

READING BETWEEN THE LINES

How the growth of denialism undermines public health

Espousing unproved myths and legends is widespread during the festive season, but some groups hold views contrary to the available evidence throughout the year. This phenomenon, known as denialism, is becoming more elaborate and widespread, and poses a danger to public health, say **Martin McKee** and **Pascal Diethelm**

Christmas is a time when many entirely rational people whose views are based solidly on empirical evidence the rest of the year suspend their critical faculties and say things they know to be untrue. Just in case any young children have picked up their parents' copy of the *BMJ*, we won't go into detail except to say that the subject of these falsehoods traditionally originates in the far north.¹ Such stories are harmless and those telling them will, when their children reach an appropriate age, abandon



GERARDO GARCIA/REUTERS

the pretence. Yet other people hold views that are equally untrue and do so with an unshakeable faith, never admitting they are wrong however much contradictory evidence they are presented with.

Some of these views are harmless, but others cost lives. It is easy to think of contemporary examples. "HIV is not the cause of AIDS."² "The measles, mumps, and rubella vaccine cannot be considered safe."³ "Second hand smoke is simply an irritant and there is no conclusive evidence that it is dangerous."⁴ And, with potentially the greatest consequences for our species, "the evidence that the world is warming is inconclusive, and, if not, the evidence that global warming is caused by anthropogenic carbon emissions is unproven."⁵

Denialism and its history

The term "denialism" has been coined to describe this phenomenon. First popularised by the American Hoofnagle brothers, one a lawyer and the other a physiologist, it involves the use of rhetorical arguments to give the appearance of legitimate and unresolved debate about matters generally considered to be settled.⁶ The term can be traced to people who deny the existence of the Holocaust, but it has subsequently been applied much more widely. Denialism can be recognised by the presence of six key features (box).^{6, 7} It is, however, important not to confuse denialism with genuine scepticism, which is essential for scientific progress. Sceptics are willing to change their minds when confronted with new evidence; deniers

are not. Unfortunately, confusion is encouraged by the liberal use of the term, such as when the current British government uses the term "deficit deniers" to attack critics of its economic policy, a group that now includes large numbers of distinguished economic researchers, among them several Nobel laureates.⁸

Although contemporary usage of the term is relatively recent, the concept of denialism has been recognised for several decades. A chapter entitled "Denial

of reality" in a 1957 book describing the phenomenon of cognitive dissonance notes how "... groups of scientists have been known to continue to believe in certain theories, supporting one another in this belief in spite of continual mounting evidence that these theories are incorrect."⁹ It highlights, in particular, the importance of selectivity, whereby "one aspect of the process of dissonance reduction [is] obtaining new cognition which will be consonant with existing cognition and avoiding new cognition which will be dissonant with existing cognition." The extent to which selectivity influences our views is now widely recognised, not least as a result of a best-selling book containing many examples of what is termed "confirmation bias."¹⁰ One explanation is that confirmation bias is how we deal with

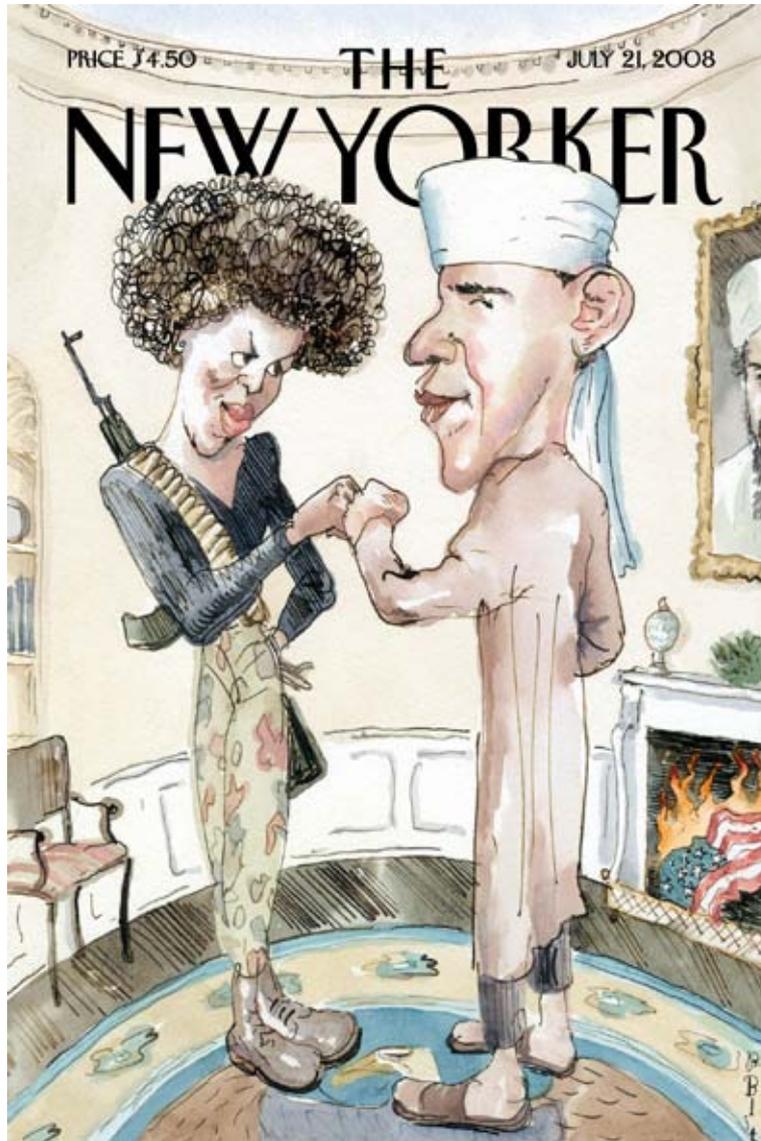
evidence that challenges our strongly held beliefs and that would otherwise threaten our self perceived status as intelligent and moral individuals.

Approaches to denialism

Recent cognitive research, some taking advantage of advances in brain scanning, has shed light on the neurological processes whereby individuals interpret a message according to who is the messenger. People subconsciously suppress recognition of clearly contradictory messages from politicians that they support, yet easily identify contradictions from those they oppose.¹¹ However, simply ignoring relevant evidence is insufficient. Evidence, including authoritative corrections, that contradicts strongly held views can, paradoxically, reinforce those views.¹² Thus, research in the United States has found that registered Republicans who are exposed to evidence on the importance of social determinants of health are less likely to support collective action to address them than are those not exposed.¹³

Yet denialism involves more than someone accumulating a collection of individual errors in information processing. Increasingly, it takes on the form of social movements in which large numbers of people come together and propound their views with missionary zeal.¹⁴ These views combine exploitation of the genuine uncertainty that characterises scientific research with the use of simple falsehood.

Denialists emphasise the limitations of statistical associations for establishing causality, which are well recognised by aetiological epidemiologists, yet ignore other criteria that are used to ascertain whether a relationship is likely to be causal, such as biological plausibility, consistency, and strength of association.¹⁵ They may also try to change “the rules of the game,” such as in the now notorious example when the tobacco industry sponsored efforts to define “good epidemiology practice.” The



As with vaccines, you can never be sure

initiative would have redefined a relative risk of less than two as being not statistically sound because of the potential for unrecognised confounding and was designed to exclude research on the risks associated with passive smoking, which typically yield a relative risk of 1.3-1.6.¹⁶ Other efforts seek to redefine concepts as essentially unresearchable, such as in an industry funded report on alcohol that stated: “violence is a nebulous concept.”¹⁷

Selective use of the scientific literature is another approach used by denialists, who either promote methodologically flawed research that supports their world view over more methodologically sound papers or undertake intensive searches of papers they oppose for anything that might cast doubt on the quality of the science. A now notorious example is “Amazongate,” in which a report by the Intergovernmental Panel on Climate

Change inappropriately referenced a statement on a report about the sensitivity of the rainforest to changes in rainfall rather than the relevant primary research. This inconsequential referencing error, in a report of more than 900 pages, was then used to undermine the entire report.¹⁸

Deliberate falsehoods are rarely used to convince people that something is true, but rather are used to seed doubt about the actual truth. For example, although only 18% of Americans believe that President Barack Obama, a church going Christian, is a Muslim, an additional 43% are unsure.¹⁹ Media commentators don’t actually say that that Obama is a Muslim, they just say that they don’t know whether he is or he isn’t, while consistently using the president’s full name: “Barack Hussein Obama.” In the health arena, this approach is commonly found in debates about vaccines, where denialists play on the argument that “you can never be sure” when it

comes to the very small risk of complications of vaccinations.

The spread of denialism

Of course, there have always been people who have held strong views in the face of overwhelming evidence to the contrary. Indeed, the Flat Earth Society, although a shadow of its former self, still exists. However, the world has changed in recent decades in three important ways, each facilitating the spread of denialism.

The first is the birth of web 2.0, which has transformed the internet from a closed publishing platform into an interactive tool allowing intensive exchange of ideas. People who might once have clung on to dissenting views in isolation can now locate individuals with similar views within seconds. Social media enable communities of denialists to grow by feeding each other’s feelings of persecution by

When a seemingly bizarre story appears in the media that risks undermining public health, health professionals should ask: “why is this story appearing now?”

CHARACTERISTICS OF DENIALISM

Identification of conspiracies: Denialists argue that scientific consensus arises not as a result of independent researchers converging on the same view but instead because researchers have engaged in a complex and secretive conspiracy. They are depicted as using the peer review process to suppress dissent rather than fulfil its legitimate role of excluding work that is devoid of evidence or logical thought.

Use of fake experts: It is rarely difficult to find individuals who purport to be experts on some topic but whose views are entirely inconsistent with established knowledge. The tobacco industry coined the term “Whitecoats” for those scientists who were willing to advance its policies regardless of the growing scientific evidence on the harms of smoking

Selectivity of citation: Any paper, no matter how methodologically flawed, that challenges the dominant consensus is promoted extensively by denialists, whereas any minor weaknesses in papers that support the dominant position are highlighted and used to discredit their messages.

Creation of impossible expectations of research: This may involve corporate bodies sponsoring methodological workshops that espouse standards in research that are so high as to be unattainable in practice.

Misrepresentation and logical fallacies: An extreme example of this characteristic is the phenomenon of *reductio ad hitlerum*, in which anything that Hitler supported (especially restrictions on tobacco) is tainted by association. Other methods of misrepresentation include using “red herrings” (deliberate attempts to divert attention from what is important), “straw men” (misrepresentation of an opposing view so as to make it easier to attack), false analogies (for example, because both a watch and the universe are extremely complex, the universe must have been made by some cosmic watchmaker), and excluded middle fallacies (in which the “correct” answer is presented as one of two extremes, with no middle way. Thus, passive smoking causes either all forms of cancer or none, and as it can be shown not to cause some it must, it is argued, cause none).

Manufacture of doubt: Denialists highlight any scientific disagreement (whether real or imagined) as evidence that the entire topic is contested, and argue that it is thus premature to take action.

a corrupt elite. This is encouraged by cynicism with existing political systems. In one study, for example, the people who were most likely to believe in 9/11 conspiracy theories were those who were disaffected and disengaged with the political system.²⁰ Such cynicism is growing, a development that should not be surprising given how politicians feel able to take their countries to war on the basis of dubious evidence.²¹

A second issue, in some countries, is the espousal of denialism by an increasingly partisan media, which expends considerable energy identifying supposed conspiracies that they then espouse to the general public.²²

The third is the growing exploitation of the first two issues by corporate interests. Although the tobacco industry has been at the forefront of such tactics, there are now examples from many other sectors, including the food and drink, asbestos, oil, and alcohol industries. Such activities received considerable official support during the administration of George W Bush, under whose aegis there were widespread attempts to politicise scientific research and advice.^{23 24}

Tackling denialism

So how should scientists respond to denialism? The first step is to recognise when it is present. Denialism changes the rules of the game. Conventional approaches to scientific progress—such as hypothesis generation and testing, and argument and counterargument—that seek to elicit the underlying truth no longer apply.

In some cases, nothing can or needs to be done. The persisting belief among many people that Princess Diana may have been murdered by the security services (32% of the British public in one poll),^{25 26} for example, has enabled some tabloid newspapers to fill many pages and has wasted much police time, but has no persisting implications for public policy.

In other areas, especially where the views reflect longstanding cultural beliefs, it may be necessary to accept that these views exist and adapt messages to take account of them when developing policies and practices. Examples include the development of health promotion campaigns to prevent the spread of HIV²⁷ or to encourage the uptake of immunisation.²⁸ Such campaigns are based on a detailed assessment of the beliefs that would undermine them if not confronted. For example, early programmes to

tackle HIV/AIDS in east Africa had to address concerns that promotion of condoms was a covert attempt to control the population. It may be necessary to accept that there are some people who cannot be convinced, but there will be many who can.

This leaves those cases where denialist views are being promulgated actively by powerful vested interests. Here, we argue, health professionals have a responsibility to confront the denialists, exposing the tactics they use and the flaws in their arguments to a wide audience. Again, the first step is recognition. When a seemingly bizarre story appears in the media that risks undermining public health, health professionals should ask: “why is this story appearing now?” Many will, however, find this approach uncomfortable because it conflicts with the common tendency to seek compromise and avoid conflict.

Confronting denialism may also require the use of less usual methods of communication, such as analogy and narrative. Crucially, it demands speed of response. However, health authorities and non-governmental organisations are rarely able to respond rapidly, especially at weekends when, in our experience, misleading stories tend to appear in the media. Equally, editors of medical journals (with a few exceptions) often seem unable to appreciate the need to counter denialist stories.

In this paper we have looked at some of the most outrageous examples of denialism. Yet denialism is often much more subtle, and researchers are far from immune to its effects. There is a wealth of evidence on how reviewers find real or imagined flaws in papers whose messages they disagree with while discounting real errors in those they agree with. Perhaps, during the Christmas break, we, as reviewers and editors, might all take some time out to reflect on our own innate cognitive biases as well as how to overcome those of others.²⁹

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References are in the version on bmj.com

Integrative medicine and the point of credulity

So called integrative medicine should not be used as a way of smuggling alternative practices into rational medicine by way of lowered standards of critical thinking. Failure to detect an obvious hoax is not an encouraging sign

It is a common, and rarely unsuccessful, ploy to change the name of something unpleasant in order to give it greater acceptability. However, changing the name of Windscale nuclear plant to Sellafield after an accident in 1981 made it no less radioactive, and the new name quickly acquires all the connotations of the old.

Increasing concern has been expressed about the presence of complementary and alternative medicine (CAM) on the NHS. For instance, the House of Commons Science and Technology Committee recently reported critically on the evidence base for the use of homoeopathy in the NHS.¹ Nationally and internationally, there has been a move to disguise the nature of CAM by renaming it “integrative medicine.”^{2,3} Of course, it is something of an insult to medical practitioners to suggest that they do not take into account their patients’ individuality, autonomy, and views as part of their daily practice. It is certainly a key tenet of evidence based medicine⁴ and to

suggest that so called integrative medicine is somehow confined to the alternative world is a canard.

It is sometimes possible to test the status of a notion (the terms hypothesis and theory should be reserved for ideas that are related to at least some form of evidence) by a process of opposition. This involves testing the status of the notion by looking at the limits to which it can be pushed.⁵ Furthermore, there is an excellent tradition of testing research areas of dubious authenticity by means of a hoax. In 1996, Alan Sokal had a paper accepted in a cultural studies journal, in which he parodied postmodern philosophy and cultural studies by making a series of exaggerated, wrong, and meaningless statements about the potential progressive or liberatory epistemology of quantum physics in the style of the field.⁵ This he subsequently described in a book, bluntly called *Intellectual Impostures*.⁶ In the spirit of Sokal, therefore, I responded to a mass circulated email invitation to submit a

paper to something called “The Jerusalem Conference on Integrative Medicine.”

The invitation announced:

An International Conference on Integrative Medicine will be held in October 2010 in Jerusalem. It will be a meeting of professionals in the field of medicine from around the world that will deal with ways to unite the scientific principles of modern medicine with the holistic principles of alternative medicine.... The scientific committee of the convention is still open to accept additional topics to the conference program.

On 1 June 2010, I sent them the following invented nonsense:

I write to ask if you would be interested in a presentation on my recent work on integrative medicine. I am an embryologist by background, with an extensive publication record, in journals including *Nature* and the *Proceedings of the Royal*



Society, and have written an award winning text book on medical embryology. Recently, as a result of my developmental studies on human embryos, I have discovered a new version of reflexology, which identifies a homunculus represented in the human body, over the area of the buttocks. The homunculus is inverted, such that the head is represented in the inferior position, the left buttock corresponds to the right hand side of the body, and the lateral aspect is represented medially. As with reflexology, the “map” responds to needling, as in acupuncture, and to gentle suction, such as cupping. In my studies, responses are stronger and of more therapeutic value than those of auricular or conventional reflexology. In some cases, the map can be used for diagnostic purposes.

Although I resisted the temptation to draw an analogy with the mappings of phrenology, I still had it in mind, and the reference to gentle suction might have been taken by a sceptical reader to refer to the idea of kissing the point of credulity.

The organisers replied on the same day.

Dear Prof. McLachlan

I thank you for your interesting and enriching mail. In order to bring the proposal to the Scientific Committee I would appreciate it if you could send me an Abstract of your proposed lecture. And a short C.V.

Yours Sincerely
[name redacted]

The Jerusalem International Conference on Integrative Medicine

I replied on the following day:

ABSTRACT

Intensive study of the development of early human embryos indicates that there is a reflexology style homunculus represented in the human body, over the area of the buttocks. This homunculus corresponds to areas of clonal expansion (“Blaschko lines*”), in which compartments of the body have clear ontological relationships with corresponding areas of the posterior flanks. The homunculus is inverted, such that the head is represented in the inferior position, the left buttock corresponds to the right hand side of the body, and the lateral aspect is represented medially. The Blaschko lines mediate energy flows to parent areas, and lead to significant responses to appropriate stimuli. As with reflexology, the “map” responds to needling, as in acupuncture, and to gentle suction, such as cupping. Responses are stronger and of more therapeutic value than those of auricular or conventional reflexology. In some cases, the map can be used for diagnostic purposes. In both therapeutic and diagnostic interventions, a full case history must be taken,

in order to define the best methods of treatment. In the presentation, anonymised case histories, “testimonies” and positive outcomes will be presented. The methodology does not lend itself to randomised double blind controlled trials, for obvious reasons.

Obviously, the involvement of a sensitive area of the body poses special challenges. Ethical practice is of significant concern. Informed consent must be obtained from all patients in writing, before either therapeutic or diagnostic procedures are commenced. Although exposure of the gluteal region is recommended, procedures can be carried out using draping if this is required in order to gain patient cooperation. Chaperones or same sex practitioners are recommended in the case of female patients.

Unfortunately, this novel paradigm may meet with closed minds and automatic rejection. Patience and understanding of “closed” mindsets is essential in order to advance this new discovery in a way commensurate with its importance.

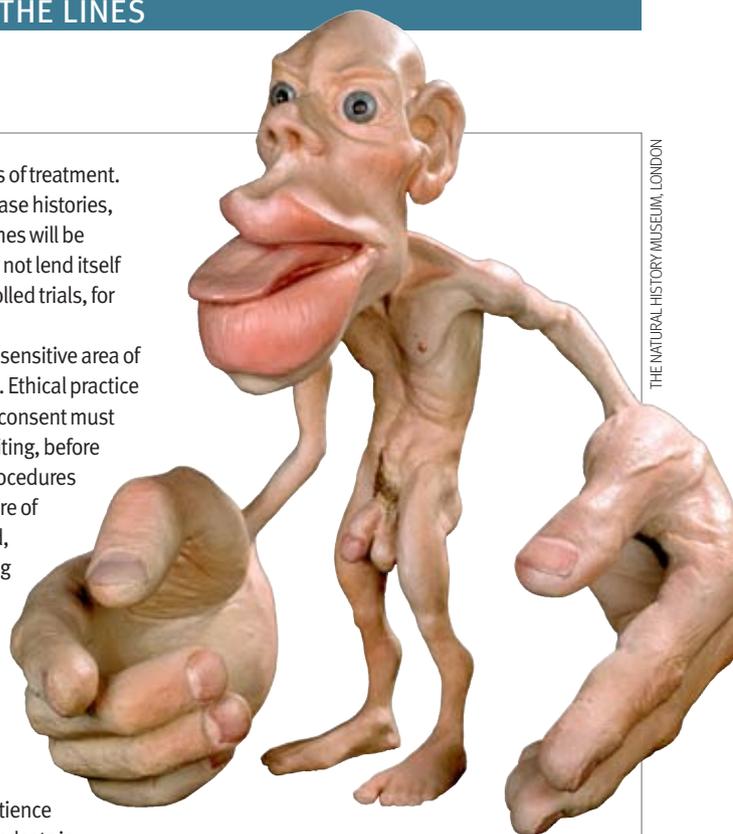
*See for example <http://dermnetnz.org/pathology/blaschko-lines.html>.

My initial email and abstract were constructed to include appeals to authority, hints of conspiracy theories, and “scienciness,” but with an absence of evidence or plausibility. I received this from the organisers on 26 July 2010.

Dear Prof. John C. McLachlan,
You have sent a proposal to the The (sic) Jerusalem International Conference on Integrative Medicine. We are happy to inform you that the Scientific Committee has reached its decision and that your paper has been accepted and you will be able to present your lecture. The time frame will be 15-20 minutes. Considering the tight schedule, I will appreciate if you’ll confirm your participation in the convention.

Unfortunately, I did not believe that I wished to carry the joke so far as to actually attend, although part of me was tempted.

I fully accept that this is just one instance, relating to a particular conference. And conference abstracts are refereed less stringently than full papers. But I also believe that the idea I proposed was intrinsically and self evidently ridiculous. Whereas Sokal’s hoax parodied the incomprehensibility and reductio ad absurdum of some proponents of cultural studies’ approach to natural sciences, this particular hoax parodied the absurdity and credulity of so called integrative medicine. I do not believe that rational medicine could have been fooled with something so



intrinsically ridiculous as in this case. Minimum standards of common sense should, I think, have led to a polite but firm rejection—or at least further inquiry. Alternative medicine is not noted for rigorous inquiry, for research designed to prove the null hypothesis, but rather accepts notions on face value. Therefore a face value test is fair.

I did also, to be honest, feel a little uncomfortable about it. There was an element of deception involved, and academic intercourse generally relies, to some degree, on good faith. I sent off the abstract in a spirit of fun, but then hesitated about making it public. I did decline the invitation (though I have never been to Jerusalem, and would have enjoyed the trip) but I didn’t want to cause harms by taking up a conference slot. But in the end, just as so called gentle teasing may reveal structures to the anatomist, so a different kind of gentle teasing may reveal something to the philosopher, and may promote an element of self awareness in proponents of alternative medicine, no matter what grand title it is disguised under. It provides, at the least, an opportunity for reflective practice, which I hope proves of some benefit to us all.

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Christmas 2009: *Secret remedies*: 100 years on (*BMJ* 2009; 339:b5432)

On the impossibility of being expert

More scientific papers are being published than ever before. **Alan G Fraser** and **Frank D Dunstan** call for that new strategies to deal with this avalanche of information

Every doctor has an ethical duty to keep up to date. Is this just getting more difficult or has it already become impossible? Since Alvin Toffler coined the phrase “information overload” in 1970,¹ the growth of scientific and medical information has been inexorable. There are now 25 400 journals in science, technology, and medicine, and their number is increasing by 3.5% a year²; in 2009, they published 1.5 million articles.² PubMed now cites more than 20 million papers.

One response of the medical profession to the increasing scientific basis and clinical capacity of medicine has been to increase subspecialisation. This may restrict the breadth of knowledge of the ultraspecialist, but can such subspecialists maintain their depth of expertise? Taking one medical subspecialty as an example, we have examined the gap between information and human capacity, and we explore the implications for any doctor who wants to practise evidence based medicine.

Methods

We searched the database of the US National Library of Medicine (PubMed) on 12 September 2010 for references relating to diagnostic imaging in cardiology. The table shows the search terms used.

Citations with any reference to echocardiography (the mainstay of diagnosis) were searched first, and then the strategy was narrowed to echocardiography as a main topic and restricted to controlled clinical trials (strategies 1-4; table). It is recommended that junior colleagues should be trained in several imaging modalities,³ and so we performed further searches for the concept of “multimodality imaging” in cardiology. This included single photon emission computed tomography (SPECT), positron emission tomography (PET), magnetic resonance imaging, computed

tomography (CT), and coronary arteriography, as well as cardiovascular ultrasound (strategies 5-6, table).

All searches were performed for each year from 1966 (the year before ultrasonics was introduced as a search term in PubMed; echocardiography was added in 1973) to 2009. Trends in papers on echocardiography were modelled; a good fit—from a cubic model containing time, the square of time, and the cube of time—was used to predict the numbers of publications to the end of 2010 and annually to 2015.

Results

The table shows the publications retrieved by each search, along with totals for the last full calendar year. Figures 1 and 2 show annual totals to 2009 and predictions from 2010 until 2015.

Search 5 without the cardiovascular system gave 700011 citations. A search for “diagnostic imaging” [Mesh] and “cardiovascular system” [Mesh] gave 195 106 papers, or 159 661 if limited to human studies, core clinical journals, and Medline.

To estimate the time that it might take a new entrant to the subspecialty to read all the previous literature, we assumed that he or she could read five papers an hour (one every 10 minutes, followed by a break of 10 minutes) for eight hours a day, five days a week, and 50 weeks a year; this gives a capacity of 10 000 papers in one year. Reading all papers referring to echocardiography (search 1) would take 11 years and 124 days, by

which time at least 82 142 more papers would have been added, accounting for another eight years and 78 days. Before our recruit could catch up and start to read new manuscripts published the same day, he or she would—if still alive and even

remotely interested—have read 408 049 papers and devoted (or served a sentence of) 40 years and 295 days. On the positive side, our recruit would finish just in time to retire.

Reading only the major studies would need more than four years for strategy 3 and more than five years for strategy 6. Alternatively, if only one year was allocated for study, then for strategy 3 our

recruit would need to read 95 papers every single day. If our recruit kept to the European Working Time Directive, he or she would have to read 138 papers a day, or for strategy 6, 162 papers a day at a rate of one every three minutes.

To keep up to date, the cardiac imaging specialist needs to read 30 papers a week on echocardiography or 43 a week on multimodality imaging. If limited to one paper every working day (estimated total 250 a year), then the chance that he or she will read any particular paper is 1 in 8.9. The chance that a colleague on the opposite side of the world will read that same paper in the same year is 1 in 79. If each reads a random selection of 250 papers a year, then the median number that both will read can be estimated at 28 (range 16-40) or 1.3% of the total.

A search strategy restricted to evidence on outcomes would not work for this subspecialty. The

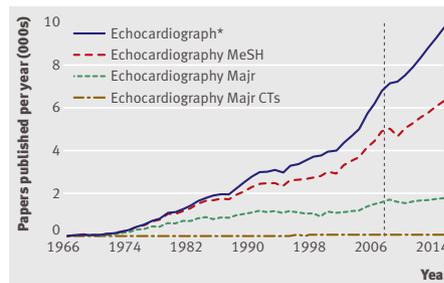


Fig 1 | Trends in numbers of papers listed each year in PubMed, according to search strategies 1-4 in table. The numbers to the right of the vertical line, after 2009, are projected totals. MeSH=medical subject heading, Major=as a main topic; CTs=controlled clinical trials

Search strategies for identifying articles on diagnostic imaging in cardiology

Strategy	Question	Total no of papers from 1966 to September 2010	Papers published in 2009
1	All papers that include any reference to echocardiography	113 976	7207
2	All papers cited with echocardiography as medical subject heading	84 689	4672
3	All papers with echocardiography as a main topic	34 577	1558
4	Papers with echocardiography as a main topic, restricted to human controlled trials	457	23
5	All papers referring to the cardiovascular system and any one of multiple imaging modalities cited as a medical subject heading; referred to in text as any “multimodality imaging”	109 604	7083
6	All papers referring to the cardiovascular system or diagnosis of cardiovascular disease and any one of multiple imaging modalities, if cited as a main topic and limited to humans; referred to in text as major “multimodality imaging”	40 496	2226

average number of controlled clinical trials that were published during the decade 2000-9 (search 4) was 26 each year. This number is not increasing, and it represents only 2% of the publications with echocardiography as a main topic (search 3) or 0.5% of all papers referring to echocardiography (search 1) during the same period.

Discussion

The gap between what we can learn and what is known is increasing all the time. We now know less and less about more and more, so being expert means knowing and publicly acknowledging the limits of your ignorance. Our analysis of one subspecialty showed no evidence whatsoever that the problem is abating, and remarkably similar patterns were reported recently for clinical trials and systematic reviews.⁴ Keeping up with the literature has already become a Sisyphean task. We are even engulfed by information overload about “information overload”⁵; searching this term on Google gives about 980 000 hits.

We did assume that all papers have equal value, which is clearly untrue, but we did not allow any time in our calculations for obtaining papers, and we ignored the projected increases. Impact factors are concentrated in a few journals,⁶ and citation errors are common,⁷ so trying to use either to select what to read would be unreliable for a topic such as medical imaging. Misconceptions are promulgated when authors do not check primary sources,^{8 9} and even when findings are contradicted by randomised controlled trials.¹⁰ Systematic reviews are not all being kept up to date.¹¹ Thus, delegating the selection of reading material to others might be unrewarding.

If anything, we probably underestimated calls on the doctor’s time for reading. Accurate diagnosis is a prerequisite for evidence based medicine, but experts in multimodality imaging should also know something about clinical and other aspects of their speciality.

Faced by the deluge of data, it is tempting to be nihilistic. After all, being ignorant of 100%

of the literature in your field is not significantly different from being ignorant of “only” 98%. On the other hand, reading even 2% is more than reading nothing at all. The average specialist reads 322 papers a year,¹⁴ and a few brave, exceptional, and overcommitted people might accept the challenge of reading more. For most ordinary mortals, this is impossible, and for clinicians who are not also researchers it may no longer be sensi-



ble. Reading the literature has become a collective rather than an individual pursuit, and each of us must change our behaviour to reflect this.

Medical students and doctors in training can be taught to search databases effectively.¹⁵ Doctors can use new information technologies to gain prompt and efficient access via the internet to the most relevant new data for their speciality.¹⁶ The Cochrane Collaboration is admirable, but its programme of systematic reviews is not comprehensive, so all academic institutions and medical professional associations should contribute to collective efforts to summarise medical evidence and build trustworthy, interactive repositories of knowledge on the internet. Authors of clinical guidelines have a particular responsibility to ensure that their recommendations are based on rigorous and re-testable meta-analyses of randomised controlled trials, health technology assessments, and systematic reviews.

Appropriate resources must be allocated for researchers and experienced senior colleagues to dedicate time to these activities. More could also be done to develop decision support tools.¹⁷

In fields such as diagnostic imaging the plethora of publications hides the fact that we still lack sufficient evidence for rational practice. The small proportion of papers that were cited as controlled clinical trials (search 4) reinforces this notion. The best way to assess any diagnostic strategy is a controlled trial in which investigators randomise patients to diagnostic strategies and measure mortality, morbidity, and quality of

life,¹⁸ but only 2.4% of diagnostic recommendations in the guidelines from the American Heart Association and the American College of Cardiology are supported by this level of evidence.¹⁹

It is time for the profession to be more imaginative. How can we reduce the number and increase the quality of publications?²⁰ Can we remove the responsibility of all researchers to publish all their results? Could they contribute instead to wikis? Can we construct open access internet resources that allow data mining? Only initiatives such as these will overcome our worrying finding that colleagues in the same medical discipline may inhabit intellectual worlds with little overlap. Happy reading!

Contributors: AGF conceived the study, performed the literature searches, and drafted the manuscript. FDD performed the modelling and revised the manuscript. AGF is guarantor.

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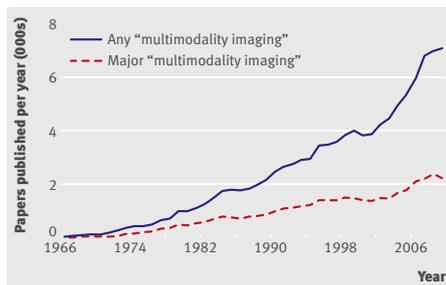


Fig 2 | Trends in numbers of papers cited each year in PubMed, according to search strategies 5 and 6 in the table

A dose by any other name would not sell as sweet

Inventors of drug names suddenly stood the alphabet on its head. Why did z and x become so attractive in the attempt to influence prescribers, asks **Rob Stepney**

If you leaf through the June 2000 issue of the *British Journal of Cardiology* you will see advertisements for Zocor, Xenical, and Cozaar before you reach a brand name that does not contain a prominent x or z (and that brand is Viagra). In an issue of *Hospital Doctor* from the same month (22 June), adverts for Celebrex, Topamax, Flomax, Vioxx, Zispin, Zyprexa, Oxis, Efexor, and Fosamax outnumber those for brands not containing letters from the tail end of the alphabet. Examination of the *British National Formulary (BNF)* from 1986 to 2004 confirms that z and x suddenly achieved remarkable and previously unexplained popularity in the branding of drugs.

Of 1436 products added to the *BNF* between 1986 and 2005, more than a fifth had names that began with z or x or contained a prominent x or z within them. In 1986, only 19 branded drugs began with one of these letters. Over the next two decades, the number of brands beginning with a z increased by more than 400% (to 63) and those beginning with an x increased by 130% (to 16). In the same period, the overall content of the *BNF* grew by only 80%.

Why did these letters suddenly become so attractive to companies trying to persuade doctors to prescribe their drugs? In linguistics, the “zuh” sound is described as a voiced fricative. The “fricative” element refers to the fact that airflow directed over the tongue becomes turbulent when passing the sharp edges of the teeth, while the “voiced” aspect reflects the vibration of the vocal cords. But there is nothing magical in the sound itself. One suggestion for the popularity of z is that it works well in the Middle East, which was becoming an increasingly important market for drug companies. This

Generic names of drugs listed in the article

Brand name	Generic name
Zocor	Simvastatin
Xenical	Orlistat
Cozaar	Losartan
Viagra	Sildenafil
Celebrex	Celecoxib
Topamax	Topiramate
Flomax	Tamsulosin
Vioxx	Rofecoxib
Zispin	Mirtazapine
Zyprexa	Olanzapine
Oxis	Formoterol
Efexor	Venlafaxine
Fosamax	Alendronic acid
Zyloric	Allopurinol
Zinacef	Cefuroxime
Zovirax	Aciclovir
Zantac	Ranitidine
Zirtek	Cetirizine
Zoladex	Goserelin
Zithromax	Azithromycin
Zoton	Lansoprazole
Prozac	Fluoxetine
Zoloft	Sertraline
Nexium	Esomeprazole
Plavix	Clopidogrel
Xanax	Alprazolam
Xylocard	Lidocaine
Xyloproct	Lidocaine
Xalacom	Latanoprost
Xenazine	Tetrabenazine
Xyzal	Levocetirizine
Xeloda	Capecitabine
Xatral	Alfuzosin
Zestril	Lisinopril
Innovace	Enalapril
Tritace	Ramipril
Pulmicort	Budesonide
Flixonase	Fluticasone
Taxol	Paclitaxel
Oncovin	Vincristine
Herceptin	Trastuzumab
Erbix	Cetuximab
Aprovel	Irbesartan

More likely, though, is that use of these letters relates to the imperative to make a brand name highly visible in a crowd. Reflecting their infrequent occurrence in English words, x and z count for 8 and 10 points in Scrabble, the highest values (along with j and q) in the game. So names that contain them are likely to seem special and be memorable. “If you meet them in running text, they stand out,” is the way one industry insider explained. Generally, they are also easy to pronounce.

That is an old insight in the wider field of marketing. But in pharmaceuticals z did not really take off as a brand initial until after 1996, with the number of drugs beginning with the letter rising steeply from 29 to 51 in 2000 (figure). And the widespread use of x (often also pronounced as “zuh”) is later still. Something additional started the bandwagon rolling.

Z and x spell Zuxess

Whatever the initial thinking that lay behind the use of the letter, the people responsible for marketing drugs spotted in the 1990s that an unusually large number of z brands had already achieved blockbuster status or were well on the way towards it.

Both Wellcome and Glaxo—then unrelated companies—showed an early liking for z and enjoyed conspicuous success. Wellcome had introduced Zyloric for gout in 1966 and Glaxo the intravenous antibiotic Zinacef in 1978. But it was in 1981 that both companies hit the jackpot with Wellcome’s launch of the antiherpes drug Zovirax and Glaxo’s launch of the H₂ receptor antagonist Zantac. In 1985, Zovirax became the world’s first billion dollar drug; and Zantac was the world’s best selling drug by 1986.^{1 2} In its first 20 years, it was used to treat more than 200 million people.³

The antihistamine Zirtek and the first agonist of luteinising hormone releasing hormone Zoladex (both introduced in 1989), the antibiotic Zithromax (1991), and the proton pump inhibitor Zoton (1994) all became highly successful; and Prozac (1987) made such an impression that its name branded a generation. In 2003, three of the world’s top 10 drugs (each grossing between 3 and 10 billion dollars annually) were Zocor, Zyprexa, and Zoloft.⁴ Also among the top

has a superficial plausibility: think of how Arab scientists launched astronomy with the terms zenith and azimuth. X, though representing the unknown for centuries, has been famously associated with medical advance since x rays. So this too would have appeal.



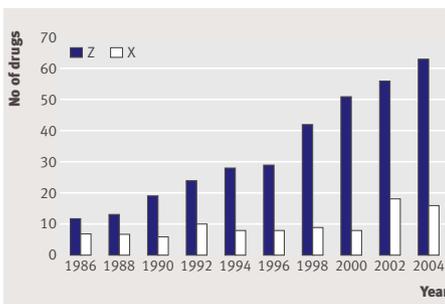


Fig 1 | Number of drugs with a brand name beginning with z or x listed in March edition of *BNF* for each year. New formulations of existing brands and zinc related compounds have been excluded

ten drugs that year were two with the X factor: Nexium and Plavix.

The widespread use of x at the start of a brand is a more recent ploy in drug marketing, seemingly designed to achieve the sound of a z while looking different. In the 1985 *BNF* there are a few (notably Xanax, Xylocard, and Xyloproct). The big year for brand introductions with this feature did not come until 2002, but by 2005 there were more than a dozen including Xalacom, Xenazine, Xyzal (successor to Zirtek), Xeloda, and Xatral.

People who work in branding speak of it as a means of making a product more than it actually is. In many areas, this is achieved by adding persuasive emotional (and some would say irrational) content. If you buy a car named after an animal famed for its exhilarating speed and elegance, that is what you associate with the vehicle. But in the tightly regulated world of pharmaceuticals, drug names are supposed to be devoid of what the Medicines Control Agency used to call “unsubstantiable beneficial” connotations.

Certain drug names have always alluded helpfully to the chemical class of the agent (as in Innovace, Tritace), its target organ (Pulmicort, Flixonase), the plant species from which the prototype drugs were derived (Taxol, Oncovin) or the drug’s molecular target (Herceptin, Erbitux). Otherwise, when they are sticking to the rules, those inventing brand names for drugs have little scope to play with anything but the sound of letters, and to some extent the appearance of the word. This is presumably why we have the odd repetitions seen in Vioxx and Cozaar) If any alphabetical quirk seems to be working well, there must be a strong temptation to follow suit.

Sometimes, though, the rules get bent or broken. Aprovel manages to convey the idea of endorsement and Celebrex and Zestril a clear *joie de vivre*. Indeed, the contrasting stories of the two brands of lisinopril, both launched in the late 1980s, would make an interesting case study. ICI Pharmaceuticals called its lisinopril Zestril. Its competitors marketed the same molecule as Carace. Whereas Zestril became one of the medical world’s most successful brands, Carace sank pretty much without trace. Was the difference due to the z, the zest, or both?

Product naming, of course, is an art that extends across all commercial activity; and z and x have played an important role elsewhere. Of the 10 cars currently listed as fastest in the world (all capable of 0-60 mph in under four seconds), four—including the Ferrari Enzo and the Jaguar XJ220—have a z or x in their names.⁵ For some brands, the prominence of a key letter is fortuitous: Zanussi, the white goods manufacturer, apparently derived its name from the early 20th century blacksmith and stove manufacturer



Antonio Zanussi. But there are many examples of brand name coinage that are as contrived as those used to market drugs and precede them. For the best part of a century, marketing has gone for certain arbitrary syllables like “ex”, “ax” or “ox.” These are stuck on to a meaningful word, as in Timex, Artex, or Tampax, or a meaningful word misspelt, as in Kleenex (introduced in 1924). Xerox, which became a trademark in 1948 (50 years before the double x stratagem became popular for drugs) is an acknowledged classic.

That said, the use of x and z in drug brands suddenly became extraordinarily prevalent. I suggest that this phenomenon arose because of the fast rate at which new products were being introduced, the fact that the difference between many “me too” drugs was more apparent than real, the immense rewards that were seen to accrue from innovative marketing, and the fact that the ploys available for use in the naming of drugs are so restricted.

I thank the staff of the BMA library for their help in enabling me to consult copies of the *British National Formulary* from 1985 to 2005.

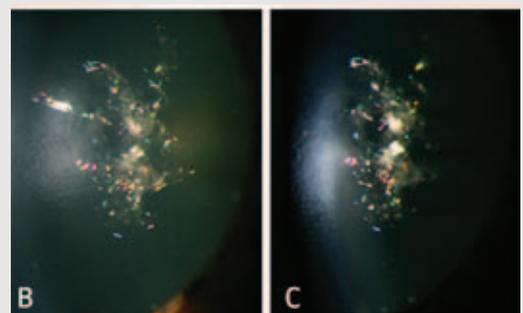
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A Christmas tree cataract



A 73 year old woman referred for cataract surgery had on examination a right Christmas tree cataract (fig 1A). Highly reflective, iridescent, polychromatic crystals were noted within the lens. Their colours varied according to the angle of the incident light, (fig 1B, C). It has been postulated that Christmas tree cataracts result from the accelerated breakdown of membrane associated proteins. The peptides and amino acids accumulate in the lumen of the reticular meshwork, and cystine is concentrated beyond the level of crystallisation, giving rise to growing crystals.

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Pie sharing in complex clinical collaborations: a piece of cake?

The Little Red Hen learns some important new lessons in K T Buddingh's cautionary, but entirely fictitious tale

A Little Red Hen lived in a university hospital where she took care of the sick animals in the different wards. She did this under the overseeing eye of her wise and learned mentors. There was the Cow, who had a degree from a prestigious overseas university. There was the Pig, who had led mergers of several high standing hospitals in the country. And there was the Sheep, who had an outstanding treatment record with almost no animal morbidity and mortality.

One day the Little Red Hen thought: "Why don't I see if I can use my scarce free hours at the end of the day and make an excellent pie. Not only will this pie add to the gastronomic knowledge, it could be that the sick animals will benefit from this pie in the long run."

So the Little Red Hen ran her idea past her mentors.

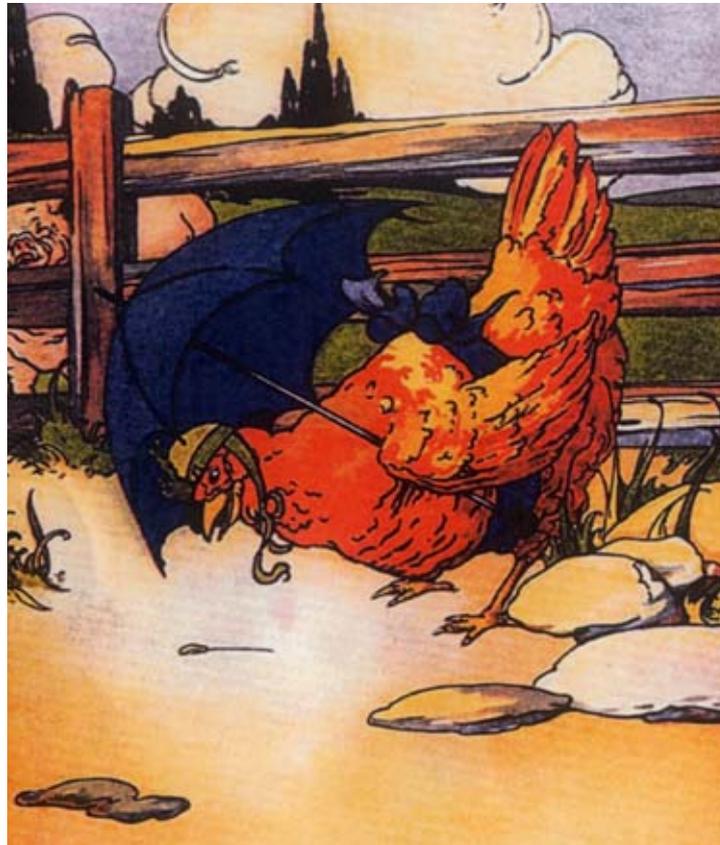
"Great idea," said the Cow. "I will supply the milk and the butter. Of course, I would like a piece of the pie when it is baked."

"Excellent," said the Pig. "I happen to know the editor of a prestigious cook book. I expect a piece of the pie once it is finished."

"Good thinking," said the Sheep. "My laboratory will provide the necessary utensils. Just make sure I get a share of the pie."

The Little Red Hen wasted no time. Every day, after taking care of the sick animals she spent the last few hours of daylight planning the pie. She took classes in pie making, wrote pie making protocols, and even obtained approval from the institutional pie review board. And after a few months, all preparations were in place.

The Little Red Hen first went to the Cow and asked for the milk and the butter. "I have the milk and the butter for you. However, I heard that the Sheep will also have a part of the pie. I



FLORENCE WHIT WILLIAMS/THE LITTLE RED HEN

her mentors to share the news.

"Welcome everyone," said the Cow. "I would like to present the outstanding result of our co-operation." She then took half of the pie and left the room. The Pig was next. "Excellent work, Little Red Hen." He cut himself a sizeable piece of the pie and left the room. Then the Sheep stepped forward. "What a feat of culinary craftsmanship did we achieve! Congratulations on your first pie." He cut a small piece of the pie, and took the rest.

The Little Red Hen sat in the conference room and stared at the small piece of pie that remained. Although happy to have baked her first pie and to have contributed to the gastronomic knowledge, she was left with an inexplicable feeling of disappointment. It did take quite some time before the Little Red Hen attempted to bake another pie.

Disclaimer: This tale is based upon coffee table stories and a compilation of reported experiences in the academic

hospital at no specific place. Any names, characters, places, and incidents are either the product of the tale or are used fictitiously. Any resemblance to actual events or locales or persons, living or dead, is entirely coincidental.

Contributors: KTB came up with the idea and wrote the first draft. LMCA gathered opinions and experiences from colleagues in the university hospital and contributed significantly to the description of the characters in the tale. GMvD ran a spell check on the document and demanded that, as senior investigator, he received a prime author position. After negotiations, he edited the paper for style, contributed to the plot of the tale, and settled for the middle author position.

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want you to make sure that my piece of the pie is larger than that of the Sheep."

The Little Red Hen continued to the Pig. "Hold on," said the Pig. "I have submitted a grant application for possibly an even bigger pie, so I cannot actively co-operate any longer on the current pie. However, if you do bake it, don't forget to give me a piece."

The Little Red Hen then visited the Sheep. The Sheep was abroad for a conference on animal wellbeing with an extended post-conference tour, and his laboratory had received no instructions to provide any utensils.

The Little Red Hen went to work. She tested her own recipes, made do with her limited utensils, and fluttered between different departments to keep everybody satisfied. Finally, after many long hours and many failed pies, an acceptable pie came out of the oven.

Overjoyed, the Little Red Hen called together