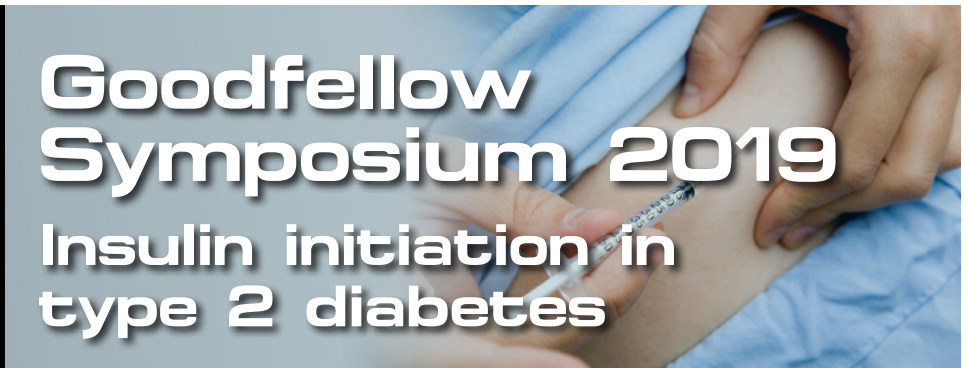
A RESEARCH REVIEW™
SPEAKER SERIES

Goodfellow Symposium 2019

Insulin initiation in type 2 diabetes



Making Education Easy 2019

About the speakers

Dr Steven Miller

BSc(Hons)
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Dr Steven Miller completed an intercalated BSc (Hons) in Genetics before being awarded MBChB with Commendation in 1999 at the University of Glasgow. He was awarded a PhD for diabetes research in 2007. After completing a 1-year Fellowship at the Garvan Institute for Medical Research and St Vincent's Hospital, Sydney, Dr Miller moved to New Zealand in 2010. He is a Consultant Physician in Diabetes and Endocrinology in Private Practice at the Waitemata Specialist Centre, Takapuna, and also at North Shore Hospital.

Dr Liesje Donkin

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Dr Liesje Donkin is a Registered Clinical Psychologist who holds dual qualifications in clinical and health psychology. Liesje holds a research Fellowship at the University of Auckland and also works in private practice. Her clinical experience includes working with people with cardiac disease, diabetes mellitus, cancer, eating disorders and chronic pain. Liesje particularly enjoys helping complex, challenging patients improve their health behaviour, self-management and quality of life.

This publication is a synopsis of presentations on insulin initiation in type 2 diabetes at the 2019 Goodfellow Symposium in Auckland in March. The Goodfellow symposium is a primary care symposium designed for GPs, urgent care physicians, nurses, nurse practitioners and registrars. Dr Steven Miller, endocrinologist at North Shore Hospital, Auckland, summarised the basics of managing diabetes in primary care and how to start insulin. Dr Liesje Donkin, clinical and health psychologist, discussed the barriers to insulin acceptance and adherence. These pre-symposium workshops and breakfast sessions were supported by Sanofi.

Diabetes – basics and beyond - *Steven Miller*

Understanding of T2DM today

Type 1 diabetes mellitus is caused by destruction of pancreatic β-cells due to an autoimmune process whereas type 2 diabetes mellitus (T2DM) results from combined insulin resistance and defective insulin secretion.[1] In fact, the UK Prospective Diabetes Study (UKPDS) demonstrated that mean β-cell function was already less than 50% at diagnosis of T2DM and progressively declined over time.[2,3] In New Zealand, the prevalence of T2DM is 1 in 20.[4]

The modern view of T2DM pathogenesis is that of the 'ominous octet'.[5] That is, hyperglycaemia is the result of eight metabolic abnormalities: decreased incretin effect, increased lipolysis, increased renal glucose reabsorption, decreased insulin-stimulated glucose uptake in skeletal muscle and adipose tissue, neurotransmitter dysfunction, increased hepatic glucose production, increased glucagon secretion, and decreased insulin secretion. Indeed, Dr Miller stated that, "the clinical syndrome we recognise as T2DM is the end result of a constellation of metabolic abnormalities. It is naive to think that all patients with diabetes will share similar characteristics or respond to therapies in the same way".

Legacy effect: early glycaemic control is key to long-term reduction in complications

Having good control of diabetes early sets patients up for a good legacy - early, strict glycaemic control is key to reducing the long-term risk of microvascular and macrovascular complications associated with T2DM.[6] The UKPDS showed that a 1% (11 mmol/mol) reduction in HbA_{1c} in newly diagnosed T2DM patients is associated with a reduced risk for complications, including lower extremity amputation or fatal peripheral vascular disease, microvascular disease, cataract extraction, heart failure, myocardial infarction and stroke (Figure 1).[7] In contrast, having poor control of diabetes early sets patients up for a bad legacy. Achieving glycaemic control late in the disease, after a prolonged period of poor control, does not improve long-term risk of macrovascular complications.[8,9] Furthermore, these complications are irreversible.

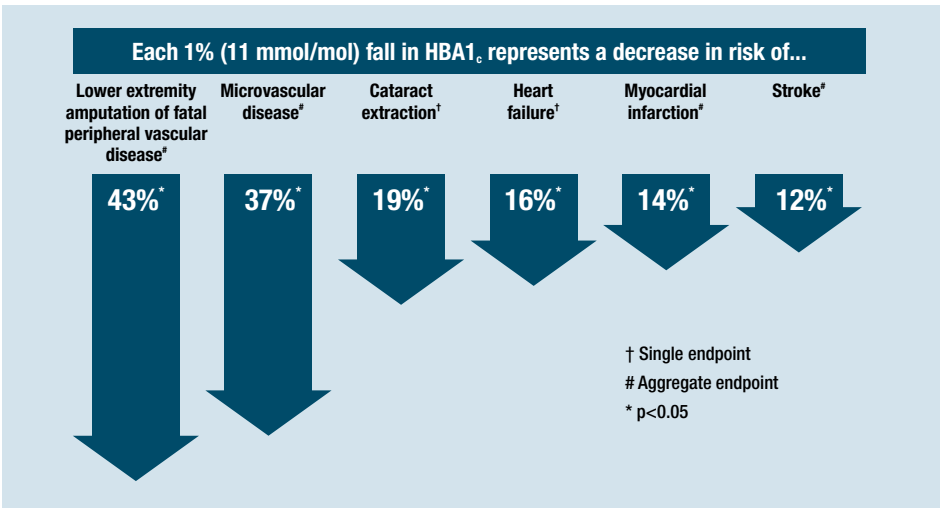


Figure 1. Association between mean HbA_{1c} and complications – UKPDS[7]

Individualised HbA_{1c} targets

Historically, there was a single HbA_{1c} target for every patient, whereas it is now recognised that it is appropriate to have an individualised target for every patient (Table 1).[10] However, approximately 50% of patients with T2DM still do not reach HbA_{1c} target of 53 mmol/mol or 7.0%.[11]

Table 1. Individualised HbA_{1c} targets[10]

Glycated Haemoglobin Range

Most Intensive Level, Approximately 6.0%*	Factors	Least Intensive Level, Approximately 8.0% *
Highly motivated, adherent, knowledgeable, strong self-care capability	Psychosocial considerations	Less motivated, non-adherent, less knowledge weak self-care capability
Adequate	Resources or support systems	Inadequate
Low	Risk of hypoglycaemia	High
Short	Duration of T2DM	Long
Long	Life expectancy	Short
None	Microvascular disease	Advanced
None	Cardiovascular disease	Established
None	Co-existing conditions	Multiple, severe, or both

Individualised HbA1c Target

* HbA_{1c} 6.0% = 48 mmol/mol; HbA_{1c} 8.0% = 64 mmol/mol.

How to treat T2DM

In New Zealand, the current treatment paradigm for treatment of hyperglycaemia in T2DM involves lifestyle modification first, with metformin as first-line drug therapy. Second-line therapy includes sulphonylureas and thiazolidinediones, while third-line therapy includes insulin, dipeptidyl peptidase-4 (DPP-IV) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors (non-funded) and glucagon-like peptide-1 (GLP-1) receptor antagonists (non-funded).[12]

The optimal treatment of diabetes is shown in Figure 2 depicting a house – with foundation therapies first (diabetes self-management education [DSME], diet and exercise, metformin), then building second-line oral therapies then third-line injectable therapies on top of this.[12]

Importantly, to avoid clinical inertia, treatment should be reassessed and modified regularly.[13] HbA_{1c} should be reviewed three-monthly if not at target, and 6-monthly if at target. Treat BP to a target of 130/80 mmHg. Conduct an annual assessment for CVD risk, urine microalbumin estimation, serum creatinine, and neurovascular foot assessment, and biannual retinopathy screening.[13]

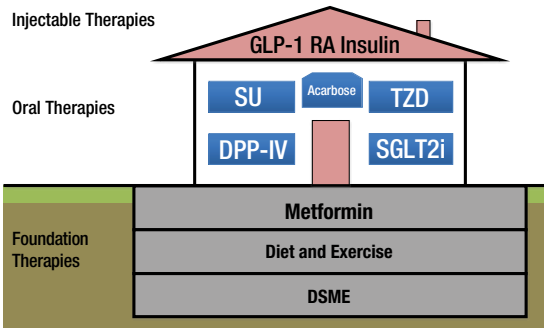


Figure 2. How to treat T2DM

DPP-IV = dipeptidyl peptidase-4 inhibitors; DSME = diabetes self-management education; GLP-1 RA = glucagon-like peptide-1 receptor agonists; SGLT2i = sodium-glucose cotransporter 2 inhibitors; SU = sulphonylureas; TZD = thiazolidinediones.

Diabetes – advanced insulin usage - *Steven Miller*

Most patients with diabetes will eventually require insulin as part of the normal progression of the disease. Insulin has the largest effect on reducing HbA1c levels of all glucose-lowering medicines.[14] Early use of insulin therapy can help normalise blood glucose and HbA_{1C} levels and thus enable patients to control diabetes.[15] The best time to start insulin is when glycaemic targets are not being met. Insulin initiation will take time – longer consultations are best, with several visits and follow-up calls required. Dr Miller suggests that if healthcare professionals (HCPs) don't understand the differences between the many available insulins, that they simplify insulin initiation by familiarising themselves with one basal insulin, one prandial insulin and one premixed insulin.

Dr Miller described his recipe for insulin initiation. Patients should self-monitor blood glucose before each meal and before bed for 3-5 days. For most patients, fasting hyperglycaemia will be present thus Dr Miller recommends bedtime basal insulin (intermediate acting or long acting). Basal insulin requires only one daily injection, patients can self-titrate, and it has a low risk of hypoglycaemia. The insulin regimen must be individualised to suit each patient. Various formulations of insulin are available with differing durations of action (Figure 3).

Patients must understand the theory behind the insulin regimen, and the relationship between carbohydrate intake, insulin dose and glycaemic response must be understood by the patient for a complex regime to be successful. Although endogenous insulin secretion is inadequate when supplemental insulin is required in T2DM, most patients retain some endogenous β-cell function capable of insulin production. This remaining β-cell function is impaired when blood glucose is elevated (so-called pancreatic glucotoxicity). Accordingly, the addition of a basal insulin alone will suppress hepatic glucose production thus controlling blood glucose between meals. In turn, this helps to restore endogenous postprandial insulin release, and euglycaemia is restored.[16]

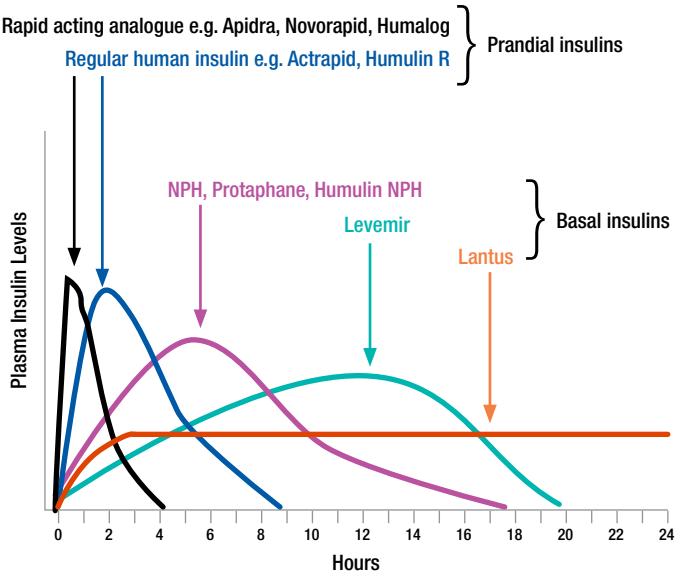
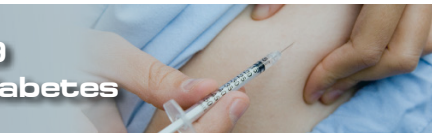


Figure 3. Insulin action over time[17]



Understanding barriers to insulin acceptance and adherence - *Liesje Donkin*

Introduction

Dr Donkin discussed known barriers to insulin acceptance and long-term adherence. She provided an overview of evidence-based approaches to overcome these barriers and delineated clear, practical strategies shown to help address barriers that can be integrated into the patient consultation.

A growing proportion of HCP time is dedicated to the management of T2DM.[18] There is a pressing need to integrate effective strategies into the HCP/patient encounter to improve diabetes self-management and reduce HCP workload.[18] While insulin treatment is a normal trajectory of disease management, insulin is often underused and initiation delayed because of concerns about patient acceptance and adherence.[19] Protracted delay increases the risk of a large number of diabetes-related complications that may compromise life expectancy and quality of life.[20]

Insulin initiation: the barriers and the challenges

There are many factors that hinder patients taking their medication, which can be grouped into three clusters: patient-related barriers, HCP challenges, and system-related barriers.[18,21,22] Patient related barriers include concerns such as: 'I have failed; insulin is a treatment of last resort'; 'life will be more restricted'; 'people will treat me differently'; 'I worry about weight gain and hypoglycaemia'; 'I fear needles and making a mistake'; and 'I worry insulin is unnatural or harmful'. HCP challenges include concerns that a patient will resist insulin or the assumption that insulin is too complicated for the patient - it may seem better to maintain the status quo and delay insulin for as long as possible. System-related challenges include HCP work load, time constraints, and lack of resources.

The health belief model

One of the many models used to underpin work in health psychology is the health beliefs model, which states that patients act rationally, in their best interests, based on personal beliefs. Patients' health decisions are made by weighing up beliefs for and against that decision. Beliefs about insulin are formed from a variety of sources and experiences such as 'Dr Google', attitudes of family and friends, past experiences, social context, pop culture, and patients' understanding of diabetes. For example, patients may recall family members on insulin, and that insulin needles are large and terrifying.[23] Family members may believe that insulin doesn't work or that it may impact their ability to drive. Patients may be concerned about others thinking they have failed once they go on insulin or that insulin is dangerous. Religious and or cultural beliefs are also factored into patients' decisions about whether to start insulin.

Strategies to overcome patient barriers to insulin acceptance and adherence

For insulin acceptance and ongoing adherence, perceived necessity of insulin must outweigh concerns about taking insulin.[24] Insulin initiation should be viewed as a normal part of the diabetes care continuum.[18] HCPs should start the initial insulin conversation and set appropriate patient expectations at, or shortly after, diagnosis.[18] At the time of insulin initiation, assist the patient to understand why insulin is necessary.[18] Explain that insulin will help the patient live a healthier life, make them feel better, and reduce their risk for complications later on. Use of analogies is recommended: "when your car runs out of gas, you need to refill the tank - our bodies need insulin like a car needs gas".

Use open questions for assessing attitudes to insulin therapy, such as:[25]

- What does it mean to you to start insulin therapy?
- Why do you think it might be helpful (or unhelpful) to start insulin now?
- How do you think using insulin will change things at home? At work?
- What worries you most about insulin?
- Do you think you can manage insulin therapy?
- What do you need to know before starting insulin therapy?
- What will make it easier for you to start insulin therapy?

Ask questions up front about fears and concerns – take cues from the patient's responses and validate patients' fears and concerns.[18,21,26] See examples in Table 2.

Table 2. Addressing patient concerns about initiating insulin

Patient concern	Healthcare professional answer
Insulin has serious side effects. My grandfather took insulin and he lost his sight.	Insulin did not cause your grandfather's blindness. It is likely he was prescribed insulin too late. It is unmanaged diabetes progression, not insulin that causes blindness. In fact, taking insulin at the right time can prevent blindness.
Isn't insulin a dangerous drug?	Insulin is a hormone naturally produced in your body. You are just topping it up to make up for what your body can't produce.
I failed! I couldn't keep it under control and now my diabetes is really bad.	Needing insulin is not a failure – everyone needs insulin to survive – diabetes changes over time and it is normal to need insulin at some point.
Doesn't taking insulin cause low blood sugar, which can be dangerous?	When you learn how to take insulin, you will also learn how to prevent low blood sugar, how to recognise the signs, and what to do if it happens.
What about weight gain? I've heard insulin can make you gain weight.	It is true that some people taking insulin gain weight and if that worries you, we can look at ways to help prevent weight gain.
I'm actually really scared of needles.	Lots of people feel that way. But there are simple techniques we can show you that help. Most people find the pain level from an insulin injection to be less than that of a finger-stick for normal blood sugar monitoring.
I'm worried I might forget to take insulin, or I won't be able to fit injecting into my day.	Address patient concerns about integrating insulin into daily life with concrete, achievable action plans - e.g. stick to a set time every day to take your insulin; set a reminder on your phone so you don't forget.

Shared decision-making has been consistently shown to encourage adherence and subsequent glycaemic control.[27] Understanding the patient's lifestyle and daily routines can provide insight into opportunities to add insulin into the patient's life with minimal disruption.[18] Collaboratively set goals that are simple and achievable, e.g. "I will fill in a daily blood glucose record". Emphasise the importance of healthy coping goals e.g. "I will make time for myself during the day". Mutually agreed upon glucose targets can serve as concrete guideposts to reinforce positive behaviour change.[18]

A pros and cons matrix is a useful tool to complete with patients to explore the positive reasons for change. An example is shown in Table 3 below.

Table 3. Pros and cons matrix of initiating insulin

Starting taking insulin	
Pros	Cons
• My diabetes will be better controlled • I can have more control over my medication • It will get my wife off my back • My health will be better for the kids • It's a serious step which makes me think about how I need to look after myself better • I'll get over my fear of needles	• Needles!! I feel scared • What if I mess up the dose? I'm worried the side effects of the medication will be worse • It's change which I don't like
Staying on my oral medication	
Cons	Pros
• My diabetes isn't well controlled • I'm worried about complications from my diabetes not being controlled	• I'm familiar with my current pills • They're easy to take (when I remember)

Addressing HCP challenges and system barriers

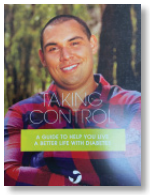
HCP reluctance to initiate insulin can be based on misperceptions about the patient.[28] Using techniques to elicit individual patient beliefs and concerns about insulin, and to collaboratively set goals and action plans should improve acceptance and adherence. Once insulin therapy has been initiated, patients often grow in confidence and feel a sense of empowerment over their health.[23] Furthermore, improving the insulin conversation and the initiation process should make the consultation more time effective; improve acceptance, persistence, and adherence; improve glycaemic control; decrease long-term complications; and reduce healthcare utilisation and HCP workload.[18]

Getting off to a good start: The Taking Control guide

An international panel of clinicians specialising in the care of people with diabetes discussed ways to introduce insulin to patients that might not only enhance uptake but also minimise future interruptions or discontinuations.[18] There was a strong consensus that helping patients get off to a good start with insulin is critical. The panel developed the 'Taking Control' guide,[29] which aims to direct and facilitate targeted patient-HCP discussion around insulin use. The evidence-based guide, designed by health psychologists, is time efficient and aligned with the recommendations of Polonsky et al.[18] It includes patient-centred take home materials, covers patient barriers to acceptance, and supports patients in long term treatment adherence.

Structured education targeting beliefs and setting action plans in relation to insulin necessity, insulin injection technique, blood glucose monitoring, diet, exercise, and hypoglycaemia prevention has been shown to improve adherence and the number of patients achieving target HbA_{1c} levels.[30]

FREE PATIENT RESOURCE



Patients often struggle when starting a new medicine through either not understanding the role of treatment or having other unhelpful thoughts around the illness itself. In partnership with Atlantis Healthcare, Sanofi has developed the Taking Control guide to help you identify these barriers quickly with each of your patients and provide tailored information to improve both acceptance and long-term self management of their diabetes.

To order copies of the booklet "Taking Control" please contact michael.lewis@sanofi.com

TAKE-HOME MESSAGES

- The legacy effect: if patients achieve target HbA_{1c} levels soon after diagnosis, they have better long term outcomes than those who do not reach target levels early, even if control is relaxed later in the course of disease.
- It is appropriate to have an individualised HbA_{1c} target for every patient.
- Most patients with diabetes will eventually require insulin as part of the normal progression of the disease.
- Insulin has the strongest glucose-lowering effect of all glucose-lowering medicines.
- Early use of insulin therapy can help patients achieve their target blood glucose and HbA_{1c} levels and thus enable patients to benefit from a favourable legacy effect.

Before patient requires insulin:

- Set treatment expectations early at or shortly after diagnosis.

At the time of insulin initiation:

- Emphasise the benefits of insulin.
- Elicit patient concerns/beliefs using open ended questions.
- Collaboratively set goals and action plans.
- Focus on integrating insulin into patient's daily routine with minimal disruption.

At follow-up appointments:

- Assess current beliefs and areas of concern.
- Check progress in relation to mutually agreed upon glucose targets.
- Adjust goals if necessary.
- Encourage strategies for healthy coping.

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