



[www.polypack.co.nz](http://www.polypack.co.nz)

## [ The polypill ]

5 low-dose medicines in a single pill, the polypill, has been described as an approach that could have a greater impact on the prevention of disease in the Western world than any other single intervention. The polypill aims to prevent cardiovascular deaths in people who are at risk. This is very different to what doctors currently do, which is treat problems after they occur. The polypill is 5-10 years away but a very similar option is available now.

Cardiovascular disease is the leading cause of death in New Zealand, causing 40% of deaths. Use of the polypill could reduce mortality due to heart disease and strokes by 50- 80% and could enable a third of the population to live an average of 11-12 years longer. The treatment is cheap, with few side effects and based on data from hundreds of trials of the individual components.

The polypill aims to prevent cardiovascular deaths in people who are at risk, which is almost everyone in Western countries. This is very different to what doctors currently do, which is treat problems such as high blood pressure after they occur.

The polypill is 5-10 years away at least, and many experts believe that they will never be made available, as pharmaceutical companies cannot patent the product. Anyone can be prescribed the pills in separate bottles, but the polypill is being developed to make it easier for people to take the medicines.

## [ Polypack ]

Polypack is a packaging service that will package medicines that are the same or similar to those that will be in the polypill. Co-packaging of medicines makes it much easier for people to take a number of medicines over a long period of time, and has been shown to improve clinical outcomes.

The Polypack can currently deliver up to five medications in a single sachet to be taken each day. The medications available are the same or similar to those that would be in the polypill if it were available and must be prescribed by a doctor. The following medicines are available and the prescribing doctor can include all or some of these medicines and can change the doses:

aspirin	100 mg e/c	Reduce clotting
simvastatin	20 mg	Reduce cholesterol
bendrofluazide	2.5 mg	Reduce blood pressure
enalapril	5mg	Reduce blood pressure
atenolol	50mg	Reduce blood pressure

Unlike the polypill, components of the Polypack can be removed if a person cannot take 1 or more of them (eg. atenolol can be removed for people with asthma). Boxed rolls of 90 sachets are dispensed and the cost is \$1 a day. Unit-of-use sachets have been shown to massively increase adherence to treatment regimes requiring multiple tablets and have been shown to improve clinical outcomes.

## [ Expert opinions ]

"It's a great shame that the polypill is taking so long to get to market and that's why I applaud Shaun's innovation. I've been an enthusiast for the polypill since the beginning, and now, aged 57, I take the five pills every night. I'm glad that others will have the chance to choose to drastically reduce their chances of having a heart attack or stroke, which otherwise will kill a third of us."



Professor Richard Smith  
*Director of the Ovations initiative*  
*Ex-editor for the British Medical Journal*

"The polypack represents a practical method whereby the New Zealand population can obtain the benefits of the polypill strategy which has been described as an approach that could have a greater impact on the prevention of disease in the western world than any other single intervention. The major advance of the polypack initiative is that it is possible to vary the doses of the medications included to meet individual patient requirements. This overcomes the major drawback of the polypill concept in which fixed dose combinations of medications are included in a single pill. As a result, the polypack represents a "second generation" version of the polypill strategy."



Professor Richard Beasley  
*Director of the Medical Research Institute of New Zealand*

## [ FAQs ]

### What effect will the polypill medications have in preventing heart attack and stroke?

There are various estimates of the reduction in a person's risk of a heart attack or stroke that can be obtained by taking the polypill medications, ranging from around 50% - 80%, but of course this depends very much on the individual person and their risk profile.

### Are the polypill medications suitable for my patients?

That's a decision between you and your patient, and as with any treatment you need to look at the benefits and risks. Many would argue that the benefits outweigh the risks if your patient has a risk factor for heart disease, listed below, and others go further and say that everyone who lives in a Western country is at high risk of cardiovascular death – it is the biggest killer in New Zealand and accounts for 40% of deaths each year.

Cardiovascular risk factors include (with approximate prevalence in people > 35yo):

Diabetes	1/10
Obesity	1/3
Raised cholesterol	1/3
Raised blood pressure	1/3
Lack of exercise	>1/2
Current or former smoker	1/4

### If a patient is not known to have high cholesterol or high blood pressure, how can it be appropriate for them to take the polypill medications?

Most heart attacks and strokes occur in people whose levels of risk factors such as blood pressure or cholesterol are about average, because even average levels (which are regarded as "normal") may be too high. Current guidelines recommend offering treatment to those whose risk factor levels are high.

Traditionally, the approach has been to treat only if certain risk thresholds have been reached. However, even though an individual maybe not reach these traditional thresholds, benefits can still accrue by further reductions in blood pressure, cholesterol etc. This is because there is a sliding scale of risk; the concept of abnormal on one side of the line corresponding to high risk and requiring treatment, and normal on the other side, being low risk requiring no treatment is now under scrutiny.

The polypill concept goes further and offers treatment regardless of risk factor levels, since any reduction will reduce risk. Research from last year showed that drugs which reduce cholesterol had health benefits for people whose cholesterol was not considered to be high.

## What are the main reasons for **not** taking the polypill medications?

Some doctors do not like the polypill approach and argue that people should be monitored regularly, encouraged to lead a healthy lifestyle and conditions such as high blood pressure should be treated if they occur. There is also the time to take the tablets each day, the cost and the risk of side effects.

However, the polypill is aimed at preventing heart attacks and strokes. Remember, around 40% of deaths are due to these conditions and almost everyone is at risk. If side effects occur then the Polypack contents can be altered or your patient can stop taking it. The cost is around \$1 a day, and the convenient packaging means that it is quick and easy to take the tablets, as opposed to opening 5 bottles.

## What if a patient has a contraindication for 1 or more of the components?

You can simply not add 1-2 medicines to the Polypack prescription.

## Why does the patient have to pay?

The Polypack is a private medicine, although it is hoped that it will be funded later. Most of the cost of \$1/day is for the production and boxing of the sachets using a specialized robot, and the processing of the prescription.

## Is there research to show that the Polypack will work?

No – but there is excellent evidence that the components work, and there is no reason to doubt that it will work. Long-term studies of thousands of patients will prove it once and for all, but these studies are 10-20 years away – if they happen at all.

## How long would a patient take the polypill medications for?

Indefinitely. It is necessary to continue taking the pills to maintain the preventive effect.

## What are the side effects?

Around 1 in 10 people may experience side effects, mostly from the aspirin component. Side effects are possible from all 5 components, however, the suggested doses in the Polypack are all low in order to reduce the chance of side effects. If your patient experience a side effect, you can choose a modified Polypack, without the tablet(s) that is causing the problems. In the recently published Polycap study, around 4% of people taking the Polycap dropped out of the study because of side effects, and in the study they did not have the option of removing 1 or more components.

The most common side effects are:

Aspirin	Stomach pain, stomach bleeding
Atenolol	Tiredness, low blood pressure, slow heart rate, dizziness, depression, shortness of breath, fatigue
Simvastatin	Very rarely - liver damage, severe muscle pain
Enalapril	Dizziness, cough, headaches
Bendrofluazide	Low blood potassium levels, impaired glucose tolerance, impotence

Are there any people who should not take the pills?

Yes, there are some contraindications, and all doctors will be very familiar with the components. You can choose a modified Polypack, without the tablet(s) that is not suitable for your patient.

Contraindications include:

Aspirin	Aspirin intolerance, peptic ulcers, asthma
Atenolol	Slow heart rate, asthma, some types of angina
Simvastatin	Few contraindications
Enalapril	Impaired kidney function, some heart valve diseases
Bendrofluazide	Known allergy to this or similar drugs, gout

Is the Polypack programme being monitored?

No, in order to launch the service as quickly as possible there is no initial research programme in place, but there are plans for several research studies around the programme.

Should I wait until there is more research?

You can do this, but most experts in the field think that the evidence from the medical literature is now strong enough for the widespread use of this approach. All of the drugs are used in low doses and have been routinely used in medical practice for many years and in millions of patients. It is estimated that the delay in the introduction of beta-blockers in the USA could have cost 119,000 lives. Medicine is a very conservative profession, and rightly so, but it often takes 10 years until a treatment is shown to be safe and effective before it becomes part of standard medical practice. No-one is being forced to take the Polypack – we are simply making this option available in a practical way.

How long will it be until the single polypill arrives?

Current estimates are over 5 years, but it could be 10 years or they may never appear at all, as there are huge regulatory hurdles to overcome and as the drugs are off-patent, the pharmaceutical industry is not developing polypills. From when the polypill concept was first raised in 2002, it has taken until 2009 for the first small study to be completed.

## Why launch the Polypack now?

There are 2 main reasons. Firstly, development of the polypill has been frustratingly slow and a product is 5-10 years away, if it appears at all – thousands of people could benefit by taking it now. Also, the first study results have just been released. There was a concern that the 5 drugs may cause too many side effects, but this was not seen in the study published in *The Lancet* in March 2009. In addition, the benefits seen in this study were very similar to what was predicted.

## Does the Polypack have any advantages over the single polypill?

Yes, it is available now, the components can be removed to suit individual people, and taking up to 5 small pills may be easier for many people than taking one large one.

## Is a prescription needed?

Currently, yes, although the aim is that eventually you will be able to buy the Polypack from a pharmacy without a prescription.

## Do patients still need to exercise and eat well?

YES, YES, YES. Exercise and a good diet are important to everyone and should definitely be encouraged in patients taking the Polypack.

## How does the packaging into sachets help?

For almost all people, taking 5 different medications, from 5 different bottles, for many years, is simply not feasible. We know for certain that adherence to treatments is inversely proportional to the complexity of the regime. Taking the contents of a single sachet is much easier. The pills are all very small and most people will be able to easily take them in one swallow with water. If you are going away for a few days or on holiday, you can simply tear off the number of sachets that you need rather than taking lots of tablet bottles with you.

Studies have shown that packing in sachets such as this is preferred over blister packs and in South Auckland, this approach in people with diabetes led to improved long-term blood sugar levels.

## At what age should patients start taking the polypill medications?

This is hard to answer and is for you and your patient to decide. The benefits are greater in those with more risk factors for heart attack and stroke and so if your patient has two or more risk factors, you might want to start your patients on the polypill medications in their 40's or even 30's. In general though, 50 and over is thought to be around the right age.

# [ Polypill Further information ]

## [ Medical Journal papers ]

1. Benefits, challenges, and registerability of the polypill. *European Heart Journal* 2006 27(14):1651-1656
2. A strategy to reduce cardiovascular disease by more than 80% *BMJ*. 2003 Jun 28;326(7404):1419.
3. The polypill: at what price would it become cost effective? *J Epidemiol Community Health*. 2006 March; 60(3): 213–217.
4. Polypill holds promise for people with chronic disease. *Bull World Health Organ*. 2005 Dec;83(12):885-7
5. Effect of combinations of drugs on all cause mortality in patients with ischaemic heart disease: nested case-control analysis. *BMJ*. 2006 April 15; 332(7546): 912
6. Improving Medication Adherence in Chronic Cardiovascular Disease. *Crit Care Nurse*. 2008 Oct;28(5):54-64
7. Polypill debate continues. People will always be sceptical. *BMJ* 2004;328:289
8. A "poly-portfolio" for secondary prevention: A strategy to reduce subsequent events by up to 97% over five years. *Am J Cardiol*. 2005 Feb 1;95(3):373-8
9. The 'polypill', friend or foe? <http://www.australianprescriber.com/magazine/28/4/82/3/>
10. Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease. *The Lancet*, Early Online Publication, 30 March 2009
11. Serum Total Cholesterol Concentrations and Awareness, Treatment, and Control of Hypercholesterolemia Among US Adults. *Circulation*. 2003;107:2185
12. Polypill and polyméal: the NHF's view on possible wonder drugs. *Neth Heart J*. 2005 June; 13(6): 248
13. Adherence to prescribed oral hypoglycaemic medication in a population of patients with Type 2 diabetes: a retrospective cohort study. *Diabet Med*. 2002 Apr;19(4):279-84
14. Impact of Pill Organizers and Blister Packs on Adherence to Pill Taking in Two Vitamin Supplementation Trials. *American journal of epidemiology* 2000;152(8):780-7
15. Can medication packaging improve glycemic control and blood pressure in type 2 diabetes? *Diabetes Care*. 2000; 23(2): 153-156.
16. Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review. *Bull World Health Organ*. 2004 Dec;82(12):935-9
17. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein (JUPITER study). *N Engl J Med*. 2008 Nov 20;359(21):2195-207

## [ Magazine articles ]

1. New Scientist. 'Polypill' promises five times the benefits. <http://www.newscientist.com/article/mg20227023.800-polypill-promises-five-times-the-benefits.html>
2. Time Magazine. A Remedy Off the Rack? <http://www.time.com/time/magazine/article/0,9171,1619678,00.html>
3. Protomag.com. A cocktail of cardiovascular drugs // Recommended for everyone over 55 // No prescription necessary // No need for a doctor's oversight // The brainchild of overly ambitious would-be pioneers, or truly the world's next wonder drug? <http://protomag.com/assets/the-polypill>