EDITORIALS

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Time to question the NHS diabetes prevention programme

Focus on individual behaviour change is unlikely to stem the epidemic of type 2 diabetes

Eleanor Barry NIHR in-practice fellow
Samantha Roberts DPhil student, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford OX2 6GG, UK
Sarah Finer honorary clinical senior lecturer, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK
Shanti Vijayaraghavan consultant diabetologist, Department of Diabetes, Newham University Hospital, Barts Health NHS Trust, London, UK
Trisha Greenhalgh professor, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford OX2 6GG, UK trish.greenhalgh@phc.ox.ac.uk

Requires multisectoral action

A new Public Health England report on the rising prevalence of type 2 diabetes proposes targeting people with non-diabetic hyperglycaemia (defined as an HbA_{1c} concentration of 42-47 mmol/mol) with behavioural interventions (diet and exercise).[1] Action for this group (10.7% of the adult population) is to be the cornerstone of the NHS Diabetes Prevention Programme, which will be rolled out nationally from 2016.[2]

Such individualised policy is divorced from the multilevel, community-wide, and politically engaged prevention plans recommended by the World Health Organization[3] and Robert Wood Johnson Foundation.[4] In its report on non-communicable disease WHO calls for "multisectoral action that simultaneously addresses different sectors that contribute to the production, distribution and marketing of food, while concurrently shaping an environment that facilitates and promotes adequate levels of physical activity."[3]

Five dubious assumptions

Targeting individual behaviour as a preventive strategy rests on five doubtful assumptions: that it is possible, on the basis of a risk score and blood test, accurately to identify a population subgroup with the highest risk of developing diabetes; that individuals thus targeted will behave like participants in research studies; that behaviour changes will be sustained indefinitely; that clinically important improvements in patient relevant outcomes will follow; and that the programme will be affordable and cost effective.

Risk scores and confirmatory tests of hyperglycaemia are imperfect. Three systematic reviews (not cited in the Public Health England report) were circumspect about the usefulness of diabetes risk scores and warned that a score's external validity may be weak if the population on which it is used differs from the one on which it was developed.[5 7 8]

The risk scores were designed to predict type 2 diabetes, but the Public Health England report seems to conflate this with their ability to detect non-diabetic hyperglycaemia. Using HbA_{1c} to identify non-diabetic hyperglycaemia defines twice as many people as "prediabetic" than does the gold standard but impractical oral glucose tolerance test[10]; it may be inaccurate in some groups.[11-14] Substantial under-diagnosis and overdiagnosis is thus likely, with huge workload implications for both primary care and community services.

Public Health England justifies its proposed policy using a new (non-peer reviewed) meta-analysis of behavioural interventions in diabetes prevention,[15] which extends a previous meta-analysis.[16] The 36 primary studies are described—somewhat curiously—as "pragmatic" and "real world." Yet each was limited to a tightly specified individual intervention delivered as part of a research study; half were randomised trials.[15] All participants met specific inclusion criteria, including willingness to engage and, in most if not all cases, speaking the same language as the researchers. Individuals drawn from an unselected, free living population are unlikely to respond similarly, given their lower health literacy, higher comorbidities, and greater ethnic diversity.[17-19]

The pathogenesis of diabetes incorporates genetic, physiological, psychological, sociological, and wider environmental influences that play out differently for different individuals in different settings.[23] Overlooking this complex reality, Public Health England's meta-analysis sought to identify components of behavioural interventions associated with "success," usually measured by surrogate endpoints. The results were used to build a specification for a complex intervention that would, its architects assumed, be maximally effective across a diverse population.

The NHS Diabetes Prevention Programme expects a 26% reduction in incidence of diabetes and implies that associated morbidity and mortality will fall. Yet the meta-analysis contains no evidence of any sustained reduction in morbidity or mortality relating to diabetes or cardiovascular disease after lifestyle intervention in prediabetes.[15] Rather, it focuses on changes in surrogate endpoints that were statistically but not clinically significant. A newly published evidence synthesis of the effect of lifestyle interventions on overall mortality in prediabetes cites 17 trials that failed to show a significant effect and one that just reached statistical significance.[27]

Astonishingly, given that this lifestyle intervention will become national policy, the Public Health England reports offer no formal estimate of the programme's cost or cost effectiveness. The assumption that it will save money is based on speculation that the intervention will produce "optimal effects whilst keeping costs to a minimum."[15] The proposed payment by results model may create perverse incentives to focus on "compliant" populations rather than those at greatest risk of diabetes, which often experience multiple barriers to achieving the desired outcomes.[29 30]

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The public consultation on England's proposed NHS Diabetes Prevention Programme runs until 18 September 2015 (www.england.nhs.uk/ourwork/qual-clin-lead/action-for-diabetes/diabetes-prevention). We have serious concerns that the programme consists entirely of a top down, highly standardised behavioural intervention offered to a fraction of the population. With an estimated 18.2% of adults in England having abnormal glucose metabolism, investment in population based strategies on healthy food choices and opportunities for physical activity are surely needed, as well as support for individuals.[10 31]

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Research into food and health is fraught with challenges, and powerful vested interests try to influence policy decisions, science, scientists, and practitioners

Dietary fats, health, and inequalities

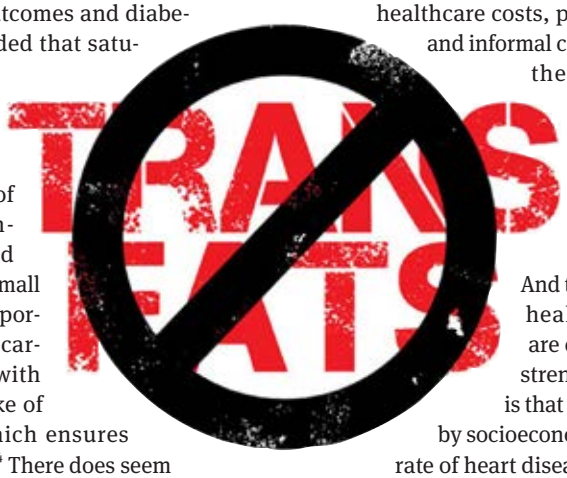
There's nothing good about trans fats; a total ban would be best for public health

J Lennert Veerman senior lecturer, University of Queensland, School of Public Health, Brisbane, QLD 4006, Australia l.veerman@uq.edu.au

The stakes are high in matters of food and health. Everyone is exposed, so everyone is personally affected. Small increases in risk translate to large health impacts at the population level. Research is fraught with challenges, and powerful vested interests try to influence policy decisions, science, scientists, and practitioners.[1]

Two linked papers focusing on dietary fats add to these debates. De Souza and colleagues reviewed the evidence on saturated fats and trans fats.[2] The verdict on the health impact of saturated fats is still open, but industrial trans fats are clearly bad for health. Allen and colleagues translate the evidence against trans fats into tangible effects on population health and health inequalities in England.[3] Here, the debate centres on the best way to phase out industrial trans fats and how much state intervention is justified.

De Souza and colleagues performed a systematic review and meta-analysis of cohort studies that examined the association between saturated fats and trans fats and a range of cardiovascular outcomes and diabetes.[2] They concluded that saturated fats were not associated with any of these outcomes. A recent Cochrane review of randomised controlled trials did find evidence of a small but potentially important reduction in cardiovascular risk with reduction in intake of saturated fat, which ensures continued debate.[4] There does seem to be agreement that it matters what saturated fats are replaced with. Broadly speaking, substitution with refined carbohydrates confers no health benefits, substitution with monounsaturated fats might be a little healthier, and polyunsaturated fats and unrefined carbohydrates (with a low glycaemic index) seem to be the healthiest sources of energy. The story for trans fats, at least the industrially produced varieties, is much clearer. Industrial trans fatty acids are often added to processed foods to improve shelf life and palatability. De Souza and colleagues found that higher intakes are associated with higher all cause mortality, and higher incidence of and mortality from coronary heart disease. This confirms the findings of previous studies.[5] Given the clarity of the evidence that industrial trans fat are unhealthy, the next question is how to reduce consumption.



This is where Allen and colleagues make a valuable contribution. In their paper, they evaluate three policy options to reduce consumption of trans fats in the United Kingdom: mandatory reformulation (complete elimination of trans fat from processed foods); improved food labelling that accelerates voluntary reformulation; and bans in restaurants and takeaway outlets.[3] The authors used a previously developed model to estimate the effects on incidence of and mortality from coronary heart disease. They found that all things considered, all three interventions pay for themselves. The projected reductions in healthcare costs, production losses, and informal care costs outweigh the cost of legislation, compliance monitoring, and food reformulation, even with assumed high costs to industry. And that is on top of the health gains, which are considerable. One strength of their study is that it estimates effects by socioeconomic position. The rate of heart disease and consumption of industrial trans fats are higher in lower socioeconomic groups, and therefore those groups stand to benefit most from measures to remove these fats from the food supply.

In modelling studies it is always possible to quibble about details. For instance, data on consumption of trans fats were not available for all socioeconomic groups, so assumptions and extrapolations had to be made. Information on socioeconomic position was available only at the area level, where there might be some mixing of rich and poor; the social gradient in benefits at the level of individuals is likely to be steeper than this study suggests. The effect estimates for food labelling are based on parallel evidence and expert opinion. By definition, all models are simplifications of reality. Given the clear evidence on the health impact of trans fats and what we know about consumption patterns, rates of heart disease, and related economic costs in England, however, we can safely conclude that these actions to accelerate the removal of industrial trans fat from the food supply are good for health, cost saving, and equitable.

Darkness visible

A total ban was found to be more than twice as effective as relying on voluntary reformulation or improved food labelling. Such policies are not extreme by any means; bans on industrial trans fats are already implemented in Denmark and several other European countries. In the United States, similar regulation is under preparation. Nevertheless it takes some political courage to implement a ban. The losers are clear, and the food industry has considerable lobbying power, while the winners are evident only from the statistics, belong to a group with relatively little political capital, and are probably mostly unaware of the problem. The value of the present study is that it makes these gains visible.

From the perspective of public health values, a ban on industrial trans fats ticks all the boxes[6]: collective action is taken in recognition of a collective responsibility for health for all; the whole population benefits without the need to target any specific individual (and risk blaming the "victim"); it addresses determinants of health and is therefore a form of primary prevention, avoiding new cases of heart disease rather than having to treat them; it requires interdisciplinary collaboration; and, as evidenced by these two papers, it has a solid basis in scientific evidence. This is public health at its best.

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Quality standards issued by NICE require that all patients . . . with unstable bleeding have an endoscopy within two hours of optimal resuscitation

thebmj.com

News: Half of UK hospitals lack essential services for managing acute GI bleeds, inquiry finds (*BMJ* 2015;351:h3488)

Deficiencies in services for acute upper gastrointestinal bleeding

Patients need rapid access to specialist care round the clock

Alan J Lobo honorary professor of gastroenterology, Academic Unit of Gastroenterology, University of Sheffield, Sheffield S10 2TN, UK, and Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK alan.lobo@sth.nhs.uk
Simon M Greenfield chair, clinical services and standards committee , British Society of Gastroenterology, London, UK, and Department of Gastroenterology, Lister Hospital, Stevenage, UK
Ian Forgacs president, Department of Gastroenterology, King's College Hospital, London, UK

Acute upper gastrointestinal bleeding is a common and serious medical emergency. There are an estimated 50 000-70 000 hospital admissions in the United Kingdom a year[1 2] and overall mortality is about 10%.[3] A new report by the National Confidential Enquiry into Patient Outcomes and Death (NCEPOD) identifies continuing difficulties in the provision of services for patients with substantial bleeding,[4] reinforcing earlier findings from national audits[5] and NHS England.[6] The report focuses on patients with severe bleeding who require transfusion of at least four units of blood.

The optimum management of acute upper gastrointestinal bleeding requires a combination of circulatory resuscitation, risk assessment to help predict the need for intervention as well as outcome, administration of blood products, drug treatment, upper gastrointestinal endoscopy with haemostatic endotherapy, interventional radiology, and surgery when necessary.[1] The NCEPOD report highlights deficiencies in each of these areas.

According to national audits, mortality from acute upper gastrointestinal bleeding fell in the UK between 1993-4[7] and 2007[3]; the reduction was attributed, at least in part, to the use—and efficacy—of endoscopic treatments such as injection of adrenaline, thermocoagulation, or application of clips.[3] Quality standards issued by the National Institute for Health and Care Excellence (NICE) require that all patients with acute upper gastrointestinal bleeding have endoscopy within 24 hours and that those with unstable bleeding have an endoscopy within two hours of optimal resuscitation.[8]

Early endoscopy is associated with improved outcomes in terms of rebleeding, need for surgery, length of stay, and cost[9] but its effect on mortality has been harder to demonstrate. It is, however, associated with lower mortality in high risk patients with non-variceal upper gastrointestinal bleeding.[10] In one UK audit, patients admitted to a hospital with a formal out of hours service for upper gastrointestinal bleeding were more likely to have their first endoscopy and receive endoscopic treatment out of hours than those admitted to a hospital without a formal out of hours service.[5]

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Common and serious emergency

In 2013, the British Society of Gastroenterology and NHS England jointly surveyed endoscopy units in all acute hospitals in England to determine their ability to meet the NICE standards on timing of endoscopy. Although 77% of hospitals were able to deliver emergency endoscopy round the clock, only 56% could provide endoscopy to all patients with acute bleeding within 24 hours.[6] The new report finds a comparable pattern, with three quarters of eligible hospitals having out of hours provision. However, only 65% of patients requiring at least four units of blood reviewed by NCEPOD had an endoscopy within 24 hours of admission. Of those with evidence of additional haemodynamic compromise, 20% had not had endoscopy at 24 hours.[4]

Organisational challenge

Insufficient numbers of endoscopists, their competing commitments to acute general medical admissions, poor availability of endoscopy nurses, and lack of executive support were all cited as barriers to providing a 24/7 endoscopy service.[6] Exchange of general medical commitments for a seven day gastroenterology service and development of out of hours endoscopy networks among endoscopists in neighbouring hospitals are potential solutions.[11] The sustainability of a dedicated out of hours emergency service staffed by consultants and the impact of such a service on consultants' elective work need to be considered as well as ensuring that training programmes deliver consultants with appropriate experience.[12]

In the NCEPOD report, 92% of patients under the primary care of a gastroenterologist received "timely" endoscopy. The report's authors call for involvement of a gastroenterologist within one hour of a patient presenting with a major bleed. The model of a dedicated gastrointestinal bleed unit allows coordination of care and has been associated with both high rates of endoscopy within 24 hours (93%) and reduced mortality.[13]

Patients should be considered for radiological interventions—computed tomographic angiography and transarterial embolisation—when therapeutic endoscopy fails to control their bleeding.[1] NCEPOD recommends that patients with an acute gastrointestinal bleed should be admitted or transferred only to hospitals with 24/7 access to on-site endoscopy and surgery, while interventional radiology must be available either on-site or within a formal network. Only 7.8% of patients in the NCEPOD review had a radiological intervention. Appropriate radiology services were available round the clock in just 30% of hospitals. Case reviewers thought that more patients could have benefited from these services, but the report suggests a shortage of at least 200 appropriately trained radiology consultants in the UK.[4]

The requirements for safe management of upper gastrointestinal bleeding have been clearly and repeatedly documented.[1 8] The new report gives a further stimulus to improve these services—and offers an opportunity that must be grasped. Senior clinicians and managers at every hospital in the UK should now examine the report's recommendations together with NICE quality standards and assess what they need to do to ensure a service that will deliver timely effective care to all those with suspected upper gastrointestinal bleeding. Each component of the care pathway should be scrutinised, but in particular the out of hours provision of emergency gastrointestinal endoscopy.

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We believe that the pay-off from a systematic effort to reactivate selected clinical trials will be high and will further justify the original huge investments of time and money

Liberating the data from clinical trials

Liberated trial data can benefit patients, prevent harm, and correct misleading research

David Henry professor, Dalla Lana School of Public Health, Institute for Health Policy Management and Evaluation, University of Toronto, and Senior Scientist, Institute for Clinical Evaluative Sciences, Toronto, ON, Canada
david.henry@ices.on.ca
Tiffany Fitzpatrick meta-data specialist, Ontario Strategy for Patient-Oriented Research (SPOR) Support Unit, Toronto, ON, Canada

Despite the importance of reproducibility in research, clinical trials are rarely subject to independent reanalysis. In a linked paper, Le Noury and colleagues have restored and reanalysed the controversial "study 329," which incorrectly portrayed paroxetine as an effective and acceptably safe treatment for children and adolescents with major depression.[1 2] The accompanying article by Doshi details the missteps of the investigators, staff from the sponsoring drug company, the lead author's home academic institution, and the publication journal.[3] Study 329 is a model example for the movement to restore invisible and abandoned trials (RIAT), which calls on investigators to publish unreported trials and republish and correct misleading reports.[4]

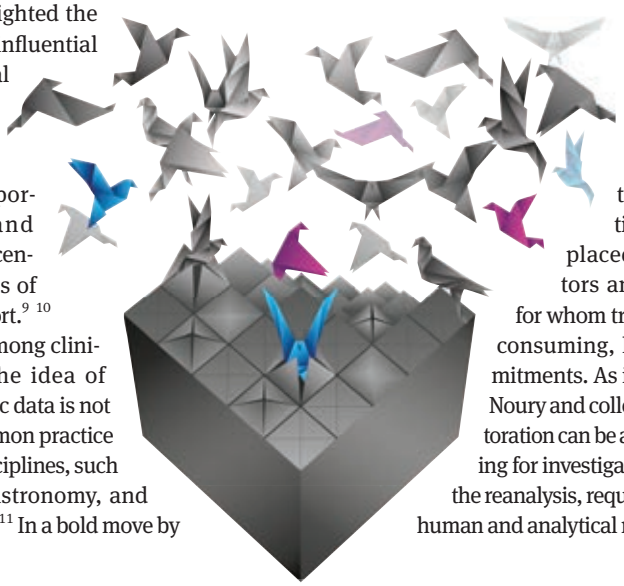
In a recent review, Ebrahim and colleagues identified just 37 published reanalyses of clinical trials.[5] Only five were conducted by investigators not associated with the original report. A third of reanalyses led to interpretations different from those of the original articles. In a recent blog, Ben Goldacre, co-founder of the +AllTrials initiative, which calls for all trials to be registered and published,[6-8] highlighted the example of an influential trial of intestinal "deworming" treatment. Reanalysis uncovered important errors and changed some central conclusions of the original report.[9 10]

While rare among clinical trialists, the idea of sharing scientific data is not new and is common practice within some disciplines, such as genomics, astronomy, and particle physics.[11] In a bold move by the standards of the time, researchers from the landmark Diabetes Control and Complications Trial (DCCT) made their data available to other investigators after they published the results of the original trial. To date, there have been over 220 ancillary studies using DCCT data, several of which have had an impact on the clinical management of diabetes.[12 13] These highlight the substantial added value that can be derived from sharing of trial data.

Groundswell

The move to access original trial data is part of the broadening open data movement in health, which has received support from major research funding agencies in the United States, Canada, the United Kingdom, Australia, and Europe.[11 14] Notably, the National Institutes of Health (NIH), which strongly encourage NIH funded investigators to share their data, provide secure data repositories for both clinical data and biological samples.[15] Recent reports from the Institute of Medicine (US), the Wellcome Trust (UK), and the Council of Canadian Academies argue for, and recommend, best practices to ensure safe sharing of clinical data.[16-18] And of course many journals, such as *The BMJ*, now encourage authors to make datasets available on request.[19]

Data sharing, however, is not without its risks.[18] As Ebrahim and colleagues point out, threats to patient confidentiality, data dredging with a risk of chance findings, and "rogue reanalyses" by investigators with their own agenda must be considered.[5] Data sharing also increases the responsibilities and burdens placed on investigators and institutions, for whom trials can become consuming, long term commitments. As illustrated by Le Noury and colleagues,[1] trial restoration can be a major undertaking for investigators carrying out the reanalysis, requiring substantial human and analytical resources.



Should restoration end with reanalysis, or should we do more? Data storage in repositories will enable independent researchers to repurpose trial data for new research questions—as shown by the successes of the DCCT.[13] If participants' data are stored with the identifying information needed to link to data stored in administrative claims or electronic medical record (EMR) databases, this will allow independent researchers to reactivate some "dormant" trials. Adding extra years of follow-up, via the linked databases, will allow the study of long term outcomes, including those not part of the original protocol.

The use of administrative and EMR data to capture clinical trial outcomes is becoming commonplace. Sometimes this has been part of the original trial protocol.[20-22] Less commonly, data linkage is used subsequently to capture additional years of follow-up.[23 24]

Reactivation of dormant trials will not be without barriers. In the case of older trials, data might have been destroyed, misplaced, exist in paper form only, or lack the variables necessary for linkage. The original trial consent forms might not have included permission to link the data, which will require research ethics boards to consider approval of "post hoc" linkage.[25]

The first step to reactivating dormant trials will be to identify which trials have been conducted and where the data are held. This can be done by searching trial registries and approaching research ethics boards, funding bodies, and investigators.[26] To enable reactivation of important clinical trials we will need to review some policies and procedures. Trial consent processes should routinely request permission to link the data to study long term outcomes. Stored data from participants should always include linkable fields, particularly health insurance numbers. Data management and retention policies should be reviewed to enable preservation of the data needed to enable long term follow-up of important clinical outcomes.

Most clinical trials are extremely expensive, and we believe that the pay-off from a systematic effort to reactivate selected clinical trials will be high and will further justify the original huge investments of time and money.

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