Preventing and controlling diabetes
Is lifestyle the drug of choice?

Statistics suggest that the number of people diagnosed with diabetes in New Zealand has now exceeded 200,000 and there could be half as many people again who have yet to be diagnosed. The disease also affects a disproportionately high number of Māori and Pacific peoples.

Type 2 diabetes is the predominant form. It usually occurs in adults, although it is increasingly seen in children, and is linked to obesity and other conditions as wide-ranging as heart disease and cancer.

That means researchers like Professor Jim Mann and colleagues from the University of Otago in Dunedin’s Edgar National Centre for Diabetes and Obesity Research, along with colleagues from the University’s Departments of Human Nutrition, Medicine and Preventive and Social Medicine, find themselves covering many of the important causes of serious ill-health and mortality seen internationally.

Professor Jim Mann has always liked being able to look at the big picture. Although he was drawn to clinical medicine, he was also vitally interested in biochemistry (in which he completed his PhD thesis) and epidemiology (the discipline of his Doctor of Medicine thesis), so getting involved in diabetes research seemed logical.

While working under Sir Richard Doll, then Regius Professor of Medicine in Oxford and best known for his work in cancer epidemiology, Professor Mann was also influenced by Professor Philip James, a physician and researcher at Cambridge who was doing obesity-related research in Britain in the 1960s and ’70s. He involved a young Jim Mann in the first Royal College of Physicians report on obesity.

What was ignored in that report, and for many years after, was the prediction that obesity was going to become the epidemic of developing and developed countries if people didn’t do something about it.

That prediction stayed with Professor Mann and he decided that, when the opportunity arose to pursue research of his choosing, that would be his focus.

His connection to Otago came at Oxford when he found himself working with a New Zealand epidemiologist by the name of David Skegg.

Professor Mann’s mentors wanted him to become a molecular epidemiologist, an area he was not that interested in, so when he was given the opportunity to do everything he wanted to do at Otago, he grabbed it.

At Otago there was acceptance of his research in all kinds of areas, from epidemiology and public health – the big picture work – to basic research in his well-equipped laboratory.
One of his first research grants – from the MRC in pre-HRC days – enabled a pilot study that suggested it was possible to reduce the chances of people with impaired glucose tolerance (prediabetes) going on to develop the disease, if they made major lifestyle changes. Confirmatory evidence came some years later, from large randomised, controlled trials in Finland and then the USA. The potential for appropriate diet and exercise to help stem the tide of the diabetes epidemic is arguably one of the most important developments in diabetes research in the past half century.

That sort of internationally recognised research has continued with projects such as the HRC-funded LOADD (Lifestyle Over and Above Drugs in Diabetes) study, led by Dr Kirsten Coppell, published in the British Medical Journal in 2010. This was a follow up to earlier work published in The Lancet and BMJ showing the potential benefits of dietary fibre and the importance of fat modification in the treatment of diabetes.

The LOADD study showed that, even when people were on a maximised drug regime, these dietary principles could produce an improvement that was as great as any of the new drugs. It received considerable publicity worldwide.

Other dietary research has involved comparisons of high-carbohydrate, high-protein and high-fat diets in the management of overweight people at risk of diabetes. They found comparable weight loss could be achieved regardless of diet composition, though more recent studies suggest that diets relatively high in protein may confer some benefits.

Weight regain following weight loss is a major issue for many but the group has shown that a simple nurse-led programme involving occasional weigh-ins and supportive phone calls is as effective as a more intensive and costly programme. Diet composition had little effect on the likelihood of weight regain.

They have also investigated how best to identify people at risk of developing diabetes before they have developed any abnormalities of blood glucose. Research by Dr Kirsten McAuley, Associate Professor Sheila Williams and Professor Jim Mann into the early diagnosis of insulin resistance eventually led to the development of the McAuley Index which has now become an internationally accepted measure.

More recently they have also worked with Professor Geoff Chase and colleagues at the University of Canterbury to develop a more sophisticated early stage test to be used for screening and for understanding the effects of interventions on insulin action.

The over representation of Māori in diabetes statistics has led to research describing appropriate use of BMI cut-offs and studies to establish the most appropriate diet composition for Māori.

HRC funding has also allowed a number of younger researchers working with Professor Jim Mann to undertake research leading to PhD degrees and researchers in the early stages of their careers to develop to the point where they now have major HRC-funded research programmes of their own.

For example, Associate Professor Rachael Taylor led the APPLE Study, one of the first community studies in the world to show that it is possible to halt excess weight gain in children through physical activity and dietary intervention. She and colleagues now have substantial HRC grants to examine ways of preventing obesity at the earliest possible stages of life.
In addition to her work on the LOADD study, Dr Kirsten Coppell - a public health physician who has also trained in general practice - has undertaken a number of epidemiological studies in diabetes including a collaborative project involving the University of Otago and Ngati Porou Hauora on the prevention of diabetes. In 2007, that was expanded to include the prevention of chronic disease and a whole-health approach, which is now being used on the East Coast of the North Island. The initial collaborative project, the Ngati and Healthy - Prevent Diabetes Project, received the gold award in the Whanau Ora Awards for Māori health initiatives.

In addition to the work on early prevention of obesity, future research will include the metabolic syndrome, in particular its relationship to gout and non-alcoholic, fatty-liver disease, and ways of reducing the risk of developing these conditions.

Professor Mann and colleagues have also set up the Centre for Translational Research, as an offshoot of the Edgar National Centre for Diabetes and Obesity Research, as an avenue to put their research into practice. One of their greatest contributions has been in the area of guidelines, with Professor Mann chairing the European Diabetes and Nutrition Guidelines group, and the Expert Advisory Group on Diabetes and Cardiovascular Disease in New Zealand. He has also chaired or served on several other relevant national and international groups, including the nutrition advisory group to the World Health Organisation – evidence of the quality of the research work of his group.

Professor Mann’s hope is that governments in New Zealand and worldwide will see the relevance of their findings and encourage implementation of the interventions they have developed.
The HRC’s Clinical Research Training Fellowship was established in 2006 to support clinicians to undertake research training and obtain postgraduate qualifications.

The scheme contributes to clinical research capacity, bridges the gap between scientists and clinicians, and enables translation of research findings. Clinicians are well placed to identify research questions, as they apply evidence-based clinical practice.

An evaluation of the Fellowship in 2010 found that it is has successfully increased clinical research capacity and contributed to the translation of research into clinical practice. Recipients of the Fellowship have undertaken innovative research with implications for the clinical setting, and have maintained a combination of clinical work and research after their Fellowship has concluded.

The impact of the Fellowship on the career and clinical practice of the Fellows has been significant. Without financial support from the HRC, many of the Fellows would not have been able to undertake research training.

Some of the research results have had important implications for policy and clinical practice. Dr Cheri Hotu, a renal fellow at Auckland Hospital, conducted a randomised, controlled pilot study to determine whether community-based monitoring could improve blood pressure control in Māori and Pacific patients with early diabetic nephropathy. The DEFEND (Delay Future End Stage Nephropathy due to Diabetes) study investigated whether monthly community visits by nurse-led Māori or Pacific healthcare assistants could break down barriers and achieve better results than usual clinic practice. The community model provided more frequent monitoring, more adjustments to medication regimens, the removal of language and transport barriers, and encouragement of medication adherence, which led to a higher utilisation of antihypertensive medications.

A significant decrease in systolic blood pressure and a significant reduction in urinary protein levels provided evidence of an overall improvement in diabetic nephropathy for patients who received community care.

The study results led to the Department of Renal Medicine at Auckland Hospital adopting the DEFEND model of care for outpatients with chronic kidney disease. Healthcare assistants undertake frequent home-based visits to patients with chronic renal impairment, monitoring their blood pressure and assisting with transportation to clinic appointments.

The Clinical Research Training Fellowship led to Dr Hotu’s appointment as an honorary clinical lecturer with The University of Auckland, and contributed to the training and professional development of the Māori and Pacific healthcare assistants, leading to employment for one assistant in a similar healthcare role.