

SMART HEALTH CHOICES

making sense of health advice



Professor Les Irwig, Judy Irwig,
Dr Lyndal Trevena, Melissa Sweet

Smart Health Choices

*In loving memory of Andre Joffe
1964–1999
He touched the lives of so many people
In so many extraordinary ways*

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Professor Les Irwig
Judy Irwig
Dr Lyndal Trevena
Melissa Sweet

Cartoons by Ron Tandberg



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About the authors

Les Irwig MB BCH, PhD is an internationally renowned expert on evidence-based medicine. Professor of Epidemiology at the University of Sydney, he has published widely in international medical journals. He is frequently invited to review evidence for the development of clinical guidelines and to serve on committees developing health policies. Professor Irwig has developed programmes to teach medical students and medical practitioners how to assess research and make health decisions. For this work, he received an Excellence in Teaching Award at the University of Sydney. He has also run courses to help journalists and the public understand how to interpret and use health information.

Judy Irwig has devoted a large part of her career to writing and recording songs for children, conveying important messages about relationships, self-respect and respect for the environment. She brings to this partnership the perspective of a healthcare consumer. Her non-medical background allows her to explain ideas clearly without resorting to technical jargon or making assumptions that often come from years of professional training

Lyndal Trevena MB BS(HONS), PhD is a general practitioner and a Senior Lecturer in the School of Public Health at the University of Sydney. She is interested in making evidence-based practice more feasible for busy clinicians and their patients, and ensuring that good quality information is at hand for making decisions with individual patients. Information about her research and other publications can be found at www.medfac.usyd.edu.au/people/academics/profiles/lyndalt.php. Information about her practice can be found at www.gpcremorne.com.au. Decision aids and resources can be found at www.health.usyd.edu.au/shdg.

Melissa Sweet is an Australian writer and journalist, who has been reporting on health and medical issues for more than 15 years.

Before you read this book

We have designed this book to cover a range of health interests. It is easiest to read at the start and becomes more complex as it progresses. Depending on your needs and level of knowledge, you may choose the appropriate parts or chapters without necessarily reading from cover to cover.

Part I: Health advice can be harmful gives an introduction to the reasons why health advice may be misleading. It discusses some of the common pitfalls for consumers and health professionals, how to identify meaningful health claims and research, and why it can be unwise to rely on the opinions of the experts.

Part II: Your body, your choice is for you if you feel you have an understanding of the pitfalls in health advice, but need to know how to make better decisions by asking the right questions. It discusses the five key questions (see next page) to help make the best possible health decisions and what to look for when choosing a practitioner.

Parts III–VI are for you if you're satisfied with your decision-making skills but need help in assessing whether your sources of information are reliable.

Part III: Stories and studies introduces the concepts of what features combine to make a good study.

Part IV: Evaluating the evidence deals with which study designs best answer questions such as whether a treatment works or what causes a disease.

Part V: Improving your healthcare explains where and how to find reliable evidence and how to use it, and suggests ways in which consumers can get involved in improving their health and healthcare services.

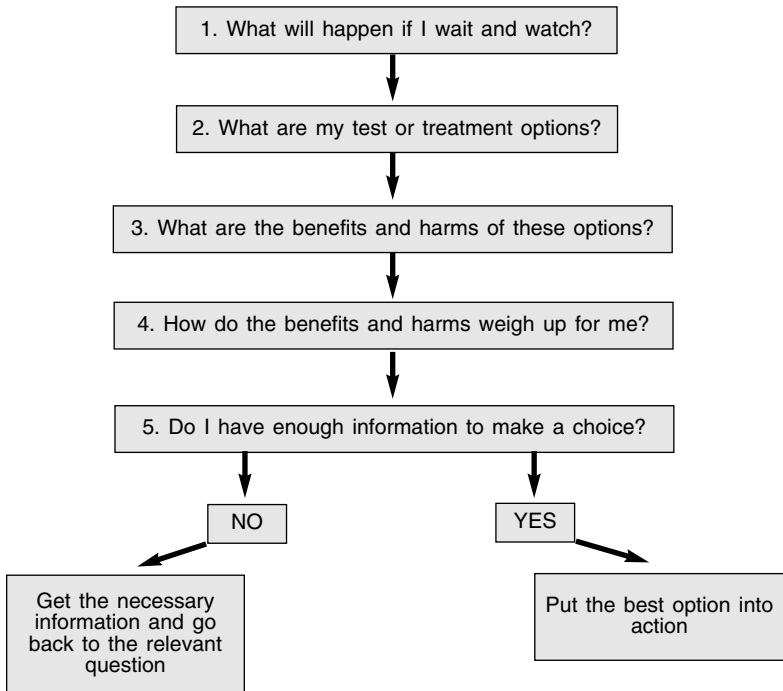
Part VI: Testing your skill starts with an opportunity to practise your skills on a range of articles from the media, internet

BEFORE YOU READ THIS BOOK

and papers in the medical literature. Later chapters are for you if you want a more advanced understanding of numerical concepts underlying health decisions.

There is a glossary at the end of the book.

There are five questions that we suggest you ask when making a smart health choice. They form the core of this book and are covered in detail in Chapter 5. They are:



Acknowledgements

The idea for this book was conceived more than 15 years ago when Judy Irwig began to realise how fortunate she was to have an epidemiologist for a husband. When so many other people that she knew were floundering in a sea of often conflicting and confusing health information, Judy was able to ask Les to help her evaluate health advice. Often, Judy was surprised to discover that health information that was being widely circulated, whether in the media or by friends or even health professionals, was not reliable.

As Judy's skills in appraising health advice developed, she began to think that everyone should have access to the same sort of information that she did. And so she started work on the themes of this book. Judy and Les then invited Melissa Sweet, a journalist who had written widely about evidence-based healthcare and the importance of patients playing an active role in their health decisions, to contribute to the project. The result was *Smart Health Choices: How to make informed health decisions*, published in Australia in 1999 by Allen & Unwin.

When it came time to update the book for this more international edition, Dr Lyndal Trevena, a Sydney GP and academic at the University of Sydney, was the perfect person for the job. Her commitment to evidence-based practice and 20 years' experience as a GP gave her a powerful clinical and academic perspective on the issues so important for smart health choices. 'I try to communicate with my patients about evidence whenever I can,' says Lyndal.

This new edition contains many extra examples and sections. But Les is delighted that the core elements remain the same. 'This suggests that the principles we recommend as important for making smart health choices will be of enduring help,' he says.

The authors are delighted that the Australian cartoonist, Ron Tandberg's work also features in the second edition.

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Disclaimer

The decision-making techniques and advice presented in this book represent the opinions of the authors based on their training and experience, and are not intended to replace appropriate consultation with health practitioners. Many of the examples and studies cited may be out of date by the time that you read the book. They are intended to illustrate various principles rather than to be used as a basis for health decisions.

The authors and publishers expressly disclaim any responsibility for any liability, loss or risk, personal or otherwise, that is incurred as a consequence, directly or indirectly, of the use or application of any comments in this book.

The characters in the hypothetical examples and the short story are purely fictitious.

I

Health advice can be
harmful

1

This book could save your life

In the past, information was the real bottleneck, so any improvement in information would lead to an improvement in thinking and in the quality of decisions. Information access and handling (by computers) have widened that bottleneck. So we move on to the next bottleneck. This is ‘thinking’. What do we do with the information?

Edward de Bono¹

Every day we make decisions about our health – some big and some small, some conscious and some subconscious. *What* we eat, *how* we live and even *where* we live can affect our health. We make decisions about where to source information about maintaining good health, as well as about whom to see for treatment when we are ill.

We are bombarded with information about health on a daily basis. ‘Good health’ is highly valued and some people will go to great lengths to achieve it. Sometimes we worry whether we are making the right decisions and we seek assurances that we are receiving the best possible care. We often want answers to questions about a specific health condition. We might wonder about the meaning of certain test results, whether there are other treatment options and, if so, how effective they are. More and more people are also beginning to question whether tests and treatments might have side effects or involve risks.

Public confidence in traditional sources of health care has been understandably shaken in recent years by a number of high-profile hospital scandals and claims of negligence. In the UK, a major enquiry found three heart surgeons guilty of professional misconduct when 29 babies died between 1988 and 1995, more than double the rate in the rest of England.² An enquiry into 29 deaths in Campbelltown and Camden Hospitals in New South Wales in Australia also found mismanagement, poor communication and under-resourcing.

Despite the intense publicity that usually surrounds such cases of medical negligence, these account for a relatively small proportion of the problems with people's health care. A much broader problem arises from the care provided by well-meaning professionals in a system that is so fragmented and complicated that it is all too easy for things to go wrong. It is estimated that as many as 30,000 people die in the UK each year as a result of medical errors³ and that tens of thousands of Australians die or are seriously injured as a result of their healthcare. Seventeen per cent of hospital admissions are associated with an adverse event caused by healthcare management.⁴ In the USA, it has been estimated that about 180,000 people die each year partly as a result of their healthcare – the equivalent of three jumbo jet crashes every 2 days. These figures suggest that there is a great deal of room to improve the healthcare that many people receive.

Some people assume that complementary or 'natural' therapies provide a safer alternative to conventional options. However, there are many examples of people suffering side effects or complications from such therapies, whether from herbal products, acupuncture or chiropractic. In Australia in 2003 hundreds of vitamin and other products had to be recalled after 19 people were hospitalised and 87 reported feeling ill after taking a 'natural' travel sickness pill. Some alternative therapies can also interact with other medicines. Prince Charles sparked debate in May 2006 when he advocated greater access to complementary therapies at the World Health Assembly in Geneva and through the Smallwood report, which was commissioned by him. Some of Britain's leading doctors followed with a letter to NHS trusts urging them to fund only therapies that

were based on scientific evidence. They were particularly concerned about NHS funds being used for homeopathic treatments, given that research has not shown them to be effective and patients were not being told this.⁵ Early in 2007, a £200,000 pilot project of complementary therapies in Northern Ireland general practice had doctors complaining that the limited government health funds could be better spent on breast cancer drugs that have been shown to be effective in scientific studies.

This book will help you to evaluate the potential benefits and harms of various therapies, whether they are part of western medicine or a traditional or complementary practice. When making smart health choices, you should bear in mind what we *don't* know as well as what we *do* know about the pros and cons associated with use.

Although many cases of harm result from human and/or system errors, there are many other ways in which harm can be done. Sometimes, bad things simply happen by chance and are unavoidable. In other cases, they are caused by the well-meaning, but ill-informed, use of treatments and tests that do more harm than good. In addition to this, there are tens of thousands of people who, although not being harmed by their care, are not receiving the best possible treatment for their situation. Studies in many countries have shown that the way the same condition is treated can vary dramatically, depending on where the patient lives or on which type of doctor or health practitioner they see. Much remains unknown about how best to prevent or treat many common conditions; however, there is widespread evidence that the information that is already available is often not put to best use.⁶

This situation has come about for many reasons. Historically, the medical and health professions have not placed sufficient emphasis on the proper evaluation of health practices, although evidence-based practice has become much more common in recent times. Commercial interests, such as pharmaceutical and medical technology companies, often drive the introduction of new practices before their harms and benefits have been carefully investigated. (More about that through the rofecoxib arthritis drug story later.) The media often disseminate misleading and even dangerous health informa-

tion. And consumers themselves often seek out and recommend the use of ineffective and even harmful remedies, perhaps encouraged by misleading advertising, websites or the advice of well-intentioned friends and family.

This book aims to help consumers and practitioners develop the skills to assess health advice – and hopefully to make decisions that will improve the quality of their care. For some people, making better-informed decisions could be life saving. We hope that it will be useful if you are struggling to come to terms with an illness or injury, and the best ways of managing it. Or you may simply want to lead a healthier life, and may be wondering how to make sense of the often conflicting flood of health information that deluges us every day, through the media, and from our friends and health practitioners.

Medicine has a long history of introducing new treatments and other interventions before they have been properly evaluated and proved beneficial. In the late 1950s, American surgeons began introducing a new treatment for people with stomach ulcers that involved freezing the stomach. The first few patients so treated showed a dramatic improvement in ulcer symptoms, and the technique was enthusiastically adopted and used on tens of thousands of ulcer patients. When a proper evaluation was finally conducted, it found that subsequent surgery for ulcers, bleeding from the stomach or hospitalisation for severe pain occurred in 51 per cent of the patients randomly allocated to stomach freezing – compared with 44 per cent of patients randomly allocated to a sham treatment (placebo). (The quality of research is increased by random allocation of patients – for example, by the flip of a coin – to either an active treatment or a placebo treatment, or a comparative treatment.) Needless to say, the stomach freezing procedure was rapidly abandoned, but only after tens of thousands of people with ulcers received the wrong treatment because of insufficient evidence.

Sometimes, the widespread introduction of unproven treatments has had disastrous consequences. In the 1980s, a new treatment for a heart disorder is estimated to have killed tens of thousands of people. This disaster, described by Thomas Moore in his book *Deadly Medicine*,⁷ might have been prevented if the drug, flecainide, had been properly evaluated before its widespread use to control irregular heart-

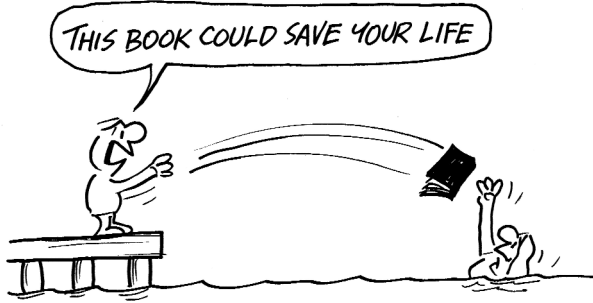
beats after a heart attack. It might have been prevented if more practitioners and consumers had been prepared to ask ‘What is the evidence to support the use of this new drug?’ The drug was approved for marketing after its manufacturer showed that it stopped several kinds of irregular heartbeats. However, it was introduced before studies had investigated whether this meant that it would also prevent deaths. When this research was finally done, it showed that the treatment had the opposite effect to that expected: it caused deaths.⁸

Unfortunately there are more recent examples of widely used treatments proving to be harmful after more rigorous evaluation has been conducted. Two examples that we will consider in more detail later in this book are the withdrawal of rofecoxib, an anti-inflammatory medicine used for arthritis, which was found to increase the risk of heart attacks and strokes, and the change in use of hormone replacement therapy after the results of a large randomised trial called the Women’s Health Initiative (WHI).

This book is in no way intended as a do-it-yourself guide to becoming your own doctor. It is hoped, however, that it will help you to assess health advice better by showing you how to recognise useful evidence and reject that which is likely to be harmful. Its underlying argument – that we should remain cautious about any intervention that has not been thoroughly investigated and proved to do more good than harm – applies to all health advice, whether it comes from mainstream medicine or complementary/alternative practitioners.

The book is based on the philosophy that consumers have a right to develop a health partnership with their practitioner, so that all decisions take account of their personal preferences, as well as being based on accurate information about the beneficial and harmful effects of interventions. We hope that it will enlighten and empower those who may be feeling disgruntled with their health-care, or who are confused by all the conflicting opinions and information that they are given, or who feel that their practitioners are not taking their viewpoints into account. The book will also be useful to readers making health decisions on their own, without consulting a practitioner.

We believe that the information in this book could have a profound impact on your health by offering simple tools to distin-



guish between good advice and potentially harmful advice. This knowledge could mean the difference between choosing the most effective treatment or choosing one that may be useless or even life threatening. Perhaps this book will save your life – or that of someone close to you.

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2

Be sceptical

What has not been examined impartially has not been well examined. Scepticism is therefore the first step towards truth.

Denis Diderot, Pensées Philosophiques

This chapter forms the basis of making ‘smart health choices’ because it encourages you to ask questions about the health advice that you receive – whether it comes from a television advertisement, a friend or a health professional. It will give you some of the tools to be sceptical, a critical thinker who can sift the misleading advice from that which has a genuine basis.

First, it is important to understand how our own biases can influence us. It is human nature to be tempted to believe explanations because they sound plausible, or because they agree with a prior belief or fit in with our value systems. Similarly, it can be difficult to give up a long-standing belief, even if not supported by the available evidence.

An example of this comes from the history of the tomato, which originated from South America and became a popular food in Europe by the mid-1500s. However, North Americans did not cultivate it until the twentieth century. They believed it to be poisonous, because it belongs to the Nightshade family, which includes some poisonous plants. The fact that Europeans had been eating tomatoes safely for centuries did not change their view.¹

There are many examples of people's health suffering because of practitioners' failure to change their thinking in response to new medical evidence. It has been estimated, for example, that tens of thousands of premature babies around the world died or suffered health problems that could have been prevented had doctors been quicker to act on research evidence showing the benefits of giving corticosteroid drugs to expectant mothers going into premature labour.

On the other hand, new tests and treatments can be adopted *too* quickly, sometimes as a result of commercial pressure and sometimes for political reasons.

It is important to be critical of your own decision-making processes. Are you choosing or avoiding a particular treatment simply because that is what you or your family have always done, without investigating its harms and benefits or whether it is your best option? Be aware that healthcare practitioners also have their own personal and professional biases; a chiropractor will take a different approach to back pain to a surgeon, whereas cardiologists may have different views from liver specialists about the health impact of alcohol.

But perhaps you should reserve your most sceptical thinking for what you read or hear in the media. Consider a news report that cites a professor saying that the latest research suggests that drug x is a breakthrough new treatment for high blood pressure. If the professor's views are being disseminated as part of a campaign by the drug's manufacturer, this is unlikely to be mentioned in the news story. Similarly, if you read a report where an expert is sounding the alarm about the safety of a certain drug, it may well be that the expert's views are being disseminated as part of a campaign funded by the manufacturer of an opposition drug. Again that will not necessarily be mentioned in the news story. Such stories often do not put the experts' claims into a broader context – for example, looking at how they compare with other research in the area. And they rarely look critically at what evidence might be available to support the experts' claims. Clearly, it would not be wise to take such stories at face value.

However, many consumers and even health professionals rely on the news media for information about health. The problem with

this is that ‘news’, by its very definition, is that which is unusual, sensational, scandalous or stirring. The media’s preoccupation with rare, sensational events tends to make us lose perspective of what is normal. News is also susceptible to distortion and misinterpretation. The media are more likely to report studies with a ‘positive’ finding, such as those linking power lines to childhood cancer. ‘Negative’ studies – those finding no link – are much less likely to be reported. It is unusual for the complexities of health information to be accurately or fully conveyed in the media.

The media may report a new ‘breakthrough’ study showing that one treatment increased the survival of people with cancer by 10 per cent. It may not mention, however, that what this actually meant was that, one year after treatment, 110 of 1000 patients were alive instead of the 100 of 1000 who would have survived without treatment. Furthermore, it may not mention that what this meant for longer-term survival was unclear, and that the usefulness of the treatment was still uncertain because of its side effects.

Media coverage of health-related news can have significant effects on people’s health behaviour. After Kylie Minogue’s diagnosis of breast cancer there was a 20-fold increase in average daily television time given to breast cancer over a 2-week period. Messages during this time emphasised that breast cancer can ‘strike at any age’. Although to some extent this is true, this message fails to point out that, while breast cancer *does* occur in women under the age of 40, it is much less common than in older women. Accompanying media messages at this time were critical of the government for not extending free mammograms to women of all ages. However, they neglected to explain that mammography is not a very accurate test in the breasts of younger women who have not yet reached the menopause. They also neglected to mention that mammography, as with most tests, is not entirely without risks. After this publicity the number of women booking mammograms went up by 40 per cent. But the increase was much higher in women aged 40–49 years compared with older women aged 50–69 years (25 per cent increase).² In other words, the intense media focus on Kylie Minogue’s breast cancer seems to have made some younger women overly anxious about their risk of the disease.

Most journalists and media managers are not qualified to assess scientific data and to discriminate between high-quality studies and the many studies that are of poor quality and dubious value. You can be more confident of the validity of a study if it is reported as being published in a well-known medical or scientific journal, but this is no guarantee. Reports of such single studies often fail to include the broader context, so that the results are reported as if conclusive fact, whereas they may be tentative and not in line with other valid studies.

And most journalists and media managers are looking for a ‘story’; the stronger and more exciting they can make the findings sound, the more chance that their story will be displayed prominently. One journalist expresses it this way:

Scientists who do poor studies or overstate their results deserve part of the blame. But bad science is no excuse for bad journalism. We tend to rely most on ‘authorities’ who are either most quotable or quickly available or both, and they often tend to be those who get most carried away with their sketchy and unconfirmed but ‘exciting’ data – or have big axes to grind, however lofty their motives. The cautious, unbiased scientist who says, ‘Our results are inconclusive’ or ‘We don’t have enough data yet to make any strong statement’ or ‘I don’t know’ tends to be omitted or buried someplace down in the story.

*Victor Cohn*³

Advertisements also have a powerful impact on our healthcare, whether by influencing a doctor’s decision about what drug to prescribe or by persuading you to buy a particular food or pill. Tips for avoiding the tricks and traps of advertising can also be useful for evaluating other forms of health advice.

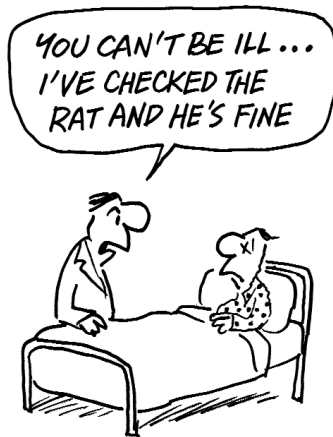
And, of course, there’s the internet! An ever-increasing amount of health information is now available to everyone online. More and more, people are turning to the internet to look up health information, to try to find out more about either their own health problem or the health of a family member, perhaps to double-check information that they’ve received from a health practitioner or to ‘chat’

with people who have the same health problem via discussion groups and 'blogs'. Health programs can be downloaded via podcasts and played through i-pods while walking the dog.

Below are some of the common strategies used in selling health messages, why they can lead you astray and how to evaluate them.

If it works on a rat, it will work on you

Many reports claim that a certain product has been scientifically proven to have various benefits. But the fine print reveals that the results come from laboratory or animal experiments. It cannot be assumed that these results will be relevant for humans. Different species respond differently to various treatments.



For years many scientists were convinced that taking supplements of the antioxidant, beta-carotene, related to vitamin A, would reduce the risk of certain cancers and heart disease. One of the reasons for their optimism was that animal studies had suggested that vitamin A was protective against cancer in some situations. The theory was strengthened by observational studies showing that people with higher blood levels of beta-carotene had lower rates of cancer and heart disease. But when proper trials were done –

randomly allocating individuals to beta-carotene or placebo supplements (dummy pills) – the results surprised many. An analysis of 47, well-conducted, randomised controlled trials showed that antioxidant supplements (beta-carotene, vitamins A, C and E, and selenium) do *not* reduce your chance of dying. In fact taking beta-carotene or vitamin A or E appeared to *increase* it.⁴ To add further weight to this, another summary of the effect of beta-carotene on preventing cancers of the bowel, liver, stomach and pancreas also showed that it increased your chance of dying! It seems that, in humans, taking beta-carotene, vitamin A and vitamin E (alone or in combination) may do you more harm than good.⁵⁻⁷

Tip

You need to know the evidence proving that the product works on humans – and that its effect is relevant to your needs and situation.

Here's how it works

A remedy which is known to work, though nobody knows why, is preferable to a remedy which has the support of theory without the confirmation of practice. . . . The question to which we must always find an answer is not ‘should it work?’ but ‘does it work?’

*Richard Asher*⁸

People selling health messages, especially advertisers, love to tell you ‘how their product works’. This strategy can be very convincing because it seems to make ‘good sense’ that, if we understand the mechanism by which something might work, the hoped-for outcome will automatically follow. But knowing how something is supposed to work is not proof that it does work.

For example, knowing that a substance changes the lining of your stomach, or plumps out your skin cells – these are examples of markers which are sometimes called *surrogate* or *intermediate measures* – may be intriguing, but is certainly no proof that you will have better digestion or smoother skin. These outcomes that matter

to you are often called ‘person-centred outcomes’. And on a more serious note, remember the story of flecainide, the drug that was meant to reduce deaths by treating irregular heart rhythms, but in fact increased the risk of death. What we really need to know is whether a product or treatment will improve our quality of life or help us to live longer.

Similarly, we should not discard treatments that have been proven to have benefits, simply because we do not understand how they work. Many thousands of women and their babies probably suffered unnecessarily because the medical profession was reluctant to accept that the anticonvulsant, magnesium sulphate, was an effective treatment for eclampsia because they did not see how it could possibly work. Eclampsia causes swollen feet, high blood pressure and fits in pregnant women, and accounts for about 10 per cent of all maternal deaths worldwide – about 50,000 deaths a year. A summary of the results of six randomised trials has shown that magnesium more than halves the risk of eclampsia and was better than other anticonvulsants, although there is a small increased risk of caesarean section (5 per cent).⁹

People who dismiss alternative health therapies because their mechanisms ‘do not make sense’ may be as misguided as those who believe a therapy will work because its mechanism suggests it ought to.

Tip

You need to know whether an intervention works in practice (empirical evidence). This can come only from seeing what actually happens to people who have the intervention. We get this information from good quality trials on people rather than from theory alone. Person-centred outcomes describe how an intervention affects your quality or length of life.

Blind you with science

Product promotions aimed at the general public and at doctors are notorious for using inconclusive or misleading research, wrapped up in scientific jargon, in an attempt to inspire support for a product.

And even if valid research is cited, you cannot assume that it will be quoted accurately or fairly. Consider this advertisement aimed at medical practitioners for a cholesterol-lowering drug called Zocor or simvastatin. In 1993 the pharmaceutical company brochure included this quote from a 1991 independent medical report:

HMG-CoA reductase inhibitors such as simvastatin ... are the most effective in lowering cholesterol levels and are more acceptable to patients than the bile acid resins. . . .

In its original form, what the report actually said was:

HMG-CoA reductase inhibitors such as simvastatin *and pravastatin* are the most effective in lowering cholesterol levels and are more acceptable to patients than the bile acid resins *although their long-term safety and effectiveness in terms of morbidity and mortality have yet to be demonstrated.*¹⁰

Another example of how science can blind comes from an advertisement for Ponstan, a non-steroidal anti-inflammatory drug. The product was advertised to doctors in Pakistan as providing:

... unsurpassed efficacy compared to acetaminophen [paracetamol] in fever control and better tolerance.

When challenged by the Medical Lobby for Appropriate Marketing (MaLAM),¹¹ the company agreed to withdraw its claim of better tolerance from future advertising. But it defended the claim of *unsurpassed efficacy* on the grounds that this meant it was equivalent, not superior, to other products – although most general readers might not understand it this way. MaLAM has been renamed ‘Healthy Skepticism’ and their website has some excellent examples of misleading advertising that you may wish to look at via www.healthyskepticism.org/adwatch.php

Tip

Just because it sounds scientific doesn't mean that it is valid. And don't assume that individuals or groups with vested interests will be objective.

Personal testimony and celebrity endorsement

Often an individual's experience is used to sell products. A leaflet for a homeopath's practice, for example, says that people such as the Royal Family, Mahatma Ghandi, Mother Theresa and Tina Turner visit homeopaths. So what if they do? Celebrities don't always get it right. Just because one person has had a good experience with a product or treatment does not mean that others can expect the same outcomes, or even that that person's recovery was a result of their use of the product. Anecdotal evidence can sound compelling, but is not a valid guide for decision-making, whether it comes from the experience of your next-door neighbour or a personal testimony published in an advertisement. Of course, such advertisements never publish the negative experiences with their product. What is needed is evidence from high-quality studies such as randomised controlled trials. For reasons that we discuss later, randomised controlled trials, in which people are allocated randomly to the treatment or an alternative treatment or placebo, are the most effective studies for evaluating the risks and benefits of health interventions.

Tip

As compelling as it may sound, anecdotal information can be unreliable as a basis for predicting an outcome. Ask to see evidence of randomised controlled trials.

Summary

- Just because a product works on rats, or cells in a laboratory test tube, does not mean that it will improve your health. The outcomes of a treatment or intervention should be relevant to people. They should tell you about quality and length of life rather than some biological measure that is supposed to predict well-being.
- Knowing how something is supposed to work is not necessarily proof that it does work in practice. We need evidence from high-quality studies on groups of people rather than from theory alone.
- Don't be blinded by 'science'. All too often what is marketed as 'scientifically proven' is based on questionable research. And be aware of the vested interests of information sources.
- What matters is not whether someone famous recommends a particular product, but whether there is evidence from randomised controlled trials showing that it is more likely to do good than harm.

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3

Bad evidence

I'm always certain about things that are a matter of opinion.

*Charlie Brown*¹

Thinking straight about the world is a precious and difficult process that must be carefully nurtured.

*Thomas Gilovich*²

What would you think of a newspaper report that said that a certain substance caused many major diseases, on the evidence that 99.9 per cent of all people who die from cancer had eaten it and that most sick people had also eaten it? Would that make you a tad nervous about trying the substance? What if another article noted that 99 per cent of people involved in air and car crashes had eaten carrots within 60 days preceding the accident and that 93 per cent of criminals come from homes where carrots are served frequently? Would you stop eating carrots?

Although this (very much tongue-in-cheek) report might make you laugh, it raises a serious issue: health advice can easily mislead, even be harmful, if not tested by high-quality studies. Studies are not always designed so that they are capable of providing reliable information. And there are different types of studies capable of providing different types of information. This chapter aims to help you understand the basics of health research and to give you some tips for distinguishing between the different types of studies.

Basic research – testing ideas

Getting back to carrots, there are several different types of studies that could investigate the killer carrot hypothesis. So-called basic research is typically conducted in the laboratory, using experiments with cells, animals or human tissue to investigate underlying mechanisms of the body and how they are affected by disease or potential treatments. In the 1920s a laboratory-based study on dogs with diabetes laid the basis for treating humans with insulin. But the early cholesterol studies done on animals were not appropriate models because animals and humans metabolise cholesterol in very different ways.

Although studies in the laboratory can provide important information, it generally would be unwise to assume that the results are applicable to people until they are tested more widely in trials on people.

The media often carries reports of promising laboratory research – for example, of potential new cancer ‘cures’ – which provide less exciting news when they are eventually tested in randomised controlled trials. Not surprisingly, the hypothetical ‘carrot report’ notes that rats force fed with 20 pounds of carrots per day for 30 days developed bulging abdomens. Their appetites for wholesome food were destroyed. Perhaps this is another example of why we shouldn’t be too quick to draw conclusions for humans from studies of rats.

Sometimes basic research is done on people to test whether a drug or procedure affects the way the body functions or reacts (for example, to test for a change in body chemistry or function such as the way muscles contract). Although done on people, this is still basic research because it is concerned with laboratory measurements rather than whether people develop diseases, feel better or live longer.

Applied research – does it work on people?

Studies involving people generally fall into three broad categories:

1. Observational studies
2. Intervention studies or trials
3. Summaries of all the best quality randomised trials.

Observational studies

Observational studies examine patterns of health and disease in different groups of people who are exposed to different environments or lifestyles.

Intervention studies (trials)

Intervention studies investigate the effects of treatments, procedures or other regimens, by intentionally changing some aspect of the status of the people in the study. These are *experimental studies* to see whether people who get the intervention are better off than those who do not.

The most reliable intervention studies are those that involve randomly allocating one group to an intervention – whether a drug, a new type of surgery or an exercise programme, for example – and comparing the results with those in a control group who are untreated or who receive a different intervention. These are *randomised controlled trials* (RCTs). Randomised controlled trials are often also called *randomised trials*. A trial that is randomised will always be ‘controlled’ because it will have a control group, but, be aware, a *controlled trial* is not necessarily randomised.

Interestingly, it was observational studies that helped raise hopes that one of the vitamins found in carrots, beta-carotene, might help prevent cancer, because it was observed that people with higher intakes of such vitamins had lower overall rates of certain cancers. But observational studies are not as reliable as randomised controlled trials; there is always the concern that there may be some other explanation. Could it be, for example, that people with high intakes of vitamins are more likely to be healthier anyway because they are also more likely to be eating other healthy foods and to be exercising and following healthy lifestyles?

Another example was the belief that hormone replacement therapy (HRT) would protect women who had gone through the menopause from heart attacks and strokes after the menopause. For years, many older women took HRT to help stave off these and other risks. It was observed that women who took HRT were less likely to have heart

attacks and strokes. Just like the beta-carotene story, the opposite was found to be the case when a randomised trial was done. One of the reasons that results from observational studies should be treated with caution is the possibility of bias. Women who choose to take HRT may be wealthier, eat a better diet, exercise more regularly, smoke less, attend health check-ups more regularly, etc. Despite the best efforts of researchers to adjust statistically for some of these factors, it is impossible to account for everything and bias can creep in.³⁻⁵

The best way of dealing with this type of concern is by testing a theory using randomised controlled trials. Randomised controlled trials are the ‘gold standard’ for evaluating treatments and other interventions because the randomisation process – where research participants are randomly allocated (for example, by the flip of a coin) to either an active treatment or a placebo or comparative treatment – helps reduce the risk of other factors influencing the results. We can be even more confident in the results when both the researchers and the research participants have been ‘blinded’ or ‘masked’, so that they do not know who is taking the active treatment. Indeed, as mentioned earlier, when the randomised controlled trials of beta-carotene supplements were finally done, they suggested that, if anything, the supplements might increase the risk of some cancers⁶ and the randomised trial of HRT showed that it increased the risk of heart attacks and strokes, particularly in the first 12 months.^{4,5}

Randomised controlled trials also allow a comparison with what would have happened without the intervention. It is all very well to say that a new antibiotic, for example, cures 90 per cent of people suffering from a respiratory infection. But what if 90 per cent would have recovered anyway, without any treatment? Too often, however, we hear reports from the media and other sources that a clinical trial has shown such and such. What we need to know is whether this was a randomised controlled trial, because clinical trials do not always include a control group and are not necessarily randomised. The results of randomised controlled trials are available for many areas of healthcare and the number is increasing. However, if such evidence is lacking, you might have to rely on the next best source of evidence. Below are some of the other points that can help you evaluate health advice and, it is hoped, avoid common pitfalls.

Summaries of all of the best quality randomised trials

In 1971, a British doctor and epidemiologist by the name of Archie Cochrane wrote an important and controversial book entitled *Effectiveness and Efficiency: Random reflections on health services*.⁷ This book suggested that many people were being over-treated in a well-meaning effort to do everything possible to ‘cure’ them. He argued that the systematic use of medical research, in particular, evidence from randomised controlled trials, should be encouraged, so that safe and effective therapies would be more likely to be used and ineffective and unsafe ones minimised.

Eventually he established the Cochrane Library which is now an online database and is available free of charge in several countries around the world, including Australia, Ireland, Norway, Finland and the UK. It is a database that contains summaries of the best research on treatments and covers a whole range of topics from ‘acupuncture treatment for depression’ to ‘zinc for treating the common cold’.

These summaries are called systematic reviews. They are usually better than just looking at just one randomised trial because, if a number of trials come out in favour of a treatment, that means the theory has been tested and proved over and over again and the results are more reliable. Systematic reviews are also more dependable because experts putting them together usually disregard any randomised trials that have been poorly conducted and keep only the good quality studies in their summary.

An example of a systematic review from the Cochrane Library is one that summarises the results of 24 randomised trials (that involved 3392 people between them all) testing the effect of over-the-counter treatments for acute cough. It showed that there is not enough research evidence for or against cough mixtures and suggests that this should be borne in mind if people choose to use them.⁸

Common pitfalls to avoid when assessing research

Just because two events occur together, does not mean that one event causes the other

You may have heard about the guy who had a habit of clapping his hands loudly several times every few minutes. When his friend

asked why, he explained that it kept the elephants away. ‘But there are no elephants around here!’ his friend exclaimed, dismayed. He replied: ‘You see, it works.’

Because two events or characteristics are associated does not mean that they are related, let alone that one caused the other. Just because people with red hair and blue eyes are more likely to get skin cancer does not mean that their risk will be reduced if they wear coloured contact lenses and dye their hair. Red hair and blue eyes are associated with an increased risk of skin cancer because they are also associated with pale skin, but are not, in themselves, a risk factor for skin cancer.

Similarly, you often hear reports suggesting that one disease or another is the result of an infectious agent. For example, one recent study was reported as showing that heart disease may result from a virus because the virus was found in clogged artery walls. Is this convincing? Not necessarily. Even if the study showed that cells from diseased artery walls were far more likely to be infected with the virus, this does not prove cause and effect. It may simply be that the diseased cell walls are more prone to infection – in other words, that the disease may precede the virus.

As the benefits and harms of many modern interventions can take decades to become apparent, it is difficult for the general consumer and health practitioner to draw conclusions about the cause and effects of diseases and treatments without the knowledge gained from proper studies. If a young woman takes a ‘morning after’ pill to avoid an unwanted pregnancy, she may be relieved when her period arrives 2 weeks later. Her anecdotal experience probably convinces her that the pill has been effective. What she may not realise is that, even if she had not taken the pill, there was a 90 per cent chance that she would not become pregnant.

Even if two events are associated, the causal arrow does not always point in the direction that is intuitively assumed; the cause-and-effect sequence may be reversed. A TV show host overlooked this point when describing a study that claimed that families who eat together have better communications. The host assumed that, if dysfunctional families wanted to improve their relations, all they had to do was share meals. In fact, meal sharing may be an effect rather

than a cause of good family dynamics – that families who get on well tend to share experiences, including mealtimes.

Anecdotal evidence can be unreliable. You cannot infer a general rule from a single experience – especially someone else’s

Anecdotal evidence is often the most difficult advice to resist because it is based on someone else’s personal experience, which can sound extremely convincing and compelling. If your next-door-neighbour recovered from cancer after a watermelon diet, that can sound very persuasive. But we already know the dangers of assuming cause and effect – just because she ate the watermelon before recovery does not mean that it caused her recovery. Remember, too, that only survivors speak: perhaps 50 other people died of cancer after trying the ‘miracle watermelon cure’. Anecdotal reports can give an unbalanced perspective. Now, if there had been a randomised controlled trial showing that patients who ate watermelon survived twice as long that would have been a different story.

Some things get better on their own (spontaneous remission). It is impossible to know whether a treatment ‘worked’ unless you know for sure what would have happened in the absence of treatment

Say you take antispasmodics – medication to stop painful bowel spasms – for irritable bowel syndrome. If the symptoms disappear over a few months after the treatment, you might assume that the antispasmodics worked. But the condition might have improved anyway. Only randomised controlled trials will answer whether the treatment will help more people to recover than would have recovered anyway. In fact, a summary (systematic review) of 11 randomised trials comparing antispasmodics with ‘fake pills’ or placebo showed that there was a slight increase in the number of people who got pain relief: 46 people out of 100 will get pain relief with the placebo and 58 out of 100 will get pain relief from the antispasmodics. In other words 12 extra people in every 100 will be helped, but

almost half of all people got better with a placebo.⁹ On the other hand, six randomised controlled trials of antidepressant drugs for irritable bowel showed no difference between them and placebo.⁹

This example also reflects what statisticians refer to as regression to the mean. This is a tendency for values in nature to shift towards average – for example, children of exceptionally tall parents are likely to grow into shorter adults than their parents, closer to the average height. And children of very short parents are likely to become taller than their parents, closer to average height.

Similarly, an unusually high or low result from a medical test is likely to reflect a more average result on repeat testing. For example, if you have a very high cholesterol count on one occasion, it is likely to be lower at the next test, even if you do nothing about it.¹⁰ To get a true measure, you should have several tests. This phenomenon also occurs because of the body's natural healing processes, which means that many abnormal states (of sickness) tend to shift towards the average (good health).

Put simply, some things just get better on their own.

Thousands of well-meaning John and Jane Does have boosted the fame of folk remedies and have signed sincere testimonials for patent medicines, crediting them instead of the body's recuperative powers for a return to well-being.

*James Harvey Young*¹¹

The placebo effect is powerful. People often report an improvement on almost any therapy, even a placebo (an inactive intervention). This is why it is difficult to discern the real effects of active treatments without randomised controlled trials

In one experiment, patients with bleeding ulcers were divided into two groups. The first group was told that their treatment would dramatically ease their pain. The second group was told that their treatment was only experimental and little was known about its effect. Of the first group 75 per cent reported sufficient pain relief. Of the second group, only 25 per cent reported a similar benefit.

Both groups had been given the identical ‘treatment’ – a placebo containing no active pharmacological ingredient.¹²

What was at work was the power of the placebo – or perhaps, more correctly, the power of the mind. The placebo effect is a well-documented phenomenon, whereby the apparent outcome of treatment can be positively influenced by the mere expectation that it will work, held by the patient and/or doctor.

You might ask why it is so important to determine what produces the benefit. After all, does it really matter what makes someone feel better – the placebo effect or an active treatment? Of course, if placebos work that’s great, but we want to know whether it is worth risking the side effects of any additional pharmacological effect of an active drug beyond its placebo effect.

Consider that earlier in the twentieth century many thousands of patients with angina (chest pain caused by constricted blood vessels) underwent various treatments that are now known to have no effect whatsoever. Many of these patients and their doctors reported remarkable (if not long-lasting) improvements after trying potentially dangerous drug treatments, and also after an invasive surgical procedure that involved tying off an artery in the chest.

This is one of the most important reasons for randomised controlled trials, which help discern the impact of the active component of a treatment over and above its placebo impact.

The placebo effect is generally seen as beneficial for patients, because it can improve symptoms. But it can also be responsible for harmful effects – what is sometimes called the *nocebo* effect. For example, some dentists say that controversy over the safety of amalgam fillings has had a *nocebo* effect. As they are worried that their fillings might be making them sick, some people have felt symptoms – regardless of whether their teeth are filled with amalgam or other substances.

Screening tests that detect disease early are not always beneficial. They can lead to people living more years with disease rather than longer lives

A screening test, as distinct from a diagnostic test, is used to identify disease in people who have no symptoms. This is great if early

diagnosis of a disease will result in more effective treatment. However, in some cases, making an early diagnosis may not be helpful, particularly if there is no effective treatment. In many countries, the advent of tests to screen healthy men for markers associated with prostate disease has led to an explosion in the number of men diagnosed with the cancer. In the UK alone, the number of men diagnosed with prostate cancer almost doubled in the 5 years from 1990 and in Australia it tripled.^{13, 14} But this dramatic increase is not believed to represent a ‘real’ increase in the cancer’s incidence and is instead believed to reflect earlier diagnosis. Thus, there are more men who now know that they have prostate cancer, but not necessarily any more men with the cancer.

For some diseases, early detection does not help to prolong life because earlier treatment is no more effective than later treatment. In these situations, early detection simply increases the years of disease from the time of diagnosis rather than increasing years of life. This is called ‘lead time bias’. To explain further, here is an example.

Andy is the same individual in all scenarios and this is what might happen to him in three different situations, as if they were happening in parallel universes (Figure 3.1):

1. Scenario 1: Andy decides against screening in 2000 and dies in 2010, 5 years after developing symptoms. He lives for 5 years with disease X.
2. Scenario 2: Andy is screened in 2000, found to have disease X and dies in 2010, 5 years after developing symptoms. Screening has not prolonged his life but merely increased the number of years lived with disease x from 5 years to 10 years.
3. Scenario 3: Andy is screened in 2000, found to have disease X and dies 15 years later in 2015. Screening has prolonged his life by 5 years.

From this example we can see that longer survival from time of diagnosis is not a reliable way of determining whether screening is effective. For this we need randomised controlled trials comparing death rates in screened and unscreened groups.

CHAPTER 3

Dates: 2000	2005	2010	2015->
Andy is not screened	In 2005 Andy presents with symptoms and is diagnosed with disease X	In 2010 Andy dies having lived for 5 years since diagnosis	
<div style="background-color: #cccccc; padding: 5px; display: inline-block;">5 years lived with disease X</div>			
In 2000 Andy is screened and diagnosed with disease X	<div style="background-color: #cccccc; padding: 5px; display: inline-block;">10 years lived with disease X Screening did not prolong his life</div>		In 2010 Andy dies having lived for 10 years since diagnosis
In 2000 Andy is screened and diagnosed with disease X	<div style="background-color: #cccccc; padding: 5px; display: inline-block;">15 years lived with disease X Screening prolonged his life by 5 years</div>		In 2015 Andy dies having lived for 15 years since diagnosis

Figure 3.1 Andy's three scenarios

Screening for prostate cancer is another good illustration of the potential for screening programmes to do more harm than good. In the UK and Australia, most authorities have not recommended that a formal screening programme be introduced for this reason, although there is a great deal of *de facto* screening occurring. (For further information about this subject, see the NHS Cancer Screening Programme's *Prostate Cancer Risk Management* website and also *The PSA Decision – what you need to know* video and booklet.^{15, 16})

Here are some statistics that help explain why screening is not necessarily beneficial: suppose 10,000 men are screened by a PSA test, which measures the blood levels of prostate-specific antigen (Figure 3.2). Of these, 8500 will have a negative result, although 765 of this group can be expected to develop the cancer anyway, because the test is not 100 per cent accurate (and nor is any test).

BAD EVIDENCE

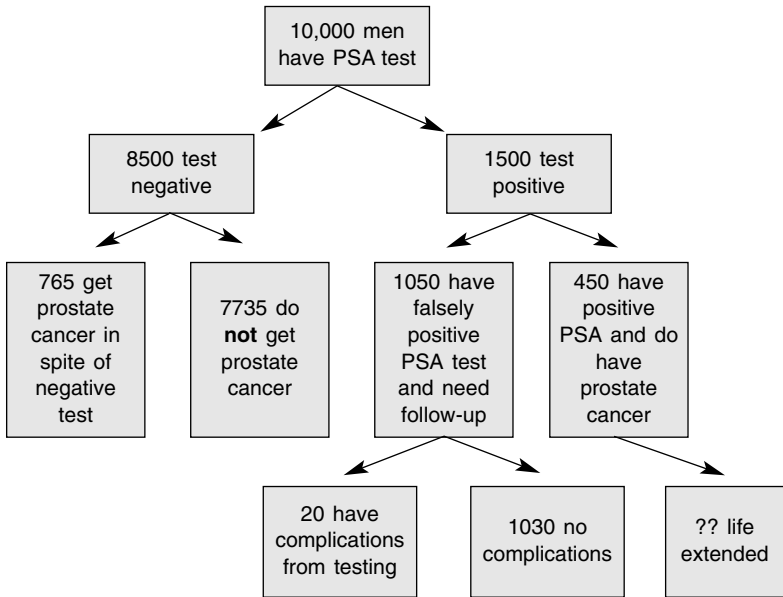


Figure 3.2 The consequences of screening for prostate cancer

Of the 1500 men with a positive result who undergo further testing, 1050 will then be given the all clear, although up to 20 may develop complications as a result of their further investigations and all could be expected to have suffered some degree of psychological stress.¹⁷

Of the 450 who are shown to have the cancer, it is not yet clear to what extent treatment will extend their lives or improve their quality of lives. Some will suffer serious consequences as a result of their treatment, such as incontinence and impotence. And because of the slow-growing nature of many prostate cancers – it is commonly said that most men die with prostate cancer rather than of it – it is quite possible that many men will have suffered adversely from investigation and treatment for a condition that may never have harmed them. The trouble is that we do not now have a good way of selecting which men might benefit from early detection and treatment.

The prostate cancer story is a powerful reminder of why you should always ask what the risks and benefits of any screening test are. Even mammography screening, which has proved to save lives when used to detect breast cancer in women aged over 40, involves some harms, and these may outweigh benefits at the younger end of that age range.

You should ask what is the chance that this screening test will accurately detect an important disease? What are the risks and benefits of earlier detection of the disease? Will it give you extra years of life, or just extra years of disease?

Summary

Assessing medical research can be complex – even for the experts. It helps to understand some of the more common pitfalls:

- Laboratory-based research on animals does not necessarily apply directly to humans.
- To test whether a treatment is effective in humans requires a randomised controlled trial on people who have the condition of interest.
- Just because health characteristics or events are associated – or occur together – does not mean that they are related, or that there is a cause-and-effect relationship.
- Anecdotal evidence can be dangerous. You cannot infer a general rule from a single experience – especially someone else's.
- Many diseases get better with or without treatment. It is impossible to know whether a treatment 'worked' unless you know for sure what would have happened in the absence of treatment.

continued

- The placebo is powerful. People often report an improvement on almost any therapy, even a placebo (a biologically inactive intervention). This makes it difficult to discern the real effects of active treatments without randomised controlled trials.
- Screening tests that detect early disease are not always beneficial. They can lead to people living more years with disease rather than leading longer lives. This is called ‘lead-time bias’. (A screening test, as distinct from a diagnostic test, is used to identify disease in people who have no symptoms.)

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4

Don't always rely on the experts

Medicine is indeed in the middle of an intellectual revolution. Methods of reasoning and problem solving that might have worked well in the past are not sufficient to handle today's problems.

David Eddy¹

Recently a friend was describing some treatment that her father had been given. It didn't sound like he was doing well on the medication. When I suggested that there may be a more appropriate treatment, her response was, 'But surely a qualified doctor would know what's best.'

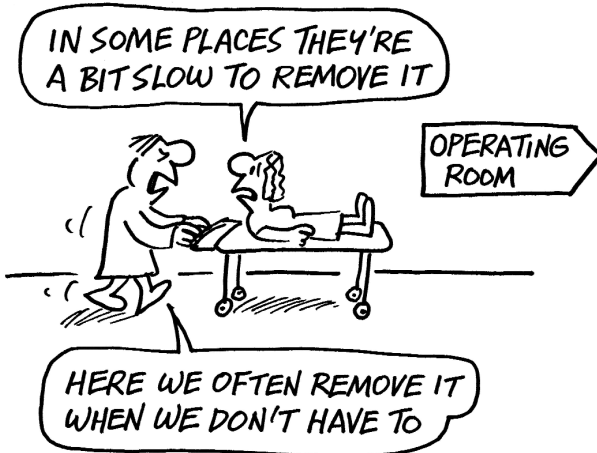
Unfortunately, it is not always safe or wise to make this assumption. It's virtually impossible for health professionals to keep completely up to date with the latest and best research treatments and tests. Gone are the days when a doctor could stay in touch by reading a few key journals each week.

To give you some idea of the extent of medical information overload, it has been estimated that about 560,000 new medical articles are published every year and 20,000 new randomised trials are registered. That's equivalent to 1500 new articles per day and 55 new trials.² There certainly has been an enormous change since the 1970s when Archie Cochrane and others suggested a more systematic approach to assessing health treatments through randomised trials.

Health professionals, like most of us, struggle with time pressures and face real challenges as they juggle clinical matters and

the need to keep up-to-date with the latest good quality research. Even if they can access such information efficiently, there are many other challenges in communicating with patients about the pros and cons of various treatment options and finding out what the patient's preferences might be. This is not easy to achieve in a 10-minute consultation in addition to taking a thorough history and examining the patient!

This problem is reflected by the many studies that have shown a widespread variation in the rates of various medical procedures that cannot be explained away by intrinsic differences in the populations. Boston and New Haven, for example, have similar populations in terms of their healthcare needs. Most of their practitioners are associated with internationally renowned medical centres. Yet New Haven residents have been reported to be about twice as likely to undergo a bypass operation for heart disease as their counterparts in Boston, who are more likely to be treated by other means. On the other hand, Bostonians are much more likely to have their hips and knees replaced by a surgical prosthesis than are New Havenites, whose physicians tend to prescribe medical treatments for these conditions. Bostonians are more than twice as likely to have arteries in their necks unblocked as a way of preventing strokes whereas



clinicians in New Haven prefer to recommend aspirin and other drug treatments. By contrast, hysterectomies for non-cancerous conditions of the uterus are more often performed in New Haven.

Other studies, in the USA, the UK and Australia, have found similar variations in medical procedures, which reflect different approaches to managing the same conditions. This may come about for a number of reasons, including differences in access to equipment or facilities, in training or in financing arrangements. But such variations can also arise because experts specialising in the same problems have different views about the best way to treat them. It is possible that some of those treatments are better than others.

But even if the experts did all agree about the best way to manage a particular condition, this does not necessarily mean that they are all correct – they may all be wrong. There are also dangers in relying on a consensus of experts – which has traditionally been the basis of many medical recommendations. Consensus may merely represent a middle ground between opposing views and may not accurately represent any expert view, or it may represent the views of the most persuasive or influential expert who might also be the most uninformed about the valid evidence. So we can't rely on advice or opinions just because they come from a so-called expert or 'a leading authority in the field'.

Why the experts disagree

It can be very confusing when the experts disagree about our health-care. Such disagreement reflects both the complexity of healthcare and the uncertainty about what will be the outcome of a particular intervention.

Healthcare decisions are complex

When our grandparents and great-grandparents were raising families, practitioners had relatively limited tools and knowledge. Their advice was far simpler than it is these days, and the outcomes of treatment tended to be more obvious and immediate. Premature death was far more common.

Say, for example, your great-grandfather complained to his doctor of a pain in the stomach. It may have been caused by a minor gastric inflammation, in which case he would have recovered spontaneously within a few days, irrespective of treatment. Or it may have been a stomach cancer that inevitably would have killed him. In the first instance, the practitioner would have been praised for the old man's recovery and the treatment hailed as a cure. In the latter situation, you and your grieving relatives probably would have taken the philosophical view that some things are beyond the ken of doctors.

If your great-grandfather had been seeking help now, he and his practitioner would have far more information to consider and weigh up, including choosing from a wide range of diagnostic tests and treatments. Healthcare has become so much more complex, increasing the choices for treatment, but also increasing the chances that practitioners will disagree about which is the best option.

Health outcomes are uncertain

Another important reason for differences in expert opinion is the uncertainty of health outcomes – the same disease will have a different effect on different people. Nor can it always be accurately predicted how an intervention – whether surgery or a medication – will affect different people. Clearly, then, different practitioners will have different experiences. The best way of dealing with this uncertainty is to turn to studies of groups of people to find out what is the most likely outcome. This probabilistic evidence predicts the chance that a particular outcome will occur for a particular intervention in a given situation.

The complexity and uncertainty of healthcare help to explain why experts today face a new era: one that demands a high level of skill in evaluating information so that they can make sense of the growing body of research literature and apply the best available evidence to their patients' care:

For centuries, the practice of medicine has been based on one huge assumption. The assumption is that physicians instinctively know the right thing to do. We call it 'clinical judgement' or the 'art of

medicine'. Somehow, the assumption goes, physicians are able to assimilate all they have learned from their medical education, their training, research, their personal experiences, and conversations with their colleagues, as well as all the information about their patients – their signs, symptoms, hopes, and fears – to determine the right thing to do.

*David Eddy*³

Fortunately, there is now an international push to ensure that health care is based on evidence rather than experts' opinions or consensus. Clearly, good healthcare requires that practitioners use clinical judgement together with the best evidence. Alone, neither is enough.

Practitioners may be poorly informed

Evidence-based healthcare is becoming more widely used by responsible practitioners worldwide. This has been possible largely because of the growth and availability of electronically accessible information offering practitioners and consumers previously unimaginable possibilities for making the best health decisions. The problem is that not all of this information is reliable. Much of it is based on poor quality studies. However, practitioners are being trained to access and assess the best quality of research.

Not all practitioners practise evidence-based health care

Although usually well intentioned, practitioners may not offer optimal care because many are not integrating the best available evidence into their decisions. This evidence is accessible through electronic databases, from good quality journals and from evidence-based guidelines.

Even when good quality evidence is available, not all practitioners are using it. This is partly because there are often delays between the results of research and the publication of easily accessible recommendations based on the research, and partly because old habits die hard. Many practitioners are resistant to changing

practices that have become routine even when they may no longer be appropriate.

Not all practitioners know where to find the evidence

Practitioners might not know where to find the relevant, evidence-based information. Traditionally, many have relied on sources such as medical education, their own experience, previous and continuing medical education, and pharmaceutical companies – sources that are often inappropriate, biased or out of date. Indeed, medical schools have traditionally concentrated on the basic sciences – such as anatomy, physiology and biochemistry – and have begun teaching skills in critical appraisal of studies only over the past decade. There is an ever-increasing number of clinical practice guidelines based on the best available research but sometimes these can be difficult to find and to use with the patient there on the spot.

We can tell that many practitioners lack the skills to judge studies because of the fact that much poor quality research is still being cited as the basis for a large number of health practices and products. We should also remember that medicine has a long history of not recognising the harms of some interventions.

The most famous example is thalidomide – a drug that was considered to be safe enough to be widely used to treat morning sickness in the early 1960s before it was found to cause limb deformities in the developing fetus. But there are many more such examples – tonsillectomies were once commonly performed on children in the belief that they prevented repeated bouts of throat infections. A number of surgical deaths forced a reassessment of this procedure and a significant reduction in its use. Early in the twentieth century, babies' mouths were routinely cleaned in the belief that it reduced germs. Only later was it recognised that this cleaning caused ulcers of the palate. In the 1950s many patients with dangerously high blood pressure underwent traumatic surgery to remove the nerves running down either side of their spines. The operation was of doubtful value, but could cause terrible side effects. More recently, the antiarthritis pill rofecoxib was taken off the market when serious side effects emerged after the drug's widespread introduction.

'Safe' does not mean 'risk free'

So when a practitioner tells you that a treatment or test is generally safe, be aware that there may be harms that have not yet been discovered. 'Safe' often means that there are no known harms. And don't assume that, because something is said to be 'natural', it is risk free. 'Natural' and 'harmless' are not the same. Vitamin supplements taken in excess and some herbal products can have dangerous side effects, ranging from headaches to liver damage. As for any intervention, their harms might not be immediately obvious and, indeed, may emerge only after years of use or after large, high-quality studies have been done. As with any other intervention, their use should be handled with care.

Evidence can sometimes be distorted by drug companies

The story of the anti-arthritis drug, rofecoxib, illustrates a number of these points very nicely.

One of the difficulties facing people with arthritis is the fact that some of the commonly used anti-inflammatory drugs can cause nausea, belching and, even more seriously, ulcers in the upper



gastric tract. A drug that would have the same pain-relieving effects but fewer side effects would obviously be desirable, and there was much interest in a newer generation of anti-inflammatories called the COX-2 (cyclo-oxygenase 2) inhibitors.

In 2000, the *New England Journal of Medicine*, one of the medical world's most prestigious journals, published the results of a randomised controlled trial (the VIGOR study), which included 8076 patients with rheumatoid arthritis. Participants were randomly assigned to receive either the new COX-2 inhibitor,⁴ rofecoxib, or the more commonly used drug naproxen. That sounds good, you might say, having read the earlier chapters of this book.

In that paper, the authors commented that the naproxen recipients had a lower rate of heart attacks (1 per 1000) over a 9-month follow-up compared with the rofecoxib group (4 per 1000). Note that the other way you could report this is that the rofecoxib group had a higher rate of heart attacks than the naproxen group. This is called a framing effect. In other words, how information is presented or framed can affect how it is interpreted.

It was thought at that time, that the difference in cardiovascular event rates was caused by the fact that a lot of the heart attack sufferers should have been taking aspirin. They also claimed that naproxen itself was protective against heart attacks, a point that had not really been proved and was questioned by outside scientists at the time. The drug company that was funding the trial, the manufacturer of rofecoxib, contacted researchers who were conducting other studies with their drug to suggest that patients could use low-dose aspirin with it for cardioprotection if required. The Federal Drug Agency (FDA), in February 2002, added a warning label to rofecoxib packaging that it may increase your risk of heart attacks and strokes, but the drug was still available to the public.

As this possible link between rofecoxib and an increased risk of heart attacks and strokes became apparent in 2000, another study was getting under way to look at whether this same drug could help to prevent bowel polyps and cancers.⁵ The researchers in that trial, which was funded by the same drug company (the APPROVE study), found that rofecoxib *was* associated with an increase in cardiovascular risk. Researchers took the preliminary results to the drug

company in September 2004, the trial was stopped and the drug was withdrawn from the market immediately. Meanwhile, the drug company had benefited from a \$US2.5 billion revenue from rofecoxib sales in the year before the withdrawal. The FDA estimates that the drug caused between 88,000 and 139,000 heart attacks, 30–40 per cent of which were probably fatal, in the 5 years during which the drug was on the market. There have been over 100,000 cases and 190 class actions lodged against the drug company concerned and millions of dollars have already been awarded to plaintiffs.

Here is where the story becomes even more interesting and rather murky. On 29 December 2005, the editors of the *New England Journal of Medicine* published an editorial claiming that data about three extra heart attack cases had been withheld from the 2000 *New England Journal of Medicine* article.⁶ The editors had become aware of these extra data when the FDA hearing occurred in February 2001, but had assumed that these heart attacks had occurred after the paper had been published in their journal and that the information was accurate when it had gone to press. However, after a drug company memorandum was subpoenaed for a court case in late 2005, it emerged that at least two of the authors knew about these extra cases well before the article was published and should have adjusted the conclusions. All three of these heart attack sufferers were people who did *not* need aspirin, thereby dispelling the original claim that, if rofecoxib were taken with low-dose aspirin in those who needed cardioprotection, all would be well.

Sadly, this is not the end of the story about misrepresentation of results from drug company-funded trials on rofecoxib. Not only do the claims of the VIGOR paper appear to be misleading, but there have also been doubts raised and a subsequent correction of the APPROVE trial results.⁷ The APPROVE study had randomised 2586 people with a history of bowel polyps to receive rofecoxib or placebo. The trial stopped after 18 months when it appeared that the drug caused a doubling in the risk of heart attacks and strokes. As the drug company defended themselves against claims of wrongful death, they maintained that there was no increased risk until after 18 months of using the drug. In July 2006, the *New England Journal of Medicine* published a correction to its paper over 12 months after

it had been published in March 2005.⁷ In this latest controversy it emerged that people who dropped out of the VIGOR study early were not included in the original analysis. By omitting them, they underestimated the number of people who had earlier heart attacks while taking rofecoxib. The corrected analysis shows that the risk may increase as early as 4 months, and definitely long before the previously claimed 18 months.

At the time of revising this book, the rofecoxib story was still unfolding and we can only hope that many salutary lessons can be learned by journal editors, doctors and their patients about the pitfalls of relying upon trials that have been funded by drug companies.

Practitioners may not take account of their patients' preferences

Over the last few decades, there has developed an appreciation that many interventions have significant harms; not all people weigh benefits and harms in the same way, and in the end it is the patient's preferences that count, not the physician's.

*David Eddy*⁸

Consumers should expect that everyone who offers health advice or who delivers health care should provide sound information about the benefits of the intervention – whether a tablet, surgery or dietary changes – and the harms. Then you will be in a position to decide, with your practitioner's help, how these benefits and harms weigh up for you.

Practitioners do not always take their patients' preferences into account. This is often easier said than done and in some circumstances not practical or appropriate. It is often difficult to find out patient preferences in an emergency situation and, in some special circumstances, the law requires a doctor to overrule an individual's preferences if it puts him or her and/or others in danger. For example, an elderly person with poor eyesight and mild dementia may prefer to continue driving a car, but for obvious safety reasons this needs to be overruled. In most cases, a patient's preferences can and should be included in healthcare decisions. Later in this book

we consider some tools that are available to help people become much more involved in healthcare decisions and help them to weigh up the benefits and harms of healthcare options.

The fact is that not all people weigh benefits and harms in the same way. One person might consider a risk to be minor, although someone else might judge it unacceptable. As you become more informed about the evidence for different treatments and tests you may want your own preferences to be taken into account when weighing up the risks and benefits of a particular intervention. You should feel confident that your practitioner is considering YOUR preferences in decision-making, rather than other factors, such as what they have traditionally done in such a situation. The best way of finding the most appropriate balance between risks and benefits of health care is by choosing a practitioner who uses an evidence-based approach to health care and whom you feel comfortable questioning when making health decisions.

You should feel comfortable enough with your practitioner to ask whether any randomised controlled trials or systematic reviews of the best randomised trials have been done on a particular therapy. Remember, these are studies that are best able to evaluate the risks and benefits of an intervention because people in the study are randomly allocated to the treatment, an alternative treatment or placebo. Practitioners should try to run their practices so that they have sufficient time to attend to patients' questions, and there is no reason for competent practitioners to feel irritated or intimidated by reasonable questions from patients; on the contrary, they should encourage them. It may mean that they look something up for you if they have time during the consultation or, if they have a full waiting room beckoning their attention, they may get back to you at a later stage.

Given what you have read so far, about the rapid pace of expanding medical knowledge, you should feel reassured rather than perturbed if your health practitioner looks something up for you. They may even ask you to do some reading yourself and perhaps point you towards some evidence-based resources for patients. As patients quite rightly want to become more involved in their healthcare decisions, the role of the practitioner will change and this is already starting to happen.

If any practitioner is too busy to answer your questions clearly or fails to help you find the evidence that you want, perhaps he or she is not the one to consult. And remember, ‘practitioner’ refers to anyone delivering any form of healthcare, whether a specialist, homeopath, dentist, nurse or counsellor.

Summary

Health and medical experts don’t always get it right.

- They vary in their opinions and approaches to managing the same conditions. Their ability to assess and interpret health information may not have kept pace with the rapidly expanding amount of such information.
- Their views may be based on unreliable sources – pharmaceutical companies, the opinions of other experts, media reports and their own personal experience – rather than the results of good quality studies.
- It is your right that your health care is based on:
 - your practitioner’s clinical skills
 - the best evidence from the research literature
 - your preferences based on the benefits and harms.

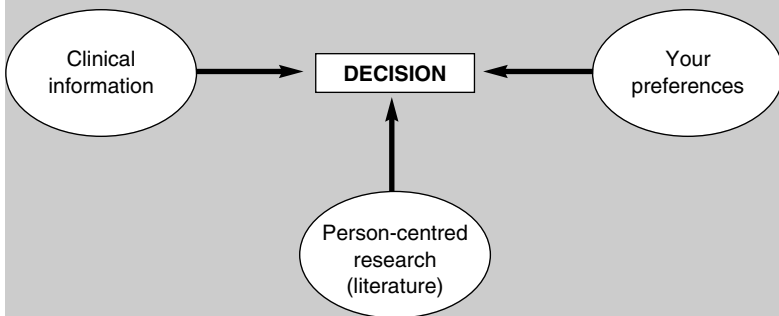


Figure 4.1 Evidence-based decision-making.

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