

Can you describe how antibiotics and probiotics can be balanced to achieve the best outcomes for children?

To make it simple, antibiotics "bad" and probiotics "good". But [it's] not always that way. Many newborns receive short courses of antibiotics... when they have a suspected infection, and then that is stopped. And [even] these short-term antibiotics might do exactly the same thing as [in] the mouse model - so that they [may] have lasting effects on immunological maturation and so on.

Probiotics promote controlled inflammation while antibiotics sort of wash away everything. Like in diarrhea patients, all microbiota is washed away and the Staphylococci... are the ones coming [back] first, and they lead to chronic diarrhea. Of course when you have a condition, you need antibiotics to stop the condition early. I'm not an anti-antibiotics person. But I would say not [to use them] for preventative purposes. For example, a caesarean section does not require antibiotics but [they are] given for some reason. We have given that up a long time ago in [Finland].

Could consuming probiotics help lower blood pressure?

By Honor Whiteman



(MNT)⁽⁶⁾ We have all heard that consuming foods with probiotics - "good" bacteria - promotes a healthy gut. But new research published in the journal *Hypertension* suggests that eating probiotics could also help lower blood pressure.

Probiotics are live microorganisms that occur naturally in the gut. These microorganisms are also present in some foods, such as live-cultured yoghurt, some fermented vegetables and aged cheeses. Past research has suggested that probiotics are good for our health by aiding digestion, intestinal function and protecting against harmful bacteria.

Earlier this year, *Medical News today* reported on a study published in *JAMA Pediatrics*, which suggested that probiotic use among infants may reduce the risk of gastrointestinal disorders. Such evidence has led to the addition of probiotics to certain foods, and they are also available as dietary supplements.

Now, research led by Jing Sun, PhD, of the Griffith Health Institute and School of Medicine at Griffith University in Australia, suggests that consuming probiotics from food sources and dietary supplements may improve blood pressure.

Probiotics 'may help reduce high blood pressure and maintain healthy blood pressure'

To reach their findings, Sun and his team analyzed nine high-quality studies that assessed the probiotic consumption of 543 adults who had either normal or high blood pressure.

They found that on average, participants who had consumed probiotics daily for 8 weeks or more had a 3.5 mm Hg lower systolic blood pressure (pressure in the arteries when the heart beats) and a 2.38 mm Hg lower diastolic blood pressure (pressure in the arteries between heartbeats), compared with those who did not consume probiotics. Such effects were strongest among participants with high blood pressure - defined as 130/85 mm Hg or more - and greater benefits were found from consumption of probiotic products that contained multiple bacteria.

However, the researchers note that consumption of probiotics with fewer than 10⁹ colony-forming units (CFU) - the level of bacteria or dose of probiotics in a product - did not improve blood pressure, nor did consumption of probiotics for less than 8 weeks. Commenting on the team's findings, Sun says:

"The small collection of studies we looked at suggest regular consumption of probiotics can be part of a healthy lifestyle to help reduce high blood pressure, as well as maintain healthy blood pressure levels."

She hypothesizes that probiotics may have a beneficial effect on blood pressure through lowering cholesterol levels, reducing blood sugar levels and insulin resistance,



and helping to regulate the hormone system that manages fluid balance and blood pressure.

Although these findings show promise for the use of probiotics in lowering blood pressure, Sun notes that doctors should not recommend them for blood pressure control until further studies have confirmed the benefits. She also points out that the team's investigation is subject to limitations. "The studies looking at probiotics and blood pressure tend to be small," Sun says. "Moreover, two studies had a short duration of 3-4 weeks of probiotic consumption, which might have affected the overall results of the analysis."

This is not the only study to suggest that the benefits of probiotics reach further than the gut. Last year, *Medical News Today* reported on a study by researchers from the University of California-Los Angeles, which suggested probiotics could be beneficial for brain function, while other research found they could be effective against psoriasis and chronic fatigue syndrome.

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Message from the Editor

14th Edition

From probiotic benefits in heart health and blood pressure to the possibility of lowering allergy risk in newborns, should pique your interest in this edition.

To Dr. Eric Chong, Senior Consultant and Director of Cardiology Service, Jurong Health, Singapore; we extend our sincere appreciation for his contribution in this issue.

For our Chinese readers, we take this opportunity to wish you a very blessed Lunar New Year and a joyous and healthy 2015.

God Bless !

Melvin Wong
Editor-in chief

The Role of Probiotics for Heart Health/Lipid Management

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Introduction

Coronary artery disease and ischemic heart disease (CAD & IHD) are common diseases in Singapore and disease prevalence is rising as a result of Singapore's rapidly aging population, increasing stress levels and increasing prevalence of triple high metabolic disease including hypertension, hyperlipidemia and diabetes.

Coronary disease can vary from simple discrete lesion that is amenable to percutaneous coronary intervention (PCI) to very complex diffuse calcified multi-vessel lesions making even bypass operation difficult due to the poor revascularization targets. Therefore, intensive medical therapy remains a key component to successful management of these patients.

Lipid lowering and anti-inflammatory therapy are some of the key concepts in the management of patients with CAD. The previous American ATP III guideline advocates a cut off value of 2.6mmol/l or 100mg/dl in patients at risk of CAD, and an even lower cut off value of 1.8 mmol/l or 70 mg/dl in high risk patients with existing CAD or IHD. ⁽¹⁾

Fig 1.
Discrete coronary artery stenosis of right coronary artery in a patient with hypertension and hyperlipidemia.

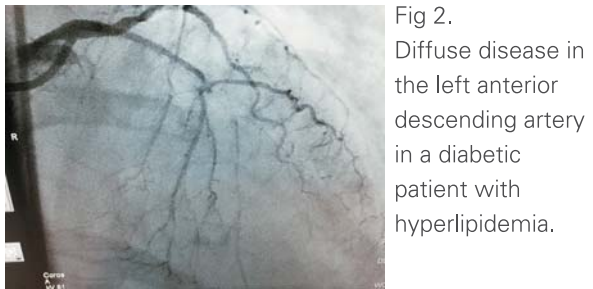
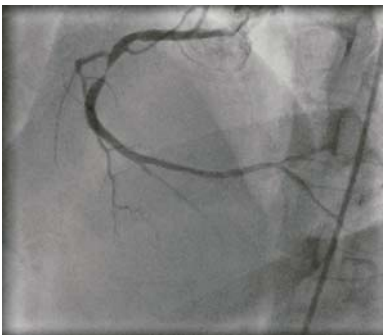


Fig 2.
Diffuse disease in the left anterior descending artery in a diabetic patient with hyperlipidemia.

The newly revised AHA/ACC cholesterol management guideline currently advocates a more stringent recommendation for lipid lowering by >50% reduction in LDL level under the high intensity therapy category for secondary prevention. ⁽²⁾

The 3 highest risks groups include patients with:

- Atherosclerotic cardiovascular disease (ASCVD). These include coronary artery disease, peripheral artery disease, acute coronary syndromes, history of coronary or other arterial revascularization, stroke or TIA.
- Familial hyperlipidemia (LDL > 190mg/dl).
- Diabetic above age 40.

For the remaining patients of age 40-75 years that do not meet the above criteria, but have a 10 year risk of >7.5% based on the AHA/ACC risk calculator, moderate intensity therapy is recommended for primary prevention of CAD. The online calculator can be found at <http://tools.cardiosource.org/ASCVD-Risk-Estimator/>

The statin therapy recommendation according to high and moderate intensity therapy is shown in the table below.

Table 1: Recommendation on high and moderate intensity statin therapy

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy
Daily dose lowers LDL-C on average, by approximately ≥ 50%	Daily dose lowers LDL-C on average, by approximately 30% to < 50%
Atorvastatin (40†) - 80 mg Rosuvastatin 20 (40) mg	Atorvastatin 10 (20) mg Rosuvastatin (5) 10 mg Simvastatin 20-40 mg‡ Pravastatin 40 (80) mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2-4 mg

Other additional risk factors may also be considered which include:

- Family history of premature CAD
- LDL > 160 mg/dl
- Increased CRP greater than 2.0
- Coronary calcium greater than 300
- Ankle brachial index (ABI) < 0.9

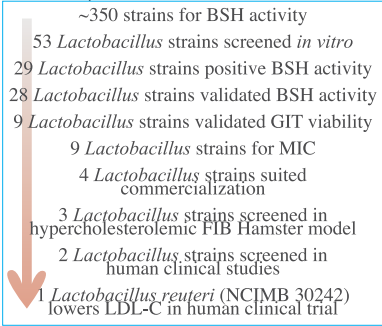
From our clinical experience, Asian patients undergoing intensive statin therapy not infrequently experience statin side effects including myalgia, myositis and transaminitis. High dose statins including atorvastatin 40-80mg or Rousuvastatin 20-40mg may not be well tolerated. In such situations, alternative combination therapy may be considered to achieve the same LDL lowering target with a reduced or more tolerable statin dose. One of the safe add-on alternatives is probiotic therapy, specifically ***Lactobacillus reuteri* NCIMB 30242**. This probiotic is a natural lactobacillus, it can be considered as an indirect form of bile acid sequestrant. It does not increase adverse muscle symptoms and offers additional benefits by improving digestive function and reducing inflammation as compared to other commonly used health supplements in the market such as omega 3 and fibers.

The mechanism of bile acid hydrolase in *Lactobacillus reuteri* NCIMB 30242

The cholesteroLowering effects can be primarily ascribed to bile salt hydrolase (BSH) activity of the lactobacillus that deconjugates bile acid.

The deconjugated bile salts are less efficiently reabsorbed which results in the excretion of larger amounts of free bile acids in the feces. Deconjugated free bile salts are also less efficient in the solubilization and absorption of lipids in the gut. Therefore, cholesterol production is reduced. The liver will then utilize more LDL for its cholesterol shortage and removes more cholesterol from the body to produce bile. The total LDL in blood will be reduced. Other possible mechanisms in LDL lowering with *L. reuteri* NCIMB 30242 therapy also include assimilation of cholesterol by the bacteria, binding of cholesterol to the bacterial cell walls, and physiological actions of the end products of short-chain fatty acid fermentation.

Based on the scientific literatures, *L. reuteri* NCIMB 30242 therapy can reduce LDL level effectively by 11.6%, total cholesterol by 9.1%, non-HDL-C by 11.3% and Apo B-100 by 8.4%. ^(3,4)



The Probiotic Discovery Process of *Lactobacillus reuteri* NCIMB 30242 is shown on the left

Summary for Statin Therapy

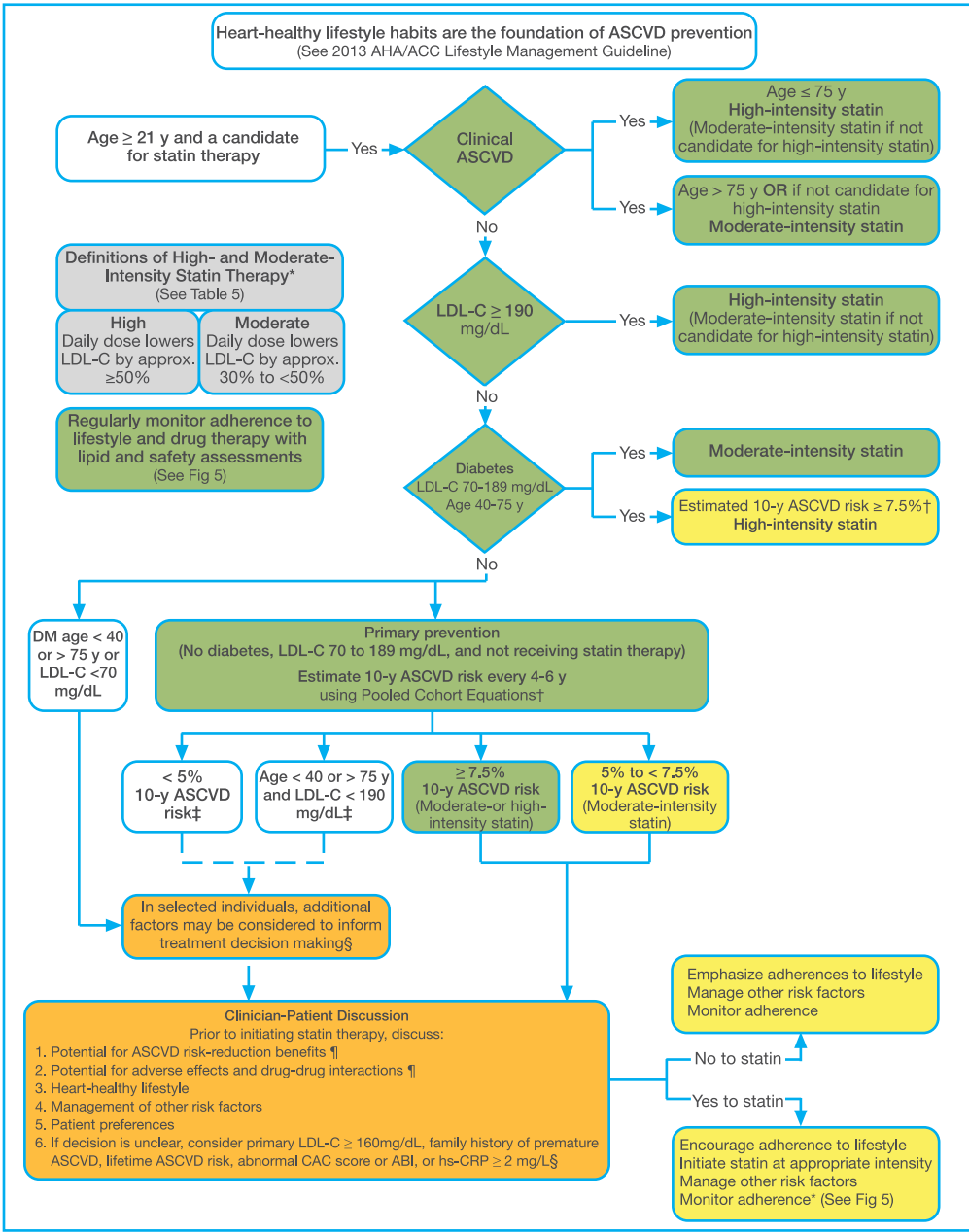


Table 2: A comparison of *L. reuteri* NCIMB 30242 and other lipid lowering health supplements
* Cardioviva™ is marketed as Pro-Lipid in Singapore

	Effective dose (g/day)*	TC reduction vs. placebo (%)	LDL-C reduction vs. placebo (%)	Effect on HDL/LDL ratio	Effect on CV inflammatory markers	Effect on GI health	Reference
Cardioviva™ (<i>L. reuteri</i> NCBIM 30242)	0.2	5 - 9	9 - 12	Yes	Yes	Yes	Jones et al., 2012a; Jones et al., 2012b; Ooi et al. 2010
Phytosterols	1.6 - 3	3 - 15	5 - 15	Yes	No	No	Abumweis et al., 2008; Ortega et al., 2006; Talati et al., 2010; FDA, 2010; EFSA 2012
Fish oil/Omega-3/DHA/EPA	0.85 - 3.4	0	0 - +3	Yes	Yes	No	Hooper et al. 2004; Skulas-Ray et al., 2011; EFSA, 2012;
Oat β-glucan	3 - 10	4 - 9	5 - 10	Yes	No	Yes	Othman et al. 2011; Tiwari and Cummins, 2011; EFSA, 2010; EFSA, 2011; NCEP-ATP III, 2002
Psyllium fiber	7 - 10	2 - 9	3 - 7	Yes	No	Yes	Wei et al., 2009; Anderson et al., 2000; NCEP-ATP III, 2002
Soy protein	25 - 40	3 - 5	4 - 6	Yes	No	No	McVeigh et al., 2006; Anderson and Bush, 2011; FDA, 1999; Erdman, 2000; NCEP-ATP III, 2002

Conclusion

LDL lowering and anti-inflammation therapies are essential components in the management of CAD and IHD. In addition to intensive statin therapy, beneficial health supplements such as *L. reuteri* NCIMB 30242 can offer further LDL lowering without the common adverse effects of statins. It is hence a reasonable and safe add-on choice for at risk patients. The AHA/ACC online risk calculator is a useful tool to assist physicians in the management of patients.

Dr. Erika Isolauri, on the far-reaching effects of probiotics

By Kristina Campbell, M.Sc.



(GMFH)⁽⁵⁾ Dr. Erika Isolauri is a professor of paediatrics at the University of Turku, and chief physician at the Department of Paediatrics at Turku University Hospital in Finland. At the 2014 Harvard Probiotics Symposium she presented a talk entitled *Probiotic Use During Pregnancy for Protection Against Childhood Diseases*. She sat down with Gut Microbiota for Health after the event to describe more about her research and clinical practice.

How did the microbiota become a topic of interest for you within paediatrics?

From patient work. I had two lines of research, one was treatment of acute diarrhea, and the other was food allergy and atopic eczema. And then we learned how you can improve: you give milk to diarrhea patients, and if you use fermented milk or probiotics milk, you can strengthen their [gut] barrier and shorten their recovery.

Then, in the other line of research, I saw that atopic eczema children have [altered antigen transfer in the gut]. And then I applied the information I got from the diarrhea studies. Actually, the idea came from my PostDoc. We were working in France, I was in Paris at that time. So we looked at how the gut barrier functions,

how diet modifies the structure in diarrhea or other impaired barrier function states, and then we applied it to patients.

I saw many effects - very good responses in practical work. So therefore I always mention: listen to the patients and learn from their experience. Believe what they say and not necessarily what the textbooks say.

What role do probiotics play in immunity through the microbiota?

It's not only through the microbiota. Probiotics have immunomodulatory effects. They do work in the lower part of the gut and modify the composition but they have many other effects. One is that they strengthen the gut barrier in the small intestine, so they affect how antigen uptake is taking place.

Also the antigen transport and the mucine layer is enhanced, and tight junctions are enhanced. And also, the pro-inflammatory gut microbiota is changed, the barrier is changed, and also [there is] some effects on antigens: they degrade antigens. They enhance IgA immunity and IL-10 production, TGF-β production.

Many of these effects take place in other locations than where we have our fecal microbiota. It is shown there also that we have a transient effect on the gut microbiota. But if we have this effect, and control inflammation during the critical stage of development, we can have lasting effects in clinical terms. So it is not about the microbiota as such.

Quick Facts

Probiotics During Pregnancy May Lower Allergy Risk In Newborns

In a 2013 meta-analysis of clinical trials, Dr Erick Forno and his team suggested that babies whose mothers took probiotic supplements during their pregnancy face lower risks of developing allergies due to a strengthened immune system. They found that babies given probiotics in utero were 12 percent less likely to have developed allergies, whereas babies who began consuming the probiotics after birth displayed no change in allergy risk. ⁽⁷⁾

