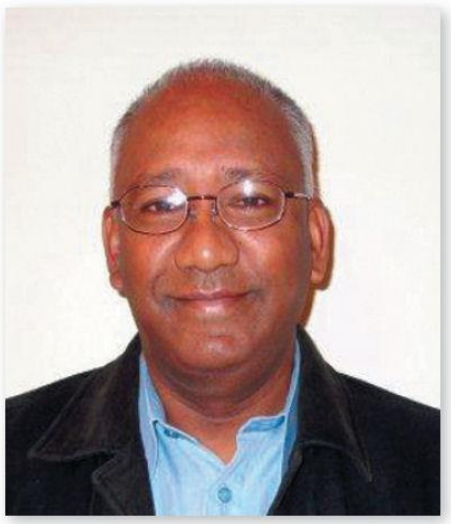
Dr Helen Lunt

Diabetes Physician

Clinical Associate Professor, University of Otago, Christchurch



Mr Rab Burtun

Diabetes Nurses Specialist

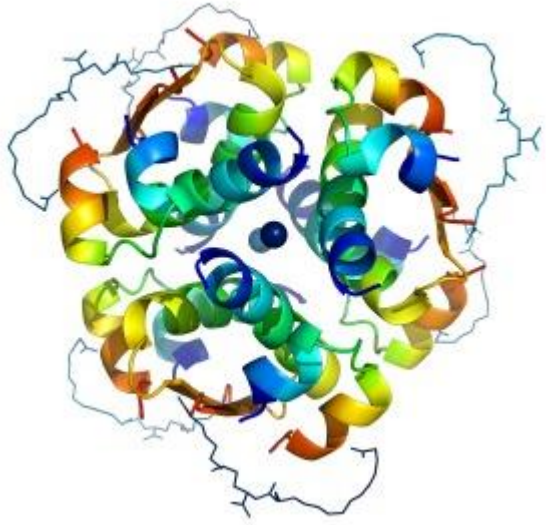
Waitakere Hospital, Waitemata DHB

Thursday, August 11, 2016 (Room 3)

8:30 - 10:30 WS #5: Starting Insulin in Primary Care

11:00 - 13:00 WS #11: Starting Insulin in Primary Care (Repeated)

Why insulin therapy?



Dr Helen Lunt

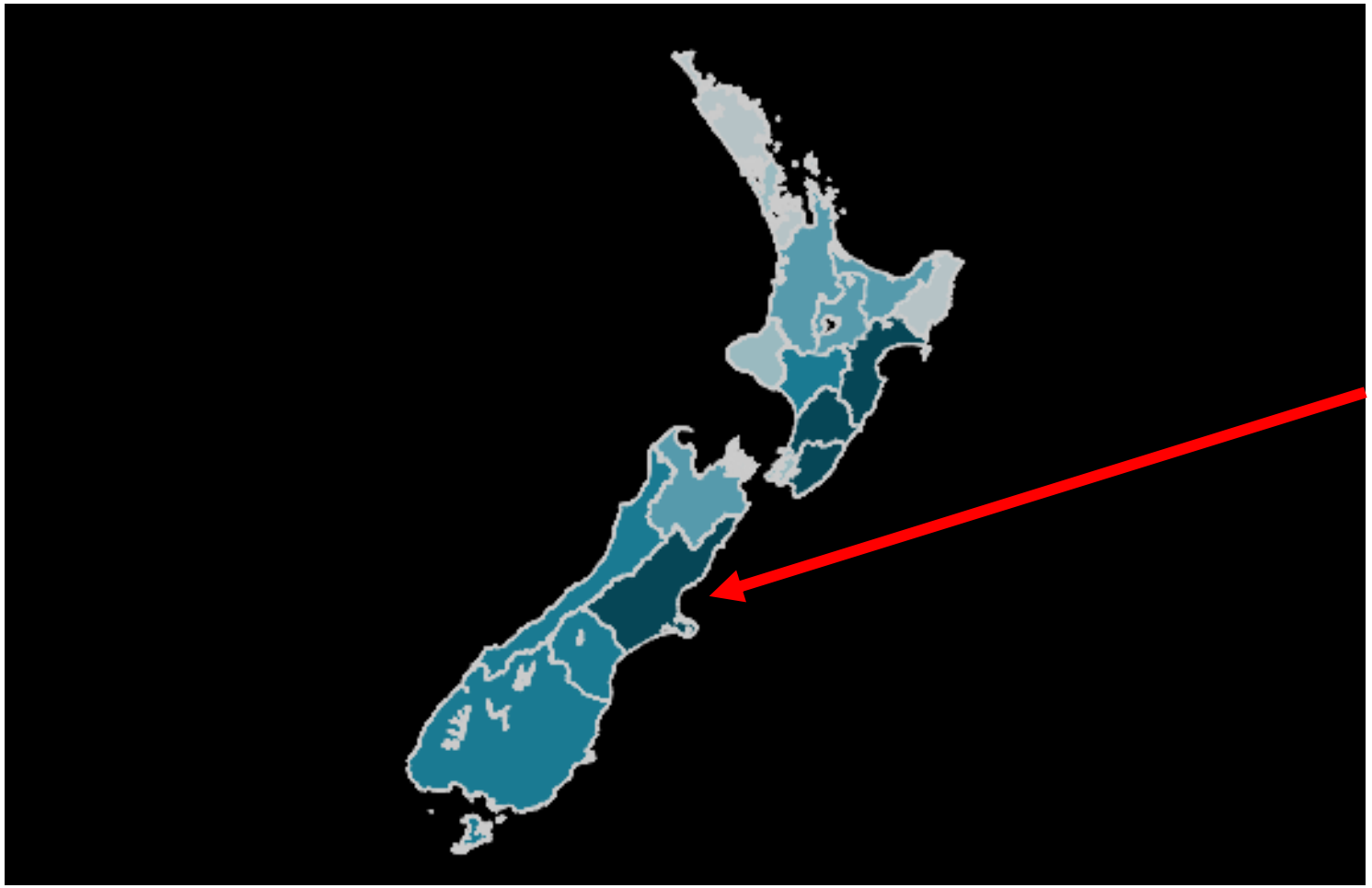
Christchurch Diabetes Centre

NZ virtual diabetes register (HQSC)

	2010	2011	2012	2013	2014	2015
Total	**196,134**	**210,759**	**224,908**	**238,890**	**251,478**	**260,458**
Canterbury	18,625	19,357	20,308	21,076	21,799	22,558
Waitemata	21,447	23,631	25,498	27,871	29,743	30,931
Counties Maukau	28,565	30,941	33,507	36,508	39,724	41,982

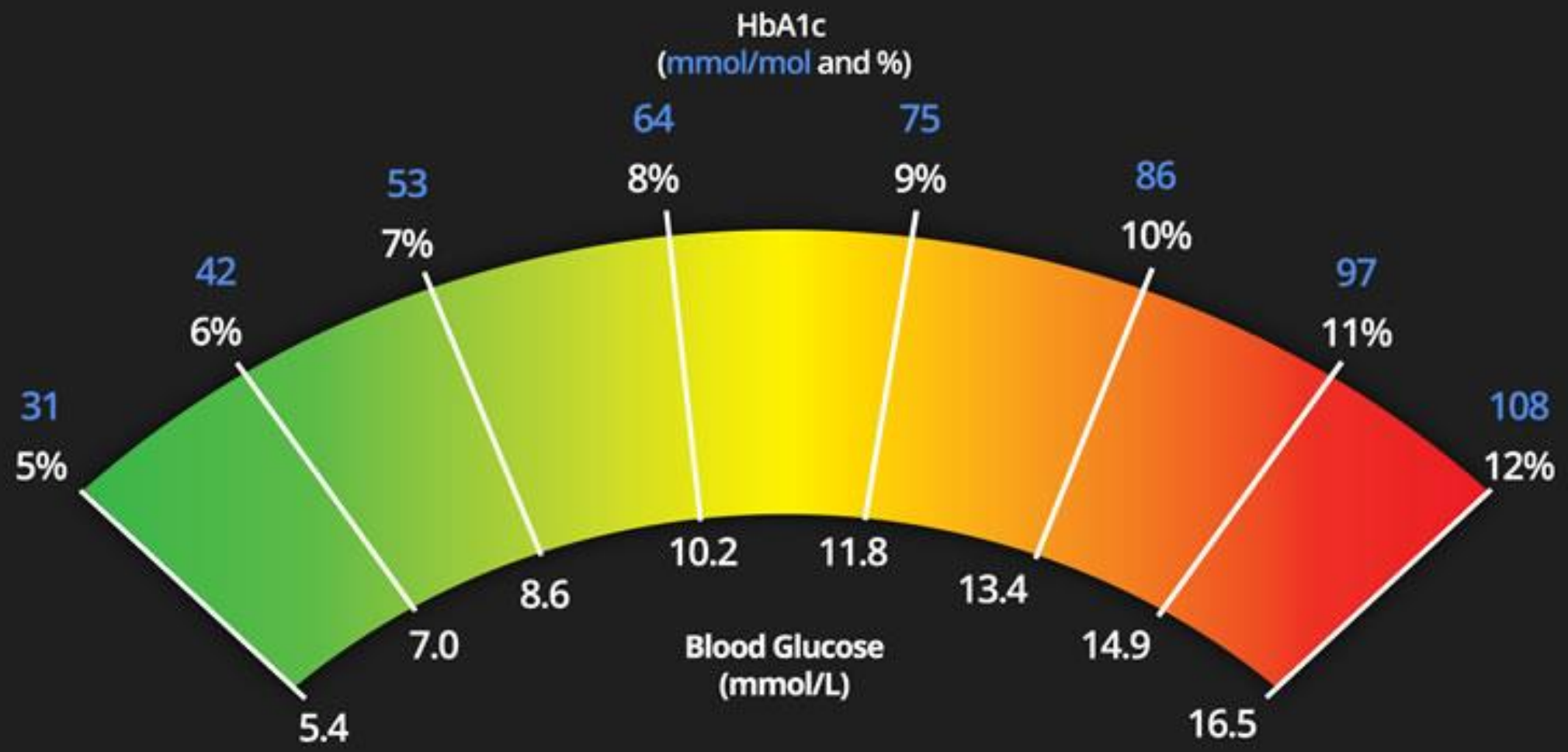
Number of New Zealanders with diabetes expected to double over the next 20 years

Patients aged 25 years and over, regularly using insulin (HQSC)



Canterbury appears to have the highest insulin use at 23% of people identified as having diabetes

HbA1c as an indicator of Diabetes Control



Diabetes.co.uk
the global diabetes community

unite for diabetes

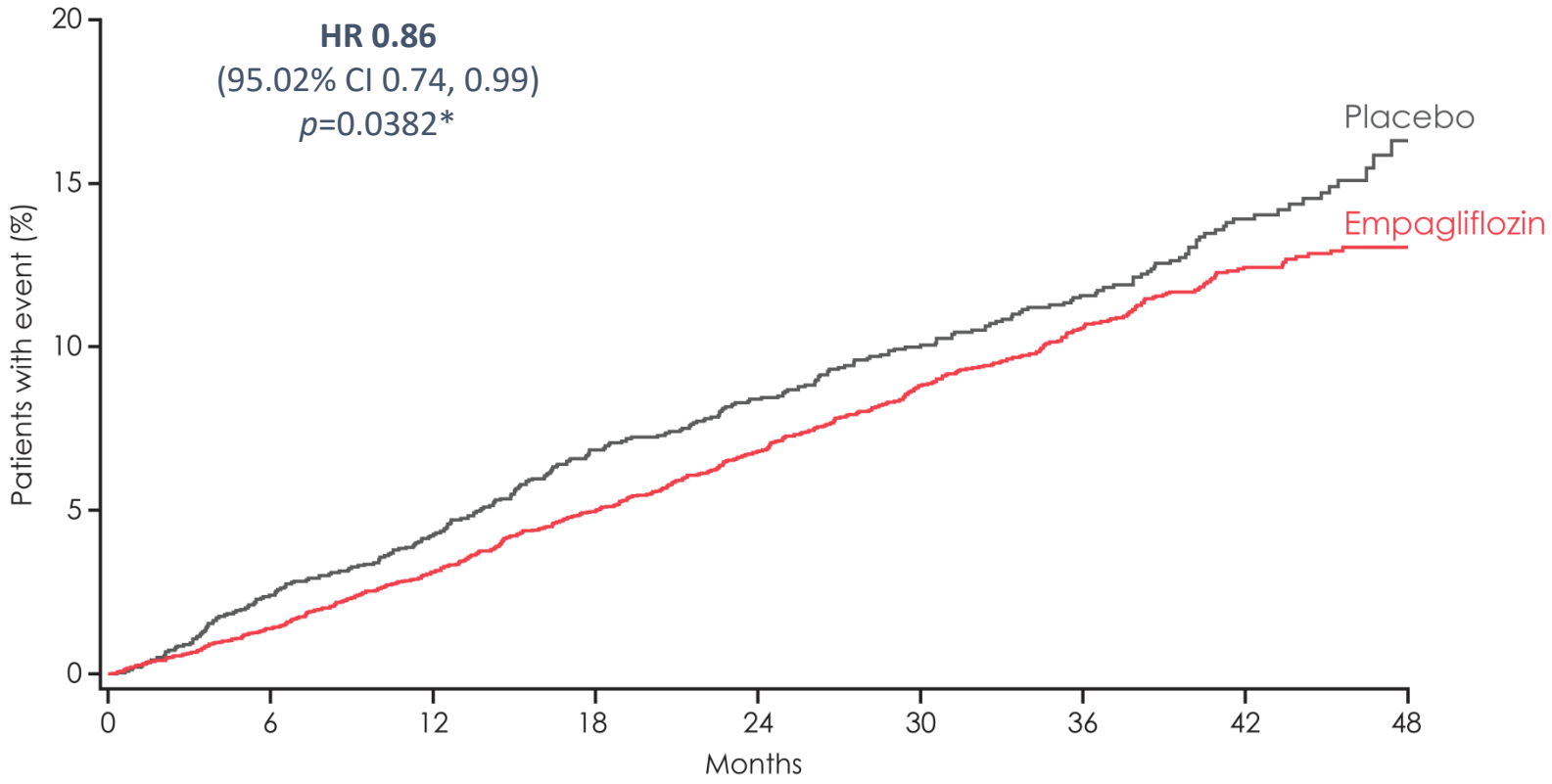
Nathan et al. Translating the A1C Assay into Estimated Average Glucose Values. Diabetes Care 2008; 31:1473-1478
Christchurch Diabetes Centre 2009

AERx inhaled insulin system- *“in looking at the market and the convenience of our device, we decided its is not really there”*

Why treat hyperglycaemia in type 2 diabetes

- Intensive anti-glycaemia therapy improves the outcome of microvascular disease in type 2 diabetes
- Epidemiological analyses show a relationship between chronic hyperglycaemia and CV disease, but there is no definitive study showing that lowering glucose reduces CV morbidity and/or mortality
- Symptomatic treatment of hyperglycaemia is an agreed priority
- Some treatments treat more than hyperglycaemia e.g. Empa-reg (empagliflozin) study:

Empa-reg primary outcome: 3-point MACE



No. of patients									
Empagliflozin	4687	4580	4455	4328	3851	2821	2359	1534	370
Placebo	2333	2256	2194	2112	1875	1380	1161	741	166

Cumulative incidence function. MACE, Major Adverse Cardiovascular Event; HR, hazard ratio.

* Two-sided tests for superiority were conducted (statistical significance was indicated if p≤0.0498)

“But I don’t want injections, what is there instead?”

‘Shot from the bow’ approach

Diet, lifestyle, metformin – then what?

Funded	Unfunded
Sulphonylureas	Incretin analogues (injections)
Acarbose	SGLT2 inhibitors
Pioglitazone	DPP IV inhibitors

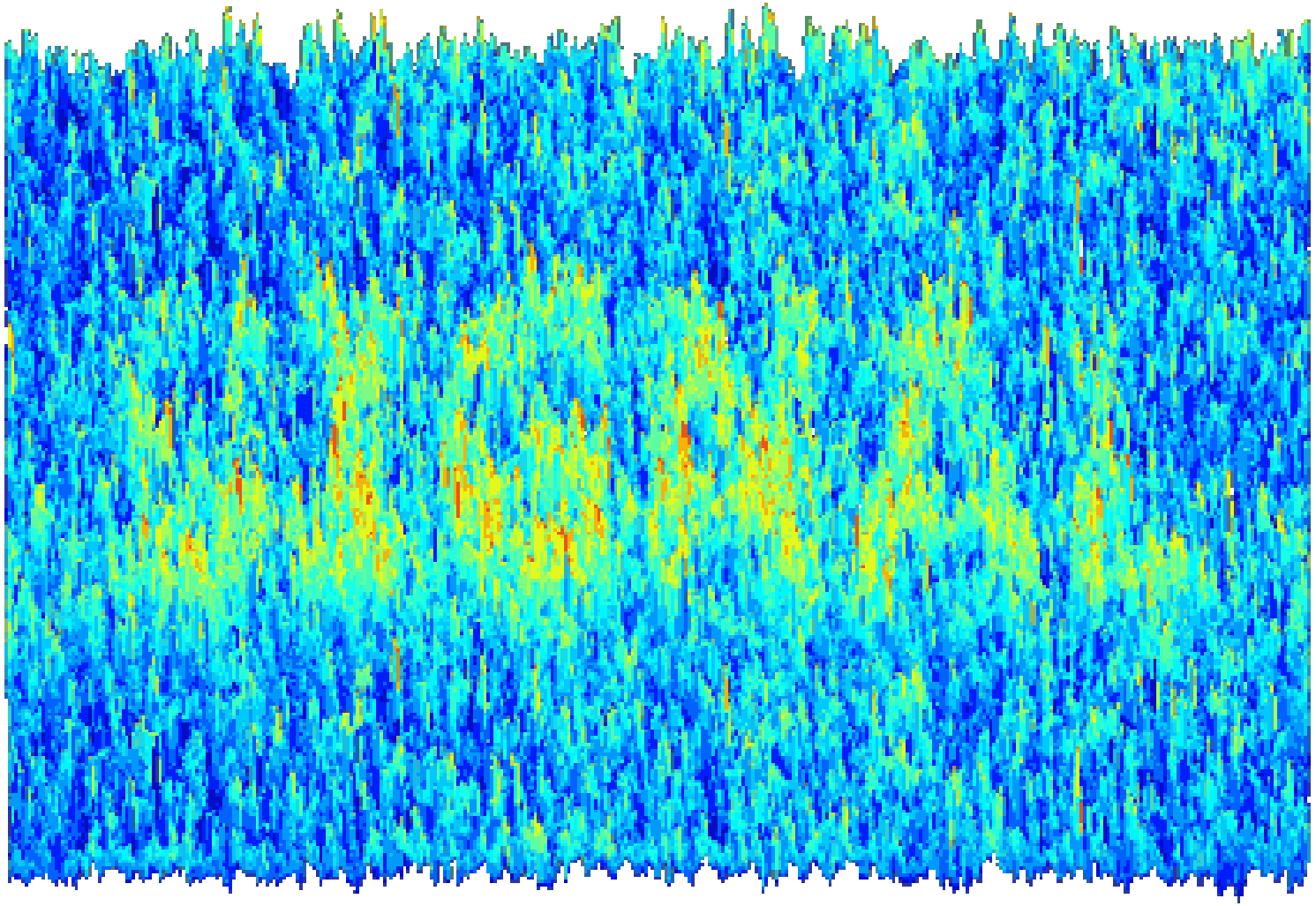
FDA and new anti-diabetic therapies – why are there so many complexities?

- The legacy of troglitazone and rosiglitazone still haunt the minds of many diabetes physicians (and also the FDA)

- All new diabetes drugs require an in depth safe review with a specific focus on cardiovascular outcomes

- Enhanced post marketing surveillance programmes

Drowning in data, starved of unambiguous meaning



“There have been reports of Y side effects with drug X”

Recent FDA communications

- 06/14/2016 Canagliflozin (Invokana, Invokamet) and Dapagliflozin (Farxiga, Xigduo XR): Drug Safety Communication - Strengthened Kidney Warnings

- 05/2/2016 FDA announced that a safety review has found type 2 diabetes medicines containing saxagliptin and alogliptin may increase the risk of heart failure

- 08/28/2015 FDA warns that DPP-4 inhibitors for diabetes may cause severe joint pain

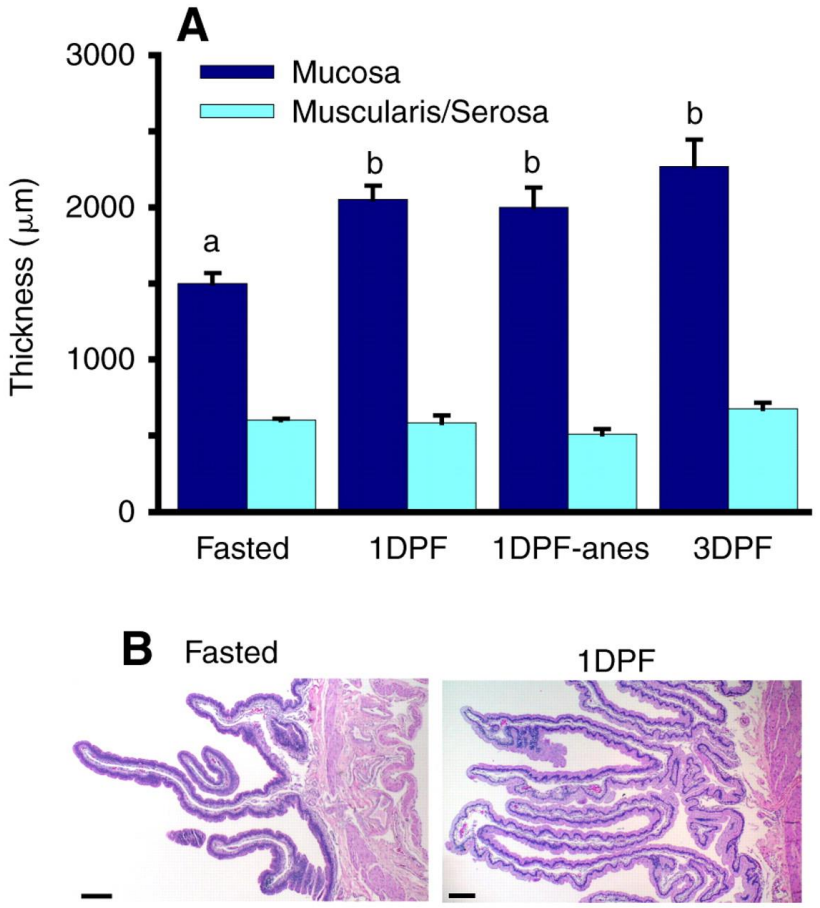
- FDA Drug Safety Communication 2015: FDA revises label of diabetes drug canagliflozin (Invokana, Invokamet) to include updates on bone fracture risk and new information on decreased bone mineral density

Medsafe data sheet – Sitagliptin and pancreatitis

- There have been reports of acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotising pancreatitis in patients taking sitagliptin.

- Patients should be informed of the characteristic symptom of acute pancreatitis: persistent, severe abdominal pain…..

Metabolic and digestive response to food injection in a binge-feeding lizard, the Gila monster (Journal of Experimental Biology 2007)



Medsafe

24 May 2016

INVOKANA® (canagliflozin):

Advice on the Risk of Lower Limb Amputation Primarily of the Toe during treatment with canagliflozin

Dear Healthcare Professional,

Janssen-Cilag Pty Ltd ('Janssen') would like to inform you of new important safety....

Approximate costs per month – NZ online pharmacy

- Exenatide injections (Byetta) $269.90
- Dapagliflozin tablets (Forxiga) 10mg $89
- Sitaglipin tablets (Januvia) 100mg $102.40
- Saxagliptin tablets (Onglyza) 5mg $72.00

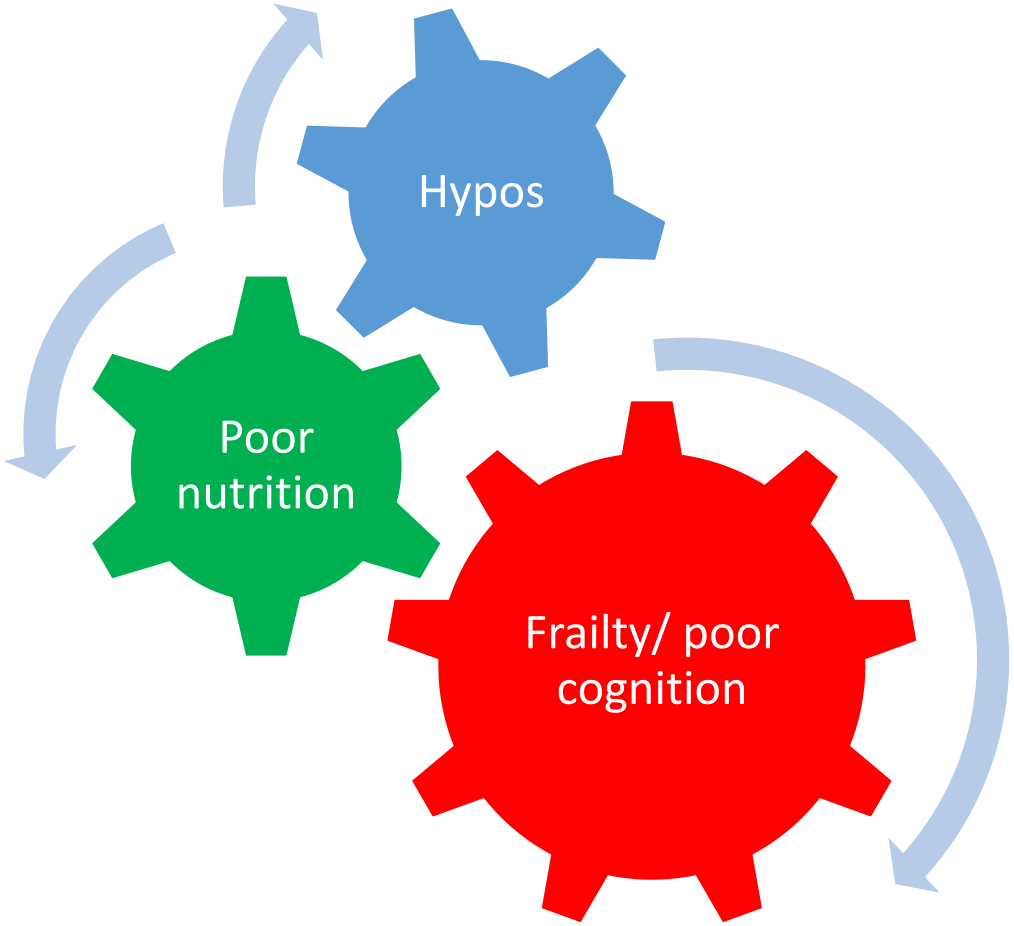
Starting insulin and the Type 2 diabetes journey: *"If you don't know where you are going, you'll end up someplace else" Yogi Berra*

- Progressive beta cell failure is the norm; in 'well' patients with diabetes, medications (including insulin) will need escalating over time
- Think about where your patient is likely to be from a medical perspective in one, two and five+ years time
- If you start with once a day injections, is the patient likely to benefit from twice a day injections longer term?
- Will your patient find that a complex regimen of 3 or 4 injections a day fits in better with their lifestyle?
- Transitions: Will your patient be changing job (shift work/no shift work), retiring etc and how will this affect their diabetes needs?.

Clinical (therapeutic) inertia = Failure to alter (intensify) therapy towards evidence based goals

- Failure to escalate oral therapy
- Failure to initiate insulin
- Failure to intensify insulin
- Failure to de-intensify (diabetes) therapies with side effects, in patients with reduced life expectancy (e.g. BMJ ‘Too much medicine’ campaign)

Avoid hypoglycaemia in frail elderly patients

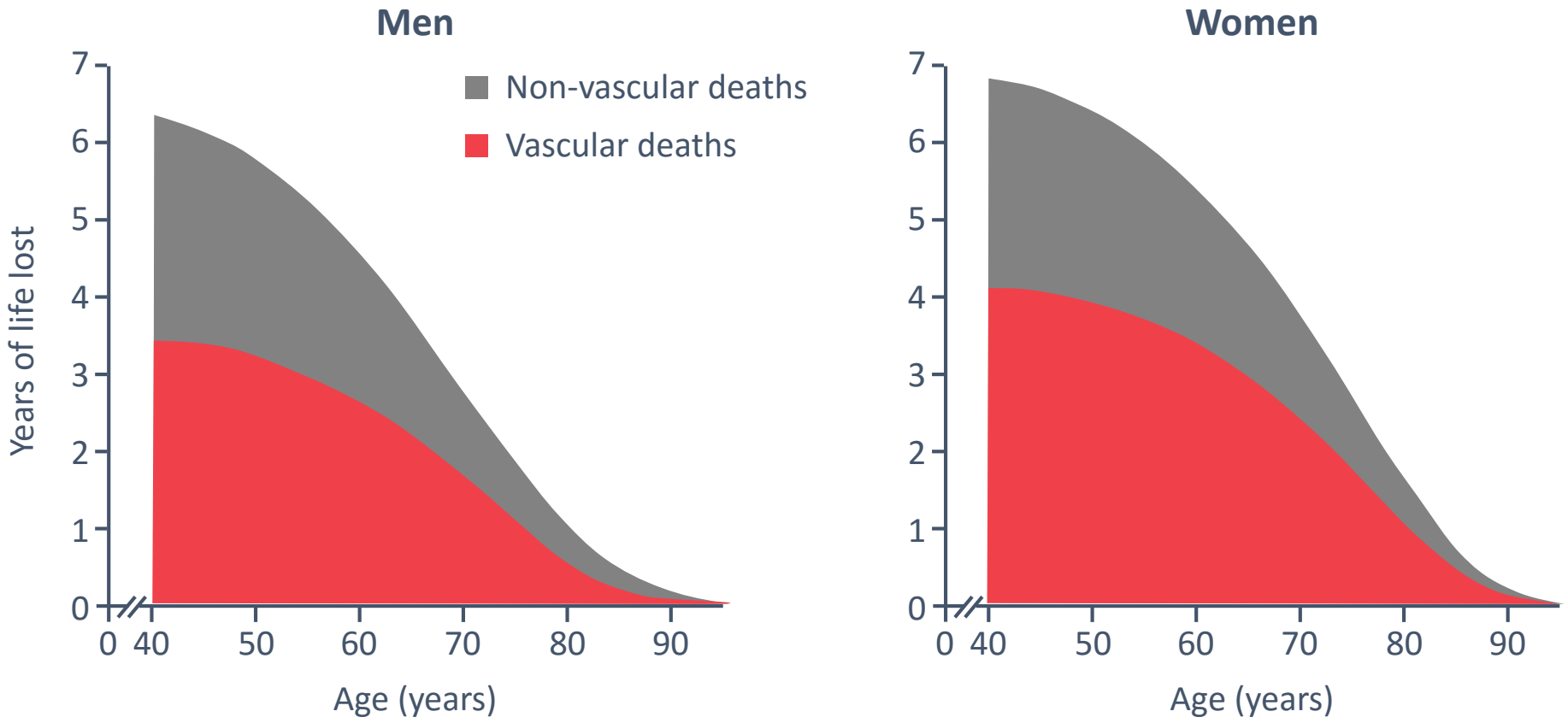


In the elderly and others with limited life expectancy, avoid hypoglycaemia and accept a more relaxed HbA1c

HbA1c legacy (metabolic memory) effect: Is a bit like having a lot of money in your pension pot – accumulate it when you are younger and spend when you are older

"The eyeball test": the medical equivalent of 'Can facial appearance reveal your lifespan?'

Diabetes is associated with significant loss of life years



On average, a 50-year-old individual with diabetes and no history of vascular disease will die 6 years earlier compared to someone without diabetes

Seshasai et al. N Engl J Med 2011;364:829-41

American Diabetes Association 2016 recommendations for CV risk reduction

- Blood pressure target <140/90, lower in high risk populations such as those with diabetic kidney disease
- Consider administering one or more antihypertensive medications at bedtime
- Use a risk calculator to decide on statin therapy (and aspirin therapy as relevant)
- Aspirin recommended for primary prevention in high risk patients
- Support smoking cessation, weight management, physical activity and healthy lifestyle choices (probably more important than insulin!)

Information that may be available at clinic, that helps with decision making about insulin starts

- HbA1c
- Tablets – is the patient ‘maxed out’ on diabetes meds or is there still some headroom? (NB Medsafe eGFR criteria and metformin)
- Random (capillary) glucose
- Meter download results or written log/diary
- Dietary history – important if considering insulin with a rapid acting component to it
- Patient preference / social, cultural and educational background / BMI

Why insulin? - Take home points

- When treating type 2 diabetes, carry on using common sense, take the patient's views into consideration and individualise treatment
- If you need a target HbA1c, knowing this is not a 'one size fits all' number, then go for a target of ≤55mmol/mol for most of your patients
- There are new non reimbursed diabetes medications available that look promising, but the diabetes specialists have difficulty keeping up with 'signals' about their side effect profiles
- Insulin may be easier than a complex diabetes tablet regimen! Insulin has been around a long time and we know its side effect profile
- Nearer the end of life, review which diabetes therapies can be reduced