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Editorial: Fibre and prevention of chronic diseases (*BMJ* 2011;343:d6938)
Research: Dietary fibre, whole grains, and risk of colorectal cancer (*BMJ* 2011;343:d6617)

Eat more fibre

The likely benefits include a lower risk of cardiovascular disease

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One of my strongest memories from medical school is the image of two collections of stool projected in a guest lecture by Denis Burkitt. One, the stool of an African schoolboy, was large and moist; the other, that of an English schoolboy, was small and dry. Dr Burkitt, who was widely recognised for his work describing a unique cancer of the jaw in African children, went on to argue that diet, particularly one high in dietary fibre, could prevent many of the diseases common in Western countries.

In the years since, dozens of studies have investigated the association between dietary fibre and chronic disease. The linked paper by Threapleton and colleagues is an important addition to this literature.[1]

The investigators performed a state of the art meta-analysis of 22 cohort studies that related intake of dietary fibre with coronary heart disease and cardiovascular disease. Consistent with most other studies, the meta-analysis showed a consistent inverse association between intake of dietary fibre and first coronary heart disease and cardiovascular disease events. For both outcomes, every 7 g per day intake of total dietary fibre was associated with a significant 9% lower relative risk of first events. The study also generated dose-response curves, rather than simply comparing high intake and low intake groups.

The authors also analysed the impact of fibre subtypes and fibre from specific food sources. Here, the number of studies was smaller and the confidence intervals wider. In the analysis of fibre subtype, only insoluble fibre was significantly associated with reduced risk of coronary heart disease and cardiovascular disease. A trend was seen between greater intakes of soluble fibre and lower risk, but the dose-response is weaker and the results are not significant.

As the authors acknowledge, this careful meta-analysis is limited by the quality of the included studies. For example, most of the data on dietary intake were obtained by food frequency questionnaires, which are better at describing dietary patterns than individual nutrient intakes. Even more important is the potential for confounding owing to the association between high intake of dietary fibre and other healthy nutritional factors and healthy behaviours. Ultimately, randomised clinical trials will be needed to confirm the link between dietary fibre and cardiovascular disease.

Despite these limitations, clinicians should enthusiastically and skilfully recommend that patients consume more dietary fibre. Although the association between increased dietary fibre and reduced risk of colon cancer remains controversial,[2] increased dietary fibre has other health benefits. These include a reduction in lipids and blood sugar, less constipation and diverticular disease, and increased satiety. Some studies show a reduction in total mortality with increased intake of dietary fibre.[3] Nutritional guidelines recommend that men should consume 30-38 g per day and women 21-25 g per day.[4] Estimates in Western countries suggest that the average dietary intake is about half of the recommended amounts.[5]

Dietary recommendations should include a mix of soluble and insoluble fibre and fibre from multiple food sources. Good sources of dietary fibre include whole grains, fruits, vegetable, legumes, nuts, and seeds. Examples of soluble fibre include oats, nuts, seeds, legumes, and most fruits. Insoluble fibres are found in whole wheat, wheat bran, brown rice, other whole grains, and most vegetables. As Threapleton and colleagues illustrate, 7 g of additional total fibre can be easily provided with one portion of whole grains and one portion of legumes, or from two to four servings of fruits and vegetables.

All of a piece

Recommendations to eat more fibre and more high fibre foods are consistent with other nutritional recommendations, including advice to eat less sucrose and high fructose corn syrup, fewer refined carbohydrates, less *trans*-fat and saturated fat, and less meat. Clinical experience suggests that many patients will respond better to dietary counselling that recommends eating more of certain foods, rather than the constant focus on eating less.

Persuading patients to eat whole grains is particularly challenging. Whole grains include barley, bulgur, millet, quinoa, brown rice, rye, oats, and whole wheat. Guidelines suggest that at least half of the daily grain input should be from whole grains. Current food labelling does not make it easy for consumers to identify which foods are whole grains, especially when consuming baked goods and cereals. One strategy is to identify food products with whole grain listed as the first ingredient. Another strategy is to teach patients to look for the ratio of grams of carbohydrates to grams of dietary fibre. Breads with ratios of less than 10:1 and cereals with ratios of 5:1 are consistent with a higher fibre product.

Persuading patients to eat whole grains—barley, bulgur, millet, quinoa, brown rice, rye, oats—is particularly challenging

Fruits and vegetables also vary in their fibre content and patients can be taught to identify the higher fibre foods that meet their food preferences. Patients should also be encouraged to eat whole fruit, rather than drinking it, because most fruit juices contain little fibre. Other practical recommendations include increasing fibre gradually and drinking adequate amounts of water.

In conclusion, the evidence for recommending higher intakes of dietary fibre comes from several lines of imperfect evidence, mostly observational studies, and expert opinion. By systematically analysing existing observational studies, Threapleton and colleagues' meta-analysis increases our confidence in the benefit—in terms of reduced cardiovascular disease and coronary heart disease events, of higher intakes of dietary fibre. Moreover, the increase in fibre needed to achieve such benefit is modest and a dose-response can be estimated. Given the alignment with other nutritional recommendations, it makes sense to increase our efforts to counsel patients and advise the public on increasing the intake of dietary fibre. The recommendation to consume diets with adequate amounts of dietary fibre may turn out to be the most important nutritional recommendation of all.

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RESEARCH, p 11

Greenaway's is the sixth report in as many years in the wake of the failings in Modernising Medical Careers . . . it deserves support before a seventh report concludes broadly the same

Postgraduate medical education and training in the UK

Time for action

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As David Greenaway's report on the future shape of postgraduate medical education and training makes clear,[1] this is the sixth report in the United Kingdom in as many years in the wake of the failings in Modernising Medical Careers.[2] All reports start from the premise that changes to the current system will be necessary to meet evolving healthcare needs. Our reluctance to adopt changes that have a broad consensus reflects at worst vested self interest in the status quo and at best an innate professional conservatism and a desire to sustain those attributes of a doctor that have served medicine well in the past.

However, reluctance to change also reflects the inherent uncertainty in predicting the future and the length of time before the outcome of profound change is evident. The fundamental problem is how we can provide rigorous, quality assured education that equips doctors with the desired range of capabilities to meet current healthcare needs without having to redesign the system every few years. The report makes it clear that "broad based beginnings" and flexibility are key to avoiding the snakes and ladders of returning to basic training if technological advances or other developments limit the value of a doctor's hard earned specialist expertise.

Education and training—never complete

Given the rapid shifts in our society's demography and the likelihood of greater expectations of healthcare among older people in the future, most programmes should have an increased focus on elderly care medicine and the complexity of comorbidity, as suggested. The proposed move from CCT (certificate of completion of training) to CST (certificate of specialty training) is key in that it emphasises that education and training are never "complete." The proposal to introduce credentialing to define adjunctive specialist capability in specific areas of clinical practice after obtaining the CST provides a practical way to adapt skills to prevailing needs. It also provides a means for clinician scientists to balance clinical, educational, and research demands while still enabling them to exhibit specialist expertise, albeit within a narrower scope of practice.

Tomorrow's ward round

Whereas the impact of demographic shifts looms large in the report's analysis, less emphasis is placed on technological developments that also drive change. For example, genomics with its potential to herald a new era of "precision medicine,"[3] and the democratisation of medical knowledge, self care, and self referral supported by digital means that will transform the transactional relationship between doctor and patient.

The recommended structural reforms also attempt to tackle another concern—that, compared with many other developed healthcare systems, the time taken to achieve independent specialist status is too long. Advancement based on evidence of competency rather than on time served may help in this regard. So too may the proposal for doctors to become fully registered as soon as they graduate from medical school, if such a move could be achieved without falling foul of European regulations on programme length. Further shortening could be achieved if the foundation programme was reduced to one year, the second foundation year being incorporated into the first year of general specialist practice. Such developments would encourage medical schools to focus on preparedness for practice and ensure that final preparations are not put at risk by displacement to another deanery as can happen now.

Full registration at graduation also provides the opportunity to lift the cap on overseas medical student numbers because overseas graduates could then return to their country of origin with a fully registered qualification without having undergone foundation training. In the likely event that there are too few UK/European Union graduates to meet demand in the future, a ready supply of UK trained graduates—familiar with the culture and practice of the NHS—will be available. This would be a more ethical solution than recruiting from overseas graduates who have had no training in the UK.

Many problems remain to be resolved if the proposed system is to work. In addition to the inherent tensions between service and training, the training environment needs attention. Shorter lengths of stay in hospital, limited outpatient follow-up, and shift working with inconsistent teams threaten "on the job" learning. As the report rightly asserts, only clinical environments that provide high quality education and training should be approved for postgraduate medical training.

Broader based doctors, better equipped for community and intermediary care roles, can play such a part only if other NHS policies and structures are aligned with this intent. For example, the hospital trust system is currently incentivised to keep patients coming to hospital, rather than encouraging the stated policy of more community based care.

The report contains an unfortunate reference to doctors who are "out of training." Whether on—or not on—a path to CCT, no doctor should be regarded as out of training if he or she is to pursue reflective practice and keep up to date.

The expectations of those entering or considering entering the profession will need to be managed. Proposals to introduce adjunctive training in, for example, management, leadership, and education during general specialist training could help inculcate a culture of adaptability.

Care in transition however should not be interpreted as an excuse for resistance to change. The broad principles espoused are the right ones, and, as the review makes clear, we should rapidly move to defining which organisations are best placed to implement the changes. The Greenaway report deserves support before a seventh report concludes broadly the same.

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- Research: Effect of longer term modest salt reduction on blood pressure (*BMJ* 2013;346:f1325)
- Research: Effect of lower sodium intake on health (*BMJ* 2013;346:f1326)

Sodium in drugs and hypertension

A threat to cardiovascular health that deserves serious attention

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Experimental, clinical, and epidemiological studies consistently indicate that excessive salt intake encourages the development of high blood pressure.[1] Because hypertension accounts for 62% of strokes and 49% of heart attacks worldwide,[2] its prevention and treatment should substantially reduce the number of these events. Recent joint guidelines from the European Society of Hypertension and European Society of Cardiology recommend reducing salt intake to 5-6 g/day as a class 1, grade A lifestyle modification.[3] Most commentators agree that any successful salt reduction policy must tackle the problem in adults and children. The high salt content of commercially marketed foods is the main reason for excessive salt intake, making it impractical to reduce salt intake simply as an individual choice. Thus, the World Health Organization promotes whole population strategies, such as characterisation of the national diet and negotiations with the food industry to reduce salt content.[2]

The linked paper by George and colleagues should focus the attention of authorities and health operators on the importance of medical preparations, which so far have been largely disregarded, as another source of sodium intake.[4] The argument is not new—it has been targeted by various health institutions and was the object of a recent pilot clinical trial.[5]

The authors used the Clinical Practice Research Datalink (CPRD) to perform a nested case-control study of the impact of sodium containing drug formulations on the incidence of cardiovascular events. The study population consisted of adult primary care patients from the United Kingdom who were prescribed at least two sodium containing formulations or matched standard formulations of the same drug between January 1987 and December 2010. The study followed up 1 300 000 patients for more than seven years, during which time more than 61 000 cardiovascular events were recorded. For each case a control was matched for age, sex, and clinical practice extraction.

The study found that for the primary composite endpoint—incident non-fatal myocardial infarction, stroke, or vascular death—cases were significantly more likely than controls to have been taking a sodium containing drug. A dose-response association was also seen—the more sodium that was cumulatively ingested through drugs, the greater the risk of an event. This result was driven by the fact that patients taking a sodium containing formulation had a higher probability of stroke and greater risk of becoming hypertensive compared with those taking the no sodium formulation of the same drugs. All cause mortality was also higher in people taking sodium-rich drug preparations, but there was no evidence of an effect on the risk of myocardial infarction or heart failure.

The authors used multivariate adjustments to take account of several potential confounders, but some potentially relevant factors, such as nutritional habits and physical activity, were not adjusted for. Whether any specific drug category was associated with worse outcomes was not defined. Despite these limitations, the authors' suggestion that doctors should prescribe sodium containing formulations with caution and not to patients with hypertension unless there are compelling reasons to do so, seems reasonable.

The group of sodium containing drugs is large and includes effervescent and soluble analgesics, cold and flu preparations, indigestion and anti-diarrhoeal preparations, cystitis preparations, laxatives, bowel cleansing solutions, and, paradoxically, diuretics and antihypertensives. Drugs are salified because the salt forms of active substances are usually more soluble, which increases their bioavailability. Generally, sodium salts of weak organic acids and hydrochloride salts of weak organic bases dissolve much faster than the respective acids or bases. The result is a more rapid diffusion of the drug to the absorption sites. Potassium salts are generally as soluble as sodium salts, and sodium is probably used instead of potassium because it is cheaper.

Previous concerns

Concern about the role of effervescent, dispersible, and soluble drugs in increasing sodium intake has been raised several times in the past. In 2004 the US Food and Drug Administration issued new rules that required over the counter drugs with levels of sodium that were potentially harmful to people with certain underlying medical conditions to be labelled with the sodium content and with a warning.[6] These rules were aimed at alerting people on sodium restricted diets to consult their doctors before using products containing more than 140 mg of sodium as the maximum daily dose. George and colleagues found that, among people taking sodium containing drug formulations, the median amount of sodium ingested daily from these drugs was almost 18 times higher than that (106 mmol or 2.5 g/day). It was also higher than the maximum dietary sodium intake recommended by WHO (2 g/day). The European Commission has ruled that the sodium content of oral and parenteral drugs containing 1 mmol or more per dose must be included on the packaging and in the package leaflet.[7] This requirement applies to all drugs currently licensed for use in the UK.

Despite these measures, none of the guidelines delivered in the past few years in support of reducing salt intake has considered the potential contribution of sodium contained in commonly prescribed and over the counter drugs to sodium intake. According to George and colleagues' findings, it is time to fill this gap and also time for the drug industry to find alternatives to the use of sodium salts in medical preparations. Last, but not least, doctors should pay more attention to the sodium content of drug products and avoid prescribing high sodium preparations to the same patients that they advise to follow sodium restricted diets.

Competing interests: I am an unpaid member of World Action on Salt and Health (WASH), coordinator of the Interdisciplinary Working Group for Reduction of Salt Intake in Italy (GIRCSI), a member of the SINU/INRAN committee for the preparation of the Italian dietary reference intakes, and a former member and treasurer of the executive committee of the Italian Society of Hypertension.

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Future generations may look back at our present tolerance of withheld trial results in the same way that we look back on medieval blood letting

Improving, and auditing, access to clinical trial results

All trials should be registered, with their full methods and results reported

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The House of Commons Public Accounts Committee delivered a remarkable report on 3 January. Its initial remit was the United Kingdom's £424m (€510m; $697m) stockpile of oseltamivir (Tamiflu), but the committee soon broadened out—with evident surprise—into the ongoing problem of clinical trial results being routinely and legally withheld from doctors, researchers, and patients.

This situation has persisted for too long. The first quantitative evidence on publication bias was published in 1986.[1] Iain Chalmers described in 2006 how progress in the 1990s soon deteriorated into broken promises.[2] Recent years have seen extensive denial. The Association of the British Pharmaceutical Industry (ABPI) has claimed that these problems are historic, and that results are now posted on clinicaltrials.gov. The recently defunct Ethical Standards in Health and Life Sciences Group,[3] which most UK medical and academic professional bodies signed up to, falsely claimed that a "robust regulatory framework" ensures access to trial results.[4] US legislation requiring all results to be posted on clinicaltrials.gov within 12 months of completion has been widely ignored,[5] with no enforcement. There has also been covert activity from industry—a leaked memo on its "advocacy" strategy included "mobilising patient groups" to campaign against transparency.[6]

Despite this, we have achieved considerable progress. The AllTrials.net campaign, started 12 months ago, calls for all trials on all uses of all currently prescribed treatments to be registered, with their full methods and results reported.[7] It now has the support of most medical and academic professional bodies as well as the National Institute for Health and Care Excellence (NICE), Medical Research Council, Wellcome, more than 130 patient groups, 60 000 members of the public, and many in industry including GlaxoSmithKline. The Health Research Authority has announced that registration will be a condition of ethics committee approval.[8] The BMA has passed a motion stating that withholding trial results is research misconduct,[9] and the General Medical Council is re-examining its guidance on the matter.

There have also been extensive new proposals for greater transparency from European Union legislators, the European Medicines Agency (EMA),[10] and industry bodies.[11] All, however, share the same loophole—they all propose improved access to information on trials conducted from 2014 onwards. This means that almost all trials relevant to current medical practice would be exempt (including, for example, those on oseltamivir).

We now have an unprecedented opportunity for change, with considerable support from medical and academic professional bodies, policy makers, patient groups, and—importantly—the public. It's time to consider what practical improvements can be made.

Firstly, by whatever means necessary, the methods and results of all previous trials must be accessible to the medical and academic community, which produces the guidelines and systematic reviews that inform patient care. It is commonly assumed that it would be difficult to enforce demands for trial results from diffuse global organisations, but we have never tried simply asking in an organised fashion. For example, the EMA could ask all research organisations and companies with a marketing authorisation for full methods and results of all trials they have conducted, so that these can be posted online, on the first ever register of trials that aspires to be a complete record of all research. If this invitation is declined, we could be told.

Bring on a trials observatory

Secondly, while the current state of secrecy continues, there is much to be done with the most basic research tool in medicine—audit. Industry is quibbling over the precise proportion of trials that go undisclosed. This should not be a matter of debate. We need a trials observatory, covering all trials on all currently used treatments, that matches registry entries and other sources of information on completed trials against sources of results, whether those are in academic papers, clinical study reports, regulatory documents, or online postings. From these data we could derive live dashboards on transparency to drive up best practice, identify the best and worst companies for missing results, the treatments where most information is missing, the best and worst investigators, and more.

This is actionable information. If routine audit shows a particular principal investigator is performing badly, with many unreported results, should ethics committees grant them access to more trial participants? Will patients participate in trials for companies that withhold results? If two treatments have equivalent benefits, but one comes from a company with a track record of transparency and the other from a company that actively undermines the transparency campaign, are those two treatments still equivalent, and which should a cautious clinician prescribe?

One aspect of the committee's report was missed by popular commentators, but it exemplifies the peculiarity of the current situation. Professor Kent Woods, head of the Medicines and Healthcare Products Regulatory Agency (MHRA), told the committee that European regulators had everything on oseltamivir. Evidence from the Cochrane Collaboration shows that this is not true. Cochrane asked the EMA for all the documents it held on oseltamivir, under that agency's contested new transparency policy, and the agency complied—on several trials it held incomplete information on the methods and results, and for many more trials, it held nothing.[12] The Public Accounts Committee expressed concern, and Professor Woods may wish to clarify this matter. But it is odd that there is any uncertainty about what evidence exists, or what the MHRA, EMA, and NICE have seen, on currently prescribed treatments (www.bmj.com/tamiflu).

It is also remarkable that the medical community needs a committee of generalist politicians to reflect these problems back to us. We spend millions on individual trials to exclude bias and often to detect subtle differences between treatments, but we let those biases pour back in unnecessarily when we permit whole trials to be withheld. Future generations may look back at our present tolerance of withheld trial results in the same way that we look back on medieval blood letting.

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