Better research for better healthcare

The ill-fated TGN1412 phase I study and Prince Charles versus the medical establishment over complementary therapies recently pushed evidence-based medicine and clinical trials into prominence. For a society with poor vocabulary about probability, risk and uncertainty, and which increasingly blurs boundaries between well and ill, moving the debates forward, and in unity, will be tough.

Prince Charles called for orthodox medicine to learn from alternative, telling the World Health Assembly in Geneva 'The proper mix of proven complementary, traditional and modern remedies, which emphasizes the active participation of the patient, can help to create a powerful healing force in the world'. Which begs the question 'What's the proof?'. In parallel, 13 eminent doctors wrote to acute and primary care trusts urging them to review practices with regard to 'ways in which unproven or disproved treatments are being encouraged for general use in the NHS'.[1]

About half of all general practitioners refer patients to alternative practitioners, and should stop if it is pointless. As clinical scientist Leslie Rose said, the letter was to 'instill equal vigour in gathering evidence for every treatment prescribed to NHS patients', adding that a business plan for refurbishing the Royal London Homoeopathic Hospital—which cost £20m to set up—put no emphasis on evidence. £20m can buy a lot of what works, and such support begs questions about government consistency in calling for hard evidence for healthcare.

The hospital's Dr Peter Fisher described the letter as an attempt to introduce 'medical apartheid' into the National Health Service, and Terry Cullen, of the British Complementary Medicine Association, said: 'There is so much anecdotal evidence that thousands of people gain benefit from using complementary medicines. We shouldn't dismiss that'.

He is right: which is where a major problem arises—confusing treating illness with 'gaining benefit', and indeed anecdote with evidence. The World Health Organization defines health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'.[2] But the NHS has enough to do without being charged—in both senses—with creating this nirvana. Hoards of sensible, bright people swear by various blends of snake oil for multiple malaises, from back pain to itchy skin to mild melancholy. And maybe it is more powerful. But we need hard evidence that we *can* cure cancer, bypass a heart or silence schizophrenic voices with homeopathy, reiki, reflexology or aromatherapy. That is not to say they are not useful adjuncts to conventional treatment, or, more importantly, that conventional care equals medicines: the evidence base for talking treatments in some mental illness is excellent.[3] But when a hard-pressed NHS has to look after the really unwell, it has got no moral or practical choice but to start by offering what works, and probably to stop there before the money runs out.

Among the very real inherent difficulties in evidence-based medicine is being able to integrate what is best for the individual with what it says in the less personal book of evidence. This takes skill, care and that rare commodity, time: a good clinician will keep one hand on their evidence-based medicine touchstone, while recognizing that what works for him may well not work for me, and may also throw unscientific, non-evidence-based human kindness into the mix, if they can find a moment. A tough but possible call.[4] More prosaically, even Homer nods: busy clinicians cannot always be experts in everything, while, in parallel, patients may need to acknowledge that health as defined by the WHO is not the job of the NHS.

An invaluable recent addition to understanding these topics is a book for non-professional readers written by a medical journalist, a breast cancer patient and a medical researcher. *Testing Treatments: Better Research For Better Healthcare*[5] asks about how we know whether a drug or treatment really works, about trial bias, and whether research is really focused on patient benefit.

The book explains why trials are essential to embedding healthcare in evidence. Its 'blueprint', distillable into honesty about uncertainty, integrity of industry and more accessible information for all about the state of play, is in part set out in an article by one of its co-authors, Sir Iain Chalmers, former Director of the first Cochrane Centre.[6] He is a founder of the James Lind Alliance (Lind was the naval surgeon who carried out a controlled trial of scurvy treatments in 1747),[7,8] which is promoting partnerships between patients and professionals to identify important uncertainties about treatments. Chalmers is passionate about the importance of clinical trials, and determined that priorities be influenced by the imperatives of patients and clinicians, as well as academics and industry. He is also working to get the trials concept embedded in the public consciousness through a 'testing treatments card'. Like an organ donor card, it would state that the holder wishes to be entered into registered, necessary and, ultimately, well-disseminated trials.

It will be interesting to see what emerges, in parallel with the UK Clinical Research Collaboration's work to push clinical trials up the agendas of public awareness and professional feasibility. As long as the curious and potentially dangerous paradox pertains—that it is easier to give a nonevidence-based unlicensed treatment to all your patients than to half of them, because setting up a

proper trial can be a bureaucratic nightmare, or because you cannot recruit patients as they do not understand the score—something must be wrong.

Competing interests The author will not gain personally from publication of this article, and these views do not necessarily reflect those of the Association of Medical Research Charities.

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Gym users and abuse of prescription drugs

Anabolic steroids are synthetic derivatives of naturally occurring testosterone. According to surveys and media reports, androgenic anabolic steroid use is widespread.[1] In 1991, data from the National Household Survey on Drug Abuse indicated that there were more than one million users in the USA.[2] Steroids became controlled drugs in America in 1990 and in the UK in 1996, but the most recent data suggest that their use has increased.[3,4]

Current estimates indicate that there are as many as three million 'steroid' users in the USA and that 2.7%–2.9% of young American adults have taken them at least once in their lives.[5] Surveys in the American field indicate that use among community weight trainers attending gyms and health clubs is 15%–30%.[4] In the UK, the majority of use was by non-competitive recreational bodybuilders or non-athletes, who use these drugs for cosmetic purposes.[1]

Self-image in obesity, as a consequence of media attention focusing on clinical and public health implications, leads us to comment on a number of possible explanations for the progressive increases observed. The prevalence of abuse of certain prescription medicines amongst health-club attendees has dramatically increased in the UK. The non-therapeutic use of such medicines was previously considered to be restricted to the professional athlete or recreational bodybuilder. As a consequence of the internet revolution, steroid abuse is becoming challenged by the more expensive designer drugs, particularly growth hormone.

The first nation-wide survey for steroid abuse in the UK surveyed 21 gyms throughout Britain, and found that 8% of respondents admitted having taken them at some time: 5% of these were current users; 9.1% were men; and 2.3% were women.[6] A survey of 100 steroid abusing athletes conducted in three South Wales counties,[7] reported high rates of polypharmacy (80%). In addition to an increase in abuse, 20% reported needle sharing utilizing hazardous injection techniques, which included injection site pain, and the reusing of needles.[8] Steroid abuse has continued, despite the advertising campaigns by successive governments, highlighting the risks of contracting serious diseases such as HIV, hepatitis B and C.

Bodybuilders have been described as suffering from an altered perception of body image, leading to psychopathology.[9] Bulimia nervosa is an eating disorder characterized by eating binges, vomiting, laxative and/or diuretic abuse and prolonged fasting. Some patients with anorexia nervosa also manifest bulimia. There has been a link established between bulimia nervosa, anorexia nervosa and bodybuilding, related to perception of body image. Unrealistic, muscular male, and slim female body ideals, put individuals at risk for negative body images, resulting in low esteem, unhealthy eating and exercise habits. Some individuals resort to drug-taking to counteract their altered body images.

Anorectics, have been publicly on trial in the USA and surreptitiously on trial in the UK, for some time now. The pharmaceutical manufacturing giants must demonstrate that a drug's benefit outweigh its risks. Expenditures by the pharmaceutical industry for direct-to-consumer advertising have increased dramatically from $1.8 billion in 1999, to $4.2 billion in 2004.[10] What are the chances of the medical profession adhering to its maxim 'first do no harm', when the source of the problem appears to have no degree of accountability?

In 2005, in male and female health club attendees,[3] we observed significant increases in the use of the following drugs: diuretics (10%), thyroxine (10%), insulin (14%),

clenbuterol (21%), tamoxifen (22%), human chorionic gonadotrophin (11%), growth hormone (24%) and ephedrine (44%). The study indicated that steroids were still the most abused drug. It would seem that both sexes are at risk, with 7% of users being female. Clenbuterol, ephedrine and thyroxine, abused by bodybuilders as a training stimulant and to increase metabolic rate and induce lipolysis, were associated with palpitations and caused extrasystoles, during functional exercise electrocardiography. Their use had increased by 3%, 2% and 6%, respectively. Insulin, abused by bodybuilders to increase total body mass, had increased by 14%. This accounted for several individuals suffering from hypoglycaemia in bodybuilding competitions, resulting in emergency rehabilitation with glucose drinks. One such subject confessed to taking 70 international units of insulin, under the presupposition that he was taking 7 IU, on two separate occasions, 1 week apart, and suffered the consequences.

Tamoxifen, abused by bodybuilders to prevent gynaecomastia had increased by 10%. Human chorionic gonadotrophin, abused by bodybuilders to stimulate the testes, when withdrawing from their exogenous androgens, was the only drug to have decreased and had diminished by 4%. Diuretics, abused by bodybuilders to counteract the adverse water retention of both steroids and growth hormone, had increased by 6% and had accounted for several bodybuilders suffering severe muscle cramps and collapsing on stage in competitions. Growth hormone, abused by bodybuilders to induce lipolysis and in the belief that it enhances muscle mass and strength, had increased by 18%: it accounted for less severe side effects, such as muscle weakness, carpal tunnel syndrome, water retention and headaches.

The results of our survey corroborate the research undertaken in the USA, which demonstrated several trends in the non-medical use of androgenic anabolic steroids. The recent results of this American survey[4] reveal several trends in the non-medical use of steroids. Nearly four out of five users are non-athletes who take these drugs with the sole intention of improving physical appearance. Steroid users are taking larger doses than previously recorded, with more than half the respondents using a weekly dose in excess of 1000 mg. Close to 100% of steroid users surveyed admitted to self-administering by intramuscular injection, with approximately 1 in 10 users reporting hazardous injection techniques. An 89% majority of users obtain drugs from aberrant sources, with more than 50% admitting to the use of drugs manufactured in back-street laboratories. Polypharmacy is practised by more than 95% of steroid users surveyed. One in four users takes growth hormone and insulin, suggesting that the use of adjuvant anabolic agents is rising. Nearly 100% of steroid users experience subjective side effects suggesting that concern over health risks does not influence the patterns of drug use.

Awareness of the psychological reasons for use is the first step in an attempt to providing the counselling and then appropriate medical treatment required.

Competing interests None declared.

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