A Winnipeg scientist and his team have shown that the humble flax seed has the power to dramatically reduce high blood pressure – a development that could help cut the incidence of cardiovascular disease by as much as 50 per cent.
Dr. Grant Pierce is not a fish person.

“I just don’t like the taste,” he says simply.
The Winnipeg scientist’s dislike of fish may seem like a trivial detail, especially when raised in the context of his research into the health benefits of certain types of foods.
But it is, nonetheless, one of the reasons why Pierce decided to embark on a major research project more than 10 years ago that now promises to change much about how we treat high blood pressure and cardiovascular disease in Canada and around the world.

At the time, Pierce, Executive Director of Research at St. Boniface Hospital, was helping to launch the newly minted Canadian Centre for Agri-Food Research in Health and Medicine (CCARM). The research facility, a partnership between St. Boniface Hospital, the University of Manitoba and Agriculture and Agri-Food Canada, is dedicated to exploring the health benefits of foods, particularly those grown on the Prairies.

As Pierce, a physiology professor in the Faculty of Medicine at the University of Manitoba, reviewed his options, he started to focus on flax seed, and with good reason.

New research at the time suggested that significant health benefits could be derived from omega 3 fatty acids found in fish. Studies indicated that, among other things, omega 3 fats could boost brain development and promote heart health.
Flax also contains omega 3 fatty acid, but it differs from the kind found in fish. Omega 3 fatty acids eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) are found in fish, while a third omega 3 called alpha-linolenic acid (ALA) is found in flax.

At the time, it was thought that the omega 3 fatty acids found in fish were more beneficial than the kind found in flax. As a result, the health spotlight shone on omega 3-laden fish, while the humble flax seed remained in the shadows – a healthy food to be sure, but not necessarily as beneficial as some others.

Pierce decided to test that theory.
“When it came to looking at flax seed, I was persuaded by the effect of fish and the omega 3 fatty acids they contain and their effect on cardiovascular health,” says Pierce.
“You hear all the time that the omega 3s found in fish are very good for brain development and a variety of things,” he says. “Well, if you follow this thinking logically, that means vegetarians haven’t had good brain development as they grew up. I don’t go for that. They must have had their omega 3 fatty acids from another source, and I bet you they fared just as well.”

Pierce figured he probably wasn’t the only one who didn’t care for fish, and concluded that there might be some interest
in researching alternative food sources to fish-based omega 3s. And since flax is grown in abundance in Manitoba, the plant seemed like the perfect choice for the first long-term study at CCARM.

"If the fatty acid in flax is structurally different than fish, then potentially it's biologically different," says Pierce. "In other words, it may have a different biological effect. It may be worse. It may be better. And we wanted to examine that."

Now, more than 10 years later, following a series of studies and clinical tests involving 110 people, Pierce believes flax is ready to step out from the shadows and claim its rightful place as one of nature’s true super foods. That’s because he and his team have recently completed a clinical trial demonstrating that flax, depending on how it is consumed, has the potential to significantly reduce blood pressure, thereby possibly decreasing the incidence of stroke by as much as 50 per cent and heart attack by about 30 per cent. The findings, in effect, that the tiny brown seeds derived from the pale blue flowering plant grown across Manitoba could be as powerful as any blood pressure medication on the market today.

The health implications flowing from the research are huge. Hypertension (high blood pressure) is a leading cause of cardiovascular illness, including stroke and heart disease. In Canada, cardiovascular disease is one of the leading causes of death, accounting for an estimated 29 per cent of all deaths, or about 70,000 people each year, according to the Heart and Stroke Foundation of Canada. In Manitoba, a report produced by Manitoba Health says about 235,683 people in this province had hypertension in 2010/11. That represents about 27.2 per cent of the population 20 years of age or older, compared to 21.7 per cent in 2000/01. The report also says about 1,514 people in Manitoba suffered a stroke in 2009/10, while 2,420 had a heart attack.

In addition to shedding light on possible new approaches to treating and preventing disease, the research also underscores the importance of the work being done at CCARM, located at the St. Boniface Hospital Research Centre.

Pierce helped launch CCARM in 1999 with a view to filling a gap in the medical research world. As he explains, drug companies spend billions of dollars annually on the research and development of new drugs, but comparatively little is spent on researching the health benefits of particular foods or how they might be used. The reason is that drug companies can’t patent the information that might come from researching the health benefits of a particular food, consequently there is no incentive to spend money researching its value. Even the health food and supplement industry – a multi-billion dollar business – spends relatively little to actually research the claims often made for their products.

That’s where CCARM comes into play. Researchers at the centre are dedicated to researching nutraceuticals or functional foods that may have some health-related benefits. A functional food is something like muffins that contain a dose of bran. A nutraceutical is an extract like ginseng or Echinacea extract.

Pierce says the goal is simple: “Either we prove that these foods or nutrients are of benefit to our health, or we prove that they aren’t. If the marketing claims hailing their benefits turn out to be unsupported by good scientific data, people can stop wasting their money on products that they thought were good for them.”

From the outset, the vision at the centre has been ambitious, focusing on long-term, complex studies that can be costly. As a result, it is important to look for locally-grown foods that are potentially healthy and marketable –
Flax magic

Flax is known to provide certain health benefits. For example, it is believed to play a role in reducing inflammation and fighting some types of cancer. But research conducted by Dr. Grant Pierce and his team suggests flax can play a major role in boosting cardiovascular health and reducing high blood pressure. Pierce says he believes that three ingredients found in flax work together to achieve this outcome. They are:

**Omega 3 fatty acids:** There are three major types of omega 3 fatty acids – docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and alpha-linolenic acid (ALA). DHA is found in fish and is believed to play an important role in brain development and function. ALA is found in flax. ALA helps reduce inflammation, which helps reduce the buildup of plaque in arteries, a prime cause of stroke and heart disease.

**Fibre:** Flax is high in soluble and insoluble fibre. Soluble fibre absorbs bad fats from the body, reducing cholesterol levels and blood pressure.

**Lignans:** These are plant compounds found in flax. When they interact with bacteria in the digestive system, they produce potent antioxidants.

two factors that can help attract potential investors.

The research into flax is a good example of how that relationship works. The study’s primary goal was to determine whether flax had significant health benefits, and involved dozens of willing participants and a host of medical researchers and clinicians at the University of Manitoba and St. Boniface Hospital. But it also drew on the expertise and support of the Canadian International Grain Institute, the Food Development Centre in Portage la Prairie, Canada Bread and the federal and provincial governments, who were interested in the economic implications of discovering the health benefits of a locally-grown crop.

From the outset, Pierce knew that his research would likely confirm that flax did indeed have a number of health benefits. One area he wanted to investigate was whether it would help reduce cholesterol.

- **2010:** Work in animals is initiated to determine if flax seed can reverse cholesterol-filled plaques once they are already established. Further animal research shows flax seed and ALA can prevent the production of plaques in arteries caused by trans fats in the diet.

- **2011:** The last patient finishes the trial and the results begin to be analyzed.

- **2012:** The effects of flax seed on hypertension are reported at the annual American Heart Association meeting in Los Angeles. A paper is submitted describing these results in detail to a major peer-reviewed journal in the heart field.

- **2013:** The first major paper from this trial is accepted for publication in the highest-ranking heart journal in the world. Work on several more papers incorporating the data from this trial continues.

Milled or ground flax is more effective in reducing high blood pressure because it is easier to digest than whole seed flax.
High cholesterol contributes to the buildup of plaque in the arteries, which restricts the flow of blood and can cause heart attacks. "Omega 3 fatty acids are anti-inflammatory and we now know that inflammation is an important component of heart disease, creating blockages in your arteries and altering how your arteries work," he says.

The first step in the multi-year research project involved basic lab work – looking at cells in a petri dish under a microscope. Once the basic tests were completed, the team began animal testing. Lab animals were fed a high-cholesterol diet. While the control group animals received regular food, others had milled flax seed added to their diet. The animal studies yielded impressive results, showing flax had the potential to significantly reduce the cholesterol-filled blockages in arteries. Further animal studies also demonstrated that flax prevents cholesterol buildup from a diet high in trans-fats.

The research team found other benefits. When researchers induced conditions in flax-fed animals that resembled heart disease, their hearts were found to have added resistance to developing an irregular heartbeat.

“One of the major complications in a heart attack is that the heart will go into something called an arrhythmia, or an irregular heartbeat, and ultimately, if it’s severe enough, that’s what kills many patients," says Pierce. “Flax prevented some of the most dangerous arrhythmias.”

In addition, researchers also discovered that flax made the animals’ smooth muscle lining in their arteries relax more than the control group. This relaxing effect on arteries could potentially reduce the incidence of adverse cardiovascular events – such as heart attacks or strokes, which occur when blood flow is substantially reduced to parts of the brain. The findings were significant enough to prompt more research involving clinical trials in humans with heart disease.

“Because of those three effects we found in the animals, we got pretty excited,” Pierce says. “The animal work was so positive, we knew it was time to move on to human studies to see if it’s beneficial to us.”

Those studies started four years ago. Even though the first phase of the clinical study involved only a year of monitoring patients, Pierce says a lot of groundwork had to be done first. His team needed to carefully design an experiment that would show as conclusively as possible that flax does or does not benefit human health.

Pierce hypothesized that previous studies that had shown minimal cardiovascular health benefits from flax had more to do with the design of the studies than with the plant itself. So he and his team carefully built their study from the ground up, with financial support from the Canola Council of Canada, Flax 2015, the Flax Council of Canada, the Agri-Food Research Development Initiative, St. Boniface Hospital Foundation and a variety of other companies and organizations.

Before working with patients suffering from heart disease – a group that could dramatically show the most potential benefit – the team ran a number of mini-trials on healthy individuals to answer a number of questions, which arose earlier in the research.

“That’s why the animal work is done, and prior to going into the clinical trials, you work on healthy people first. There were some basic questions that needed to be answered prior to setting up a major trial in a diseased population,” says Pierce.

One of the most important of these questions was how much flax would a patient need to ingest in order to achieve optimal results? But before they could find an answer to this problem, they had to figure out the best way for the patients to ingest flax. Was it better to eat flax as whole seed, as a milled product or as an oil?

During this part of the research, they discovered that patients eating whole seeds showed no increase in omega 3 fatty acids in their blood. But significant levels of omega 3 did show up in the blood tests of participants ingesting flax oil or the milled product.

With that problem solved, Pierce and his team moved onto a trial to determine how much flax seed someone would have to consume in order to derive a benefit.

Eventually, they determined that 30 grams of milled flax provided a dose of ALA that would likely provide heart-healthy benefits. But uncertainty persisted because flax seed omega 3 oils (ALA) have a different molecular structure than the (DHA and EPA) omega 3s found in fish.

In a nutshell, the ALA found in flax has a shorter molecular structure. This type of beneficial fat is also found in walnuts, hemp seed, kiwis, canola and soybean, but flax contains the highest concentrations.
“The only difference amongst different omega-3 fatty acids we found was the way they’re absorbed,” explains Pierce. “If I gave you a pill that contains fish oil and a pill that contains flax oil, the EPA and DHA seemed to be absorbed a little bit better, so you have to take a little bit more of the flax oil to get the ALA levels in your bloodstream to a level equivalent to the fish oils.”

Yet, arguably, the most important research work, contingent to the success of the larger clinical research puzzle, was developing food products that would contain enough flax to be beneficial while still being palatable.

And that is not an easy thing to do, according to Dr. Michel Aliani, Director of the Weston Sensory and Food Research Centre in the Department of Human Nutritional Sciences at the University of Manitoba, and a member of the CCARM research team.

Flax on its own is not exactly tasty. The seed is bitter and quite granular, potentially making any product containing it bland, dry and largely unappealing. “We knew more or less that the food would be healthy, but the challenge is whether people can eat it on a daily basis,” says Aliani.

That’s where Canada Bread and the Food Development Centre in Portage la Prairie stepped in. They developed food products using flax donated by Pizzey’s Milling and Glanbia Nutritionalss. From buns, bagels, biscuits and muffins to pasta and snack bars, they developed a variety of baked goods and other products that would appeal to clinical trial participants’ tastes.

“Developing foods that contain the required amount of flax has been a major challenge in and of itself, let alone making them tasty,” he says. “We had to have 30 grams of flax seed in one muffin or bagel, and that’s huge (equal to three heaping tablespoons of flax) because it amounts to about one-fifth to one-sixth of the entire muffin or bagel,” he says. “The study participants had to eat one of these per day and this was a very long study.”

Researchers had to figure out how to include that much flax into a recipe without compromising the integrity of the food product. Would a muffin or bagel with that much flax even hold together?

“Even today,” Aliani says, “recipes for future studies are

BIO: Dr. Grant Pierce

Dr. Grant Pierce was born in Welland, Ontario, and moved to Winnipeg in 1979. During his career, Pierce has published over 200 research manuscripts and written or edited eight textbooks on a variety of topics concerning metabolism, nutrition and cardiovascular health. His research papers have been cited well over 4,000 times. He has delivered over 250 invited lectures in 31 countries and organized more than 50 international meetings.

Pierce’s work on diabetic cardiomyopathy and ischemic heart disease has been pioneering and highly cited. He has served on the editorial boards of the top basic science cardiovascular journals in the world, including Circulation Research, American Journal of Physiology and the Journal of Molecular and Cellular Cardiology. He is currently Co-Editor of the Canadian Journal of Physiology and Pharmacology and Associate Editor of Molecular and Cellular Biochemistry.

In 1986, Pierce returned to Winnipeg from studies at the University of California at Los Angeles (UCLA) to help found the Canadian Centre for Agri-Food Research in Health and Medicine (CCARM), a partnership of St. Boniface Hospital, the University of Manitoba and Agriculture and Agri-Food Canada, to investigate the health-related benefits of nutraceuticals and functional foods. Over the years, the centre has expanded to include researchers from Agriculture and Agri-Food Canada. In 1994, Pierce was appointed a professor in the Department of Physiology, Faculty of Medicine, University of Manitoba. He is currently the Executive Director of Research at St. Boniface Hospital.

Awards/Distinctions:
Throughout his career, awards for research excellence have been received from the American Heart Association, the International Society for Heart Research, the Heart and Stroke Foundation of Manitoba, the Canadian Institutes for Health Research, the Life Sciences Association of Manitoba, the University of Manitoba and institutions in several different countries. He recently received the Queen Elizabeth II Diamond Jubilee Medal from the Government of Canada. He is the only Manitoban to serve as the Chair of the Scientific Review Executive Committee for the Heart and Stroke Foundation of Canada, where he was responsible for all peer review conducted by the foundation. He is an elected Fellow of seven different international organizations.

Education:
1976: B.P.H.E., Lakehead University;
1979: M.Sc., Dalhousie University
1983: PhD in Physiology, University of Manitoba.
1983 to 86: Postdoctoral training, University of California at Los Angeles.

Dr. Grant Pierce holds a sample of the milled flax seeds that can help reduce high blood pressure.
Flax has tremendous potential to reduce the risk of developing cardiovascular disease. But unlocking the benefits of this remarkable little oilseed can be tricky.

For example, just eating flax seeds will not reduce your risk of stroke or heart attack. That’s because flax seeds are not easy to digest, and chances are they will pass through your system without imparting any health benefits, according to Dr. Grant Pierce.

Flax seeds do become easier to digest when they are ground or processed into flax oil. In Pierce’s study, some hypertensive participants consuming just over 30 grams of milled flax a day for six months experienced blood pressure reductions of 15 mmHg systolic and seven mmHg diastolic.

Pierce says, “So we wanted a population of patients with those types of problems.” They found a good match in the patients under the care of Dr. Randy Guzman, Director of the I.H. Asper Clinical Research Institute and Vascular Research at St. Boniface Hospital and an associate professor of surgery in the Faculty of Medicine at the University of Manitoba. His patients suffered from peripheral arterial disease, a condition that clogs arteries and blocks blood flow. “These are patients with arterial problems outside of the chest – or cardiac area – and instead, they often have problems in their lower extremities,” says Guzman. “The same plaques that block up the arteries that feed blood to the heart can block up other arteries, like in the legs.”

About 80 per cent of the patients were on medication for high cholesterol while 75 per cent took medication for high blood pressure. Because these patients are considered to be very ill, even though they’re under medical care and making efforts to improve their health, Pierce says they were ideal candidates for the clinical phase of the study. “They have a high incidence of heart attacks and strokes. They have a lot of arrhythmias, and they have all the characteristics that made us think, ‘Hey, this is exactly the group that flax seed may help.’”

Although the study set out to measure cholesterol levels, with the hypothesis that flax would reduce blood cholesterol over the course of a year, Pierce says they discovered an unexpected and pleasant surprise. Patients’ blood pressure fell. “Approximately 75 per cent of the patients who came into our trial were hypertensive,” Pierce says, adding their average blood pressure was 158 millimetres mercury (mmHg) systolic over a diastolic of about 81 mmHg. “These patients were already on anti-hypertensive drugs and still their blood pressure was poorly controlled, partly because they had so many things going on with them that the physician can’t keep up in treating all of the problems.”

After a month into the trial, their blood pressure decreased and continued to fall until the six-month mark when it stabilized. By the end of the study, the average study participant’s blood pressure decreased 15 millimetres mercury (mmHg) systolic and seven mmHg diastolic.

Unlocking flax’s health benefits

Flax has tremendous potential to reduce the risk of developing cardiovascular disease. But unlocking the benefits of this remarkable little oilseed can be tricky.

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You can find ground flax seed in numerous products, including bagels, cereals, snack bars, and even some types of tortilla chips.

You can also add flax to your foods at home. The Flax Council of Canada has a number of suggestions on its website. They include:

- Add ground flax seed to cereal, salads or yogurt.
- Drop some ground flax seed into your soups, stews and chillies.
- Use ground flax seed when making muffins and cookies.

For more information about flax seed, including nutrition facts and recipes, visit the Flax Council of Canada website at www.flaxcouncil.ca
Research Team

Some members of Dr. Grant Pierce’s research team. Top row, from left to right: Dr. Randy Guzman, Wendy Weighell. Second row: Dr. Grant Pierce, Dr. Bram Ramjiawan, Renée La Vallée, Matthew Lytwyn. Third row: Andrea Edel, Thane Maddaford, Stephanie Caligiuri, Alex Austria, Dr. Michel Aliani. Bottom row: Riya Ganguly, Dr. Marketa Hlavackova, Justin Denisel, Brittany Devaney, Dr. Elena Dibrov.
At first, Pierce wasn’t sure what to make of the results. “I’m not a blood pressure researcher, so, to be honest, when we got the results, I said, ‘Hmnn, okay, I guess these are good. Let’s consult with some hypertension experts,’” he says. “Their response was, ‘Your results are fantastic.’ So we went into the blood pressure literature and that’s when we realized, ‘Wow! We have a major effect here.’”

Guzman concurs with the results. “It’s a significant finding and the magnitude is substantial,” he says. “The exact mechanisms as to how high blood pressure can cause heart attacks or strokes is complicated,” says Guzman. “But the bottom line is if you can reduce blood pressure in patients, you can also decrease their risk of having a stroke or heart attack.”

Pierce attributes the reduction in blood pressure to three main ingredients in flax:
- **Omega 3 fatty acids**: These are known to reduce inflammation, and a buildup of plaques in the artery walls is suspected to be a by-product of an immune system response to high-fat diets, stress and other factors that lead to arterial inflammation.
- **Fibre**: Flax is high in soluble fibre, which absorbs bad fats from the body, reducing cholesterol levels and blood pressure.
- **Lignans**: These are potent antioxidants, more potent than Vitamin E.

Pierce believes it was these three ingredients working together that created the synergistic effect that reduced the study participants’ blood pressure during the trial.

“You have to remember, one millimetre difference is a huge impact on heart attacks and stroke,” he says. That’s a result even better than those found from consuming fish. “Fish can reduce blood pressure in hypertensive patients by about four millimetres mercury systolic, so it’s nowhere near the level for flax.” Furthermore, flax may be more beneficial than fish because it contains less cholesterol than fish.

In addition to a drop in blood pressure, the participants also experienced a cholesterol reduction of about 10 per cent, but Pierce says those findings are currently being written up for publication in a medical journal later this year.

But Pierce says it’s the blood pressure findings that are the most compelling at this stage. No other food or supplement comes close. “There’s no comparison. Flax seed is better than any other dietary intervention ever shown,” he says. That includes the DASH diet (Dietary Approaches to Stop Hypertension), the Mediterranean-style diet prescribed to patients with high blood pressure. “And it’s at least as good as many of the drugs that are on the market today,” he says.

For Pierce, the findings are exciting. “I would hazard to say this is the most significant finding our lab has produced, and I doubt that I will ever find anything better,” he says. “If this has an influence on reducing heart attacks and stroke by as much as the research suggests, I don’t think it gets much better than that.”

Still, the research is only getting started. “Our paper on flax and hypertension is currently being revised for publication in the best heart journal in the world,” he says “and we continue to learn more about how it works from animal trials.”

Aliani says like any good science, Pierce’s research has opened up many new avenues of investigation. “In scientific research, if you have a question, and answer it – case closed – that’s not really good science,” says Aliani, who is now working on a study investigating flax’s benefits for Type 2 diabetes patients. “In good science, the answer to one question should open a lot of others, and that is the case here.”

Indeed, questions abound for Pierce. A lot of research is still left to do.

“For example, these patients were on hypertensive medication so, really, I don’t know whether flax reduces blood pressure in these patients on its own, or did it boost the effects of the drugs?” he says. “In our next trial, that’s what we want to look at – take patients who are not on drugs yet and see if we can reduce the number of them who end up taking drugs, or eliminate the need for them to go on anti-hypertension drugs altogether.”

“The good part is that past work shows flax does not reduce blood pressure in people who are not hypertensive. Our study confirms that.” In other words, people with normal blood pressure won’t lower their blood pressure where they may be at risk of passing out.

Eventually, Pierce would like to examine whether flax can help prevent high blood pressure. “Technically, as a scientist, I cannot say it (flax) will prevent the development of high blood pressure because you’d need another study to determine if that’s the case,” he says. “That’s a super study, one we’d love to do – it won’t be the next study we do – but honestly, that’s where I believe the real gold is; that’s where I believe the real beneficial effects are to be found. If it does prevent or delay disease, then it is a realistic approach for reducing health-care costs in Manitoba and Canada.”

Joel Schlesinger is a Winnipeg writer.
It’s unlikely the groundbreaking research into the health benefits of flax seed would have seen the light of day without the Canadian Centre for Agri-Food Research in Health and Medicine.

Founded in 1999, CCARM is the first nutraceutical and functional food research group organized in Manitoba, and is believed to be the only one of its kind in the world.

“There is no other research group like it,” explains Dr. Grant Pierce, who helped found and chair CCARM, and is now one of 12 principal investigators and over 50 support staff working out of the centre, located at the St. Boniface Hospital Research Centre.

One reason for its uniqueness is that CCARM’s organizational structure brings together many experts across diverse disciplines under one roof.

“We have a teaching hospital, (St. Boniface Hospital), a major university (the University of Manitoba) and a national agricultural organization (Agriculture and Agri-food Canada) coming together here,” he says. “From an organizational standpoint, I’m not aware of any other nutraceutical/functional food group with a national agriculture organization heading clinical medical trials.”

The research carried out at CCARM also sets it apart from other centres because scientists can do bench-to-bedside research into food’s potential health benefits.

“We can look at cells. We can look at animal models of disease,” he says. “We can then move that right into studying the effects on healthy people, and even disease populations, like we have done with the flax seed study. We can eventually evaluate what we all want to know: does this food reduce heart attacks, stroke and other chronic diseases.”

With this one-of-a-kind mandate, CCARM is forging new avenues of understanding about foods’ potential medicinal benefits to human health.

But without the $17-million start-up funding from the federal government, as well as support from the University of Manitoba, St. Boniface Hospital Foundation, the province, and numerous international and national health research agencies, Pierce says research like the flax study might not have ever got off the ground because CCARM wouldn’t be around.

“The widespread support has allowed CCARM to become a centre-point for exciting research with wide-ranging benefits over the last decade. Its research will benefit farmers and the economy – as well as the health of everyone,” says Pierce.

“Our goal at CCARM is not to just do the best science that we can. It's really about knowledge translation and bringing basic science research and clinical research not only to the bedside, but also to the general public in a way where we're all benefitting.”

CCARM is currently led by Dr. Peter Zahradka, professor of physiology in the Faculty of Medicine at the University of Manitoba. This large research group continues to excel in identifying the health-related benefits for pulse crops (beans, peas, lentils, etc.), canola, buckwheat, berries and their components (resveratrol), vitamins, and a variety of extracts from natural vegetation in field and forest.