Calorie labelling on the high street
A step forward, but changes in food supply must follow

In the linked cross sectional surveys, Dumanovsky and colleagues assess the effect of a menu labelling regulation on calories (1 kcal=4.18 kJ) per purchase at fast food chains in New York City.1

The need to find new approaches to stimulate dietary change is self evident. More than 60% of adults are overweight, and diet related ill health is estimated to account for 10% of morbidity and mortality in the United Kingdom.2 Years of traditional information based health promotion have heightened awareness of the elements of a healthy diet, with 87% of consumers claiming that healthy eating is important to them.3 Nevertheless, changes in eating habits have been slow, and much remains to be done.4 The challenge is to find and test innovative approaches to drive dietary change within populations.

Front of pack nutritional labelling on products in the supermarket is now widespread in the UK, but with an estimated 20-25% of calories consumed away from home, it is logical that labelling should extend beyond supermarket purchases. Dumanovsky and colleagues report on the New York experience of the mandatory provision of calorie information on menus and menu boards in chain restaurants.5 It is the latest in a series of diverse studies that began with simple analogue experiments of food choice in an experimental laboratory context, whereby participants were asked to make food choices with and without nutritional information.

The recent policy introduced in New York City has provided opportunities for researchers to study the effect of menu labelling in a real life setting. Dumanovsky and colleagues’ observational study, which is the most extensive to date, assessed food purchases on the basis of till receipts from lunchtime customers across a large and random sample of outlets before and after the introduction of menu labelling. The study found no significant difference in calories purchased before and after introduction of the regulation. However, in the 15% of customers who reported using information on calorie content, purchases contained fewer calories (106 kcal) after the regulation was introduced.

Although the study estimates the likely effect on the energy content of purchases at the population level, it leaves many questions unanswered. Taste, price, and prevailing social norms are all important influences on consumer food choices, and it is difficult to isolate the effects of menu labelling from the wider contextual characteristics of the environments in which food choices are made.

Previous evidence of the effect on the calorie content of purchases has been equivocal and elicits strong opinions.6 Few would disagree that more effort is needed to raise awareness of the importance of energy intake to successful weight control, and labelling itself will contribute to a growing “calorie consciousness,” which may yield sustained benefits. What happens beyond the restaurant is a matter of speculation. There is the potential for compensatory behaviours, but it is equally plausible that lessons learnt on the high street about the relative energy content of different items can inform food choices elsewhere.

High street chains in England are about to embark on a similar, although voluntary, scheme as part of the government’s public health responsibility deal. Companies committing to the out of home labelling pledge will display calorie information clearly and prominently (in a size and font similar to the price), at point of choice (usually menu boards in quick service restaurants, or shelf edges in coffee and sandwich shops), and across all standardised items available for 30 days or more each year. To date, 32 companies—covering more than 5000 high street outlets and representing 14% of the total number of meals served outside the home—have signed the deal. This is an overtly pro-choice intervention that empowers consumers when making food choices. In the voluntary context in which it is being enacted in England, it gives businesses autonomy too, and consumers will be able to choose whether to receive such information by their choice of where to eat. Consumer response will be a key part in driving change among businesses not yet engaged in the responsibility deal. It may also act as a barometer of the public appetite for further action to make healthier choices easier.

But knowledge alone may be insufficient to induce sustained changes in dietary habits. There is growing recognition that automatic behaviours may be a more dominant influence on eating habits than reflective processes.7 The experience of salt reduction has shown that industry action using a “health by stealth” approach has delivered measurable improvements in diet.8 Anecdotal reports suggest that menu labelling can drive wider changes on the part of businesses, including reformulation, portion control, or changing the default option such as substituting reduced fat for full fat milk or mayonnaise. These “supply side” measures may...
Improving the disclosure of medical incidents

A genuine apology is only the first step in the process

A central component of a just, patient safety culture includes the disclosure of serious medical incidents to those who are affected (open disclosure). The concept of openly disclosing the details of medical incidents has been adopted by several organisations and medical authorities including ones in Canada, New Zealand, the United Kingdom, the United States, and perhaps the earliest adopter, Australia, which implemented a national open disclosure policy in 2003. The qualitative study by Iedema and colleagues (doi:10.1136/bmj.d4423) explores, from individual patients’ perspectives, the successes and problems associated with the execution of the Australian open disclosure policy. The study underscores many important messages for organisations that have or are considering an open disclosure policy.

The findings indicate that much work is needed to engage patients and families in open disclosure, and the study provides a long list of important activities and behaviours associated with successful open disclosure. Research and clinical experience suggest that several items from the list are central to effective disclosure, including a true belief in the process, the timing of the process, an apology and expression of empathy, a knowledgeable and neutral person to help collect information and deal with patients’ questions, and attention to the financial implications of the event.

The patient quotations suggest that it is still common for medical organisations to approach open disclosure with less than full high level commitment and belief in the process. This is not surprising: developing and maintaining a just patient safety culture requires ongoing effort, as organisations such as the Dana-Farber Cancer Institute have found. The results should prompt leaders within medical organisations, particularly those in risk management, to critically examine their commitment to open disclosure.

Furthermore, the study shows that disclosure was often delayed. Disclosure should begin shortly after a medical incident is recognised, not when all the internal fact finding and analysis are complete. Those affected by a medical incident deserve specific and timely information, not just generic information that is packaged for everyone. Not surprisingly, clinicians need help in effectively delivering an apology and indicating their empathy for the patient’s current situation. This may require coaching and role playing before the first disclosure meeting.

But it is crucial that the care team does not abandon patients or families when something goes wrong.

Disclosure needs to be viewed as a process, not a single meeting. Affected people rarely understand all the components or complexities of the incident in one meeting. Organisations should expect a multi-visit process, even if the clinicians are involved only in the initial meeting. A single meeting often cannot deal with more than reviewing the event, expressing an apology, and answering questions. Subsequent meetings allow for additional questions, further information disclosure, discussion of steps taken to lessen the chance of a recurrence, and financial discussions. The number and flow of meetings vary from incident to incident, but more than one meeting is usually needed. Finally, those affected need someone who can help them

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It is essential not to miss potentially treatable causes of new onset confusion or amnesia. Once toxic and metabolic causes have been excluded, infectious encephalitis must be considered and treated. However, the results of a recent surveillance study in the United Kingdom found that only 42% of patients with encephalitis had an identifiable infectious cause. Even just a decade ago, the cause of encephalitis in those without an identifiable infection may well have remained obscure. There is now unequivocal evidence that specific autoantibodies directed against neuronal proteins crucial to the control of neurotransmission are responsible for a proportion (~8% in one series) of such cases. Importantly, these autoimmune encephalitides may be treatable with immunotherapy.

Antibodies against two targets, the voltage gated potassium channel (VGKC) complex and the N-methyl-D-aspartic acid (NMDA) receptor, have emerged as important causes—more than 100 related or relevant articles have been published in the past two years alone. These autoimmune encephalitides have distinctive clinical features and can be diagnosed by simple serological tests. Despite almost certainly being underdiagnosed, about 400 patients with clinically relevant raised VGKC complex or NMDA antibody titres have been identified at the UK diagnostic centre in Oxford in the past three years (A Vincent, personal communication, 2011), and 400 patients with NMDA antibody associated encephalitis have been identified in the United States over a similar time period, showing that these conditions are not uncommon and have worldwide prevalence.
Prompt diagnosis and treatment with immunosuppression can improve or even reverse symptoms. If left untreated, retrospective case series show that these conditions can lead to irreversible cognitive deficits, ongoing seizures, and death.3 4

Limbic encephalitis associated with VGKC complex antibodies usually presents in middle aged or elderly people and is twice as common in men as in women.3 5 6 Patients typically develop personality change, amnesia (often with dense anterograde and retrograde components), and confusion over days to weeks. Seizures are common and may contribute to confusion. A highly characteristic focal seizure disorder with very brief, frequent, unilateral dystonic face and limb jerking is often seen, and can predate the development of cognitive impairment.7 About 60% of cases have low serum sodium consistent with the syndrome of inappropriate antidiuretic hormone (SIADH).3 5 6 A similar proportion have medial temporal lobe high signal on magnetic resonance imaging, consistent with localised inflammation, which if untreated may lead to focal hippocampal atrophy,8 a substrate for both memory impairment and adult onset medial temporal lobe epilepsy.9

In contrast, encephalitis associated with NMDA receptor antibodies is mainly seen in children and young adults, with women being affected about three to four times more often than men.3 7 8 Patients typically present with psychotic features, anxiety, or depression, which may initially be considered non-organic. Symptoms often evolve in a stereotypical sequence, with the emergence of episodic memory impairment and seizures, followed by stereotypical dystonic movements, autonomic dysfunction, and reduction of consciousness, which often necessitates admission to intensive care.4 7 8 More subtle phenotypes associated with lower NMDA receptor antibody titres include first episode psychosis10 and adult onset focal epilepsy.11 The full spectrum of symptoms associated with antibodies to both the VGKC complex and NMDA receptor remains to be determined.

Although definitive diagnosis requires detection of the relevant autoantibody in serum or cerebrospinal fluid (at a lower concentration), recognition of the distinctive phenotypes may allow for prompt treatment while awaiting diagnostic confirmation. Occult cancer should be excluded because although this is uncommon (<5%) in limbic encephalitis associated with VGKC complex antibodies, 20-50% of patients with NMDA receptor antibodies have a tumour, most commonly a benign ovarian teratoma.4 8 Early tumour removal, particularly in NMDA receptor antibody cases, improves prognosis.4 7 8

Although the evidence base is limited to retrospective series and case reports, best available data suggest that early treatment with intravenous immunoglobulin or plasmapheresis (or both), followed by long term immunosuppression (typically with corticosteroids) is associated with better outcomes.3 5 8 Other treatments, including cyclophosphamide and rituximab, have been successful in individual patients, particularly in the more protracted NMDA receptor antibody encephalitis.7 Seizures are often refractory to standard treatments, but may remit with immunotherapy.7 Patient and carer support and information for encephalitis in general, and these conditions in particular, are offered by the UK Encephalitis Society (www.encephalitis.info).

Further studies are needed to assess the epidemiology of these conditions and the full spectrum of clinical features, particularly at lower antibody titres, as well as formal clinical trials to determine optimal treatments. Unlike the controversial entity “Hashimoto’s encephalitis,” the specific and probably pathogenic antigenic targets for these antibodies and other novel neuronal antibodies associated with encephalitis are now being determined.7 9 11 12 A notable recent advance has been the demonstration that VGKC complex antibodies have several different antigenic targets, which probably explains some of the phenotypic diversity seen in this condition.8

Autoimmune encephalitis syndromes associated with VGKC complex antibodies and NMDA receptor antibodies are now well established entities, and they should be included in the list of treatable causes of encephalitis, seizures, and cognitive decline. These patients present not only to neurologists but to a wide range of clinicians, including general physicians, paediatricians, intensivists, and psychiatrists. All such clinicians need to be able to recognise these clinical phenotypes if these disorders are to be diagnosed and treated promptly, and potentially irreversible cognitive impairment prevented.

Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coiDisclosure.pdf (available on request from the corresponding author) and declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; AV and the University Department of Clinical Neurology in Oxford hold patents (SRI co-applicant on patent) and receive royalties and payments for antibody assays.

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Potential withdrawal of bevacizumab for the treatment of breast cancer
Calls into question the approval of drugs based on surrogate outcomes

On 29 June the oncology drugs advisory committee to the US Food and Drug Administration (FDA) voted unanimously to recommend withdrawing approval of bevacizumab for the treatment of metastatic breast cancer. The panel concluded that bevacizumab (Avastin, Genentech) is neither effective nor safe for the treatment of breast cancer, and the Food and Drug Administration is inviting public comment on the decision for one month before issuing a final ruling. Why has this happened and what implications does it have for the approval and passage of other new cancer drugs into everyday practice?

The success of targeted treatments such as trastuzumab for HER2 positive breast cancer has given rise to the potential for personalised medicine. It is hoped that our understanding of cancer biology and the ability to develop highly specific drugs for molecular targets will generate targeted treatments for individual cancers that result in improved survival combined with less toxicity. Bevacizumab is a humanised monoclonal antibody that inhibits vascular endothelial growth factor A, which is important in stimulating neoangiogenesis in cancer. The efficacy and safety of this drug in patients with first line metastatic breast cancer were shown in a multicentre randomised trial (E2100), which randomised women with metastatic breast cancer to conventional chemotherapy (paclitaxel) alone or in combination with bevacizumab. The trial showed that bevacizumab significantly improved the primary end point of progression-free survival from a median of 5.8 months to 11.3 months but produced no improvement in overall survival in all designs. Adverse events—including hypertension, neuropathy, and infection—increased by 20% with bevacizumab, although these were moderate and manageable (as assessed by patients and trialists).

Accelerated approval in the United States in 2008 for the use of bevacizumab for this indication on the basis of improved progression-free survival but no survival benefit was controversial. Subsequent publication of other trials of bevacizumab and chemotherapy in first line metastatic breast cancer failed to show improved survival and also showed excess toxicity and less benefit in terms of progression-free survival than the E2100 trial. Consequently, the oncology drugs advisory committee has reviewed its earlier decision and recommended withdrawal of this agent for metastatic breast cancer. Bevacizumab is still approved for breast cancer treatment by the European Medicines Agency but has not been approved by the National Institute for Health and Clinical Excellence in the United Kingdom.

Why is progression-free survival a controversial surrogate end point? Traditionally in the US an improvement in overall survival was a clear and unambiguous end point that needed to be met before a drug was deemed suitable for approval for everyday use. Progression-free survival has been suggested as an alternative in the past five years and is increasingly used as the primary end point in randomised clinical trials. However, a poor correlation exists between response rates and progression-free survival as surrogate end points for overall survival in metastatic breast cancer. In the E2100 trial, bevacizumab combined with paclitaxel had among the best results of any chemotherapy regimen used in terms of response rates or progression-free survival but it did not translate into an overall survival advantage in this unselected population.

There are challenges in persisting with overall survival as an end point. Factors in trial design, especially when crossover is allowed, and the fact that patients often take multiple drugs during the course of their disease may make it unrealistic to attribute a difference in overall survival to an individual drug or regimen.

The use of progression-free survival allows these problems to be circumvented but creates a new set of challenges. What is the value of a tumour shrinking if it does not eventually improve survival? A treatment that delays progression may be worthwhile, but how much of a delay is meaningful? If progression-free survival is to be used routinely then increased rigour is needed in trial design. The interventions need to be blinded, blinded assessment should be done by independent radiologists, and the timing of assessments should be carefully standardised. Without such rigorous data can be contaminated and bias introduced. Finally if progression-free survival assessment becomes routine then survival data may never be forthcoming. Powering trials with overall survival as the primary end point is expensive and may involve large numbers and long follow-up. It remains, however, the definitive outcome of importance for patients.

If specific groups of patients who will respond to a particular treatment can be identified it may be easier to identify a real survival benefit from these treatments. A meta-analysis of trials of bevacizumab in breast cancer has given some insight into clinical subgroups that may derive more benefit by subset analysis. Other studies have suggested the development of hypertension during...
treatment as a surrogate for likelihood of response. These observations are only a guide to future research because although bevacizumab is widely thought of as a targeted treatment it does not currently have a biological or clinical marker to predict activity in specific patient groups. The key to assessing the usefulness of bevacizumab would be to develop a robust validated companion biomarker that can identify those patients who would live longer as a result of receiving the treatment and enable the large numbers of patients who would gain little or no benefit to avoid being treated. For the time being enough data exist to explore this drug further, especially in clinically high risk patients such as those with triple negative breast cancer, and trials are continuing in this setting.

For patients already taking bevacizumab, it would seem reasonable that they should continue until disease progression or toxicity dictates otherwise. For practising oncologists in Europe the combination of bevacizumab and paclitaxel remains a well tolerated alternative to double cytotoxic chemotherapy regimens if funding permits.

The lessons learnt from bevacizumab apply more generally. A molecular target may indeed be potentially manipulated for therapeutic effect but is only relevant if the pathway is understood and the patients most likely to benefit are enrolled in clinical trials. This will require a concerted approach to tissue banking, with mandatory tissue collection and well designed trials that will identify companion diagnostics (a test that allows a specific protein to be targeted, for example the Her2 assay for trastuzumab).

Global Health 2011

BMJ Group and NICE International have joined forces to co-host a unique two day conference on policies for sustainable and effective healthcare. Taking place on 29 and 30 September 2011 at BMA House in London, Global Health 2011 will bring together experts from around the world to discuss and promote cost effective and evidence informed policy making as a means to improve health outcomes.

Global health has been defined as “An area for study, research and practice that places a priority on improving health and achieving equity in health for all worldwide” (Lancet 2009;373:1993-5). It is a huge endeavour, which no country or donor can hope to tackle alone. It must be multidisciplinary in the widest sense, encompassing not only clinical practice and public health but also economics, culture, and politics. It must go well beyond providing low and middle income countries with access to health technologies such as vaccines and retroviral drugs: these are important but they are not ends in themselves. They must be part of a journey towards developing healthcare systems that are ultimately self sustaining.

Low and middle income countries face a raft of common challenges: how to provide universal healthcare, how to manage publicly and privately funded healthcare, how to allocate finite resources, empower healthcare professionals, and integrate and improve the quality of clinical practice and public health.

Developed countries face similar challenges and are far from having all the answers. They can and must transfer vital knowhow that will support accountable and cost effective decisions. But they also have a lot to learn. America’s massive spending on healthcare—17% of gross domestic product, and forecast to rise to 20%, is recognised to be unsustainable. Rapid economic growth in China, India, and Brazil is lifting hundreds of millions out of dire poverty. What policies should these and other emerging countries pursue now that they can afford to spend 4-5% of GDP on healthcare? How can they maximise the public good from their growing economic resource without repeating the mistakes of the developed nations?

Global Health 2011 is your opportunity to hear and interact with an impressive array of influential speakers, including government ministers, funders, donors, and policy makers from both developed and developing countries. We hope it will be the first of what will become an annual event, contributing to building a healthier and more equitable world. For more information about the meeting and to register to attend, please go to http://globalhealth.bmj.com.