Hard To Swallow

Animal experiments for obesity

A report by

The Dr Hadwen Trust for Humane Research

Dr Hadwen Trust
Replacing Animals in Medical Research

The Dr Hadwen Trust

The Dr Hadwen Trust is the UK's leading medical research charity that funds and promotes exclusively non-animal techniques to replace animal experiments. Our vital work benefits humans with the development of more relevant and reliable science whilst also benefiting laboratory animals. We believe that excellence in medical research can and should be pursued without animal experiments.

Our portfolio of high-quality, peer-reviewed and innovative research combines strict ethical principles with scientific excellence, and has involved projects in a range of fields including epilepsy, cancer, meningitis, asthma, diabetes, drug testing, arthritis, Alzheimer's disease, lung injury, whooping cough, vaccine testing, dentistry, heart disease, tropical illness, fetal development and pregnancy, brain tumours and AIDS. The Dr Hadwen Trust is internationally recognised as a leading authority on replacing animal experiments and actively promotes the concept and practice of non-animal research through publications, workshops, debates and the media.

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In the UK there are 24 million overweight or obese people

Obesity – a global epidemic:

Human obesity[1] is a major global epidemic. There are 300 million obese people today and almost 1 billion overweight adults. In this country obesity is thought to be responsible for more than 9,000 premature deaths each year, and the prevalence of obesity and overweight is rising at alarming rates. Obesity in children aged under 11 increased from 9.9 per cent in 1995 to 13.7 per cent in 2003[2]. The number of children who are demonstrably obese has trebled since the 1980s, and more than half of all UK adults are either overweight or obese. That's an astounding 24 million adults. In the USA the situation is even more worrying - where extreme obesity affects one in twenty.

Without question, obesity is a major social and health issue for the 21st century. However, in order to tackle it effectively, it is imperative that we focus our attention and resources in those areas that are likely to yield positive and meaningful results. Animal research conducted in the name of obesity is not the key to a solution. Not only does it cause animal suffering, it is also a distraction from the real socio-economic, dietary and lifestyle issues that we need to address on a global scale.

[1] Obesity is extreme overweight. It is usually defined as a Body Mass Index of 25 or more. Body Mass Index is calculated by dividing the subject's weight in kilograms by the square of his/her height in metres (BMI = kg/m^2).
[2] Health Survey for England: Obesity among children under 11, published April 2005, National Centre for Social Research, Department of Epidemiology and Public Health at the Royal Free and University College Medical School.

Animal experiments:

A range of animal experimentation is undertaken in the field of obesity research, claiming to address the processes which lead to human overweight and obesity and the provision of a 'cure'. In the UK this research uses mainly rodents (rats and mice) and non-human primates (monkeys), in often invasive, stressful and ultimately terminal experiments. Experiments range from subjecting monkeys to invasive brain research where electrodes are used to study how the brain interacts with the senses and hormonal systems which influence food choices and satiety mechanisms; to genetically modifying rats or mice to produce 'obese' animals, a process which itself involves immense wastage (a high percentage of animals are killed because of failure to express the desired gene) as well as physical discomfort, and pain or distress caused by gene alterations leading to diabetes, liver disorders and high blood pressure.

Ethical & scientific opposition to animal experimentation:

The Dr Hadwen Trust is ethically opposed to all experiments on sentient animals. We believe that deliberately harming non-consenting individuals who will not benefit from an experiment, cannot be morally justified. It is clearly established that other animals have a shared ability to feel pain as well as psychological distress, indeed British and European Union legislation specifically classifies an animal experiment (procedure) as that likely to cause "*pain, distress, suffering or lasting harm*"[3].

The brain centres and circuits that underlie the unpleasant emotional aspects of pain, including fear, anxiety, memory and anticipation, are not unique to humans. In obesity research, as with all areas of animal research, it is important to look at the totality of suffering for those animals involved in experiments. As we will see, factors such as long-haul flight transportation from the USA to the UK (importing live genetically modified rodents is still very common); single housing; regular handling or restraint, sampling and injections; unnatural and sterile laboratory conditions eg: artificial lighting,

[3] Animals (Scientific Procedures) Act 1986, page 2 paragraph 2(1), published HMSO.

"The 'obesity epidemic' is entirely related to lifestyle changes which are, in the end, human choices. It is completely unjust – and scientifically dubious – to experiment on animals in obesity-related research. Where needed, this research should be conducted using non-animal methods: in the test tube, with the help of human volunteers and in population-level studies. This human approach will save animals from suffering and avoid reliance on overly simplistic animal tests which can be misleading when applied to people."

Dr Gill Langley
Science Director – Dr Hadwen Trust

excessive noise, small metal caging, food or water restriction, insufficient environmental enrichment etc. – all these and more can add to an animal's stress and distress, particularly in the case of highly sentient animals like non-human primates. In addition to this is the suffering caused by the experimental procedures, and of course the fact that in almost all cases the animals will be killed at the end of the experiment.

From a scientific perspective, the Dr Hadwen Trust believes that animal experiments have significant limitations which are of particular concern given the degree of confidence that is generally placed in them, invariably without proof of validity. Species differences in anatomy, metabolism, physiology or

pharmacology inevitably will arise, underlain by further species-specific genetic variations. Even subtle molecular differences can have a significant effect on the validity of results for extrapolation from animals to humans.

In the case of obesity research, we believe that animal experiments are a scientifically inappropriate, often simplistic and wholly unnecessary route of enquiry which can never hope to usefully replicate the multifactorial nature of obesity. Human obesity has been shown to involve not only excessive food intake, low energy expenditure, and many genes (except in cases of rare single gene obesity conditions), but also ethnicity, gender, age, socio-economic status, smoking status and other factors. Human culture, environmental, socio-economic and psychological factors play a very large role in food choice and consumption.

It is simply not possible to replicate these significant factors in animal experiments, and often used mechanisms such as 'food reward' are too simplistic to make meaningful comparisons with humans. Genetic (and transgenic[4]) studies in other animals are flawed too, as the genetic factors that contribute to human obesity involve multiple genes (except in extremely rare cases) whereas classic animal models have a single gene mutation.

[4] Transgenic means inserting an unnatural gene into animals.

Non-human primates are used in UK obesity research © PETA

Recent UK obesity animal experiments:

University of Oxford[5]: The brain and mechanisms underlying taste, appetite and the signals of satiety.

Researchers at the University of Oxford have, since the 1970s, been using non-human primates to identify areas of the brain involved in the control of eating, especially taste and the range of sensations. Data from humans have indicated there are complex processes reinforcing the eating of high-energy food, including taste and texture. The researchers in Oxford have used invasive brain recording methods with electrodes to look at taste in primates, (usually Rhesus macaques) and the areas of the brain responsible for representing the rich sensory properties of food especially temperature, texture and viscosity. The researchers have also looked at satiety mechanisms in primates and how appetite is related to associations with other stimuli.

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[5] The primate amygdala: neuronal representations of the viscosity, fat texture, temperature, grittiness and taste of foods. 2005. *Neuroscience* 132:33-48.

Eating and its various disorders in humans is complex and multidimensional. Animals, including us, have evolved to eat when food is available and to respond in very specific ways to food. It is too simplistic to compare the food reward and satiety mechanisms in non-human primates (particularly primates kept in unnatural laboratory conditions) with those in normal or overweight humans. Human culture and psychological factors play a very large role in food choice and consumption. Obesity involves not simply eating for physical or emotional reasons but also involves various genetic factors which have evolved within human cultures.

Invasive brain recording methods with electrodes involve opening the monkey's skull (under anaesthesia) and if the experiments are long-term, a small box is cemented to the opened skull with various electrodes inserted deep into the brain. The raw edges of the cut scalp and skull can cause the animals physical pain and enduring having a permanent box of electrode holders and cables running to recording equipment is likely to cause additional distress during and between test sessions.

Although not made clear in the published papers, brain recording will almost inevitably involve some kind of physical restraint, either head-only or head and body. Particularly in the case of larger primates such as macaques, both the physical restraint methods and the handling which is involved in the testing of different forms of food, will lead to further distress and discomfort, particularly arising from their inability to exhibit their most natural 'flight' response – escape. This is exacerbated when testing over long periods, as physical and psychological stress are likely to increase from being subjected to repeated sets of tests, as well as from living in a completely artificial and restricted environment. This will be particularly distressing to highly mobile and sentient animals like primates who are social, agile and inquisitive animals and who will also be emotionally affected by the distress of cage mates or others enduring procedures in the same room.

An 'obese' mouse and a normal mouse.

University of Newcastle[6] & Imperial College London[7]: Genes & obesity

There are many 'naturally' bred overweight and obese rodent strains such as the ob/ob and the agouti mouse and the Zucker rat. These animals are used extensively in the UK and USA to study the metabolic factors controlled by either single genes or sets of genes. Zucker rats show disorders in insulin control (found in diabetes) and are used to trace the role of hormones and other molecules in obesity.

Researchers at the University of Newcastle used Zucker rats in an attempt to understand the role of leptin in sugar metabolism in the liver and the onset of diabetes-like features. Young Zucker rats had liver cells removed and tested for the various enzymes involved in insulin and leptin activity. No detail was given as to how the liver cells were obtained from the rats, but it is a reasonable assumption that the animals were killed and their liver removed.

Research undertaken at Imperial College, London also used 'naturally' obese rodents - agouti mice - to investigate how a defective signaling process in the brain might impact on satiety and feeding - and hence induce obesity - in humans. A breeding colony was set up from animals purchased from the

[6] Increased sensitivity of glycogen synthesis to phosphorylase-a and impaired expression of the glycogen-targeting protein R6 in hepatocytes from insulin-resistant Zucker fa/fa rats. 2006. *FEBS Journal* 273:1989-1999.
[7] Pre-obese and obese agouti mice are sensitive to the anorectic effects of peptide YY3-36 but resistant to ghrelin. 2004. *Int. J. Obesity* 28:886-893.

USA. It is not uncommon for animals used in laboratory experiments to be imported from overseas; in 2005 there were 13,479 mice alone used in UK experiments who were sourced from outside the UK[8]. Mortality is likely to be a problem when flying animals long distance, and conditions in transit are often cramped and vulnerable to rough handling and temperature differences.

During the experiments at Imperial College, the animals were individually caged despite the fact that isolation of animals (particularly over time) can in itself cause additional distress. The mice also had to endure a series of injections into their body cavities, also likely to cause stress and pain. Furthermore, if severely obese, animals such as those used in these experiments could suffer movement problems and possible damage in ways which can be seen in obese humans, such as varicose blood vessels and joint pain.

At the end of the procedure, the mice were killed by carbon dioxide (CO_2) inhalation which has been the subject of intense discussion as an inhumane method of euthanasia. Recent reports, including one by the UK government's Animal Procedures Committee published in 2006[9], assert that CO_2 is 'aversive' (unpleasant) in rats and mice. Studies indicate that its use in euthanasia can, in some circumstances, cause the animals physical pain.

As indicated earlier in this report, human obesity is a complex multifactorial condition that has been shown to involve not only excessive food intake, low energy expenditure, many genes (except in cases of rare single gene obesity), but also ethnicity, gender, age, socio-economic status, smoking status and other factors. Experiments using rodents carrying either single or a few genes related to weight gain cannot hope to model this complexity.

Human obesity develops within the context of learned food preferences, emotional triggers, environmental pressures and poor lifestyle patterns. For example, limitless access to high-calorie foods, comfort eating when

[8] *Statistics of Scientific Procedures on Living Animals*, Great Britain 2005 (Published Home Office, July 2006).
[9] Review of schedule 1 of the Animals (Scientific Procedures) Act 1986 Appropriate methods of humane killing December 2006, page 8.

depressed, learned poor nutrition or limited exposure to healthy foods from childhood, and societal (including advertising) pressure to associate certain high-fat high-sugar foods with enhanced mood or lifestyle. Most of these factors and more are either completely absent from these animal studies, or minimized to such a degree as to have no value whatsoever.

Inherited genetic propensities in humans have been shown to be involved in almost all kinds of energy processing in the body, including maintenance of body weight and the effectiveness of dietary and physical activity and their usefulness in treating obesity and overweight. But all these genetic factors involve multiple genes, whereas classic animal models like the Zucker rat and ob/ob mouse have a single gene mutation implicated in their weight disorders. Even though studies of human genetic predisposition and environmental factors in obesity and overweight are complicated by variations between individuals, they are not confounded by species variations.

Mice are routinely used in gene-altering experiments

Edinburgh University[10] & University College London[11]: Transgenic animal models for studying obesity

The creation of transgenic and 'knockout' animal models - rats and mice with artificially altered genes - has recently been used to investigate the involvement of genes in obesity. To date more than 500 animal 'models' have been generated to address the function and role of fat tissue and weight balance. Mice are the favoured rodent because they are easiest to genetically modify (as well as cheap and easy to breed and house in large numbers) and the main focus has been on how genes control the presence and activity of specific molecules in the fat tissue, which might play a role in obesity.

Researchers at Edinburgh University used genetically modified mice to look at various enzymes which influence glucose and fat metabolism and the steps leading to obesity. The mice suffered from mild diabetes, liver disorders and high blood pressure, all associated with the altered gene. In humans these

[10] Metabolic syndrome without obesity: Hepatic over-expression of 11-B-hydroxysteroid dehydrogenase type 1 in transgenic mice. 2004. *PNAS* 101:7088-7093.
[11] Critical role for peptide YY in protein-mediated satiation and body-weight regulation. 2006. *Cell Metabolism* 4:223-233.

conditions are accompanied by mood disorders, pain and discomfort. In addition the mice became obese, resulting in persistent discomfort and stress. Again, animals in this study were singly housed and subjected to blood sampling - both cause stress and the latter, if handled badly, can be painful.

At University College London scientists used genetically modified mice to examine satiety and the role of gut hormones. The mice had been modified to be resistant to satiety (in other words, they did not become 'full up') as well as the weight-reducing effects of a particular gut hormone. Here again, mice were singly housed and given injections into the abdominal cavity, both likely to cause stress and in the latter, pain. Animals also had infusion pumps surgically implanted in their backs; as no details of analgesia were given in the paper, it can only be assumed that the mice also may have endured pain following from this procedure. The startlingly obvious conclusion of one set of experiments showed "*that through alteration of specific diet constituents a rational therapy for obesity*" could be devised. Hardly groundbreaking news to those who reduce their intake of calories in order to lose weight.

As has been previously stated, genetically modified animals are created to study one or a small set of genes and their role in bodily processes. By contrast, human obesity is mainly not genetic and anyway, rarely involves a single gene. These experiments in mice succeed only in demonstrating with certainty how mouse genes operate within a uniquely mouse context. Genetically modified animals also show compensatory mechanisms which change simple gene effects, a process that may well mask 'normal' interactions between genes or sets of genes and bodily processes, including those which lead to weight gain and obesity.

The creation of genetically modified animals involves both wastage of animal lives and can cause significant stress. In general, manipulated embryos in gene transfer are very likely to die, with only 20% to 30% surviving to birth and only about 25% of these full-term embryos actually incorporating the transgene. Any newborn animals who do not express the desired transgene,

will simply be killed. The next set of offspring from these 'founder' mice also do not always carry the transgene and if the embryos do survive and become adult, they can succumb to a variety of diseases such as diabetes, liver disorders and high blood pressure. These conditions may be accompanied by mood disorders, tiredness, lethargy and a propensity to suffer strokes and heart attacks.

The capacity to suffer of such small animals as mice should never be underestimated. Despite their small size, mice are sentient and sensitive creatures. Obesity in mice has the potential to result in physical discomfort and pain, and the relentless routine of blood sampling, surgery, handling, injections, not to mention the social isolation and insecurity of single housing, in restricted and often sterile laboratory environments, can cause an accumulation of stress and distress – outcomes which themselves have the potential to affect test results.

Advanced non-animal test methods are available

A better way forward: non-animal research approaches

The more someone is overweight the greater is their risk of a variety of serious health conditions, including: diabetes mellitus, high blood pressure, heart disease, strokes, sleep disorders, a variety of cancers and a host of psychological problems, including severe depression. Many hypotheses have been put forward to explain the current epidemic of life-threatening weight increase globally, but it is clear that present-day lifestyles promote weight gain. Increased dietary energy intake (especially high fat and sugary food and 'super-sized' portions) coupled with decreased energy expenditure through less daily physical activity, stimulates fat deposition.

People make complex choices in the food they eat, the quantities consumed and the lifestyles that they embrace, especially how active they are. Additionally, food composition and meal size is influenced by taste, psychological factors such as emotion and loneliness and family setting and broad cultural norms. Significant national variations in obesity prevalence also exist, detailed human-based studies of which point to cultural factors

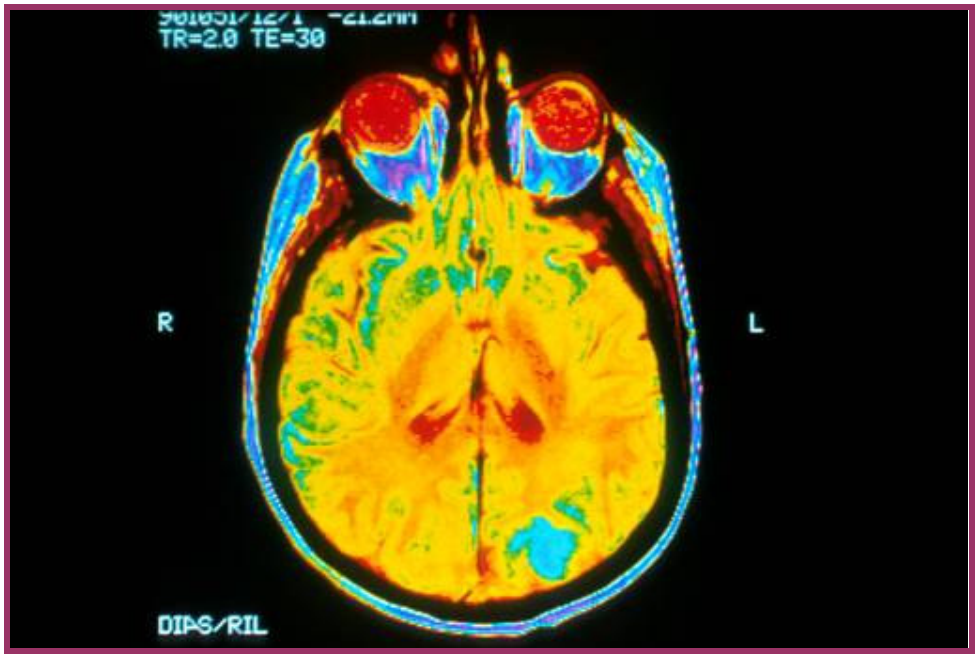
being central[12] - obesity is only half as common in Sweden as in the USA. So, trying to understand human obesity and overweight by using 'surrogate' animals and looking at isolated elements such as metabolism, simple genetic factors or how the brain influences taste, is not the answer.

Far more relevant and ethical approaches are already yielding a huge amount of data directly applicable to the human situation. For example, a great deal has already been learnt about how some people are especially susceptible to obesity and overweight, from human volunteer and clinical studies. Studies of human populations also hold great promise in understanding the role of genes and the interaction with environmental factors in weight control.

The researchers at the University of Oxford conducting invasive brain electrode experiments in monkeys, also conducted simultaneous non-invasive functional magnetic resonance imaging experiments using human volunteers and patients. Neuroimaging techniques like fMRI are a safe and non-invasive method which follow changes in the brain when tissues are actively working such as responding to colour in the outside world or the taste of food. fMRI can be used together with other imaging techniques to provide a good picture of neurological processes and activity.

Animal scientists often argue that imaging in volunteers cannot provide the same data (single cell activity) as electrode experiments in animals. This is true, however we argue that the data provided by human studies is far more informative and relevant in ways that animal studies can never achieve. This is particularly the case with understanding human appetite (particularly the role of taste and smell individually and together) and the brain regions involved. Indeed these human studies performed by the Oxford group yielded information of particular value since the human subjects were able to talk about various cognitive aspects of food, including the names of food and their

[12] see R J Stubbs and B J Tolkamp. 2006. Control of energy balance in relation to energy intake and energy expenditure in animals and man: an ecological perspective. *British J. Nutrition* 95: 657-676: D D Hensrud & S Klein. Extreme obesity: a new medical crisis in the United States. 2006. *Mayo Clinic Proc.* 81: S5-10; and P G Kopelman. Obesity as a medical problem. 2006. *Nature* 404: 635-643.



Human brain imaging offers more relevant data © NCI

visual preferences. Using human volunteers provided high resolution information which paralleled, and was of far more relevance than, that obtained from the non-human primates. It is absurd (but sadly not uncommon) that such invasive brain experiments on highly sentient primates were permitted when more relevant human-based research techniques were not only preferable and available, but being utilized by the same research team.

For genetic studies, cells and tissue from obese and non-obese human volunteers can produce information of more relevance to treating chronically obese humans than potentially misleading animal experiments. These cells can have their proteins and other natural chemicals compared, together with the genes which they possess and the gene activities, to investigate possible links with energy metabolism, for example.

Studies of human genetic predisposition and environmental factors in obesity and overweight conditions, take into account significant variations between individuals, human variations that animal studies can never replicate. Families and children, including twins, can be compared in volunteer studies, to see

which factors related to obesity are lifestyle-based and which might be gene-based. Are there common genes in obese families, for example? Do people with other metabolic problems like diabetes have genes which possibly play a significant role? How might this be dealt with by changing habits and diet?

Conclusion:

Human obesity is largely a disease of post-industrial society. Understanding the disease and finding effective ways to control the epidemic will come from changing our attitudes, certain foods and their composition, as well as our patterns of activity. Encouraging healthy diets and regular exercise on a wide scale from childhood and beyond, has a vital role to play. Non-invasive and human volunteer-based (non-animal) research techniques such as advanced functional neuroimaging can give data of far more relevance to understanding human appetite (particularly the role of taste and smell individually and together) and the brain regions involved. This gives information of particular value since the subjects are able to talk about various cognitive aspects of food, including the names of foods and their visual preferences. Researchers can also utilize clinical or volunteer samples of human cells and tissues which can produce information of more relevance to treating chronically obese humans.

If current obesity trends persist, it is estimated that by 2010 there will be an astounding 6,658,953 obese men and 6,000,000 obese women in the UK[13]. Clearly something more effective than the current strategy needs to be employed.

The Dr Hadwen Trust believes that dispensing with animal experiments – which waste lives and valuable resources – and utilizing a combination of human-specific, non-animal approaches coupled with targeted nutrition/lifestyle programmes, will provide far more relevant and reliable routes to tackling obesity, for the benefit of humans and animals.

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[13] Forecasting Obesity to 2010, Paola Zaninotto, Heather Wardle, Emmanuel Stamatakis, Jennifer Mindell and Jenny Head, Joint Health Surveys Unit (National Centre for Social Research and Department of Epidemiology and Public Health at the Royal Free and University College Medical School) published August 2006, for the Department of Health).

"I believe that going vegetarian is one of the most effective ways to be kind to yourself as well as to animals and the planet. Vegetarians are far less likely to suffer from obesity, coronary heart disease, high blood pressure and cancers. We don't need painful animal experiments to tell us that following a balanced, healthy diet low in saturated fat, cholesterol and animal protein, coupled with banishing the sedentary lifestyle, is the key to tackling obesity. I believe that animals should not suffer so that we can eat them, particularly when doing so can be so harmful to us. I also believe that animals should not suffer in laboratories so that we can seek answers to human problems for which we already have the solutions."

Rose Elliot MBE
Vegetarian Cook

Beat obesity - Go veggie!

Changing to a vegetarian or vegan diet, and getting active, can be a great way to lose weight as well as help to eliminate animal suffering from your lifestyle. In the UK alone, a staggering 850 million animals and hundreds of millions of fish are killed every year for human consumption - that's more than three million animals a day, with the average meat-eater consuming around 2,000 animals in their lifetime (excluding fish). Vegetarians do not eat meat,

poultry, game, fish and slaughterhouse by-products such as gelatine and animal fats. Instead, a balanced vegetarian diet includes a huge variety of nutritious and delicious foods such as fruits, vegetables, legumes, grains, seeds, nuts, tofu and other soya (as well as dairy products and free-range eggs, unless you go vegan and cut eggs and dairy too!).

There is no doubt that going veggie or vegan is a healthy option. According to the American Dietetic Association, "*Vegetarian diets offer a number of nutritional benefits, including lower levels of saturated fat, cholesterol, and animal protein as well as higher levels of carbohydrates, fiber, magnesium, potassium, folate, and antioxidants such as vitamins C and E and phyto-chemicals. Vegetarians have been reported to have lower body mass indices than non-vegetarians, as well as lower rates of death from ischemic heart disease; vegetarians also show lower blood cholesterol levels; lower blood pressure; and lower rates of hypertension, type 2 diabetes, and prostate and colon cancer.*[14]"

In one study published in the British Medical Journal, researchers studied 3,947 men and 17,158 women during 1994 and 1995, including meat-eaters and vegetarians. The report stated that, "*Among both men and women, mean body mass index was highest among the meat eaters, lowest among the vegans, and intermediate among the fish eaters and vegetarians… Among the meat eaters, after adjustment for age, 6.4% of the men and 9.2% of the women were clinically obese (body mass index >30) … In contrast, the prevalence of obesity was well within these targets in all the groups that did not eat meat."* The report concluded that "*These data suggest that a meat free diet is associated with a low prevalence of obesity.*[15]"

A separate study by EPIC-Oxford (a UK cohort of the European Prospective Investigation into Cancer and Nutrition) recruited people with a range of diets between 1993 and 1999. The study found that nutrient intake differs

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[14] Position of the American Dietetic Association and Dietitians of Canada: Vegetarian diets. *J. American Dietetic Assoc.* 2003. 103:748-765.

[15] Key T, Davey G. 1996. Prevalence of obesity is low in people who do not eat meat, *British Medical Journal* 313:816-817.

substantially between meat-eaters and vegetarians or vegans. "*… the prevalence of obesity is much lower in vegetarians than in meat-eaters … [T]he lowest weight gain seen over a five-year period was seen among those who had changed to a diet containing less animal foods.*[16]"

Take action:

You can help the Dr Hadwen Trust replace animal experiments with cutting-edge non-animal research techniques, by supporting our work. To make a donation or to become a member, contact us at:

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If you have a problem with obesity and you would like to go veggie, here are some key resources to help you. Before making any change to your diet or exercise regime, always consult your doctor.

Viva! (Vegetarians International Voice for Animals)
8 York Court
Wilder Street
Bristol, BS2 8QH
Tel: 0117 944 1000
www.viva.org.uk

People for the Ethical Treatment of Animals
PO Box 36668
London SE1 1WA
United Kingdom
Tel: 020 7357 9229
www.peta.org.uk

Dr Gillian McKeith – holistic nutritionist
www.drgillianmckeith.com

Rose Elliot – vegetarian cook
www.roseelliot.com

[16] For further information go to www.epic-oxford.org