



# The *big fat* truth

*More and more studies show that being overweight does not always shorten life — but some public-health researchers would rather not talk about them.*

BY VIRGINIA HUGHES

**L**ate in the morning on 20 February, more than 200 people packed an auditorium at the Harvard School of Public Health in Boston, Massachusetts. The purpose of the event, according to its organizers, was to explain why a new study about weight and death was absolutely wrong.

The report, a meta-analysis of 97 studies including 2.88 million people, had been released on 2 January in the *Journal of the American Medical Association (JAMA)*<sup>1</sup>. A team led by Katherine Flegal, an epidemiologist at the National Center for Health Statistics in Hyattsville, Maryland, reported that people deemed 'overweight' by international standards were 6% less likely to die than were those of 'normal' weight over the same time period.

The result seemed to counter decades of advice to avoid even modest weight gain,

provoking coverage in most major news outlets — and a hostile backlash from some public-health experts. "This study is really a pile of rubbish, and no one should waste their time reading it," said Walter Willett, a leading nutrition and epidemiology researcher at the Harvard school, in a radio interview. Willett later organized the Harvard symposium — where speakers lined up to critique Flegal's study — to counteract that coverage and highlight what he and his colleagues saw as problems with the paper. "The Flegal paper was so flawed, so misleading and so confusing to so many people, we thought it really would be important to dig down more deeply," Willett says.

But many researchers accept Flegal's results and see them as just the latest report illustrating what is known as the obesity paradox. Being overweight increases a person's risk of diabetes, heart disease, cancer and many

ILLUSTRATION BY GARY NEIL



other chronic illnesses. But these studies suggest that for some people — particularly those who are middle-aged or older, or already sick — a bit of extra weight is not particularly harmful, and may even be helpful. (Being so overweight as to be classed obese, however, is almost always associated with poor health outcomes.)

The paradox has prompted much discussion in the public-health community — including a string of letters in *JAMA* last month<sup>2</sup> — in part because the epidemiology involved is complex, and eliminating confounding factors is difficult. But the most contentious part of the debate is not about the science per se, but how to talk about it. Public-health experts, including Willett, have spent decades emphasizing the risks of carrying excess weight. Studies such as Flegal's are dangerous, Willett says, because they could confuse the public and doctors, and undermine public policies to curb rising obesity rates. "There is going to be some percentage of physicians who will not counsel an overweight patient because of this," he says. Worse, he says, these findings can be hijacked by powerful special-interest groups, such as the soft-drink and food lobbies, to influence policy-makers.

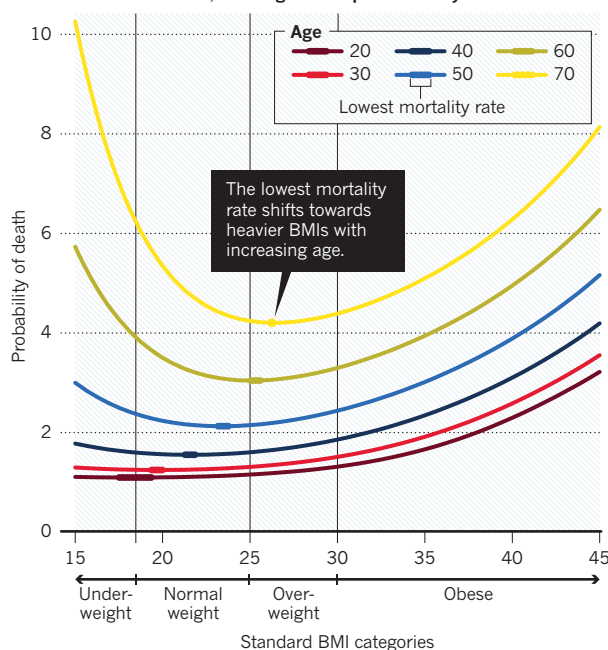
But many scientists say that they are uncomfortable with the idea of hiding or dismissing data — especially findings that have been replicated in many studies — for the sake of a simpler message. "One study may not necessarily tell you the truth, but a bulk of studies saying the same thing and being consistent, that really is reinforcing," says Samuel Klein, a physician and obesity expert at Washington University in St Louis, Missouri. "We need to follow the data just like the yellow brick road, to the truth."

### THROWING A CURVE

The notion that excess weight hastens death can be traced back to studies from the US insurance industry. In 1960, a thick report based on data from policy-holders at 26 life-insurance companies found that mortality rates were lowest among people who weighed a few kilograms less than the US average, and that mortality climbed steadily with weight above this point. This spurred the Metropolitan Life Insurance Company (MetLife) to update its table of 'desirable weights', creating standards that were widely used by doctors for decades to come.

In the early 1980s, Reubin Andres, who was the director of the US National Institute on Aging in Bethesda, Maryland, made headlines for challenging the dogma. By reanalysing

**WEIGHT WATCHING**  
In some studies, being overweight is associated with increased survival time, creating a U-shaped mortality curve.



actuarial tables and research studies, Andres reported that the relationship between height-adjusted weight and mortality follows a U-shaped curve. And the nadir of that curve — the weight at which death rates are lowest — depends on age (see 'Weight watching'). The weights recommended by MetLife may be appropriate for people who are middle-aged, he calculated, but not for those in their 50s or older<sup>3</sup>, who were better off 'overweight'. It was the first glimmer of the obesity paradox.

Andres's ideas were roundly rejected by the mainstream medical community. In an often-cited *JAMA* paper<sup>4</sup> published in 1987, for example, Willett and JoAnn Manson, an epidemiologist at the Harvard School of Public Health, analysed 25 studies of weight–death relationships and claimed that most were tainted by two confounders: smoking and sickness. Smokers tend to be leaner and die earlier than non-smokers, and many people who are chronically ill also lose weight. These effects could make thinness itself seem to be a risk.

Manson and Willett backed up that idea in a 1995 report that analysed body-mass index (BMI) — the 'gold-standard' measure of weight, defined as weight in kilograms divided by height in metres squared — in more than 115,000 female nurses enrolled in a long-term health study<sup>5</sup>. When the researchers excluded women who had ever smoked and those who died during the first four years of the study (reasoning that these women may have had disease-related weight loss), they found a direct linear relationship between BMI and death, with the lowest mortality at BMIs below 19. (That is about 50 kilograms for a woman

who is 1.63 metres tall.)

"It didn't seem to be biologically plausible that overweight and obesity could both increase the risk of life-threatening diseases and yet lower mortality rates," Manson says. The study proved, she says, that this idea "was more artefact than fact".

Around the same time, the world was waking up to obesity. Since 1980, rates of overweight and obesity had begun to rocket<sup>6–8</sup>, and in 1997, the World Health Organization (WHO) held its first meeting on the subject, in Geneva, Switzerland. That meeting resulted in the introduction of new criteria for 'normal weight' (BMI of 18.5–24.9), 'overweight' (BMI of 25–29.9) and 'obese' (BMI of 30 or higher). In 1998, the US Centers for Disease Control and Prevention (CDC) lowered its BMI cut-offs to match the WHO's classifications. "We used to call [obesity] the Cinderella of risk factors, because nobody was paying attention to it," says Francisco Lopez-Jimenez, a cardiac physician at the Mayo Clinic in Rochester, Minnesota. They were now.

### STATISTICAL SPARRING

Flegal was one of those raising the alarm. At the statistics centre, which is part of the CDC, she has at her fingertips data from the agency's National Health and Nutrition Examination Survey (NHANES). Based on interviews and physical examinations of about 5,000 people a year, the NHANES has been running since the 1960s. Flegal and her colleagues used it to show that rates of overweight and obesity in the United States were climbing<sup>6,7</sup>.

In 2005, however, Flegal found that NHANES data confirmed Andres's U-shaped mortality curve. Her analysis showed that people who were overweight — but not obese — had a lower mortality rate than those of normal weight, and that the pattern held even in people who had never smoked<sup>9</sup>.

Flegal's study got a lot of press, says Willett, because she works at the CDC and it seemed to be a sanction for gaining weight. "A lot of people interpreted this as being the official statement of the US government," he says. Just as they did earlier this year, Willett and his colleagues criticized the work and put together a public symposium to discuss it. The academic kerfuffle drew a lot of negative media attention to Flegal's study. "I was pretty surprised by the vociferous attacks on our work," says Flegal, who prefers to focus on the finer points of epidemiological number-crunching, rather than the policy implications of the resulting statistics. "Particularly initially, there were a lot of misunderstandings and confusion about our

findings, and trying to clear those up was time-consuming and somewhat difficult.”

Over the next few years, other researchers found the same trend, and Flegal decided to carry out the meta-analysis that she published earlier this year<sup>1</sup>. “We felt it was time to put all of this stuff together,” she says. “We might not understand what it all means, but this is what’s out there.” Her analysis included all prospective studies that assessed all-cause mortality using standard BMI categories — 97 studies in total. All the studies used standard statistical adjustments to account for the effects of smoking, age and sex. When the data from all adult age groups were combined, people whose BMIs were in the overweight range (between 25 and 29.9) showed the lowest mortality rates.

The Harvard group contends, however, that Flegal’s approach did not fully correct for age, sickness-related weight loss and smoking. They say that the effect would have vanished in younger age groups if Flegal had separated them out. They also argue that not all smokers have the same level of exposure — people who smoke heavily tend to be leaner than occasional smokers, for example — so the best way to remove smoking as a confounder is to focus on people who have never smoked. Willett points to one of his studies<sup>10</sup>, published in 2010, that was not included in Flegal’s analysis because it did not use standard BMI categories. Analysing data from 1.46 million people, Willett and his colleagues found that among people who have never smoked, the lowest mortality occurs in the ‘normal’ BMI range, of 20–25.

Flegal, in turn, criticizes the Willett study for scrapping large swathes of the raw data set: nearly 900,000 people in all. “Once you delete such large numbers, and they are really large, you don’t quite know how the never-smokers in the sample differ from the others,” she says. Never-smokers could be richer or more educated, for example. What is more, says Flegal, Willett’s study relies on participants’ self-reported heights and weights, rather than objective measures. “It’s a huge deal,” Flegal says, because people tend to underestimate how much they weigh. This could skew death risks upwards if, for example, people who are obese and at high risk say that they are merely overweight.

## HEALTHY BALANCE

Many obesity experts and health biostatisticians take issue with the harsh tone of Willett’s statements about Flegal’s work. They say that there is merit in both Willett’s and Flegal’s studies, that the two are simply looking at data in different ways and that enough studies support the obesity paradox for it to be taken seriously. “It’s hard to argue with data,” says Robert Eckel, an endocrinologist at University of Colorado in Denver. “We’re scientists. We pay attention to data, we don’t try to un-explain them.”

What they are trying to explain is the reason for the paradox. One hint lies in the growing number of studies over the past decade showing that in people with serious illnesses such as heart disease, emphysema and type 2 diabetes, those who are overweight have the lowest death rates. A common explanation is that people who are overweight have more energy

# “WE NEED TO FOLLOW THE DATA JUST LIKE THE YELLOW BRICK ROAD, TO THE TRUTH.”

reserves to fight off illness. They are like contestants on the television show *Survivor*, says Gregg Fonarow, a cardiologist at the University of California, Los Angeles: “Those that started off pretty thin often don’t come out successful.”

Metabolic reserves could also be important as people age. “Survival is a balance of risks,” says Stefan Anker, a cardiology researcher at Charité Medical University in Berlin. “If you are young and healthy, then obesity, which causes problems in 15 or 20 years, is relevant,” he says. With age, though, the balance may tip in favour of extra weight.

Genetic and metabolic factors may also be at play. Last year, Mercedes Carnethon, a preventive-medicine researcher at Northwestern University in Chicago, Illinois, reported that adults who develop type 2 diabetes while they are of normal weight are twice as likely to die over a given period as those who are overweight or obese<sup>11</sup>. Carnethon says that the trend is probably driven by a subset of people who are thin yet ‘metabolically obese’: they have high levels of insulin and triglycerides in their blood, which puts them at a higher risk for developing diabetes and heart disease.

All this suggests that BMI is a crude measure for evaluating the health of individuals. Some researchers contend that what really matters is the distribution of fat tissue on the body, with excess abdominal fat being most dangerous; others say that cardiovascular fitness predicts mortality regardless of BMI or abdominal fat. “BMI is just a first step for anybody,” says Steven Heymsfield, an obesity researcher and the executive director of the Pennington

Biological Research Center in Baton Rouge, Louisiana. “If you can then add waist circumference and blood tests and other risk factors, then you can get a more complete description at the individual level.”

If the obesity-paradox studies are correct, the issue then becomes how to convey their nuances. A lot of excess weight, in the form of obesity, is clearly bad for health, and most young people are better off keeping trim. But that may change as they age and develop illnesses.

Some public-health experts fear, however, that people could take that message as a general endorsement of weight gain. Willett says that he is also concerned that obesity-paradox studies could undermine people’s trust in science. “You hear it so often, people say: ‘I read something one month and then a couple of months later I hear the opposite. Scientists just can’t get it right,’” he says. “We see that time and time again being exploited, by the soda industry, in the case of obesity, or by the oil industry, in the case of global warming.”

Preventing weight gain in the first place should be the primary public-health goal, Willett says. “It’s very challenging to lose weight once you’re obese. That’s the most serious consequence of saying there’s no problem with being overweight. We want to have people motivated not to get there in the first place.” But Kamyar Kalantar-Zadeh, a nephrologist at the University of California, Irvine, says that it is important not to hide subtleties about weight and health. “We are obliged to say what the real truth is,” he says.

Flegal, meanwhile, says that the public’s reaction to her results is not her primary concern. “I work for a federal statistical agency,” she says. “Our job is not to make policy, it’s to provide accurate information to guide policy-makers and other people who are interested in these topics.” Her data, she says, are “not intended to have a message.” ■ [SEE EDITORIAL P.410](#)

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