Obesity, genetic risk, and environment

Genetic makeup can inflate effects of bad diet

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The alarming global rise in prevalence of obesity is caused by unhealthy obesogenic environments. In westernised societies we are all exposed to calorie dense food, sedentary lives, stress, and sleep deficit. Some people seem relatively insensitive to these environmental pressures, while others are severely affected and become obese.

In a linked paper, Qi and colleagues examined the interaction between common genetic variants associated with body mass index (BMI) and frequency of fried food consumption in over 37 000 people.1 The large study size was necessary to obtain adequate statistical power because the individual effects of these variants (single nucleotide polymorphisms, SNPs) on BMI are relatively subtle.2 The authors combined the weighted individual effects of 32 SNPs into a single “genetic risk score” for each participant.

As expected, participants who ate fried food more often tended to have higher BMI, and, independently, those with the highest genetic risk score also had higher BMI. The novel finding in this study is the observed interaction between genetic risk and fried food consumption: people in the highest risk groups for both had the highest BMI overall. Eating fried food more than four times a week had twice the effect on BMI for those in the highest third of genetic risk score as those in the lowest third.

**Genetic risk scores robust at population level**

This work provides formal proof of interaction between a combined genetic risk score and environment in obesity. Similar studies have already shown interaction between genetic risk scores for obesity and physical activity3 and dietary calcium.4 These results are unlikely to have a direct impact on personal healthcare because, though such genetic risk scores are statistically robust at the population level, they have poor predictive power for any given individual. Similarly, the results of the latest study are unlikely to influence public health advice, as most of us should be eating less fried food.

It would be a great shame, however, to assume that genetics can be ignored in the management of obesity. This widespread misconception arises from confusion of the common SNPs that have relatively subtle effects on BMI (the strongest of which, close to the FTO gene, raises body weight by only a mean of 3 kg even in those who inherit a double dose of the variant) with more dramatic genetic alterations that cause “Mendelian” forms of obesity.

There are, in fact, at least 15 single gene forms of obesity, with new ones reported almost monthly with advances in DNA sequencing technology.5–8 There are also chromosome microdeletions that cause Mendelian obesity.9 10 Mutations in just one of the obesity genes (MC4R) cause around one in 20 cases of severe childhood obesity,11 and the total number of obese adults with Mendelian obesity is likely to be substantial.

Where molecular mechanisms are understood, obesity-causing genetic mutations disrupt appetite control systems in the brain, so affected people are unlikely to be able to maintain long term dietary restraint. It might also be unwise to offer them some types of weight loss surgery, such as adjustable gastric banding.

Why is this important? Our current options for management of morbidly obese people are limited, though several new therapeutic approaches are in development. Different types of obesity might require different management. For example, lifestyle interventions are likely to be much more successful in people whose BMI is not too far from the desirable range. The UK’s National Institute for Health and Care Excellence (NICE) already implicitly recognises that lifestyle and medical approaches are unlikely to help those with the most severe forms of obesity. Weight loss surgery is recommended as the first line treatment in people with BMI >50.

As researchers, policy makers, and healthcare professionals, we should adopt an evidence based approach. Unfortunately, clinical logic is not always applied in the consideration of obesity—health professionals commonly recommend the same lifestyle based interventions to those with overweight or mild obesity as to those with more severe problems. We would not adopt this approach with hypertension or type 2 diabetes, where it is well recognised that diet and appropriate physical exercise might be sufficient for mild cases, but more severely affected people need drugs (or even surgery) and a lifelong care plan. There is a danger that issues surrounding blame and “personal responsibility” in obesity might lead to lack of appropriate support for extremely obese people, who often have complex care needs. This can be the case in families with undiagnosed inherited obesity: genetic screening and counselling is rarely offered in those with morbid obesity.

In summary, use of combined genetic risk scores in gene-environment interaction studies allows joint analysis of factors influencing obesity. Inclusion of multiple genetic variants into a single risk score is helpful in terms of power for such investigations. It would be useful if similar studies could be carried out in individuals with Mendelian forms of obesity, who might show even more striking gene-environment interactions. Complex analyses integrating thousands of common variants have the potential to explain yet more of the genetic contribution to traits such as BMI.12 Predictive power at the individual level, however, remains low when only common genetic variants are considered. Integration of rare genetic alterations that cause Mendelian forms of obesity might improve this, providing clinically useful predictions for individuals and enabling stratification of patients for appropriate care and treatment.

Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

References are in the version on bmj.com.

Cite this as: BMJ 2014;348:g1900

RESEARCH, p 11
Takeaway food and health

Change the menu, not the venue

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Takeaway or fast food has been a tempting target for public health advocates but a confounding one for researchers. It makes intuitive sense that people with ready access to takeaway food will eat more of it, yet results of research linking fast food access to diet or weight have been quite mixed.

In a linked study, Burgoine and colleagues take a novel approach to describing food environment exposures. Unlike most research, which considers only the home neighbourhood, this study measured food outlets around the workplace and along commuting routes as well as near the home. The authors even adjusted the commute route “buffer” based on travel mode: because drivers might deviate farther from their route than other commuters, Burgoine and colleagues counted takeaway outlets within 500 m of the route for drivers and only 100 m for pedestrians and cyclists.

The study population was drawn from the Fenland Study, which is tracking a cohort of adults born in Cambridgeshire, UK, between 1950 and 1975. Consumption of “takeaway food”—defined here as hamburgers, pizza, fried food, and chips—was measured using food frequency questionnaires. Height and weight were measured objectively. Locations of takeaway food outlets, including limited service restaurants offering hot food for eat-in, take-out, or delivery, were compiled from listings maintained by local governments. Only adults working outside the home were included.

Burgoine and colleagues found that people with higher takeaway food exposure had a higher body mass index and were more likely to be obese. Takeaway food exposure also had a modest association with dietary intake: people with the highest exposure ate 5.7 g of takeaway food per day (about half a small serving of French fries per week) more than those with the lowest exposure. For the workplace but not in home or commuting contexts, there was evidence of a dose-response relation in the association between food exposure and diet and weight outcomes. As the authors note, “This result suggests the notion that such consumption [of takeaway foods] is both place and time specific.”

This work takes a step forward by measuring the food environment of the activity space rather than the home neighbourhood. If takeaway or fast food access does influence diet and weight, its effect is likely to be modest in size and moderated by individual and environmental characteristics. Carefully crafted studies like this one can clarify when, where, and for whom the food environment matters.

Nutritional “whack-a-mole” may not work

It is unclear, however, that efforts to restrict takeaway restaurants will have much effect on obesity or population health. Restrictions on food outlets face legal and political obstacles and are difficult to enact.

Moreover, takeaway food has a role in our city, economic, and family life, and restricting it could have costs as well as benefits. Vibrant urban spaces are distinguished by the density of shops and restaurants that fuel the restless activity of city life. A restaurant can promote social capital, serving as a “third place” where people in the neighbourhood gather. Takeaway restaurants provide entry level jobs for young workers and a toehold in the economy for entrepreneurs, including immigrants who may face barriers elsewhere in the labour market. Food-on-the-go also eases the complex lives of families without a stay-at-home parent or partner; it can be a critical convenience for those who work long hours or face long commutes or lack facilities for cooking. Ensuring access to healthy food in supermarkets and farmers’ markets, while important, will not deal with the demand for food away from home.

Instead of restricting takeaway food, we seek to transform it. Healthy takeaway food should not only be available, it should be as visible, tasty, and cheap as unhealthy food. Healthy eating should, in fact, be the default option. It is difficult now to imagine a world in which broccoli rivals chips at the takeaway counter, but small steps in this direction are already being taken. As well as limiting fast food outlets, the Greater London Authority’s Takeaway Toolkit advocates working with industry to offer healthier takeaway foods. In the United States, public agencies have required calorie labelling, banned “trans fat” from restaurant meals, proposed taxing or limiting sales of sugar sweetened beverages, and modified the market basket of foods available under subsidy programmes for low income families. To affect population health, food policy must go beyond action that promotes some types of outlets and curbs others. In the food environment, what matters is the menu—what food is offered, at what price—not the venue.

Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

References are in the version on bmj.com.

Cite this as: BMJ 2014;348:g1817

*RESEARCH, p 12*
Independent Commission on Whole Person Care for the UK Labour Party

Proposals would be good for patients and a big change for doctors

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The Independent Commission on Whole Person Care report for the UK Labour Party proposes that health and social care should do more to support people with long term conditions to become engaged in managing their health and healthcare. The commission goes further than the NHS Plan and the Wanless Report, which contained similar proposals. It highlights that health has physical, psychological, and social domains, and that an integrated understanding of health should inform how public services work with people with long term conditions and how services are organised and paid for locally and nationally.

The terms of reference for the commission required John Oldham and members from voluntary, NHS, local authority care, and social care to identify how to move from “the current system to one where coordinated, fully integrated care is the norm without major structural change and within existing resources.” The report broadly achieves this aim, and brings all the themes of whole person care into one document, which focuses on the needs of people who live with multiple long term conditions. However, in such a wide ranging report, the absence of recommendations on end of life care seems short sighted.

The report’s case for change is well made. It is hard not to agree that care should be organised around what matters to people who live with long term conditions (their personal outcomes, such as maintaining independence), and that the default place for care delivery should be in people’s homes. The organisation of public services to achieve this requires a major shift. Personalised care planning should be the norm, with carers, health and social care teams, and the voluntary sector working together as alliances of care and support providers. Some of this thinking is embedded in current national guidance for England. However, fewer than 4% of people who live with long term conditions currently have a care plan, and an understanding of how diverse organisations can be successfully integrated is only just emerging.

Local organisations need to align around clear objectives to implement this vision. The report proposes that commissioning for outcomes that matter to patients would help achieve this aim, with local integrated teams of providers working together with patients and their carers to create a set of person centred objectives. These teams would work within a single capitated budget, and commissioning responsibility for the system would sit with health and wellbeing boards. Such boards would be the local stewards of health and social care strategy; previous plans to place commissioning within local authorities have clearly been dropped. This systematic integration of physical and mental health and social care would resonate upwards through the whole structure of the NHS, with NHS England becoming Care England and Health Education England becoming Care Education England.

Competition doesn’t have a strong role within this system, and although the document contains some inconsistencies, the overriding message is “care first, competition second.”

The report predicts major changes to clinicians’ work in the future, with primary care working more closely with secondary care, social care, and the voluntary sector, and secondary care doing more to understand whole person care and work more effectively in local communities. The Royal College of General Practitioners and the Royal College of Physicians have already begun this work. But the report makes it clear that hospital specialists need to do much more to engage in the whole person care agenda, proposing that the financial incentives offered by the clinical excellence scheme should be awarded for whole person care. Interestingly, however, the report is relatively light on mechanisms to strengthen primary care, other than proposing that incentives are aligned with local system outcomes. Instead, it focuses on strengthening the (currently means tested) social care system.

Several challenges remain, not least the risk of social care funding being subsumed into health budgets both locally and nationally, and the challenge of embedding person centred outcomes into a system dominated by clinical outcomes data. The report emphasises the role of information in supporting patients to manage their health and proposes that all patients should hold their own care record. However, the current confusion around record sharing across primary and secondary care in the NHS suggests that information governance might prove to be a considerable hurdle.

If fully implemented, the report’s recommendations would bring benefits to patients and substantial changes to the way that doctors work. Public services in the United Kingdom face unprecedented financial challenges, and the real lesson from the report is that we all need to change to ensure the medium term sustainability of public services.

Needed: a seismic shift in thinking

This commission may not herald another structural change, but it does represent a seismic shift in the way we need to think about the delivery of care. The financial, moral, and clinical need for such a shift is clear. As the report highlights, this isn’t just about policy, it is about people’s lives. While appreciating the frustrations of political election cycles, for the sake of people who live with long term conditions, staff, and our health and care system, we can’t delay making whole person care a reality.

Competing interests: AdI has none; AC is a paid consultant for the independent charity the Health Foundation.

Provenance and peer review: Commissioned; not externally peer reviewed

References are in the version on bmj.com.

Cite this as: BMJ 2014;348:g2136

BMJ BLOG, p 41
Therapist guided internet delivered cognitive behavioural therapy

Can be highly effective and is used to increase access to psychological treatment

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There are two main forms of internet delivered cognitive behavioural therapy—fully automated open access programmes without therapist contact and programmes guided by a therapist, which are conducted in a context similar to that of regular healthcare. This editorial focuses on therapy that is guided by a therapist, with scheduling that mirrors face to face treatment.1

Because the mechanisms for improvement are the same for internet delivered cognitive behavioural therapy as for face to face therapy, the patient should be exposed to the same interventions. So, if exposure to a feared object—such as snakes in patients with a phobia about snakes—is important in face to face therapy, then it is equally important in internet delivered therapy. In essence, internet delivered therapy is not a new treatment in itself but rather a new framework for providing psychological treatments.

The patient accesses the treatment through a personal account in a secure internet based treatment platform. The most important elements of the treatment are modules, often eight to 15, whose content reflects that of sessions in face to face therapy and provides patients with the information needed to change their behaviour. The modules mainly consist of text but can also include images and audio and video files. Throughout the treatment, the patient has contact with an identified therapist who provides guidance on how to apply the interventions to the patient’s symptoms.

Contact is provided mainly through a messaging system in non-real time, which resembles email. On average, therapists spend about 10 minutes on each patient per week,2 which is about a quarter of the time spent in face to face therapy. Evidence suggests that therapist contact, as compared with unguided internet-delivered therapy, is associated with larger treatment effects.3 Because the module content is relatively inflexible, diagnostic assessment before the treatment starts is at least as important as in face to face therapy.

Internet delivered cognitive behavioural therapy has several advantages. Firstly, and perhaps most importantly, it can drastically increase accessibility to effective treatment. In most countries common barriers to conventional cognitive behavioural therapy include lack of therapists but also stigma and difficulty in taking time off from work to attend therapy.4 5 Internet delivered therapy avoids these problems because each therapist can treat up to 80 patients simultaneously and the lack of face to face appointments means that geographical separation is not a problem.

A second advantage is that internet delivered therapy provides an excellent framework for testing the relative effects of treatment components because large scale trials can be conducted with limited resources. For example, in a recent randomised controlled trial that tested internet delivered exposure therapy against stress management for irritable bowel syndrome, all 195 patients could be treated simultaneously by only six therapists.6 Finally, because internet delivered cognitive behavioural therapy saves time, limited therapist resources can be devoted to those patients who require intensive face to face treatments.

For what problems does internet delivered cognitive behavioural therapy work and how effective is it? A recent systematic review showed that therapist guided internet delivered therapy has been evaluated for 25 clinical disorders in at least 103 randomised trials since 2000.7 Internet delivered therapy has been developed for most common psychiatric disorders, such as anxiety disorders and depression, but applications also include functional disorders such as tinnitus, irritable bowel syndrome, chronic pain, and sexual dysfunction. The disorders for which the therapy currently has strong empirical support are depression, social anxiety disorder, and panic disorder.7

A meta-analysis of 13 randomised trials, mostly of these three disorders, which compared internet delivered cognitive behavioural therapy with face to face therapy, found that the between group effect across all studies was g=−0.01 (95% confidence interval −0.13 to 0.12).8 This suggests no significant difference between the two treatment approaches and that the effect of the intervention type is likely to be small. Because there were relatively few studies, the results should be interpreted with caution, but they suggest that internet delivered therapy could be as effective as face to face therapy for some of the most common psychiatric disorders. Studies of the long term effect of internet delivered therapy show that treatment effects can last up to five years after the completion of therapy.9

Now part of regular healthcare in some countries

Internet delivered cognitive behavioural therapy has been implemented as part of regular healthcare in the Netherlands10 and Australia.11 In Stockholm, Sweden, the ICBT Clinic has treated more than 3000 patients with depression, social anxiety disorder, or panic disorder with internet delivered therapy in the context of regular psychiatric care, which is subsidised by a national health system. Therapy is integrated within a regular outpatient clinic at a university hospital and patients receive care on the same terms as patients within conventional psychiatric care. Patients can self refer, and treatments are provided by licensed psychologists, with psychiatrists conducting diagnostic assessments before and after treatment. Studies suggest that internet delivered therapy provided in this routine setting can be as effective as in published randomised trials.12

Although internet delivered cognitive behavioural therapy has been generally well studied, several important challenges remain. These include testing treatments against face to face therapy in non-inferiority trials, developing and testing treatments for children and adolescents, and, not least, ensuring that treatments have strong empirical support.

Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed

References are in the version on bmj.com.

Cite this as: BMJ 2014;348:g1977