Combining multiple meds into a single pill reduces cardiovascular deaths, study confirms

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Taking a single pill that combines medications targeting cardiovascular disease-related conditions was shown long ago to lower the risk of death

from such causes, including heart attacks and strokes.

The concept of using such "polypills" to prevent and treat atherosclerotic cardiovascular disease was introduced nearly 25 years ago. Shortly thereafter, the strategy was the focus of a seminal modeling study that promoted polypills to reduce cardiovascular disease at the population level. Still, many years and a body of supportive research later, use of such pills remains low throughout the world.

Now, a new study from researchers at Washington University School of Medicine in St. Louis published in *Nature Medicine* bolsters previous findings and provides additional evidence that polypills are beneficial in preventing heart attacks and strokes and reducing deaths among people with cardiovascular risk factors, including high blood pressure and high cholesterol.

As a result of the study, the World Health Organization (WHO) has added such polypills to its most recent Model List of Essential Medicines. The list comprises medicines considered key to public health due to their importance in treating common diseases, as well as their safety, efficacy and cost-effectiveness.

"The main takeaway here is that polypills work," said first author Anubha Agarwal, MD, an assistant professor of medicine in the Cardiovascular Division. "And if polypills were widely accepted and used for prevention of cardiovascular disease, we would be in a much better position to equitably reduce the impact of cardiovascular disease globally. This strategy would simplify treatment options—replacing multiple medications with a single pill—and likely expand access across economic levels around the world due to its potential affordability."

The researchers performed a systematic analysis of data gleaned from 26 clinical trials. The data synthesized the effects of polypills on

atherosclerotic cardiovascular disease prevention. To be included in the analysis, the trials had to evaluate polypills that included at least one statin—a cholesterol-lowering drug—and at least one blood pressure-lowering drug.

The analysis found that the polypills were associated with an 11% lower risk of death from any cause compared with people who did not take polypills, and a 29% lower risk of atherosclerotic cardiovascular disease events compared with people who did not take polypills.

"These findings support adoption and implementation of polypills to lower risk for all-cause mortality for cardiovascular disease," Agarwal said.

The researchers also found that polypill usage was associated with lower low-density lipoprotein (LDL) cholesterol and lower systolic blood pressure—the first number in a blood pressure measurement, which indicates the pressure in one's blood vessels when the heart beats. Some who used polypills experienced adverse side effects such as muscle pain or coughs.

Agarwal and her colleagues sought the data to determine whether broader use of polypills should be encouraged for cardiovascular disease prevention. The review served as the foundation of the research team's successful application to the WHO to include polypills on the organization's 23rd Model List of Essential Medicines, for high-risk primary and secondary prevention of cardiovascular disease.

The WHO endorsement may make national governments and international agencies more willing to fund such polypills and may prompt health-care providers to prescribe them. Agarwal said the decision ultimately could improve global access to polypills, particularly in low- and middle-income countries.

Agarwal said one reason polypills are not widely available is that companies are not incentivized to invest in manufacturing polypills including generic medicines, even when potential benefits to public health are significant.

"The polypill field will continue to evolve," said Mark D. Huffman, MD, the study's senior author and a professor of medicine. "The next challenge will be to learn how to best implement and sustain polypill use to prevent millions of heart attacks and strokes every year."

More information: Anubha Agarwal et al, Fixed-dose combination therapy for the prevention of atherosclerotic cardiovascular disease, *Nature Medicine* (2024). DOI: 10.1038/s41591-024-02896-w

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