Twenty years of ground-breaking research from The George Institute has proven the effectiveness of combining multiple medications into one pill to prevent heart attacks and strokes – the world’s leading causes of premature death. By simplifying treatment regimens and making recommended medications more affordable for people at highest risk of cardiovascular disease, our researchers have challenged conventional thinking about how cardiovascular risk factors should be treated, with the potential to save millions of lives if implemented globally.

Hypertension, otherwise known as high blood pressure, is the leading risk factor for premature death and significantly increases the chances of cardiovascular diseases such as stroke, heart attack and kidney disease – the number one killers of people worldwide. Despite the availability of proven and effective blood pressure lowering drugs and established management guidelines, control of high blood pressure remains poor. Only a third of people globally receive treatment for high blood pressure and of those treated, less than a quarter have their blood pressure controlled optimally. Furthermore, most patients on treatment are not able to continue long-term as recommended.

“The scale of the problem is staggering,” says Professor Anthony Rodgers, Head of the Cardiovascular Program at The George Institute. “Over a billion people globally have hypertension and several hundred million are living with cardiovascular disease...”

Conventional treatment usually involves starting one drug, increasing the dose if blood pressure is not controlled, and then sequentially adding additional medications.

Fast facts: high blood pressure
- 1.13 billion people suffer globally
- More than half of strokes and heart attacks are from high blood pressure
- Majority of burden is in low- and middle-income countries, where 20-40% of adults suffer from the condition
- Only 37% of people globally adhere to recommended treatment
- 9 million people die every year worldwide due to cardiovascular complications resulting from high blood pressure such as stroke, heart, kidney and brain disease
- 80% of premature deaths from cardiovascular disease occur in low- and middle-income countries
Once you start taking multiple medications, it’s hard to keep track of how many you are on,” says Ruth. “It becomes expensive, time-intensive and involves multiple trips to the doctor. Medicine adherence rates drop and patients are at greater risk of life-threatening diseases like stroke, heart attack and kidney disease.”

With these challenges in mind, researchers at The George Institute started to think differently about how to address the problem.

“This was the beginning of a new direction for a lot of our research,” says Professor Anushka Patel, a cardiologist and Vice-Principal Director and Chief Scientist of The George Institute. “We knew there were lots of treatments that work, but we also knew that people who most needed these treatments were not necessarily receiving them.”

“We realised that there is as much to gain globally from improving use of existing treatments than discovering new ones - the question was how do you get the proven treatments to be used more optimally among those who need them most?”

“Better access to polypills resulted in better adherence, better blood pressure control and better cholesterol control...”

Professor Anthony Rodgers

The trials sought to answer whether using polypills (containing two blood pressure lowering drugs, a cholesterol lowering drug and aspirin) improved the proportion of patients who were prescribed and taking recommended medications, which would in turn lower their blood pressure and cholesterol and therefore reduce the risk of cardiovascular events such as heart attacks and strokes. Part of the aim of these trials was also to see whether such polypills were acceptable to doctors and patients as well as whether they lowered treatment costs.

At the time, the SPACE Collaboration represented the most comprehensive real-world study of its kind, showing a 43% increase in patient adherence to medication after a year with the polypill.

“Better access to polypills resulted in better adherence, better blood pressure control and better cholesterol control,” explains Anthony.

“However, the really surprising thing was that we were expecting people who were already taking lots of pills to see the greatest benefit from the polypill, as they would be able to take fewer pills. However, in fact the opposite was the case, most of the clinical benefit in these trials was seen in people who just weren’t on the medication they needed to be.”

The evidence was clear – the most significant benefit from polypills was patients being able to access or afford treatment in the first place, and then adhere to their medication.

“Polypills represented a simple, yet powerful step - to get people from no treatment, or one or two drugs - right up to all the recommended medications they need to be on, and stay on, to prevent cardiovascular disease,” says Anthony.

Tackling the world’s biggest killers:
The PILL, IMPACT, Kanyini GAP, UMPIRE & TRIUMPH studies and the SPACE Collaboration

Trailblazing innovation
In 1999, The George Institute staff commenced researching polypills - two years before a program of research was outlined at a World Health Organization (WHO) and Wellcome Trust meeting of medical minds in 2001.

The polypill being investigated at the time was a single capsule containing four different medicines: a cholesterol lowering medication, two blood pressure lowering medications and aspirin. These medicines are recommended as preventive treatment for people who have survived a heart attack or stroke, and for people who are at high risk of such an adverse health event.

By 2006, the next series of polypill clinical trials were underway as part of the Single Pill to Avert Cardiovascular Events (SPACE) Collaboration. The SPACE Collaboration examined data from three clinical studies (UMPIRE, Kanyini-GAP and IMPACT) involving 3,140 patients with or at risk of cardiovascular disease from Europe, India and Australasia.
**Increasing adherence**

Building on the success of this research and other evidence that suggested a triple low-dose pill could reduce blood pressure faster and more effectively, The George Institute commenced the TRIUMPH study in 2012.

Conducted in Sri Lanka with 700 out-patients from urban public hospitals, TRIUMPH was the first trial of its kind to evaluate the use of a triple combination blood pressure lowering pill in the early management of hypertension compared to standard care. Only 41% of patients were receiving hypertension treatment at the start of the trial. All medications, including triple pills, were provided free of charge to the study participants, as per usual practice in Sri Lankan public hospitals.

The results from TRIUMPH showed that using a low-dose combination pill lowers blood pressure swiftly and effectively: 70% of participants on polypills had reached their blood pressure targets, compared to 55% receiving normal care. Importantly, more than 85% of TRIUMPH participants said they would ask their doctor for a polypill if it was available.

“The TRIUMPH study was turning point in the Institute’s polypill studies, with the results demonstrating its use was both safe and effective for hypertension, with global implications,” says Anushka. “The priority now is expediting the uptake of polypills in practice globally so they can have the greatest impact on health outcomes.”

**Harnessing the market, scaling impact**

With TRIUMPH’s results supporting early use of low-dose triple therapy, the key to driving global impact from the research lay in effective implementation and scale-up.

In 2014, George Health, the commercial arm of The George Institute for Global Health, was established to fast-track the commercialisation of affordable, scalable treatments and technologies arising from the Institute’s research and expertise.

George Medicines, one of the four entities comprising George Health, was tasked with translating the polypill research into a scalable and viable business model.

In 2016, the commercial development of the polypill commenced with the establishment of SmartGenRx, a $4.5-million joint venture between The George Institute and Bupa Australia.

Polypill commercialisation was given an additional boost in 2020 with one of Australia’s largest ever private-public health partnerships - a $53-million investment to fast-track the growth of George Health and George Medicines. The financial boost will contribute to the development and commercialisation of several pioneering drug treatments, including polypills and triple pills.

**The challenge ahead**

A concerted global effort is now needed to truly realise the potential impact of polypills.

“We need to work with communities and like-minded partners, such as other researchers, health professionals and governments, to advocate for the implementation of the polypill so it is widely used in all health settings,” explains Anthony.

“This will be especially important when our polypills are close to market - we’re hopefully going to be in that position in the next six to 18 months.”

By rethinking the way high blood pressure is treated globally, increasing patient adherence rates and reducing treatment costs, polypills can play a key part in achieving the ambitious WHO target of at least a 25-per cent reduction in premature mortality from non-communicable diseases by 2025. It can also help to meet the WHO goal for coverage of preventive medications in at least 50 percent of the population with symptomatic cardiovascular disease.

“Globally, we have really just scratched the surface in terms of achieving access to proven treatments,” Anushka says. “We need to use every strategy possible and polypills are a simple, low-cost and effective part of the solution.”

**TRIUMPH findings at a glance**

- 70% of patients using the triple pill treatment reached their blood pressure target after six months, compared to 55% using conventional treatment
- After six months, 83% of patients who used the triple pill treatment continued to use it, compare to approximately 50% of patients in conventional treatment using only one pill, and 33% using two or more pills
- These results were achieved without a significant increase in adverse side effects
Tackling the world’s biggest killers:
The PILL, IMPACT, Kanyini GAP, UMPIRE & TRIUMPH studies and the SPACE Collaboration

Projects:
Program to Improve Life and Longevity (PILL), Improving Adherence using Combination Therapy (IMPACT), Kanyini Guidelines Adherence with the Polypill Study (Kanyini GAP), Use of a multidrug pill in reducing cardiovascular events (UMPIRE), SPACE Collaboration (IMPACT, Kanyini-GAP and UMPIRE trials), Triple pill vs. usual care management for patients with mild-to-moderate hypertension (TRIUMPH)

Research leads:
Professor Anushka Patel, Professor Anthony Rogers, Professor David Peiris, Associate Professor Ruth Webster

Project cycle:
1999–2020

Partners and supporters:
PILL: Wellcome Trust; Brazilian Ministry of Health; Dr Reddy’s Laboratories, India
SPACE Collaboration and trials: National Health & Medical Research Council (NHMRC) Australia; European Commission; Imperial College London, UK; British Heart Foundation; Health Research Council, New Zealand; National Heart Foundation, New Zealand; Dr Reddy’s Laboratories, India; Clinical Trials Research Unit, University of Auckland; Centre for Chronic Disease Control; Public Health Foundation of India; Royal College of Surgeons in Ireland; University Medical Centre Utrecht, Hospital do Coração (Cardiac Hospital), Brazil; Medical Research Council of South Africa
TRIUMPH: Global Alliance for Chronic Disease (GACD); NHMRC Australia, The George Institute Australia, The George Institute India, George Clinical, RemediumOne, Sri Lanka;

About The George Institute for Global Health:
The George Institute for Global Health is focused on generating robust evidence to create better treatments, better care and healthier societies. This means not only generating evidence to determine what works, and doesn’t work, but also which health service or treatment is value for money and where the cost of healthcare can be reduced. Paramount to our work is finding new ways to fund healthcare so health systems can become more sustainable, as well as operate more equitably.

About The PRISM Initiative:
Through interviews with investigators and research partners, project staff and peers in the research community, The Project & Research Impact Story Mapping (PRISM) Initiative examines key research milestones of The George Institute and explores the impact of its projects on health sectors and systems, government policies, communities and more. Join us as we explore key research achievements of the past 20 years, examine how conventional thinking was challenged, who benefitted and what led the research to be transformed into practice.

George Health at a glance
Four social enterprises developing innovative treatment and care solutions for the global chronic disease market:
• George Clinical: A leading contract research organisation in Asia-Pacific with global capabilities
• George Medicines: Innovative affordable treatments for the leading causes of death globally
• George Health Technologies: Affordable, personalised digital health care for all
• Ellen Medical Devices: Developing the world’s first affordable dialysis system