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Science souring on sugar

Accumulating evidence points towards a role for sugar and other refined carbohydrates in the development of overweight

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Sugar—most importantly sucrose (table sugar) and high fructose corn syrup—has long been thought to have adverse health effects, such as contributing to dental caries, overweight, diabetes, and heart disease. A linked feature (doi;10.1136/bmj.e7800) comments on the 40th anniversary of the publication of the popular book—*Pure, White and Deadly*—written by the British physiologist John Yudkin, which claimed that high sugar consumption was associated with heart disease.[1 2]

The association between sugar and poor health has remained contentious over the past few decades. This is partly because of weaknesses in the data (Yudkin's conclusions were largely based on comparisons of sugar intake and disease rates among different populations, which is generally considered a weak form of evidence) and because powerful economic interests are invested in the production and sale of sugar based products. The tension between industry and scientists can be illustrated by a 2003 recommendation from the World Health Organization that sugar intake be limited to 10% of energy intake,[3] which was heavily attacked by the sugar industry and many governments, but was ultimately sustained. Because WHO plans to update its recommendations, a systematic review of the literature on the association between sugar consumption and body weight was commissioned, the findings of which are presented in the linked paper by Te Morenga and colleagues.

Te Morenga and colleagues limited their analysis to prospective studies and randomized trials that examined freely consumed sugar—they excluded studies in which weight loss was emphasized. Both types of studies supported an adverse effect of sugar on body weight in adults. Randomized trials of children were limited by the low number, size, challenges of blinding, and adherence to assigned diets, but the findings of prospective studies supported an adverse effect of high sugar consumption on body weight. A broader review of studies that included trials where sugar was restricted provides further evidence to support Te Morenga and colleagues' conclusions.[5] This evidence includes two recent randomized trials in children,[6 7] one of which was the first double blinded study in which an artificially sweetened drink was used as control.

Although the finding that sugar is adversely associated with adiposity is important, recommendations on sugar intake should take all its health effects into account. Consumption of sugar, and carbohydrates in general, raises postprandial plasma glucose and adversely affects manifestations of the metabolic syndrome—it increases concentrations of insulin and triglycerides and reduces concentrations of high density lipoprotein cholesterol.[8] Not surprisingly, the consumption of sugar sweetened drinks has been associated with an increased risk of type 2 diabetes and coronary artery disease.[9 10]

Te Morenga and colleagues' results suggest that sugar increases body weight mainly by promoting overconsumption of energy (although the effects of sugar on body fatness independent of changes in weight could not be assessed). This, and other evidence, suggests that sugar intake should be limited, but questions remain. What is a desirable limit? No clear threshold exists for the many adverse effects of sugar intake; in general the association seems to be roughly linear, which makes a limit somewhat arbitrary. Current intake of added sugar in the United States and United Kingdom is about 15% of total energy. Thus a limit of 10% could be viewed as a realistic goal. In contrast, the American Heart Association suggests a limit of about 5% of energy,[11] which would be more consistent with a goal for optimal health.

What mechanisms underlie the effects of sugar on weight, and what is the relative importance of sugar in liquid versus solid form? As Te Morenga and colleagues noted, many of the studies they identified examined the role of sugar sweetened drinks. Sugar in this form does not induce satiety to the same degree as it does in solid form, which makes overconsumption easier. Because of this, and the large amounts of sugar consumed in drinks, reducing the intake of sugar sweetened drinks is a high priority. Overconsumption of sugar is surely, in part, due to sweetness itself, and food technologists exploit this fact to encourage greater consumption of their products. This results in a food supply that is permeated by a high level of sweetness, which may promote behaviors akin to addiction.[12]

What are the relative roles of glucose and fructose? Popular attention has focused on high fructose corn syrup as a specific danger, but its composition is almost identical to that of sucrose (half glucose and half fructose). Although fructose is metabolized by different pathways from glucose, both seem to have adverse effects, and there is no good evidence that replacement of fructose with glucose would be beneficial. Furthermore, many starchy foods, particularly highly processed grains and potato products, have a high glycemic index, raising blood glucose and insulin more rapidly than an equivalent amount of sucrose.[13] Unfortunately, the 2003 WHO report disregarded evidence suggesting that refined grain and potato products have metabolic effects comparable to those of sugar. In contrast to added sugar, sugars occurring in the form of whole fruit have generally not been associated with weight gain, perhaps because of their relatively low glycemic index and high amounts of accompanying fiber.

What actions are needed? Efforts to reduce sugar intake are appropriate, but they should form part of a broader effort to improve the quality of carbohydrates, which would include reducing intakes of refined grain products and potatoes. Action should include educational programs, improvements in foods and drinks provided in schools and worksites, and supplemental nutrition programs for people with low incomes. Reducing the amount of sugar consumed in drinks deserves special attention. Policy approaches, such as imposing taxes on sugar laden drinks,[14] are useful, as are restrictions on advertising to children and limits on serving sizes, as have been tried in New York.[15] Healthcare providers could play an important role by routinely asking about consumption of sugar sweetened drinks as well as tobacco and alcohol use, by setting a good example, and by assuming leadership in public efforts to limit sugar as a source of harm.

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The automation of systematic reviews

Would lead to best currently available evidence at the push of a button

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The Cochrane handbook stipulates that systematic reviews should be examined every two years and updated if needed,[1] but time and resource constraints mean that this occurs for only a third of reviews.[2] Indeed, it may take as much time to update a review as it did to produce the original review. If this effort were redirected at developing methods to automate reviews, then updating might one day become almost effortless, immediate, and universal.

In his novel *Player Piano*, Kurt Vonnegut Jr described machines that record the hand motions of artisans and replay them to reproduce a perfect copy of the artefact, more quickly and more economically. Such automation is needed in the update and even creation of systematic reviews, because the capability of the human machinery for review increasingly lags behind our capacity to produce primary evidence.[3] The current reality is that many reviews are missing or outdated,[4] and it is hard to imagine a solution that does not involve some automation.[5]

Throwing our limited resources at the diminishing returns of hand crafting systematic reviews is no longer sustainable

Technology has advanced such that software can be used at least to semi-automate evidence discovery and synthesis. The idea of automating aspects of systematic review is not new, and computer systems that can reason from the literature to support clinical decision making have long been imagined.[6]

Four basic tasks underpin systematic review—retrieving the relevant evidence in the literature, evaluating risk of bias in selected trials, synthesising the evidence, and publishing the systematic review—and technology can help in each.

Evidence retrieval is now well understood and easily done, and it should be the primary function of automation. Meta-search engines can retrieve published trials from multiple databases, automatically translating between different query languages.[7] This is aided by specialised databases for clinical trials, which include well structured trial information.[8] Whether curated manually by experts or automatically by computer, such structured trial banks are suitable for further automation. Machine learning systems are being developed to help further with the process of citation screening.[9]

The effort devoted to evaluating risk of bias and evidence synthesis can be reduced by text extraction algorithms that identify specific information elements in a document.[10] ExACT, for example, is designed to help systematic reviewers by highlighting sentences and phrases containing information about population, intervention, control, outcome ("PICO") and randomisation. This algorithm has a reported precision and recall of greater than 90%.[11]

Moving from information extraction to its synthesis is far more challenging and will depend on computational reasoning across multiple documents.[12] An early example is a system that monitors the literature and alerts reviewers when new evidence appears that is likely to change the conclusions of a systematic review.[13] Although text extraction algorithms typically use statistical methods to identify specified elements in a document, multi-document synthesis will probably require mixed methods that harness specific knowledge about the structure and process of clinical trials to guide interpretation.[14] Multi-document methods are needed both for multi-trial meta-analyses and for single trials reported in multiple places—for example, if randomisation is reported in a protocol paper but not in the results paper.

Natural language generation algorithms can help publish systematic reviews by generating human readable text from trial reports or banks. Together with visualisation tools (for example, for creating CONSORT diagrams), introducing automation here may lead to more uniform and systematic accounts of the evidence.

In light of systems already available, intelligent systems could probably be derived to help across these four main tasks of performing systematic reviews, to learn from reviewers, and then to replicate their approaches. As reliability improves, these tools will move from aiding humans to becoming reliable autonomous systems that can update systematic reviews with the latest available evidence.

Currently, many systematic reviews, and all Cochrane reviews, require well structured peer reviewed protocols before any review of the evidence starts,[1] to ensure objectivity and repeatability of the review. These protocols are a formal representation of the actions that a reviewer is about to execute and can become the recipe for automation. Developing these protocols is distinct from conducting the reviews. We envisage development environments that allow protocols to be edited, tested, and then executed at the push of a button, freeing the reviewer to focus on developing and validating the review question and protocol. Validated protocols could be disseminated to open repositories that archive and index them. These repositories could then conduct reviews on demand.

For this vision to become reality, computer scientists, informaticians, and clinicians must join forces. Throwing our limited resources at the diminishing returns of hand crafting systematic reviews is no longer sustainable. Instead, some of that energy and creativity needs to be diverted into building the machinery for the next stage of evidence based medicine. The size of the task need not be daunting. Automating even small steps in the process of systematic review will shorten the time before reviews are published and increase the number of questions for which reviews are created. With time and trust, more of the process will be delegated to automation.

Eventually, the notion of a review having a fixed publication date and becoming almost immediately out of date will disappear as autonomous agents sift the evidence continuously and use their protocols to provide updated reviews on demand.[15] Furthermore, providing systematic review "machines" at the point of care will mean that clinicians will know that they always have access to the best evidence.

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News: More polio workers are killed in Pakistan
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What must be done about the killings of Pakistani healthcare workers?

It's time to stop trying to accommodate those who spread fear and terror

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In December 2012 nine volunteer polio workers, six of whom were young women, were murdered in Pakistan.[1] A day later five female education workers were murdered on their way to work in Swabi (Khyber Pakhtunkhwa). The coordinated attacks sent a chilling message to civic society that female workers and volunteers, hitherto protected by a strict Pashtun moral code, were now terrorist targets. These murders begin to fade into a background of incessant conflict and insurgency around the border areas of Khyber Pakhtunkhwa, the federally administered tribal areas, and Baluchistan. The city of Karachi is caught in a spiral of targeted killings and kidnappings for ransom.[2] In Baluchistan, the law of the government has all but collapsed and the Hazara minorities have been forced to demand army rule in the main city, Quetta, to protect themselves from the threat of ethnic cleansing at the hands of a well connected and funded underground network of terrorist organisations.[3] The nation is inured to reports of violent deaths on a daily basis, however, and the recent targeted killings of health workers are already off the news and public debate in Pakistan.

It is astounding that, despite these obvious hazards, health workers and vaccinators were back at work within a few weeks of the recent killings. It is a testament to the resilience and bravery of these frontline workers, who stand tall where their comrades have fallen. Pakistan has made enormous progress over the past year in restricting polio, with just 58 cases in 28 districts in 2012, compared with 198 cases in 60 districts in the previous year. Despite the current dangers inherent in polio and child immunisation programmes, polio vaccination cannot be allowed to slip. With the massive measles outbreak in Sindh claiming more than 300 lives over the past few weeks,[4] it is even more important to have robust vaccination programmes in place in Pakistan.

The targeted killing of health workers in Pakistan for political or so called religious reasons is not new. Polio workers have been targeted sporadically in the past.[5] In Karachi, a sprawling mega-city of almost 19 million inhabitants, 85 doctors have been assassinated since 1990, often those belonging to the Shiite sect.[6] Few culprits are ever caught, and the term "hidden hands," regularly used by those in power, has become clichéd.[7] It is clear that, although these acts of violence and murder may be perpetrated by a variety of obscurantists and organisations, their motives are similar. Whether it is blowing up girls' schools or targeting health and education workers, they aim to create a climate of maximum fear and despondency so as to impose their will. This was the method used in the peaceful district of Swat a few years ago, which saw a virtual takeover of the population of more than two million by a few hundred hardcore followers of a religious leader, who spread his message of fear using a state approved FM radio channel.[8]

FAISAL MAHMOOD/REUTERS

Ordinary Pakistanis are fighting for survival in a spiral of incessant energy crises, food price increases, and political insecurity

The ordinary Pakistani is paying the price of years of bad governance and appalling policies by successive generations of military dictatorships and corrupt civilian governments. Over the past 50 years several wars with India, ongoing political tension in Kashmir, and successive Afghan conflicts have fostered the creation of armed militant organisations that have now run amok.[9] Sadly, in both Afghanistan and much of the federally administered tribal areas and Baluchistan, a whole generation has been raised witnessing constant conflict. These "children of war,"[10] often the product of a medieval education system in religious schools (madrassahs) and unemployable in a shrinking job market, are easy bait for those who would recruit them to a "holy" cause. The contribution of conflict in the Islamic world to the growth of a Jihadist mentality cannot be underestimated. Suicide bombings in Afghanistan and Pakistan were unheard of until recent years, and the advent of killing by remote control through drones has led to a veritable bonanza for recruiters to the cause of the Taliban from among the survivors, a fact well recognised by many analysts.[11]

Although this is all depressing and chilling, it must not detract from the need to act and support the silent majority in Pakistan who want to see progress and improvements in public health programmes. Ordinary Pakistanis are fighting for survival in a spiral of incessant energy crises, food price increases, and political insecurity that sees political forces in the country at loggerheads over rapidly shrinking geographical and regional mandates. It is inevitable that terrorist organisations and obscurantists will take advantage of crises of governance and leadership, but this cannot be allowed to happen. What we urgently need is active provision of security to health workers and a visible, vociferous condemnation of violence against volunteers and health workers by all political and religious parties.

Providing security to the civilians and frontline health workers in Pakistan must also involve active pursuit of those determined to destabilise public health and education programmes. Mere dialogue and attempts to accommodate obscurantists and murderers serves only to embolden them. The experience in the Swat valley has shown that where there is a will the state security systems can effectively take on the few who hold entire populations at ransom. It is time to accept that Pakistan is "reaping the whirlwind" of creating and nurturing those who would think nothing of taking the country back to the dark ages.[12]

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Suggesting that a person's life expectancy should be an arbitrary 10 years for them to benefit from screening is misguided

Benefits of cancer screening take years to appreciate

Risks are seen more immediately

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There has been much debate in recent years about the relative benefits and risks of screening. Debates about breast cancer screening have been particularly heated, even though such screening is recommended in most developed countries. Concerns raised in a recent major review of the benefits and risks of the UK breast screening programmes are also at the heart of discussions about prostate specific antigen testing, where there is evidence of benefit but also of considerable risks.[1 2] In a linked research paper, Lee and colleagues consider how long it might take for the benefits of screening to show in a population invited for breast or bowel cancer screening.[3]

Where benefits are considered to outweigh risks then screening can be recommended. In developed countries and jurisdictions where a population model of health is delivered, screening for breast, cervical, and bowel cancer is often offered on an organised basis.[4 5] Evaluation of the effectiveness of such programmes is demanded ethically and by the programmes' funders, as well as by the populations screened and their doctors. Although it has never been evaluated by a randomised controlled trial (RCT), cervical screening has been shown to have a large effect, with five yearly screening probably preventing 63-73% of cervical cancers in women over 50 years.[6] Evidence from RCTs suggests that an invitation for bowel or breast cancer screening prevents around 20% of deaths from these cancers.[1 7] The effect of cervical screening can be shown more easily using observational data than can the effect of breast or bowel cancer screening, because the effects of breast and bowel cancer screening are much smaller.

Although population screening is offered as a public health measure, the benefits and risks affect individuals. At invitation for screening, many of the risks are immediately evident to the person concerned. These include the anxiety associated with participation, awaiting results, and referral for diagnostic investigation—which often proves that cancer is not present. The testing and diagnostic procedures, such as mammography or needle biopsy of the breast, or endoscopy, also have associated complications. These immediate risks can be readily quantified and affected people identified. By contrast, almost all the benefits of screening take years to appear, and we can never know for certain who exactly has benefited.

JAMES KING-HOLMES/SPL

Bowel cancer screening test for occult blood

The main benefit sought from breast and bowel cancer screening is the reduction in mortality from that cancer. This takes years to accrue, partly because even after symptomatic diagnosis of these cancers people normally survive for several years, and partly because of the additional lead time applied by earlier diagnosis through screening. In randomised trials where the population is free of cancer at the start, randomisation should account for temporal changes in other factors. Benefit, if it occurs, can be seen more clearly in such trials, whereas in public health screening programmes, where there is no control group and the population includes people diagnosed with cancer before screening started, analyses based on time trends can be difficult to interpret.

Lee and colleagues used data from RCTs of breast and bowel cancer screening to estimate how long it takes for one death to be prevented for each 1000 people screened.[3] They conclude that, for patients over age 50 years, the time lag for either of these screening programmes is around 10 years. It is important to acknowledge such a time lag, so that benefit is not sought too soon.

The authors' choice of one in 1000 to determine what is worth while underlies their conclusions, but it is an arbitrary choice, and they assume that the benefit of screening is constant at all ages. The risk of developing and dying from breast or bowel cancer, however, increases with age, and the absolute benefit of breast cancer screening rises as women get older.[8] In addition, the confidence intervals around Lee and colleagues' estimates of "10 years" are wide, with a range of 5 to 16 years. This shows that the estimates are too uncertain to justify any recommendation.

Doctors advising individual patients and public health practitioners considering population screening programmes should take account of the different time scales for benefits and for risks to accrue. Likely life expectancy is only one of many factors that may play a part in determining how someone responds to an invitation or recommendation for screening. However, suggesting that a person's life expectancy should be an arbitrary 10 years for them to benefit from screening is as misguided as saying that everyone will benefit.

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