Atlantic Modern Medicine Is Too Reliant on Short-Term Studies

Vigilant, long-term monitoring of patients is the future.



Researchers may soon have much more advanced devices for tracking blood pressure than the one pictured here, at a medical clinic in Los Angeles.

Lucy Nicholson / Reuters

JESSA GAMBLE | 9:00 AM ET | HEALTH

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It has been 30 years since the first findings that heart attacks are most common in the early morning. Since then, research has revealed that those first three hours after waking are also when a cardiac event is most damaging. In fact, the whole cardiovascular system is controlled by circadian rhythms that influence the likelihood of stroke, kidney failure, and

heart attacks.



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If this new knowledge about circadian rhythms has taught us anything, it is the value of time as a dimension in medicine. Many physiological changes are tied to 24-hour body rhythms, and these changes have been revealed, in part, through continuous monitoring of the same individuals through time. Other forms of vigilant patient-tracking—sometimes over decades for a single person—have demonstrated that to understand how diseases develop, there is no substitute for watching someone's health change in

real time.

"Aging studies are based on age cohorts. They look at trends in the likelihood of having diseases as a function of age," says Germaine Cornelissen, the director of the Halberg Chronobiology Center at the University of Minnesota. "Longitudinal monitoring can look at trends as a function of age in the same person, starting with presumably healthy subjects."

There is an inherent story-telling appeal to the longitudinal study. *The Up Series*, a British documentary that revisits the same children every seven years of their lives, demonstrates the entrenched nature of the class system in England. Unfolding before the audience's eyes, each child's life follows a course seemingly predestined by his or her circumstances of birth.

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The longitudinal study's main limitation is that it is not an experiment, where one factor is intentionally manipulated by a scientist. To draw more solid conclusions, babies in the documentary series would have been randomly assigned to families along the socioeconomic spectrum. In recognition of basic ethical standards and to be true to life, studies

like these are based on observation.

The 75-year Study of Adult Development at Harvard Medical School followed hundreds of American men who came of age during the Second World War. For this generation, alcoholism was the largest cause of divorce, and smoking was the greatest contributor to early death. Even levers of life happiness—overwhelmingly determined by warm relationships—could be teased out from this study.

The longitudinal study has great power because it can compare later values with the same person's baseline state. Many of the established baselines in medicine have been much better studied in men than in women, who tend to have lower blood pressure and higher heart rates, among other differences. What is average for the general population may represent an alarming shift for any given person.

The trouble is, long-term observation is only possible if it is as unobtrusive as possible. The moment monitoring becomes burdensome for subjects, the results may not be representative of normal life—and subjects may start disappearing from a study.

Take blood pressure, which is particularly hard to observe in real time over the course of months in a healthy person. "A major hurdle to the kind of longitudinal monitoring we would like to do is reluctance to use the monitor," says Cornelissen. "We are looking for a non-invasive way to monitor continuously for a week or longer that does not use uncomfortable cuffs."

One potential avenue would be a flexible electronic circuit like the one John Rogers, a materials scientist at Northwestern University, has developed. Dubbed "epidermal electronics," the device sticks like a temporary tattoo over a vein or artery on the forearm. It delivers continuous heat, and based on the rate of cooling, infers the amount of blood flow carrying that heat away.

The contemporary craze for health-monitoring smart-phone apps has prepared a wide segment of society for tracking their medical data through time. Cornelissen is hopeful that a long-term crowd-sourcing approach to blood pressure measurement could contribute much more to our understanding than one-off studies.

Blood pressure and heart rate rise during the day and fall at night. The changes are under control of the brain's master clock, the suprachiasmatic nucleus, which orchestrates the body's circadian rhythms. Some diagnosed cases of high blood pressure are accompanied

by large swings; a daytime measure of high blood pressure may actually become low blood pressure at night, and there are some indications that this change may be a bigger concern than blood pressure itself.

New research suggests that these vascular variability disorders—or circadian overswing—may be masquerading as high blood pressure when it is measured only at mid-day doctor's appointments. Some patients even suffer a shift in the timing of their rhythm, experiencing peak blood pressure at night and lowest blood pressure in the day, out of sync with the rest of their physiology.

A study at Tokyo Women's Medical University tracked blood pressure over a 48-hour period to separate straightforward hypertension from high blood pressure with vascular variability problems—either in the size of the change or in its timing. Over the next six years, fewer than 10 percent of the hypertensive subjects had a cardiovascular "morbid event" such as heart attack or stroke. Of those with a vascular variability problem, however, that number rose to 29 percent, and even higher for subjects with multiple rhythm problems.

With every increase in blood pressure, the risk factor for cardiovascular problems goes up, but the daily change in blood pressure is healthy until it crosses a threshold. Above that threshold, stroke or kidney failure in the next six years becomes much more likely.

Longitudinal studies are the opposite of today's quick-and-dirty experiments that yield publishable results before the current round of Ph.D. students turns over. Often researchers who start them have long retired or died before a longitudinal study comes to fruition. But that's exactly the sort of commitment needed. The word "monitoring" is rarely sexy, but it represents the sort of slow receptivity that has built a solid case around the climate crisis, and other steadily evolving conditions. To understand how people change, one must watch them changing.

ABOUT THE AUTHOR

JESSA GAMBLE is a writer based in Yellowknife, Canada. She is a co-owner of the science blog The Last Word On Nothing and the author of The Siesta and the Midnight Sun: How Our Bodies Experience Time.