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A polypill for secondary prevention: time to move from intellectual debate to action

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The concept of a fixed-dose combination pill—or 'polypill'—for cardiovascular disease prevention was first proposed by Wald and Law in 2003. Using data from published trials and their own meta-analysis, they claimed that a six-component polypill administered to every individual older than 55 years could reduce the incidence of cardiovascular disease by more than 80%. Since then, a storm of controversy has surrounded this idea.

Detractors of the polypill concept argue that a 'magic pill' such as this could wrongly be considered as a substitute for healthy lifestyles by many patients and that the 80% estimated risk reduction could be overwhelmingly optimistic. Patients' and doctors' level of acceptance is also predicted to be less than expected. Furthermore, those skeptical of the polypill concept highlight that in primary prevention the efficacy of any polypill should be proved beyond doubt by adequate trial findings.

Recently, the potential value of applying the polypill strategy in high-risk patients only, with or without previous cardiovascular events, has been recognized by the Combination Pharmacotherapy and Public Health Research Working Group, the WHO and the World Heart Federation. Even if polypill use is restricted to high-risk patients, its potential benefit is still huge, enabling the prevention of a large number of events while treating a smaller population than that for primary prevention.

The WHO estimates that worldwide there are 100 million people with either ischemic heart or cerebrovascular disease. Although tailored treatment to correct risk factors is advocated by many physicians, the efficacy of such an approach is limited. First, more than four-fifths of cardiovascular deaths occur in developing countries where accessibility to drugs and medical care is very restricted. Implementation of healthy lifestyles and a cost-effective polypill strategy in selected patients from these countries would avoid a number of deaths.

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Competing interests
The authors declared they have no competing interests.

www.nature.com/clinicalpractice
doi:10.1038/ncpcardio0858

Second, more than 50% of patients with chronic conditions show poor adherence to treatment, and less than 30% follow the recommended lifestyle modifications. The lack of adherence correlates with many different factors, complexity of treatment (i.e. number of drugs and frequency of administration) being one of the most important. Lack of treatment compliance results in reduced drug efficacy, increased mortality and a sizable number of hospital readmissions—an economical burden for the health system. Thus a polypill containing three generic components—aspirin, a statin and an angiotensin-converting-enzyme inhibitor, an effective combination for secondary prevention in high-risk populations—could be an attractive option for doctors and for patients already taking these drugs separately.

The strategy of a fixed-dose combination for cardiovascular prevention, however, is not free from problems. Galenic formulation is a formidable challenge. The manufacture of fixed-dose combinations to ensure drug stability, physicochemical compatibility, control of impurities and adequate bioequivalence, all in an attractive, low cost, once-a-day, easy to swallow tablet, is technically demanding.

Moreover, it needs to be proved clearly that the polypill improves treatment adherence; stopping the polypill intake because of side effects caused by one of its components will result in discontinuation of the entire treatment. In addition, the cost-effectiveness of the whole strategy and impact the polypill has on patient's adherence to healthy behaviors should also be evaluated.

Following the recommendations of the WHO and World Heart Federation, there seem to be enough reasons to encourage the development and testing of a polypill for secondary prevention as a component of an affordable, globally available, comprehensive treatment strategy, along with lifestyle interventions.