Post-SPRINT trial headaches

October 1 2015, by Hilda Bastian


BMI, Waist Circumference and Associated Risks
Disease Risk* Relative to Weight and Waist Circumference**
Know Your Numbers
Everyone needs to know their blood pressure numbers as there are often no signs or symptoms of high blood pressure. That is why high blood pressure is called the silent killer
Normal Blood Pressure
Systolic pressure
Diastolic pressure
Less than
120/80 mmHg
millimeters of mercury
lifeclinic.
BETTER HEALTH THROUGH AWARENESS
www.lifeclinic.com
STOP

Blood pressure measurement kiosk

On 11 September, some 9,300 participants in the SPRINT trial were sent a letter from the National Institutes of Health (NIH).

The letter told them the part of the trial where they needed to meet a set blood pressure target is over – but follow-up on other questions will go on (PDF).

Larry Husten reported that SPRINT results will be presented on 9 November at the American Heart Association meeting, a full publication "later this fall".

SPRINT (the Systolic Blood Pressure Intervention Trial) aimed to be the "definitive clinical trial in non-diabetic hypertensive participants" on whether lowering systolic blood pressure to 120 mm Hg is better than 140 mm Hg in preventing deaths and serious cardiovascular disease. That had been designated by the heart Institute of the NIH as "the most important hypothesis to test regarding the prevention of hypertension-related complications."

It's an extremely important trial. But now that the intervention is over so much earlier than planned, can it still be as definitive as planned?

In my earlier post, I discussed the risks of stopping a trial early. Even if the trial is ideal in every other respect, stopping early throws at least a small spanner in the works. Some would give a trial one "high risk of bias" check right off the bat, just if it's stopped early because of interim results.

What actually happened in this trial, though, and how might stopping

early have an impact on the results?

The participants are all over 50, with above normal blood pressure, and at least one other risk factor for heart disease and stroke. You can see how well the randomization worked in the baseline data in their 2014 methods publication.

There were 2 arms to the trial: "standard" and the intervention to drive blood pressure down low. People in both groups got standard educational materials. Lifestyle interventions and non-medication therapies weren't restricted. There is a second study embedded, to find out if there is an impact on cognition.

Everyone was supposed to get monthly visits for the first 3 months, then every 3 months for the rest of the trial. The people in the standard group were expected to have reached their blood pressure goal in 3-6 months. The intervention group were to get additional monthly visits until they reached their goal: 8-12 months was expected.

To keep the planned differences between the groups, medicines were to be reduced in the standard group if blood pressure was getting down towards 130 mm Hg. For those in the intervention group, doses/extra medicines were to be added until the systolic blood pressure dropped down low enough.

There was a Recruitment, Retention and Adherence Subcommittee. Adherence was monitored regularly with a patient report scale at each medication visit. Measures to improve adherence got more intense if people were on 4 meds and still not reaching the target. The commitment of the participants and the trial teams seems extraordinary.

The recruitment mix shifted as the trial went along, because there was difficulty reaching the goals for some subgroups. At the end there were

fewer women than intended (36% not 50%), people over 75 (28% not 40%), people with chronic kidney disease (28% not 46%), and people with cardiovascular disease (20% not 40%).

The study's start date was October 2010. There were some early protocol changes (for example, the age criteria for inclusion dropped from 55 to 50): the final (2012) version of the protocol is online and packed with useful detail (PDF).

Participants were meant to be followed for a minimum of 4 years, with 2 years of recruitment – the press release suggests recruitment may have gone on a little longer though. The original final data collection date was 2018. The final round of data collected before the blood pressure intervention stopped was reported by Suzanne Oparil, one of the investigators, as being in August 2015.

The trial was stopped because of a clear impact on the primary outcomes (death or a composite of serious cardiovascular outcomes). From the press release:

…reduced rates of cardiovascular events, such as heart attack and heart failure, as well as stroke, by almost a third and the risk of death by almost a quarter.

Sarah Hedgecock reported that at the press briefing, the results were said to be "consistent for the overall study population". From the different reports, it appears adverse events data was not fully analyzed.

There aren't enough tea leaves here to read much into. If the primary outcome turns out to be rock solid and confirmed in the future, other aspects of the study – including the cognition study – are vulnerable to the shorter intervention period. That includes knowledge about longer term and less common adverse events, and the impact on subgroups of

sicker people.

Stopping this trial would have been a very tough judgment call. There are stories about other trials in my previous post, if you want a peak behind the curtains of this part of the clinical trial process.

One thing is very sure though, and reading the SPRINT materials is enough to give you a headache about it. Keeping your blood pressure driven down very low, consistently, for decades is a mindbogglingly daunting prospect. And Oparil points out that the risks of going too low might be a little different outside the intensively supported clinical trial.

Hypertension, especially mild hypertension, is a risk factor, really. If we move ever more closely to treating "pre-hypertension" very intensively, too, we'd be throwing the medical book, in effect, at "pre-pre-disease". Even if we are very sure about it, the question of feasibility remains wide open.

This story is republished courtesy of PLOS Blogs: blogs.plos.org.

Provided by Public Library of Science