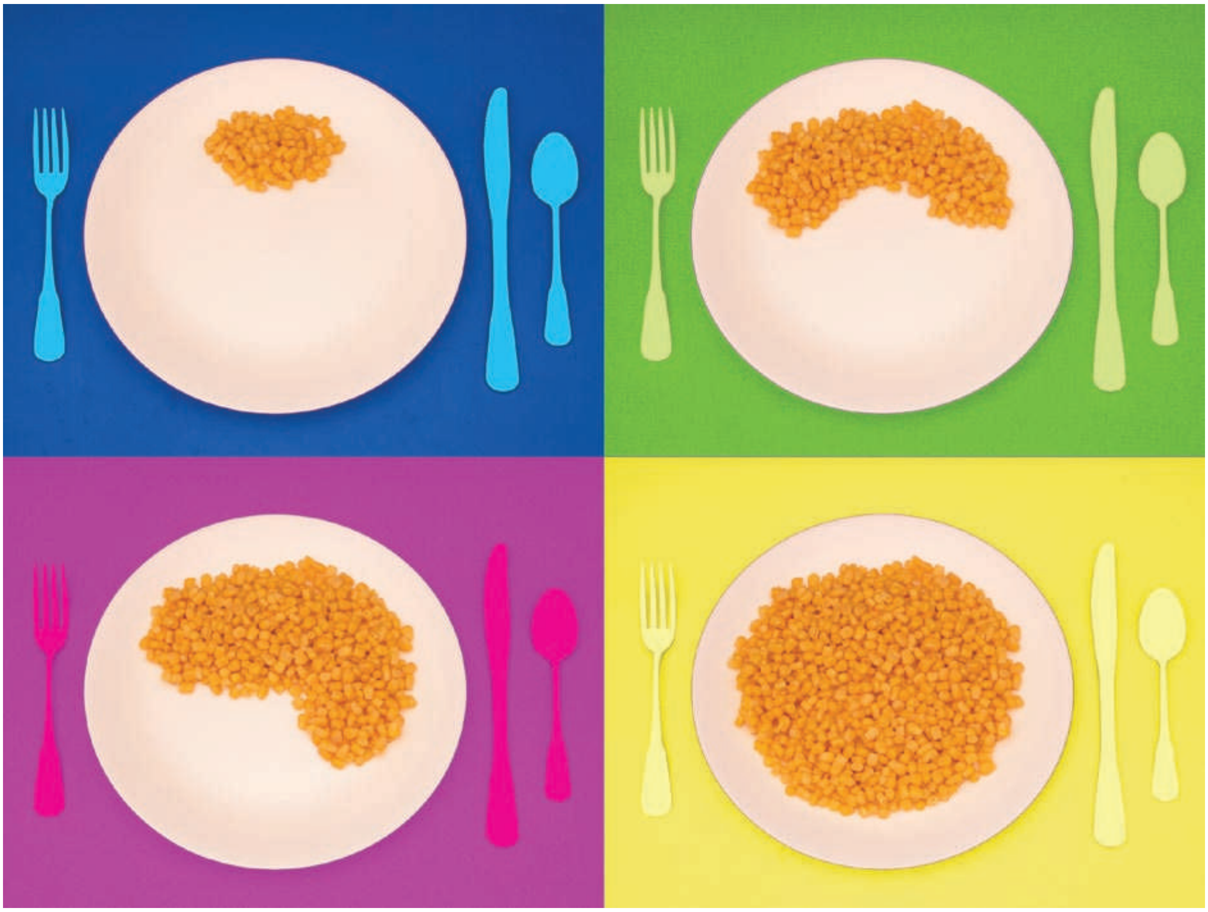


Portion truths: photos help people recall what they ate.

EVERY BITE YOU TAKE

If a camera snaps everything you eat, you can't lie about it later. That's why scientists are building high-tech gadgets to measure the human 'exposome'.

BY BRENDAN BORRELL

A decade ago, as part of a study on diet, psychologist Tom Baranowski was asked to recall everything he had eaten the previous day. A chicken dinner, he said confidently, remembering that he had prepared it for himself and his wife Janice. The thing was, he hadn't made chicken that night. It was only later that he realized he'd treated himself to a hamburger.

If Baranowski, who studies children's diets at Baylor College of Medicine in Houston, Texas, was an unlikely candidate for making such a mistake, consider how abysmal the dietary memories of everyone else must be. By observing his study subjects one day and following up the next, Baranowski has found that children routinely forget about 15% of the foods they have eaten, and more than 30% of the foods they do recall turn out to be figments of their imagination. Adults show similar patterns. "The errors of dietary assessment are overwhelming," says Baranowski.

These mistakes are more than a reminder of the human memory's fallibility: they threaten to undermine the foundations of modern medical epidemiology. In this field, researchers make associations between past events and experiences, and later ones such as the emergence of cancer or other diseases. But if the initial records are inaccurate, these associations can be weak, misleading or plain wrong. Although the problem is most jarring in studies of diet, it also infects investigations of exercise, stress, pollution or smoking — basically, anything that relies on people reporting their own

N. ISLAM/H. DADABHOY/BAYLOR COLLEGE OF MEDICINE

exposures through interviews or questionnaires. "This is the weak part of epidemiology," says Paolo Vineis, an environmental epidemiologist at Imperial College London.

Baranowski and Vineis are at the forefront of a movement among health researchers to develop measurements of environmental exposures that are more precise and objective than questionnaires. Some are working to develop personalized exposure profiles using blood-based tests. Others want their study subjects to trot around town with sensors dangling off their bodies capturing their movements, snapping photos of their lunch and taking samples of the air they breathe. "We are getting to the point where you can conceive of doing a study with 500,000 people and giving them a cellphone-sized device that they put in a charger every night," says David Balshaw, the exposure-biology programme manager at the National Institute for Environmental Health Sciences in Research Triangle Park, North Carolina.

Some researchers foresee a day when they will keep track of the entire spectrum of environmental exposures for a single individual, dubbed the 'exposome' (see 'How to measure everything'). That's a long way off. In the meantime, *Nature* takes a look at efforts to measure three key elements of the exposome: air pollutants, physical activity and diet. Each of these is bringing the exposome one step closer to reality — and the questionnaire, with all its flaws, a step closer to extinction.

BREATH BY BREATH

The contraption fitted snugly inside a child's backpack. The tangle of green plastic tubes, filters, pumps, circuit boards and a hefty battery weighed about 3 kilograms and made a low hum when it was switched on and began sucking in air. Tiny filters were designed to collect continuous records of all the grit and grime a child in the Bronx would be exposed to during their pilgrimage from their apartment, through the New York City subway system to school and back again.

For geochemist Steven Chillrud, whose team built the device in 2004, it represented the future of exposure biology. In the United States, environmental scientists have traditionally estimated human exposure to airborne pollutants by analysing data from building-mounted sensors. But the shortcomings of this approach became clear in a landmark study[1] published in 2005, in which researchers showed that levels of many hazardous compounds were higher inside homes than out. The findings made sense to Chillrud, who had already been thinking about the exposures of people living in New York City. "People do not live on buildings," he says.

To the New York City Police Department (NYPD), though, Chillrud's contraption was a potential terrorist threat. After four terrorists detonated bombs on London's public transport system on 7 July 2005, the NYPD had been conducting random searches on the subway system. When Chillrud stopped by the local police precinct to alert them to his planned study, officers were aghast, and even Chillrud admits his device looked intimidating. "We put a lot of effort into it," Chillrud says now, as he hoists it onto his desk at Columbia University's Lamont–Doherty Earth Observatory in Palisades, New York. "Then, the police shut us down." But they also offered the team a way forwards. "If we could shrink it to the size of a Walkman, we'd be back in business."

Last November, after several iterations with his collaborators, the first of Chillrud's Walkman-sized environmental sensors finally arrived. When participants in the study leave the vicinity of a 'home' beacon, the device switches between two filters, making it possible for Chillrud to distinguish between exposures at home and elsewhere; a Global Positioning System (GPS) device helps to differentiate exposures during the commute from those during the school or work day. After several days of use, the filters can be chemically analysed to identify different sources of black carbon and other chemicals. And the NYPD will be pleased: the pared-down version slips neatly into a special vest with an air inlet near the collar.

The first health studies with the contraption will be aimed at more accurately measuring passive contact with tobacco smoke. Chillrud will be studying 50 adults and a handful of children using portable sensors and a method developed by Avrum Spira, a pulmonary specialist at the Boston University School of Medicine in Massachusetts, which uses changes in gene expression in cells brushed from the nostril to assay smoke exposure[2]. Spira believes that a more precise measure of cumulative smoke exposure can pin down the reasons why some smokers — but not all — develop lung cancer and conditions such as chronic obstructive pulmonary disease. "We are not measuring just exposure, but how you are responding to exposure," Spira says.

STEP BY STEP

Another aspect of daily exposure is charted in Kevin Patrick's maps of San Diego, California. They take a few minutes to understand. The blue Pacific lapping against the shore on the left is immediately recognizable, as is the city itself, a false-colour patchwork of highways, buildings and parkland. Finally, you begin to notice the green, yellow, orange and red dots, and it all starts to come together. The dots show an individual's heart rate at different points in time: widely spaced green dots represent the sedentary drive to work; a day at the office generates green dots layered on top of each other; and finally, a jog or bike ride along the bluffs appears as a string of heart-thumping orange and red (see 'Every step you make').

Patrick, a director of the Center for Wireless and Population Health Systems at the

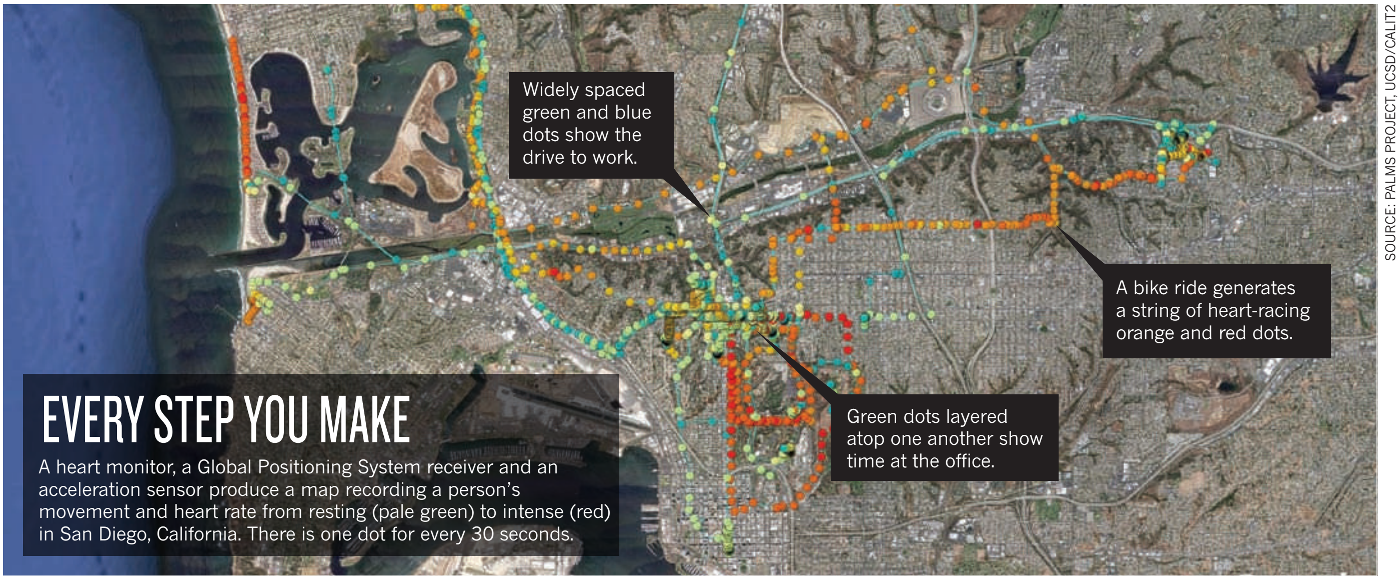
HOW TO MEASURE EVERYTHING

In the 1998 film *The Truman Show*, the central character Truman Burbank gradually discovers that his entire life since conception has been broadcast through thousands of cameras hidden throughout a giant film set. Add to that surreal vision the chemical analyses of Burbank's air, food and water, samples of his gut flora, and blood tests for endocrine-disrupting chemicals, heavy metals and metabolic products, and you have some idea of the overwhelming nature of the 'exposome' — the full catalogue of a person's environmental exposures throughout their life.

The ability to draw up this catalogue could reveal which exposures contribute to developing disease in the future. But it is as technically difficult as it is conceptually overwhelming. "People may think it's so complex that it's not achievable," says Christopher Wild, head of the International Agency for Research on Cancer in Paris, a branch of the World Health Organization, who coined the term exposome in 2005.

Sensors worn on the body can record some aspects of the 'external' exposome. But "those devices are not going to contribute more than a few per cent to our understanding", says Stephen Rappaport, an environmental-health biologist at the University of California, Berkeley. That's why he and others are working on ways to record the 'internal' exposome, profiles of biological molecules that reveal the effects of diet, toxins and other exposures. Metabolites from the pesticide DDT, for instance, can be detected in blood 20–30 years after exposure. But researchers are many years from a unified approach that could profile tens of thousands of compounds and extract from this a full history of life's onslaughts. Part of the problem is that one person's metabolic response to a change in diet, say, can be completely different from another's.

For now, some investigators are combing existing exposure data for associations with specific diseases. Since 1999, for example, the Centers for Disease Control and Prevention in Atlanta, Georgia, has conducted the National Health and Nutrition Examination Survey, which includes interviews, medical examinations and biomonitoring of hundreds of chemicals in the blood. Last year, Atul Butte, a bioinformatician and paediatrician at the Stanford School of Medicine, California, used these data in an environment-wide association study to hunt for correlations between type 2 diabetes and 266 environmental factors. The biggest surprise came from the discovery that a form of vitamin E increased the risk of diabetes[5]. **B.B.**



EVERY STEP YOU MAKE

A heart monitor, a Global Positioning System receiver and an acceleration sensor produce a map recording a person's movement and heart rate from resting (pale green) to intense (red) in San Diego, California. There is one dot for every 30 seconds.

University of California, San Diego (UCSD), says that these maps measure physical activity more accurately than the pedometers and questionnaires he and other researchers used for years. "We realized we needed to know not only how active someone is, but where that activity occurs," he says. Such monitoring can help the researchers understand how the layout of a city — with its parks, hills and smog traps — influences physical activity and, ultimately, public health.

Patrick launched the mapping project in 2007. Called the Physical Activity Location Measurement System, or PALMS, it combines heart-rate monitors, a GPS device and acceleration sensors to record body movements in detail. More than 1,500 people have already worn the US$60 devices, after which they sit down to explain what they were doing at different points during the day. Working with computer scientists, Patrick hopes to develop a pattern recognition system to automatically distinguish different activities.

The first proposed health application of PALMS will measure physical activity among San Diego-based participants in the Hispanic Community Health Study/Study of Latinos, run by the US National Heart, Lung, and Blood Institute among other bodies. He also has plans to measure the effects of interventions, such as campaigns encouraging people to spend more time in parks than city streets.

Patrick works on another project, CitiSense, led by software engineer William Griswold, also at UCSD. This aims to measure physical activity and airborne pollutants with gadgets similar to Chillrud's. In one planned study, Patrick will give these devices to San Diego cyclists, providing them with real-time feedback on the quality of the air they breathe during bike rides. Patrick says he looks forward to the day when researchers can link up the data that he is collecting with those on social networks, psychology and genetics to understand how these factors in combination contribute to disease. "I don't think it's going to be very long before that happens," he says.

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For more on detecting exposures see:
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GULP BY GULP

No study of human exposure will be complete without examining food. That's why, on a rainy afternoon in December, Baranowski was looking closely at a dinner plate of maize (corn) on a flat-screen monitor. In fact, it was one of eight plates of maize, identically positioned on a blue table, differing only in their portion sizes from a few spoonfuls to a few cups. "The kids' job," Baranowski says, "is to pick which size comes closest to the portion they consumed."

Over the past few years, Tom and Janice Baranowski have taken serial pictures of foods prepared in the 'metabolic' kitchen on the third floor of the Children's Nutrition Research Center, ranging from breakfast cereal to chicken nuggets to grapes, amassing some 15,000 photographs altogether. The photos are part of an effort funded by the US National Cancer Institute to improve the Baranowskis' food intake recording software, called Automated Self-Administered 24-hour Dietary Recall (ASA24), and adapt it for use by children. During trials, the photo-prompts help children estimate portion sizes of meals they ate with about 60% accuracy, Baranowski says. The goal is to build a web-based tool that other researchers can use in place of food diaries to, for instance, link up dietary habits, genetic signatures and risk of disease.

Electrical engineer Mingui Sun of the University of Pittsburgh, Philadelphia, is trying to circumvent self-reporting entirely. He has built an all-purpose exposure-biology device that hangs around the neck and contains 5–8 sensors including a GPS device, an audio recorder, accelerometer and a digital camera programmed to take 2–5 pictures a second over the course of a week[3]. Image-processing software can automatically recognize dinner plates or a glass of milk, segmenting the video stream so that meals and cooking procedures can later be reviewed by dieticians. Sun says the devices will soon be used in a pilot study estimating the caloric intake and physical activity levels of people who are obese.

Vineis, though, has taken a very different tack to measuring the dietary component of the exposome, as part of his work on the ten-country European Prospective Investigation into Cancer and Nutrition cohort. In November, his group published a proof-of-principle paper[4], in which they compared blood-plasma analyses and dietary assessments of 24 people who went on to develop colon cancer over a seven-year period, compared with 23 healthy controls. They found one biomarker — a derivative of benzoic acid produced by fibre-digesting gut bacteria — that correlated with dietary fibre intake and a reduced colon cancer risk. Vineis calls this the "meet-in-the-middle approach" to discovering biomarkers that measure exposure at the same time as showing how the exposure might foreshadow disease.

But fibre is just one of the known and unknown environmental exposures to which a human body is subjected, and colon cancer just one of its many downfalls. A comprehensive exposome is many years off — so for now, Vineis is just hoping for a better way to measure one exposure at a time. "I don't think we'll completely give up on questionnaires," he says. ■

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1. Weisel, C. P. *et al. J. Expos. Anal. Environ. Epidemiol.* **15,** 123–137 (2005).
2. Spira, A. *et al. Proc. Natl Acad. Sci. USA* **101,** 10143–10148 (2004).
3. Sun, M. *et al. J. Am. Diet. Assoc.* **110,** 45–47 (2010).
4. Chadeau-Hyam, M. *et al. Biomarkers* **16,** 83–88 (2010).
5. Patel, C. J., Bhattacharya, J. & Butte, A. J. *PLoS One* **5,** e10746 (2010).