

Grasping for Any Way to Prevent Alzheimer's

By PAM BELLUCK

Is there a way to prevent Alzheimer's disease? Last week, a study presented at the Alzheimer's Association International Conference in Paris suggested there might be, something that would give hope to millions who worry that one day they may be struggling with dementia.



The new study, by researchers at the University of California, San Francisco, estimated how many Alzheimer's cases might be attributable to certain behaviors or conditions: physical inactivity, smoking, depression, low education, hypertension, obesity and diabetes.

The authors used a mathematical model to surmise that these behaviors and conditions, all of which can be modified, are responsible for about half of the roughly 5.3 million Alzheimer's cases in the United States and 34 million cases worldwide.

And they calculated that if people addressed these risks — by exercising, quitting smoking, increasing their education or losing weight, for example — a significant number of Alzheimer's cases could be prevented. Reducing the prevalence of these risk factors by 10 percent, the researchers estimated, could prevent 1.1 million cases worldwide; reducing these risk factors by 25 percent could prevent more than three million cases.

The operative word was “could.” As the researchers pointed out, there is not yet scientific proof that any of these risk factors in fact cause Alzheimer's. Only if they are shown to do so could the new analysis be considered a practical recipe for preventing the disease.

“These things are not definitive,” said one author, Dr. Kristine Yaffe, a professor of psychiatry, neurology and epidemiology. “We're assuming that these are sort of causally related to the risk of dementia and Alzheimer's, but unless you have a great trial, you just don't know.”

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But while experts may have understood that distinction, not everyone else did. Some headlines made things sound more certain: “7 Things You Can Do to Fight Alzheimer’s” or “7 Steps to Prevent Alzheimer’s.”

In an editorial accompanying the study, both published in the journal *Lancet Neurology*, Dr. Laura Fratiglioni, director of the Aging Research Center at the Karolinska Institute in Sweden, suggested that the report was valuable, but said that the estimates “could be regarded as only theoretical” until more rigorous research is done.

“We have been able to identify some possible preventive factors,” Dr. Fratiglioni said, “but we do not have the final answer because we do not have the experimental studies.”

Indeed, research on prevention of Alzheimer’s is in its infancy. It has only been since the 1980s that dementia has not been considered a symptom of normal aging. And studies on preventing Alzheimer’s can be complicated and costly, especially the randomized controlled trials that provide the strongest evidence. Such trials have to follow people for years, and isolating individual risk factors — separating obesity from hypertension, diabetes, nutrition and physical inactivity, for instance — is challenging.

Last year, a National Institutes of Health panel of experts with no vested interest in Alzheimer’s research concluded that “no evidence of even moderate scientific quality exists to support the association of any modifiable factor (such as nutritional supplements, herbal preparations, dietary factors, prescription or nonprescription drugs, social or economic factors, medical conditions, toxins or environmental exposures) with reduced risk of Alzheimer’s disease.”

Most research, the panel found, involved observational studies, showing that people who did or did not get Alzheimer’s had certain characteristics beforehand, but not whether the characteristics were causal.

The panel found the strongest evidence for only one conclusion: that the herb ginkgo biloba does not prevent Alzheimer’s. There was moderate evidence that neither vitamin E nor drugs called cholinesterase inhibitors, used to treat dementia symptoms, decrease risk of Alzheimer’s. And there was moderate evidence that the gene ApoE4 significantly increases Alzheimer’s risk, as does menopause therapy with estrogens and progestins.

Evidence for or against any other causal factor was poor, often because studies were small, used vague or changing definitions, or did not rigorously monitor what subjects were doing.

“We debated for hours and hours and hours how to write the report, because certainly we didn’t want it to be the carrier of bad news,” said Dr. Martha Daviglus, the panel’s chairwoman and a preventive medicine expert at Northwestern University. But “we wanted the public to realize that at this point nothing that people can sell to them is

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proven to work.”

Many members of the Alzheimer’s community were stung, considering the panel’s conclusions a “glass half empty,” said William Thies, the Alzheimer’s Association’s chief medical and scientific officer. “We would agree that we haven’t proven any of these risk factors, but there’s data that are pretty good for some of them. And in a world where we have lots of Alzheimer’s disease and no definitive medical intervention, prevention strategies that are based on lifestyle changes are certainly attractive.”

Dr. Yaffe and her colleague Deborah Barnes excluded risk factors like nutrition or brain exercise because they believed research was not solid enough. They used a more elastic threshold to evaluate research than the N.I.H. panel because, Dr. Yaffe said, the panel “didn’t quite do the field justice.”

Their model weighed the strength of existing research and how widespread the risk factors were. In the United States, they estimated that 1.1 million Alzheimer’s cases, or 21 percent, may be linked to physical inactivity. Fifteen percent may owe to depression, 11 percent to smoking, 8 percent to midlife hypertension, 7 percent to obesity, 7 percent to low education and 3 percent to diabetes.

Their estimates for the risk factors worldwide differed because some behaviors and conditions are more common than in the United States. So low education accounted for 19 percent, or 6.5 million cases, worldwide, while physical inactivity accounted for 13 percent and obesity 2 percent.

Dr. John W. Williams Jr., a professor of medicine at Duke University who led an analysis of Alzheimer’s prevention research for the N.I.H. panel, said studies like Dr. Yaffe’s can be informative “when we don’t have other evidence” and can help shapers of public policy “make decisions about where to invest to reduce risk.”

But he said: “What should individuals do with it? Probably not much.”

Among the limitations, he said, was that some risk factors, like physical inactivity and obesity, “are darn hard to change.”

And does a risk factor like depression cause Alzheimer’s — or is it the other way around?

Still, everyone agrees these risks merit attention for other reasons: preventing cancer or heart disease, improving overall health.

“It’s good if you can do it, but not in the name of Alzheimer’s,” Dr. Daviglius said. “But maybe we will find out that by doing this for other diseases, we are also doing it for Alzheimer’s.”