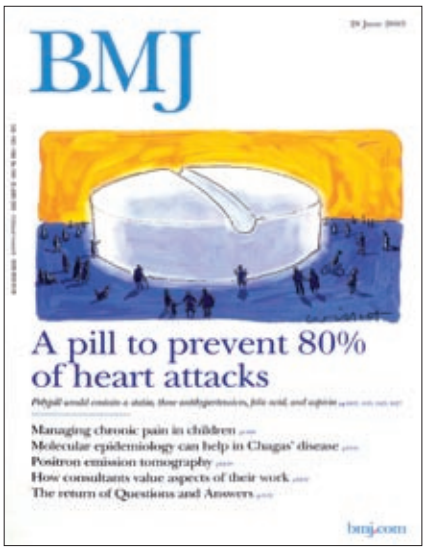


# WHAT HAPPENED TO THE POLYPILL?

A single pill to prevent cardiovascular disease sounds like a perfect solution, but little progress has been made since the idea was first suggested. **Geoff Watts** investigates why

When Nicholas Wald, head of London's Wolfson Institute of Preventive Medicine, and his colleague Malcolm Law published their case for the prevention of heart disease using a "polypill",[1] an accompanying editorial described it as "one of the boldest claims for a new intervention."[2] The substance of the claim was that, if taken by everyone with established cardiovascular disease and—most importantly—all those aged 55 or over, the polypill could reduce rates of heart attack and stroke by more than 80%.

Now, more than five years later, you might imagine that research groups would be competing to test this innovative suggestion. Not so.

As conceived by Professors Wald and Law, the polypill comprised a statin, aspirin, three types of blood pressure lowering drug, and folic acid—intended to lower serum homocysteine concentrations. The logic was that most people in Western society are at raised risk, that cardiovascular disease is consequently common, and that the drugs to treat it are effective and safe. "No other preventive method," they wrote, "would have so great an impact on public health in the Western world." Since that time, Professor Wald says, nothing has happened to change his mind.

The few trials that have been planned lack the scope and ambition of Professor Wald's original proposal. One, for example, is being organised by Anthony Rodgers of the University of Auckland's clinical trials research unit. His pilot study is recruiting 400 participants from New Zealand, Brazil, India, and elsewhere for a 12 week placebo controlled trial of a pill containing blood pressure and cholesterol lowering drugs together with aspirin.[3] But all his participants are selected because they are at increased risk of heart attack or stroke; they are not intended to reflect a section of the population at large.

Another study is being led by Valentin Fuster of Mount Sinai Hospital in New York. He is also the scientific director of Spain's National Centre for Cardiovascular Research, the body through which the trial is being organised. His polypill variant comprises aspirin, a statin, an angiotensin converting enzyme inhibitor, and a beta blocker. But all the participants have had a myocardial infarction, and his intention is to learn whether having to swallow only a single pill will improve compliance. At present, he says, only one third to half of patients take all the drugs necessary to prevent a second heart attack.

Professor Fuster is keen to explore the relevance and affordability of a polypill in low income countries. One of his hopes when full trials start—subject to US Food and Drug Administration approval—is to show how secondary prevention of heart disease can be made available in the developing world.

## Primary concerns

Professor Wald knows of no plans to run a trial of the polypill on a general healthy population. So, mindful of its potential impact on public health, why the reluctance?

It is likely that Professor Fuster speaks for others besides himself when he explains why his study is limited to secondary prevention. "This is not the solution for primary prevention," he says. "Primary prevention requires education of the public. As a priority this is much more important than any polypill."

It's a view that Professor Wald has been confronting ever since he published his *BMJ* paper. "Yes, in an ideal world our saturated fat intake would be lower and we'd exercise more, and we'd have less salt and sugar in our diet. But this is not going to happen tomorrow." He is puzzled that people seem to regard these strategies as mutually exclusive. "It's a mistake to think that when you can do things two ways it has to be one or the other."

The polypill concept is also accused of "medicalising" whole populations. "Quite the reverse," Professor Wald insists. "If you test people to see if they've got high blood pressure or high cholesterol, give them a disease label, and then have them come back regularly to find out if things have changed, you've created a patient." This, he argues, is the real medicalisation—not universal access to a pill.

Does he sense a moral objection of some kind to the use of drugs rather than lifestyle changes? He does. "There's an unstated view that if you're not a patient, taking pills may be regarded as a weakness. Once you're a patient you're relieved of that burden." Such a view, he thinks, is unreasonable. "Is getting vaccinated a moral weakness?"

The only people currently contemplating a trial in a population defined by age seem to be Professor Wald and his colleagues. With a polypill developed by the Indian generics company Cipla he hopes to set up a project in the developing world. This choice of location would be partly to minimise cost, but also because guidelines on cardiovascular screening in the UK would require participants in the placebo group with problems identified by baseline tests to get some treatment, so making it harder to show the polypill's effects.

At present no polypill formulation has been licensed in Europe or America. But if and when a combined pill for treating hypercholesterolaemia and hypertension as part of secondary prevention wins regulatory approval, new possibilities will open up. "Once a polypill is on the market, doctors can prescribe it as they see fit." It's this, Professor Wald suspects, that will eventually lead to a wider exploration of its benefits.

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2 Rodgers A. A cure for cardiovascular disease? *BMJ* 2003;326:1407-8.
3 University of Auckland Clinical Trials Research Unit. *PILL pilot: programme to improve life and longevity*. 2008. www.ctru.auckland.ac.nz/content/view/37/35/.

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