
THE TRUTH IS THAT IT IS COMPLETELY UNCERTAIN WHETHER BREAST SCREENING IS USEFUL AT THEIR AGE, AND THERE ARE VERY REAL RISKS TO WOMEN WHO ACCEPT PHE’S INVITATION. “IT CONTAINS NO DATA FROM THE PILOT STUDY—SPECIFICALLY THE DOUBLING OF ‘RECALLS’ AND FALSE POSITIVES,” SAYS BEWLEY, PROFESSOR OF COMPLEX OBSTETRICS AT KING’S COLLEGE LONDON. NEITHER DOES IT MENTION THE RECENT DUTCH STUDY WHICH CONCLUDED THAT THE BENEFITS OF SCREENING ARE LIMITED IN THE OVER-70’S, WITH SIGNIFICANT AND HIGH RISKS FROM OVERDIAGNOSIS. 4

SO MUCH FOR THE NEED FOR INFORMED CONSENT. AND AS A TRIAL THIS ONE, WHICH MAY BE THE LARGEST EVER HUMAN EXPERIMENT, HAS OTHER MAJOR FLAWS. THE MESSY EIGHT PAGE STUDY PROTOCOL, DISCLOSED ONLY AFTER REPEATED FREEDOM OF INFORMATION REQUESTS, CONTAINS TWO REFERENCES AND HAS NO STATISTICAL ANALYSIS PLAN. 5 IT CAN BE VIEWED ON THE HEALTHWATCH WEBSITE, ALONG WITH A DETAILED CRITIQUE THAT IS BEING UPDATED AS NEW INFORMATION BECOMES AVAILABLE. 6

BEWLEY AND OTHERS HAVE BEEN FIGHTING FOR YEARS TO ENGAGE THE NHS BREAST SCREENING PROGRAMME WITH THEIR CONCERNS AND THEY PRESS ON DESPITE REPEATED REBURF. THE CHARITY BREAKTHROUGH BREAST CANCER RECENTLY REFUSED TO MEET WITH HER AND MICHAEL BAUM (THE BREAST SURGEON AND HEALTHWATCH FOUNDER) TO DISCUSS THE TRIAL. THE CHIEF EXECUTIVE OF PHE HAS PUT OFF REPLYING TO CONCERNS RAISED IN AUGUST AND SEPTEMBER BUT IS EXPECTED “TO BE IN TOUCH” BY EARLY DECEMBER. HOWEVER THE NATIONAL RESEARCH AUTHORITY HAS PROMISED TO REVIEW THE ETHICAL APPROVAL.

“SURELY, ‘IMPLIED CONSENT’ BASED ON FALSE INFORMATION IS NOT VALID?” ASKS BEWLEY. A RECENT DAILY MAIL REPORT OF A TRIAL PARTICIPANT WHO RECEIVED A DOUBLE MASTECTOMY AND WENT ON TO CALL FOR SCREENING TO BE MAINTAINED EVEN MORE WIDELY AVAILABLE DEMONSTRATES HOW POORLY RESEARCH AND SCREENING RISKS ARE UNDERSTOOD BY WOMEN, AND IT IS DIFFICULT TO ESCAPE THE IMPRESSION THAT THE BODIES PROMOTING THE PROGRAMME ARE COMPLICIT IN PERPETUATING DANGEROUS MISCONCEPTIONS, SHE ADDS. “IN SUCH A CASE ALL WE CAN KNOW FOR CERTAIN IS THAT SCREENING LED DIRECTLY TO THE MASTECTOMY. BY FAR THE MOST LIKELY SCENARIOS ARE EITHER THAT THE CANCER DETECTED MAY STILL LEAD TO HER DEATH DESPITE THE SURGERY OR THAT IT WOULD HAVE BEEN CURED EVEN IF SHE’D WAITED FOR SYMPTOMS. ALL THE EVIDENCE SUGGESTS HER LIFE CHANCES ARE UNAFFECTED BY SCREENING. IT IS A SHAME THE JOURNALIST DIDN’T ASK MORE QUESTIONS ABOUT THE RESEARCH TRIAL.”

IN THE WORDS OF THE SWISS MEDICAL BOARD: “IT IS EASY TO PROMOTE MAMMOGRAPHY SCREENING IF THE MAJORITY OF WOMEN BELIEVE THAT IT PREVENTS OR REDUCES THE RISK OF GETTING BREAST CANCER AND SAVES MANY LIVES THROUGH EARLY DETECTION OF AGGRESSIVE TUMOURS. WE WOULD BE IN FAVOR OF MAMMOGRAPHY SCREENING IF THESE BELIEFS WERE VALID. UNFORTUNATELY, THEY ARE NOT, AND WE BELIEVE THAT WOMEN NEED TO BE TOLD SO.”

MANDY PAYNE

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WE WILL CONTINUE to oppose the introduction of Lord Maurice Saatchi’s Medical Innovation Bill, despite it receiving the backing of the Government this month. The bill proposes that dying patients could be given access to untested medicines without their doctors being in fear of litigation. It was proposed by Lord Saatchi, the advertising magnate, who started to campaign on the issue after his wife, the novelist Josephine Hart, died from ovarian cancer.

Under the new law, doctors would be able to try out experimental treatments on the terminally ill subject to another specialist’s agreement, and the patient giving informed consent. According to recent reports the bill now has a 75% chance of becoming law and could be in place as early as March 2015.1

Michael Baum, professor emeritus of surgery at University College London and a founder of HealthWatch, told the Telegraph: “Never once have we encountered interference or obstruction due to fear of litigation. There are of course many other obstacles to progress but changing the law with this bill is not going to accelerate innovation in cancer therapy, but might, as a result of unintended consequences, endanger our patients by uncontrolled experimentation.”1

A recent broadcast is still available online for readers who would like to get up to speed on the debate. In BBC Radio 4 Sunday,2 Nigel Poole QC explains that the British Medical Association and the Medical Defence Union have found no evidence that fear of litigation is deterring doctors from using new treatments where available and appropriate. What is more, he says, by removing the patient’s right to sue in the event of something going wrong, however rarely that right may be exercised in practice, leaves patients more vulnerable. Professor Raymond McAllister of University College Hospital London argues that the bill is unnecessary as he describes how innovation is already being carried out in specialist units. “People have not been crying out for this bill.” He says, on the contrary, it raises false hope and opens the door to mavericks.

References

OPPOSING THE SAATCHI BILL

THE HEALTH REGULATOR has granted official backing to a register of homeopaths in a move that has been described as “potentially dangerous” and “odd”.

The Professional Standards Authority for Health and Social Care (PSA), which also oversees the General Medical Council and the Nursing and Midwifery Council, has added a register run by the Society of Homeopaths to a voluntary scheme for professionals without legal protection, such as counsellors and psychotherapists.

Harry Cayton, the PSA’s chief executive, told The Times that the move will offer potential customers “reassurance” that practitioners met the training and standards set out by homeopaths themselves. But Simon Singh, this year’s HealthWatch Award winner, warned that consumers might assume homeopathy had been given official backing. “It is a slap in the face to serious health professionals who come under the PSA’s umbrella and, more seriously, it will encourage patients to make potentially dangerous decisions.”

In the Times’ letters page the following day, columnist Stephen Pollard wrote: “This is, to put it mildly, odd.” He described the PSA’s decision as “another triumph of ignorance over knowledge. Of all the bodies in the land, the organisation overseeing medical professionals should be safe from the idea that medicine is a matter of opinion rather than empirical science.”

The Times, 16 and 17 September 2014

PSA BACKING FOR HOMEOPATHS REGISTER: “ODD”

THE WORLD Health Organization is seeking comments on a draft statement on the public disclosure of clinical trial results. This is an opportunity to press the WHO to call for publication of the results of every trial that has taken place, as well as those from now on, and to remind them that the accepted time to report results or offer a reason for delay is 12 months. The consultation is open until 15 November.

Go to: http://www.who.int/ictrp/results/en/

IN CASE you are not convinced of why we need all clinical trials registered and reported, Sense About Science has produced a series of brief videos featuring 2006 HealthWatch Award winner Ben Goldacre explaining the result of the non-publication of trials of the heart drug Lorcaimide and Reboxetine, and the withholding of data on Tamiflu. All are 3-minute views, worth sharing on social media.

Go to: http://www.alltrials.net/find-out-more/videos/

THE 16TH EUROPEAN Skeptics Congress is to be held at Goldsmiths College, London, from September 11 to 13, 2015. It is jointly organised by the Association for Skeptical Enquiry and the Goldsmith College’s Anomalistic Psychology Research Unit, and will include a presentation by Professor Edzard Ernst.

Go to: http://euroscepticscon.org/

ANDREW DOWSON, the investigator who co-led the MIST (Migraine Intervention with STARFlex Technology) trial, will appear at the Medical Practitioners Tribunal Service for an eight week hearing starting on 29 October. He faces charges over his conduct of the trial. His co-investigator Peter Wilmshurst was sued by STARflex’ manufacturers after he cast doubt on the accuracy of the trial’s results, a case which triggered last year’s reform of English libel law.

BMJ 2014;349:g6141

THE TEXAS Court of Appeals has upheld the dismissal of a libel suit brought by Andrew Wakefield against the BMJ Publishing Group, editor-in-chief Fiona Godlee, and reporter Brian Deer. The libel suit concerned coverage of Wakefield’s 1998 Lancet paper on the MMR vaccine and autism, since retracted.

Go to: http://www.casewatch.org/foreign/wakefield/libel_suit/appeal_opinion.pdf

NEWS IN BRIEF
THE IRLEN EXPERIENCE

MY FATHER used to say that humanity is divided into those that see the world through a moral framework and recognise their place within it, and Tories. When a concerned mother came to the paediatric clinic bearing literature from the Irlen Institute and claiming that her daughter was a sufferer of the syndrome therein I remembered his words.

I was studying for the fellowship exam at the time and had not come across ‘Irlen Syndrome’, a condition that the leaflet told me afflicted a very sizeable proportion of the population. Until that moment I’d been happily oblivious to this phenomenon, whose treatment took the form of tinted lenses available not from optometrists but only from ‘Irlen Centres’. As the cost of the treatment was not readily findable I speculated that they might be charging handsome fees at the same time.

Much like a course of hepatitis B vaccination each new encounter with an ‘Irlen’ sufferer induced in me a growing sense of righteous indignation. I wrote a ‘personal view’ article for the BMJ which was published online at the end of July and in print some two weeks later in which I attempted to raise awareness of this practice among fellow medical practitioners.

Friends and colleagues chuckled nervously when I told them the BMJ had accepted the article. My boss at Singleton Hospital advised me to get a flak jacket in readiness, while another consultant was more than a little perturbed by the fact that my place of work would be displayed in the article next to my name. I laughed in what I thought was a morally upstanding and brave way. What was the worst that could happen? Was it not a service of good for the benefit of mankind? Was I not putting things right what once went wrong, like Dr Becket on Quantum Leap? I would clearly be regarded as a hero by the profession and by the specialty. I had nothing to lose.

“I was accused of insulting a US marine and his family while at the same time questioning my right to have an opinion on this matter as I worked at a ‘provincial hospital’”

I knew when the article had been published online even before the BMJ told me. I was idly checking my phone at 9:30pm when I noticed I had seventeen new emails. I had never in my life before had seventeen new emails all at once. I was at first excited as I started to open the messages and realised that my crusading article was being read. My excitement diminished somewhat when I realised that all seventeen emails were written by Americans hostile to my article and to me personally. Most of my newfound friends seemed to be suffering from Irlen Syndrome, the rest were affiliated with the company itself. I confess to not reading every word of every email as I was becoming increasingly disheartened by being called a trouble maker, a fool, a member of the ‘establishment’ (somewhat surprisingly), and an ill-educated poor excuse for a medical student.

I replied to two of the more sensible emails trying to explain my point of view, and noticed that another three emails had arrived in the time it had taken me to craft my replies. I did not open these new ones and tried to sleep as best I could. The morning would bring supportive messages for sure. Why was I getting so much correspondence in such a short space of time? Surely the BMJ website could not have so many interested people browsing its contents all at the same time?

The answer became clear the following day after I had deleted a further thirty-eight messages from my inbox, this time without reading a single one. The Irlen Institute of Long Beach, California had reacted to the article by tweeting my personal email address to their followers, with an invitation to “email your response directly to the author”. To be fair to them, they were loyal in a way that patients rarely are to a syndrome and offered their comments in large numbers, mostly by telling me how disgusted they were.

Rapid responses for the article started to be published on the BMJ website the following day and as the numbers were far less than the emails I had received I judged the journal was filtering them more than a vitiolic ones. I was somewhat pleased to see one or two supportive messages appearing but again the responses were mostly negative. A particular favourite accused me of insulting a US marine and his family while at the same time questioning my right to have an opinion on this matter as I worked at a ‘provincial hospital’. Many people assumed I was a medical student for some reason and one contributor invited me to attend her clinic in Brazil, all expenses paid, where I could examine files that would convince me that the syndrome was valid. I was curious enough to Google this particular individual but discovered that not only was she married but her husband appeared to be something of a big cheese in the Irlen world. The prospect started to look a whole lot less attractive.

My inbox was groaning under the weight of new emails and I cursed my stupidity in not starting up a new email address just for the purposes of the article. Grudgingly I admitted that my work colleagues were right in recognising the true danger of putting your head above the parapet and that my initial bravery was nothing more than naivety.

Then I had a more worrying email by far. It was from a man who had read my article on the amusingly named chronic fatigue syndrome website "http://constantfuckingshit.wordpress.com/” and who claimed to live in Swansea. It was my lucky day apparently as he was going to find me at work so that he could tell me all about Irlen. He said I would do an MRI scan on him so that I would know he was truthful in his assertion that his coloured lenses helped. I swallowed hard and decided that I should reply to this man lest I have a bad day at work and after a few emails he seemed to agree that he was probably best off not coming down to the eye department. He hasn’t come as yet.

I learnt a valuable lesson. Truth and righteousness are all well and good and are probably excellent for reflective learning and 360 degree assessments of probity. But in the real world you end up being called a medical student from a provincial hospital causing endless people to be ‘disgusted’ at your ‘vile’ comments while a scary man threatens to call in to see you at work and make you do an MRI scan on him. While my father may have been right, at the end of the day Tories live longer.

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THE LANGUAGE OF CLINICAL TRIALS

A NEW BRIEF GUIDE to understanding and reporting clinical trials has been published online by the Medical Journalists’ Association. In The Guide to Clinical Trials, written by HealthWatch Committee member John Illman, the MJA aims to encourage journalists to ask the right questions and to know when to seek independent expert help for further information and clarification. The 27-page guide is downloadable from the MJA website free of charge to their members, but for the benefit of HealthWatch members we are reproducing some helpful nuggets of information with the MJA’s kind permission.

In 1994 Professor Doug Altman, one of the world’s leading medical statisticians, estimated that only 1 per cent of medical research was free from flaws.1 In 2006 Dr Trisha Greenhalgh, in her book How to Read a Paper, claimed that only 10-15 per cent of published scientific research would be of lasting value.2 In 2009, Sir Iain Chalmers, co-founder of the Cochrane Collaboration, and his Australian colleague Professor Paul Glasziou, estimated that as much as 85 per cent of research investment was wasted.3

This extraordinary claim has been followed up in 2014 by a supplement in The Lancet.4 But research drives progress. There have probably been more advances in the understanding and application of medical science in the last 60 years than in the previous 2000. Clinical trials of drugs and some other treatments follow pre-clinical (pre-people) research with laboratory and animal studies. The most common types of clinical trials of drugs progress through five phases in the US and four phases in Europe. Each phase follows on only if the previous one is successful. Failure rates are high. For example, phase 2 success rates were reported in one analysis to have fallen from 28 per cent in 2006-2007 to 18 per cent in 2008.5 Definitive figures are elusive because many trials are not registered or reported. This can encourage reporting bias and conclusions that treatment is better than it really is. The James Lind Library reports that tens of thousands of deaths could have been avoided in the second half of the 20th century if all the studies into giving drugs to reduce heart rhythm abnormalities in patients having heart attacks had been reported.

There are many different types of clinical trial. Some are more reliable than others.

A case report or study features an individual patient who may have a rare diagnosis or unusual complications. Case studies have no statistical weight but can have profound consequences. For example, premature babies now routinely receive steroid therapy to prevent breathing problems, after clinical testing confirmed the value of this practice. This followed a case study with a premature lamb that developed unexpectedly strong lungs after its mother had received a cortisol steroid injection.

Case series investigate groups of patients undergoing similar treatment of illness. They may highlight rare side-effects and unexpected results in these patients, but since they do not compare different therapies, they cannot identify optimal treatments.

Cohort studies compare differences in populations—for example, between women who take hormone replacement therapy and those who do not. HRT was found to be very effective in reducing menopause-related hot flushes and further evidence suggested that it might prevent osteoporosis (bone thinning). There were also claims that it could prevent heart attacks and strokes, but large cohort studies then showed that rather than preventing heart disease, it could actually increase it. Further studies, such as the Million Women Study, have shown that HRT also increases the risk of stroke and breast cancer. This research underlines the importance of early testing. If the effects of HRT had been evaluated properly when it was first introduced, women would not have been misinformed and many would not have died prematurely.

Randomised controlled trials (RCTs) compare two or more treatments, sometimes with a placebo. Each patient has an equal chance of being allocated at random to a particular treatment group. This process is designed to prevent allocation bias. The clinicians responsible for allocating treatment are unlikely to be deliberately biased, but they may feel, for example, that a gravely ill patient would be better off in a particular group.

After random allocation to treatment comparison groups, the groups are likely to be similar in all characteristics other than the one under investigation—this means that there will be similar proportions of gravely ill patients in the groups.

The most reliable RCTs are masked or ‘blinded’. In a single-blind RCT, only the researchers know in advance who is getting what treatment. In a double-blind RCT, neither clinicians nor patients know.

Systematic reviews of research studies are done as assembly as high a proportion as possible of the reliable evidence relevant to addressing a particular question. Researchers carry out a thorough search, weed out poorly done studies, synthesise the results statistically (meta-analysis) if possible and appropriate, and draw conclusions.

Systematic reviews provide stronger conclusions than individual studies, both by reducing biases and by identifying small differences that remain undetected in single studies.

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For more information about the Medical Journalists’ Association visit their website on: http://www.mjauk.org/

References
EVIDENCE TO COMMONS ON SCREENING

EARLIER THIS YEAR we submitted a robust 3000-word response to the House of Commons Science and Technology Committee’s inquiry into the scientific merits of national health screening programmes. Our response drew on the combined expertise of members of the HealthWatch committee. So we were delighted when the Select Committee invited HealthWatch Award winners Professor Michael Baum and our patron Dr Margaret McCartney to give oral evidence this June.

The first session began with the question: Does the public understand how to screen for cancer? As you can see from the extracts below, Mike was in his element. The Chairman, Mr Andrew Miller, opened the second session with questions to Margaret McCartney. As a general practitioner, Margaret believes the number of patients who have screening is influenced by targets, but she fears that targets are distorting clinical practice.

Margaret raised the issue of the NHS Health Check. This screening programme, which is available to all between the ages of 40 and 74, has not been approved by the National Screening Committee and there is little evidence of benefit. Far more important than any health check, she said, was to advise patients to lose weight, cut down on smoking, reduce their alcohol consumption and take exercise.

Margaret introduced the problem of private screening organisations who advertise vigorously and encourage people to pay for tests without any reference to their GP. As a result of these private health checks, individuals become worried and turn to their GP. They want to know if the lump that has been discovered or the small aortic aneurism that has been found should be treated. The Chairman asked about the ethical issues and Margaret explained that in her view private screening should be regulated and their claims must be evidence-based.

Keith Isaacson Chairman of HealthWatch

WITNESS: Professor Michael Baum

ON WEDNESDAY 11 June 2014, I was invited to provide oral evidence on behalf of a campaigning group “Advocates for Honesty and Transparency in Breast Screening”. The committee was chaired by Mr Andrew Miller and included; Mr David Heath; Stephen Metcalfe; David Morris; Stephen Mosley; Graham Stringer; and David Tredinnick—the member of the health committee and the science and technology committee who has lately spoken publicly of his belief in astrology and his desire to incorporate it into medicine.1 The latter was conspicuous by his absence although I suspect he was following the proceedings on his crystal ball.

The meeting was held in a committee room at Portcullis house next door to the Houses of Parliament. The question and answer sessions were conducted in a very friendly way that showed MPs on their best behaviour, genuinely trying to get at the truth in a rhetoric free zone.

Reading the transcript of the exchanges where I was involved,2 surprised and almost embarrassed me, yet at the same time reflected the free and easy exchange of ideas that we enjoy amongst members of HealthWatch. I include some examples that provide an insight into the process:

Q54 Chair: In my experience when I have been treated by doctors, in hospitals in particular, the level of information one gets about the risks one is undergoing as a result of some intervention is communicated in a way that is unintelligible to most lay people.

Professor Baum: Your opening point gets to the very heart of the problem as far as I am concerned. The fundamental problem with screening for cancer is that the proponents of screening use relative risk reductions, which not only lay people, but most of my professional colleagues, fail to understand. The fact that screening for breast cancer has a relative risk reduction of 15% in breast cancer mortality sounds very impressive. When you translate that into absolute terms, it means that you have to screen between 1,000 and 2,000 women for 10 years to avoid one breast cancer death. I would hope the very first thing you can grapple with is how on earth we are going to display risks and benefits in absolute terms that lay people can understand?

Q55 Chair: Can an infographic approach be applied to screening?

Professor Baum: The infographic approach is improving all the time. I was a member of a panel advising a committee on how the new invitation for breast cancer screening should be put together. We urged infographics. Our advice was ignored. What I have witnessed first hand is an intention, no doubt in good faith, by the people running these screening programmes, to maintain a very high uptake, on the assumption that they know best. I am challenging this Committee to recognise that the individual layperson knows best, if given the appropriate information in an understandable format.

Q81 Stephen Metcalfe: On that basis, is there anything we are screening for at the moment that if you applied your new criteria, or applied different criteria, we would stop screening for?

Can we learn from the experience of other countries?

Professor Baum: It is somewhat ironic that one wealthy country, Switzerland, has learned from the experience of other countries! The Swiss health board has just advocated closing down their breast cancer screening programme based on our experience. I think that is a bit radical because it might throw the baby out with the bathwater. We have a fantastic infrastructure. It would be tragic if we lost the expert pathologists and radiologists. I have little doubt that we could use that infrastructure to better effect.

I hope that brief and redacted extract gives a flavour of the free and easy give and take of the select committee. In addition they were very generous with their time. I left feeling that no stone was left unturned and that the members enjoyed a clear view of the creepy crawlies that wriggle below the surface gloss of screening or as I would put it, disease-mongering amongst the worried well. I have little doubt that the committee’s report will accurately reflect my opinions and those of others such as the feisty Dr Margaret McCartney who followed me into the hot seat. But then the politics will start all over, and the ugly face of parliament will show itself again.

Michael Baum
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References
Number of articles have appeared in the popular press and online suggesting that sugar is now the demon, and we can forget about fat and saturated fat (e.g., a recent Times article). Not so. We have to consider that both fat (and the relative amounts of saturated and unsaturated fat) and sugar are hazardous in excess.

The message that an excessive intake of fat, and especially saturated fat, is a cause of elevated serum cholesterol and hence an increased risk of atherosclerosis and coronary heart disease, is well established. The consensus is that fat should comprise no more than 30% of our total energy intake (compared with a western average of 40%); and only one third of that fat should be saturated fat (the western diet contains nearly twice that amount). Mono-unsaturated fats should provide 12% of our energy and polyunsaturated fats 6%.

By contrast, recommendations for reducing sugar intake (the western diet contains nearly twice that amount). Dietary fat enters the bloodstream from the lymphatic system in chylomicrons—large lipid-rich lipoproteins that are assembled in the intestinal mucosa. Tissues around the body take up such fatty acids as they require from chylomicrons, leaving lipid-depleted remnants that are cleared by the liver. The uptake of chylomicron remnants is by the same receptor as that for LDL, so chylomicron remnants and LDL compete with each other for clearance by the liver. Like LDL, chylomicron remnants can also be taken up by macrophages, and hence contribute directly to the development of atherosclerosis.

We can provide the biological mechanism to explain this. Mono- and polyunsaturated fatty acids are good substrates for the formation of cholesterol esters in the liver, while saturated fatty acids are not. The result of a high intake of saturated fat is to reduce the esterification of cholesterol, leading to an increase in free cholesterol. In response to increased free cholesterol in the liver, there is reduced synthesis of the receptors for uptake of low density lipoprotein (LDL) into the liver, because the liver does not require to take up additional cholesterol from LDL. Because of this the serum concentration of LDL rises. The longer LDL remains in the bloodstream, the more likely it is to be taken up by macrophages, which burrow under the lining of blood vessels, and are killed by the cholesterol they have liberated by hydrolysis of the cholesterol esters that they have engulfed from LDL. The dead macrophages lay down plaques of cholesterol-rich lipid under the blood vessel walls—the process of atherosclerosis that will lead to occlusion of blood vessels and coronary heart disease.

Not all saturated fatty acids are equally bad. Myristic and palmitic acids (14 and 16 carbons respectively) are especially damaging, since they also downregulate the synthesis of LDL receptors in the liver. On the other hand stearic acid (18 carbons) has little effect, since it is rapidly desaturated to oleic acid, which is a good substrate for cholesterol esterification.

We can also explain the adverse effects of a high fat diet, regardless of the degree of saturation or unsaturation. Dietary fat enters the bloodstream from the lymphatic system in chylomicrons—large lipid-rich lipoproteins that are assembled in the intestinal mucosa. Tissues around the body take up such fatty acids as they require from chylomicrons, leaving lipid-depleted remnants that are cleared by the liver. The uptake of chylomicron remnants is by the same receptor as that for LDL, so chylomicron remnants and LDL compete with each other for clearance by the liver. Like LDL, chylomicron remnants can also be taken up by macrophages, and hence contribute directly to the development of atherosclerosis.

Unfortunately, the debate between protagonists of excessive dietary fat or sugar as factors in the development of atherosclerosis became unscientific, with people on each side taking the position ‘I am correct and therefore you are wrong’.

We can provide the biological mechanism to explain this. Mono- and polyunsaturated fatty acids are good substrates for the formation of cholesterol esters in the liver, while saturated fatty acids are not. The result of a high intake of saturated fat is to reduce the esterification of cholesterol, leading to an increase in free cholesterol. In response to increased free cholesterol in the liver, there is reduced synthesis of the receptors for uptake of low density lipoprotein (LDL) into the liver, because the liver does not require to take up additional cholesterol from LDL. Because of this the serum concentration of LDL rises. The longer LDL remains in the bloodstream, the more likely it is to be taken up by macrophages, which burrow under the lining of blood vessels, and are killed by the cholesterol they have liberated by hydrolysis of the cholesterol esters that they have engulfed from LDL. The dead macrophages lay down plaques of cholesterol-rich lipid under the blood vessel walls—the process of atherosclerosis that will lead to occlusion of blood vessels and coronary heart disease.

Not all saturated fatty acids are equally bad. Myristic and palmitic acids (14 and 16 carbons respectively) are especially dam
suggested a link between consumption of high-fructose corn syrups and obesity. High fructose corn syrup is manufactured from corn starch by hydrolysis to yield glucose, followed by isomerisation of much of the glucose to fructose. The resultant syrup is sweeter, on a dry weight basis, than sugar, cheaper, and easier to incorporate into manufactured foods and drinks. We can provide a biological mechanism for an adverse effect of fructose consumption. The metabolism of glucose is regulated mainly by the need for energy, and after a meal much of the glucose arising from foods is used for energy-yielding metabolism or synthesis of the storage carbohydrate glycogen in liver and muscle. Some, in excess of immediate requirements or for glycogen synthesis, is used to synthesise fat, either in adipose tissue immediately, or in liver, whence it is exported in very low density lipoprotein, mainly for storage in adipose tissue. By contrast, fructose enters the main pathway of carbohydrate metabolism after the regulatory step, and its metabolism is not controlled by the need for energy. This leads to formation of excessive amounts of the intermediate acetyl CoA in the liver, which can only be used for fat synthesis. A high intake of fructose is therefore an important factor in synthesis of fat, which is exported from the liver in VLDL, so contributing to high circulating levels of LDL, and hence to the development of atherosclerosis.

"at the end of the last century a number of reports suggested a link between consumption of high-fructose corn syrups and obesity"

The glycaemic index of a dietary carbohydrate is the extent to which it raises the blood concentration of glucose, ranging from 0 for undigested carbohydrates to 1 for glucose and completely digested carbohydrates. Ordinary table sugar is sucrose, a disaccharide of glucose and fructose. Although it is technically correct to describe sucrose as having a low glycaemic index (0.5), this is misleading in terms its possible health effects, since the fructose will, as described above, be used mainly for synthesis of fat which is exported from the liver in VLDL, so contributing to high circulating levels of LDL, and hence to the development of atherosclerosis.

It is true that obesity in the UK continues to increase, despite a modest reduction in average fat intake over the last decade. However, the take home message is that both fat (and especially saturated fat) and sugar are important factors in the aetiology of atherosclerosis and CHD. Both can be regarded as demons. If you are concerned about overweight and obesity, then the simple answer is that too much food, be it fat (saturated or unsaturated), carbohydrate (starches or sugars), or protein, is the problem.

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THE STATISTICAL ARGUMENT AGAINST ALTERNATIVE MEDICINE: WHY IT “CANNOT BE CONSIDERED EVIDENCE-BASED”

MOST OF THE underlying assumptions of alternative medicine (AM) lack plausibility. Whenever this is the case, according to the argument put forward by an international team of researchers in a recent paper, there are difficulties involved in obtaining a valid statistical significance in clinical studies.

Using a mostly statistical approach, they argue that, since the prior probability of a research hypothesis is directly related to its scientific plausibility, the commonly used frequentist statistics, which do not account for this probability, are unsuitable for studies exploring matters in various degree disconnected from science. Any statistical significance obtained in this field should be considered with great caution and may be better applied to more plausible hypotheses (like placebo effect) than the specific efficacy of the intervention.

The researchers conclude that, “since achieving meaningful statistical significance is an essential step in the validation of medical interventions, AM practices, producing only outcomes inherently resistant to statistical validation, appear not to belong to modern evidence-based medicine.” To emphasize their arguments, the researchers make the following additional points:

- It is often forgotten that frequentist statistics, commonly used in clinical trials, provides only indirect evidence in support of the hypothesis examined.
- The p-value inherently tends to exaggerate the support for the hypothesis tested, especially if the scientific plausibility of the hypothesis is low.
- When the rationale for a clinical intervention is disconnected from the basic principles of science, as in case of complementary alternative medicines, any positive result obtained in clinical studies is more reasonably ascribable to hypotheses (generally to placebo effect) other than the hypothesis on trial, which commonly is the specific efficacy of the intervention.
- Since meaningful statistical significance as a rule is an essential step to validation of a medical intervention, complementary alternative medicine cannot be considered evidence-based.

Further explanations can be found in the discussion of the article where the authors argue that the quality of the hypothesis tested should be consistent with sound logic and science and therefore have a reasonable prior probability of being correct. As a rule of thumb, assuming a “neutral” attitude towards the null hypothesis (odds = 1:1), a p-value of 0.01 or, better, 0.001 should suffice to give a satisfactory posterior probability of 0.035 and 0.005 respectively.

In the area of AM, hypotheses often are entirely inconsistent with logic and frequently fly in the face of science. Four examples can demonstrate this instantly and sufficiently. I think:

- Homeopathic remedies which contain not a single ‘active’ molecule are not likely to generate biological effects.
- Healing ‘energy’ of Reiki masters has no basis in science.
- Meridians of acupuncture are pure imagination.
- Chiropractic subluxation have never been shown to exist.

Such arguments are by no means new; they have been voiced over and over again. Essentially, they amount to the old adage: if you claim that you have a cat in your garden, a simple picture may suffice. If you claim there is a unicorn in your garden, you need something more convincing. An extraordinary claim requires an extraordinary proof! Put into the context of the current discussion about AM, this means that the usual level of clinical evidence is likely to be very misleading as long as it totally neglects the biological plausibility of the prior hypothesis.

Proponents of AM do not like to hear such arguments. They usually insist on what we might call a ‘level playing field’ and fail to see why their assumptions require not only a higher level of evidence but also a reasonable scientific hypothesis. They forget that the playing field is not even to start with; to understand the situation better, they should read this excellent article. Perhaps its elegant statistical approach will convince them—but I would not hold my breath.

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Reference

This article was written by Professor Ernst for his blog http://edzardernst.com/ and appears here with his kind permission

Skin care advice makes uncomfortable reading

A HealthWatch Committee member sent some text from the patient information leaflet for Diprobase Cream MSD:

“What Diprobase is and what it is used for: In adults and children, Diprobase Cream is used to treat red, inflamed, damaged, dry or chapped skin and to protect raw skin areas.

“Possible side effects: Skin reactions including itching, rash, redness, peeling, burning, pain, dryness and skin inflammation (dermatitis) have been reported with product use.”

A case of being cruel to be kind?”