Case studies diabetes and complications

The role of the diabetes team.

This afternoon:

- Brief overview of diabetes:
  - The size of the problem
  - diagnosis
  - type 1 and type 2
- Brief overview of diabetic complications
- Brief overview of treatment options
- Clinical cases

IS DIABETES IMPORTANT?

The cost of diabetes health services in New Zealand in 2001/02 was an estimated **$247 million**, with large future increases expected.

http://www.foe.org.nz/facts6.html; accessed 04/10/2007

Cost of treating Type 2 diabetes could increase to approx $1770million by 2022

Increased investment of $60million/year in prevention, self-management and early detection for Type 2 diabetes could potentially save the government $260million in 2022.

- http://www.diabetes.org.nz/news/nz_news/2008_type_2_update_report *Accessed* 09/04/2009

The problem (numbers for type 2 diabetes)

- 285 million worldwide 2010 (6.4%)
- 439 million 2030 (7.7%)
- Rise in prevalence greatest in the developing countries rather than in the developed countries.
- Directly linked to development of western lifestyle (high energy diets and reduced physical activity)

Type 1 diabetes: Epidemiology

- Disease of childhood…
- Enormous international variation in incidence.
- Annual incidence 3.2-40.2/100,000
- Annual rate of increase in incidence 3-4%
- Type 1 diabetes accounts for 5-10% of all diabetes
- Peak incidence between 10-14 yrs of age

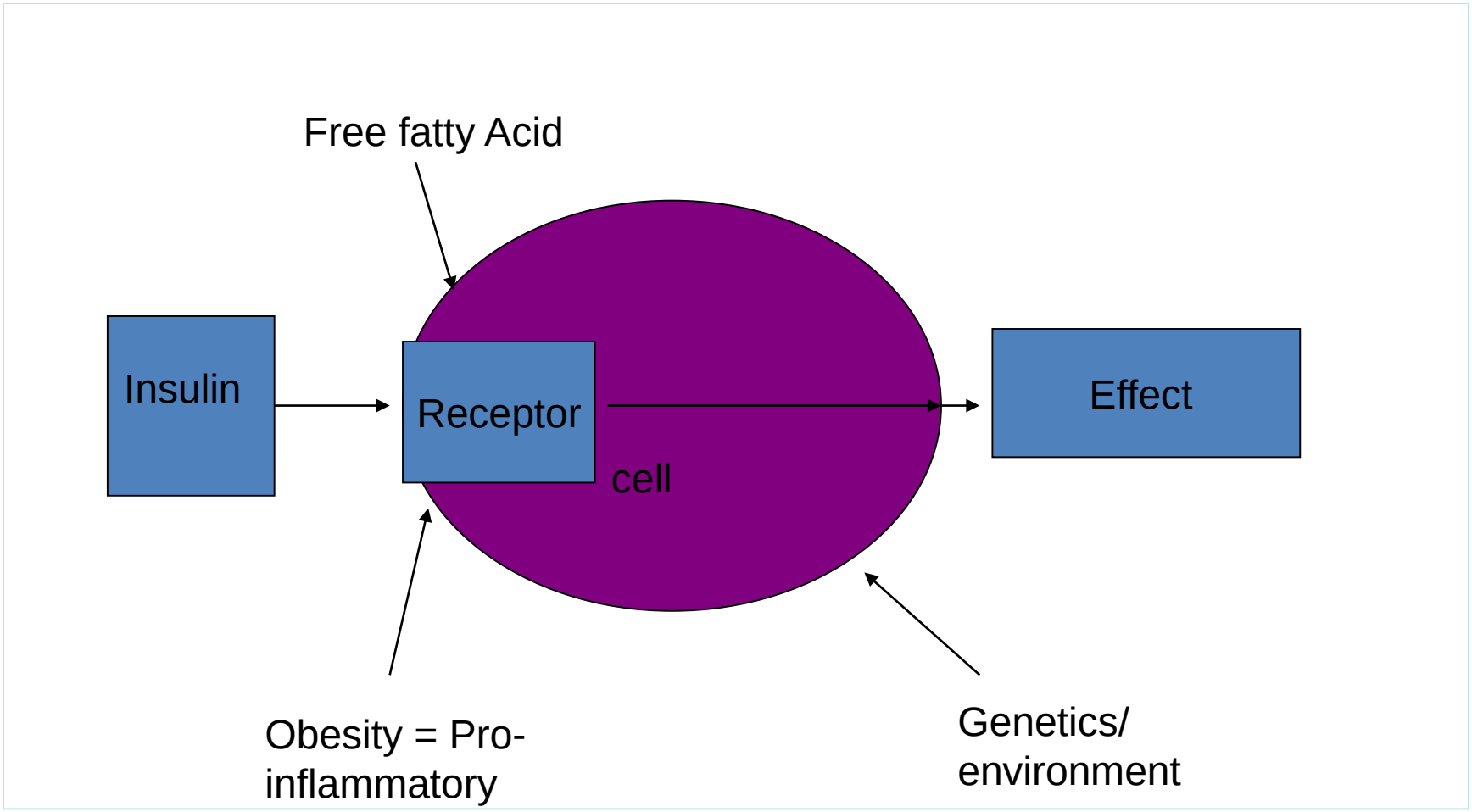
Hyperglycaemia in type 1 or type 2

- Type 2 diabetes: pancreatic function retained, “not enough insulin to overcome the insulin resistance” (beta cell function/Insulin resistance balance)
- Type 1 diabetes : no insulin production. Autoimmune Destruction of the pancreatic islet cells.

Insulin resistance

- The inability of insulin to produce its usual biological effects at circulating levels that are effective in normal subjects.
- Impaired ability to: inhibit hepatic glucose production, stimulate glucose uptake by skeletal muscle, suppress lipolysis in adipose tissue (thus increasing circulating NEFA-further stimulates gluconeogenesis, Tg synthesis, and glucose production in the liver, and reduced uptake by skeletal muscle!!!)

Insulin resistance at a cellular level



Clinical Picture of hyperglycaemia

- Symptoms related to osmotic diuresis:
  - Polyuria,nocturia
  - Increased thirst, polydipsia
  - Blurred vision
  - Drowsiness, dehydration
- Symptoms/signs linked to lack of insulin:
  - Hyperglycaemia, glucosuria
  - Extreme fatigue
  - Muscle wasting
  - Weight loss
  - Ketosis/ketoacidosis

- Symptoms of decreased resistance to infections:
    - Skin infections
    - puritis
- Symptoms related to caloric depletion:
    - Increased appetite
    - Weight loss

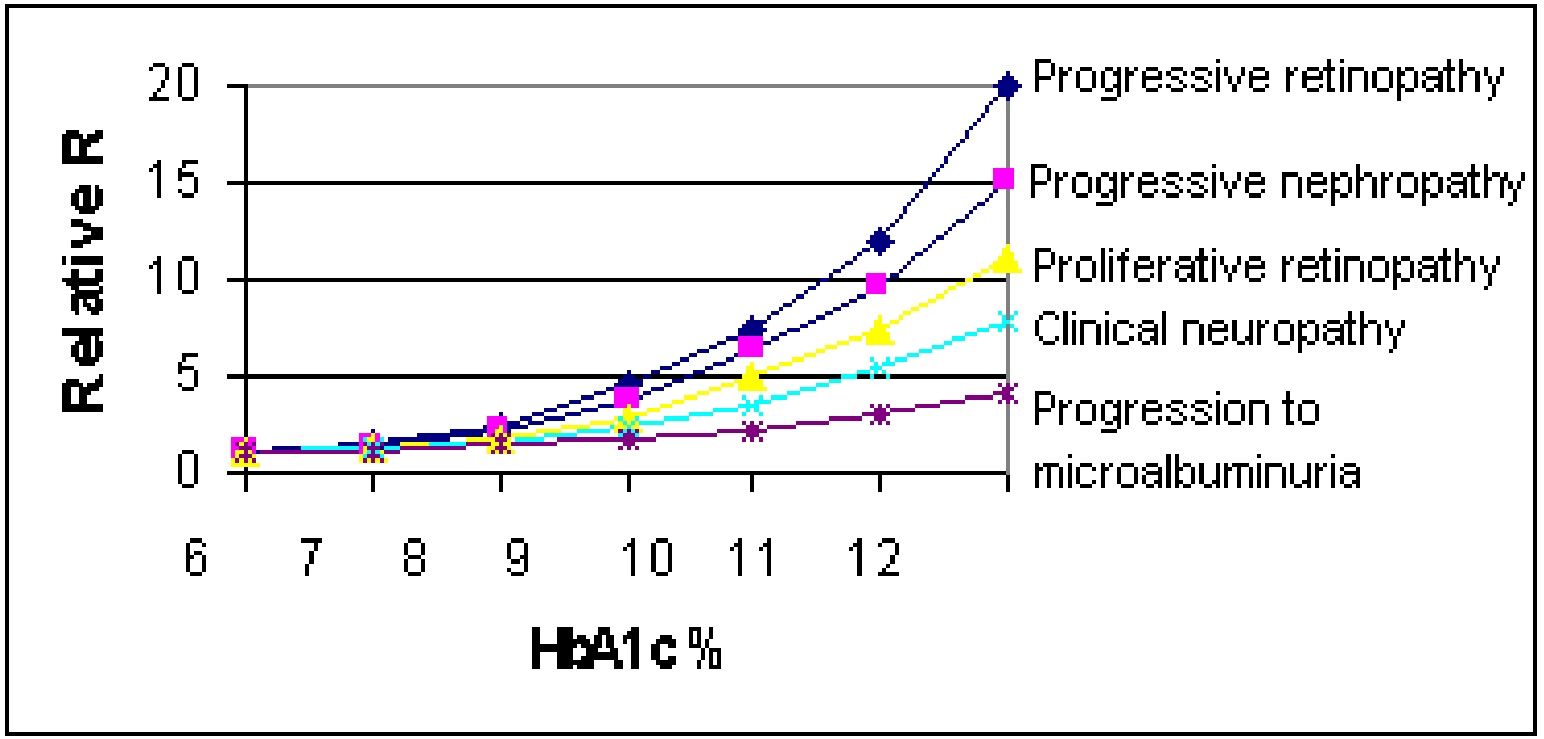
Diagnostic criteria

	Normal	WHO/ADA diabetes	IFG and IGT (WHO)	Pre-diabetes (ADA)***	
HBA1c	<5.7% ADA **<39mmol** <6.0% WHO **<42mmol**	>6.5% **>48mmol**	NA	>5.7% - <6.5% **>39 - <48mmol**	
Fasting plasma glucose mmol/L	<5.5% ADA **<37mmol** <6.1% WHO **<43mmol**	>7.0% **>53mmol**	>6.1% **>43mmol** and <7.0% **<53mmol**	>5.6% **>38mmol** and <7.0% **<53mmol**	
75gm Post load GTT mmol/L	<7.7% **<60mmol**	2 hours >11.1% **>98mmol**	IGT 2 hours >7.8% **>61mmol** and <11.1% **<98mmol**	2 hours >7.8% **>61mmol** and <11.1% **<98mmol**	
Random glucose		>11.1	NA	NA	

Complications of Diabetes

- Microvascular
  - Retinopathy
  - Nephropathy
  - Neuropathy
- Macrovascular
  - Cardiovascular disease
  - Cerebrovascular disease
  - Peripheral vascular disease
- Psyco-social
- Cognitive
- Infections: typical and atypical

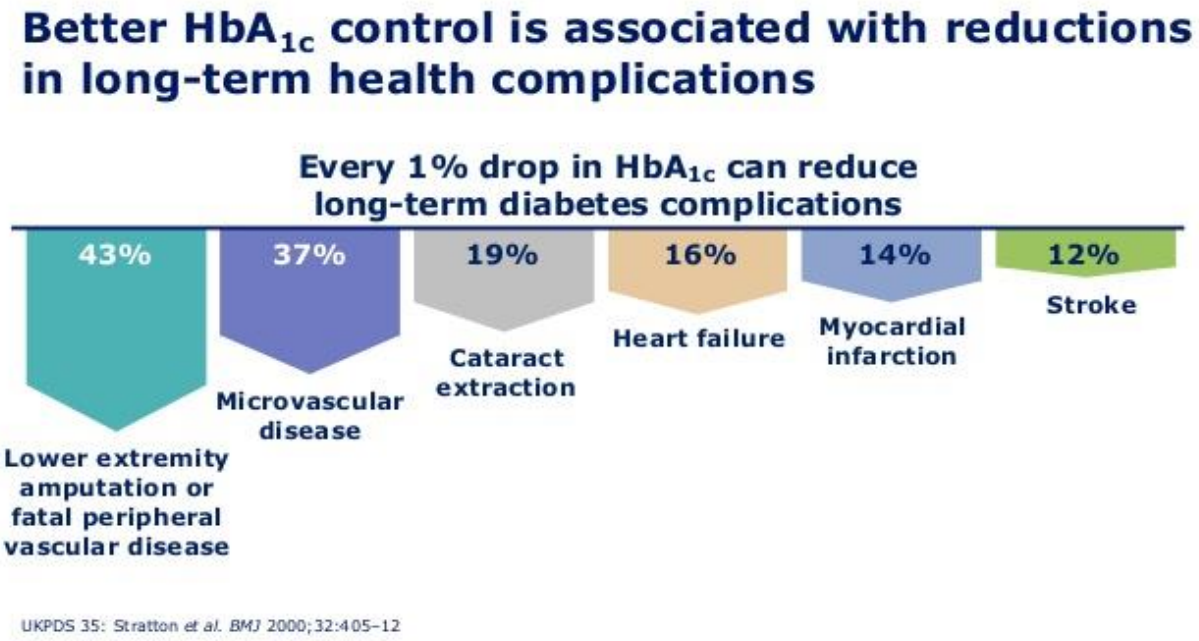
Risk of progression of Complications: Diabetes Control and Complications Trial



http://www.diabetestechnologies.com/images/chart1.gif. Accessed 04/10/2007

HbA_1c & risk of complications

1% = 5mmol



Associated vascular risk factors

- SMOKING
- Weight
- Lipids
- BP
- Obstructive Sleep Apnoea

Markers of good control

- Blood sugar levels
- HBA1c (normal **<40mmol/mol** <5.8%, diabetes control **≈55mmol/mol** 7.2%, individualised)
- BP
- Lipid profile

HbA_1c – what does it mean?

Useful in assessing accuracy of individual's tests / overall glycaemic control

HbA_1c Result		Average Blood Glucose Level
5% - 6%	**40**	4 – 6mmol/l
7% – 8%	**60**	7.5 – 9mmol/l
9% - 10%	**80**	11 – 13mmol/l
11% - 12%	**100**	14.5 – 16mmol/l
13% - 14%	**115**	18 – 19.5mmol/l
> 14%	**130**	> 20mmol/l

treatment

- Diet and exercise (lifestyle)
- Medication
- Testing……

- Must also treat: smoking, BP, Lipids…
- Must also check for complications

Blood Glucose Monitoring

When?

- Depends upon the individual and their treatment
- Initiating / modifying drug treatment
- If suspicious re very high or very low BGL
- During illness, surgery, stress

Freestyle Libre

Medication

Type 1: insulin. Life preserving hormone.

- different insulin preparations, and forms of delivery.

Type 2:

- Treat insulin resistance-metformin, pioglitazone.
- Assist pancreatic insulin production-sulphonyureas, GLP-1 agonists.
- Treat relative insulin deficit-insulin
- Treat hyperglycamia-SGLt2 inhibitors

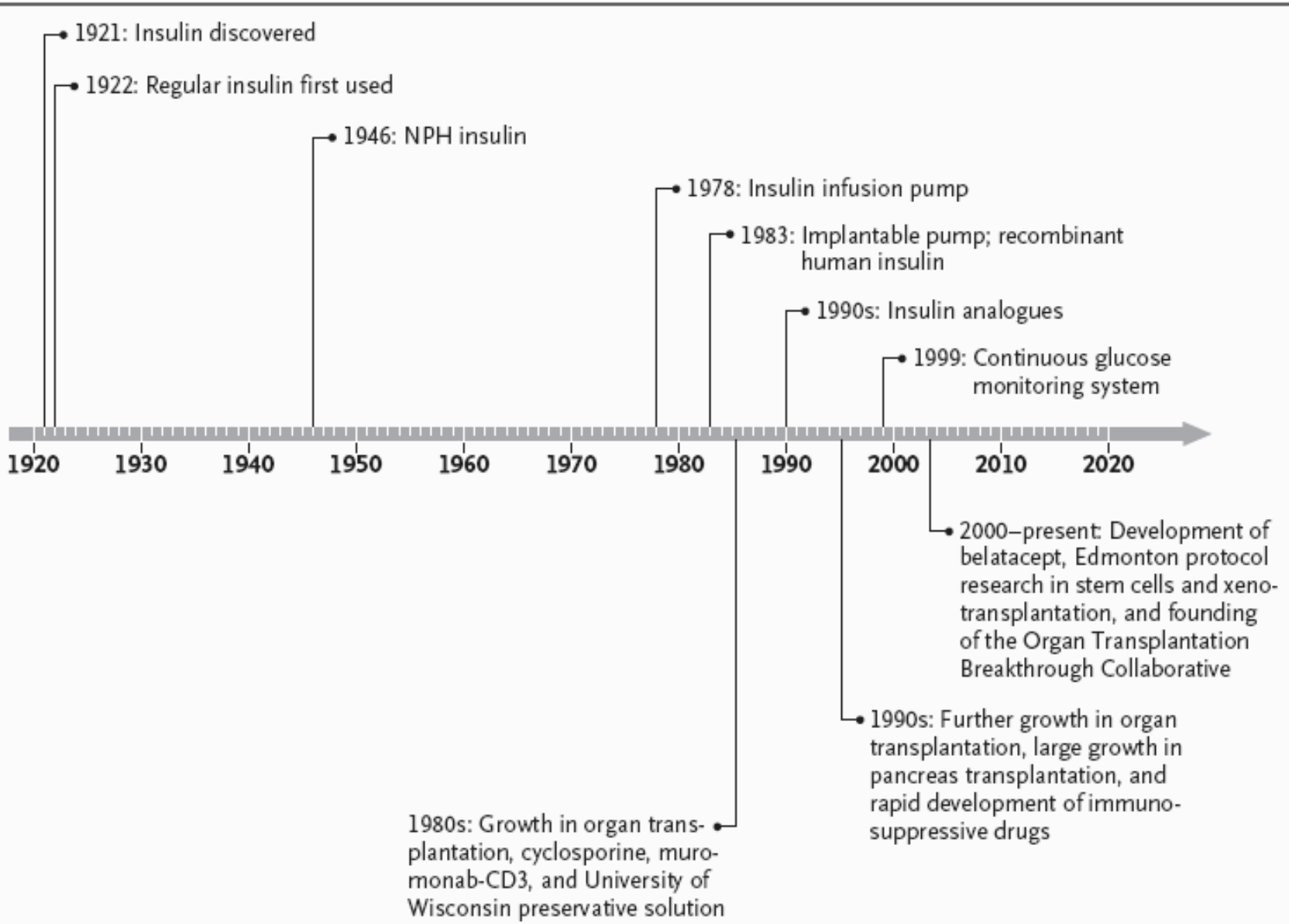


Figure 1. Milestones in the Treatment of Diabetes.

NPH denotes neutral protamine Hagedorn.

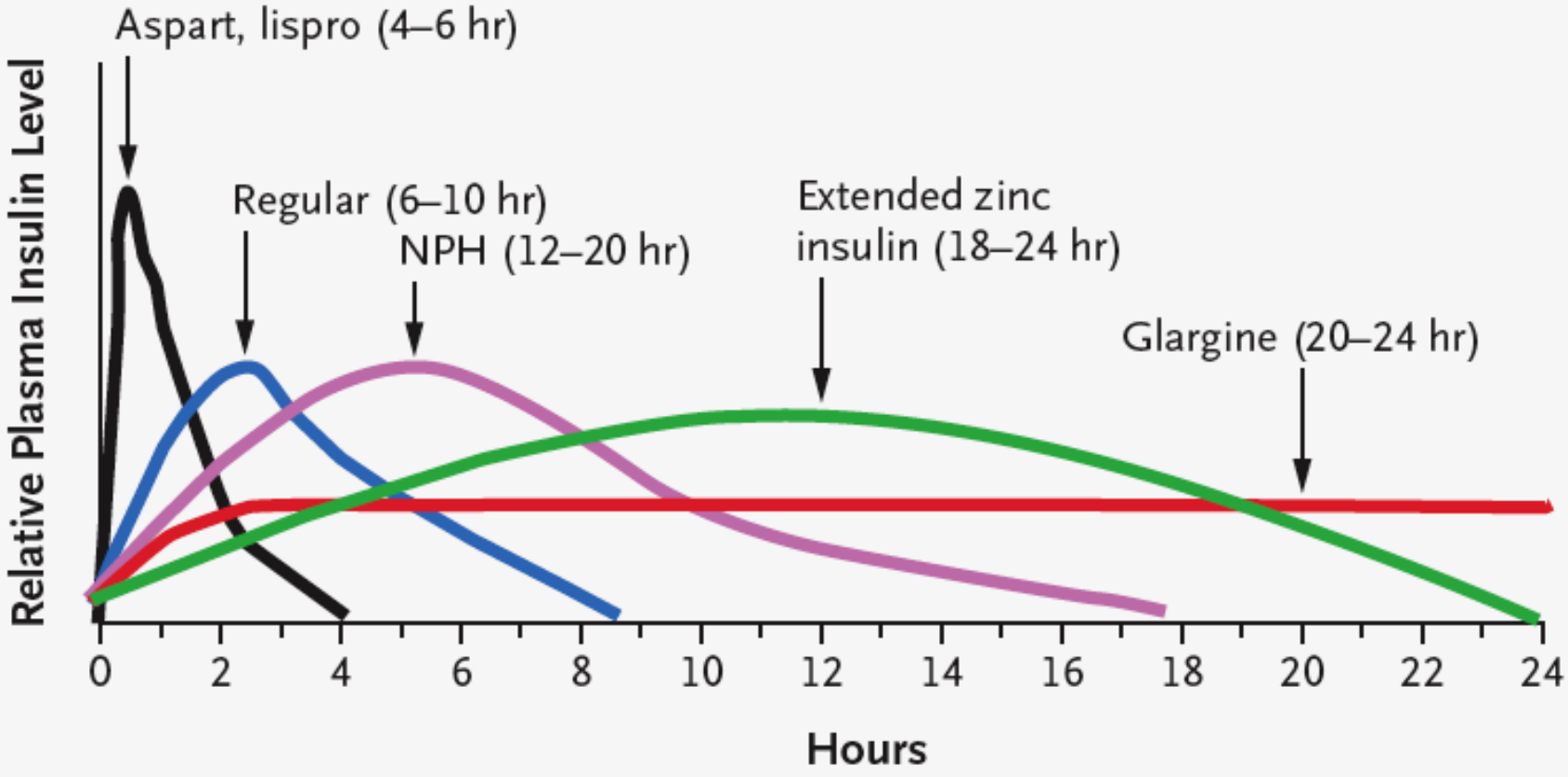


Figure 2. Approximate Pharmacokinetic Profiles of Human Insulin and Insulin Analogues.

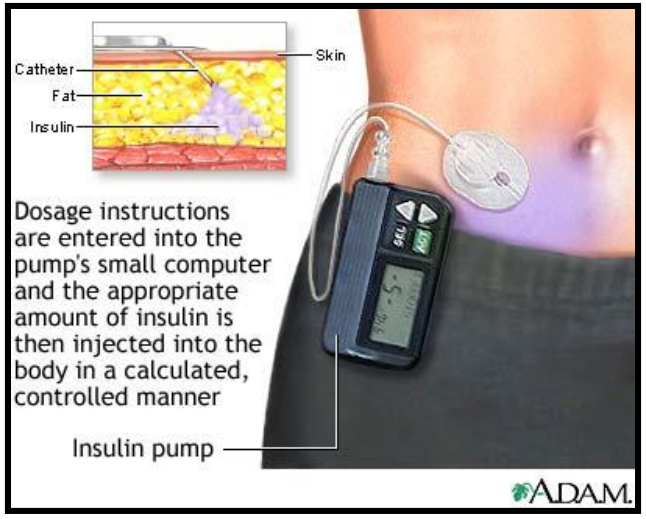
The relative duration of action of the various forms of insulin is shown. The duration will vary widely both between and within persons.

Insulin pump

- Indications: control, hypoglycaemia,blood sugar variability, social..
- National clinical priority assessment criteria
- Improved glycaemic control
- Use of fast acting analogues
- Bolus for meals and delayed bolus (1st and 2nd phase)
- Implantable!…not yet closed the loop

Insulin Pump

- Continuous Subcutaneous Insulin Infusion



Diabetic Foot Ulcers

- Risk of death at 5 years for a patient with DM and foot ulcer is 2.5 X that of DM without foot ulcer
- Lifetime incidence of foot Ulcer in DM = 15-25%
- More than half become infected
- 20% of mod-severe ulcers lead to lower limb amputation
- Peripheral artery disease independent risk factor
- High mortality following amputation – 70% at 5 years
- Consider a healed foot as a foot in REMISSION.
- Healing affected by CHF, Renal disease, PVD, and the ability to walk independently.

Armstrong DG et al. NEJM 2017

Prevention is the KEY

- On going professional foot care
- Good diabetic control
- Attention and treatment of PVD
- Adherence to care
- Early recognition of a problem

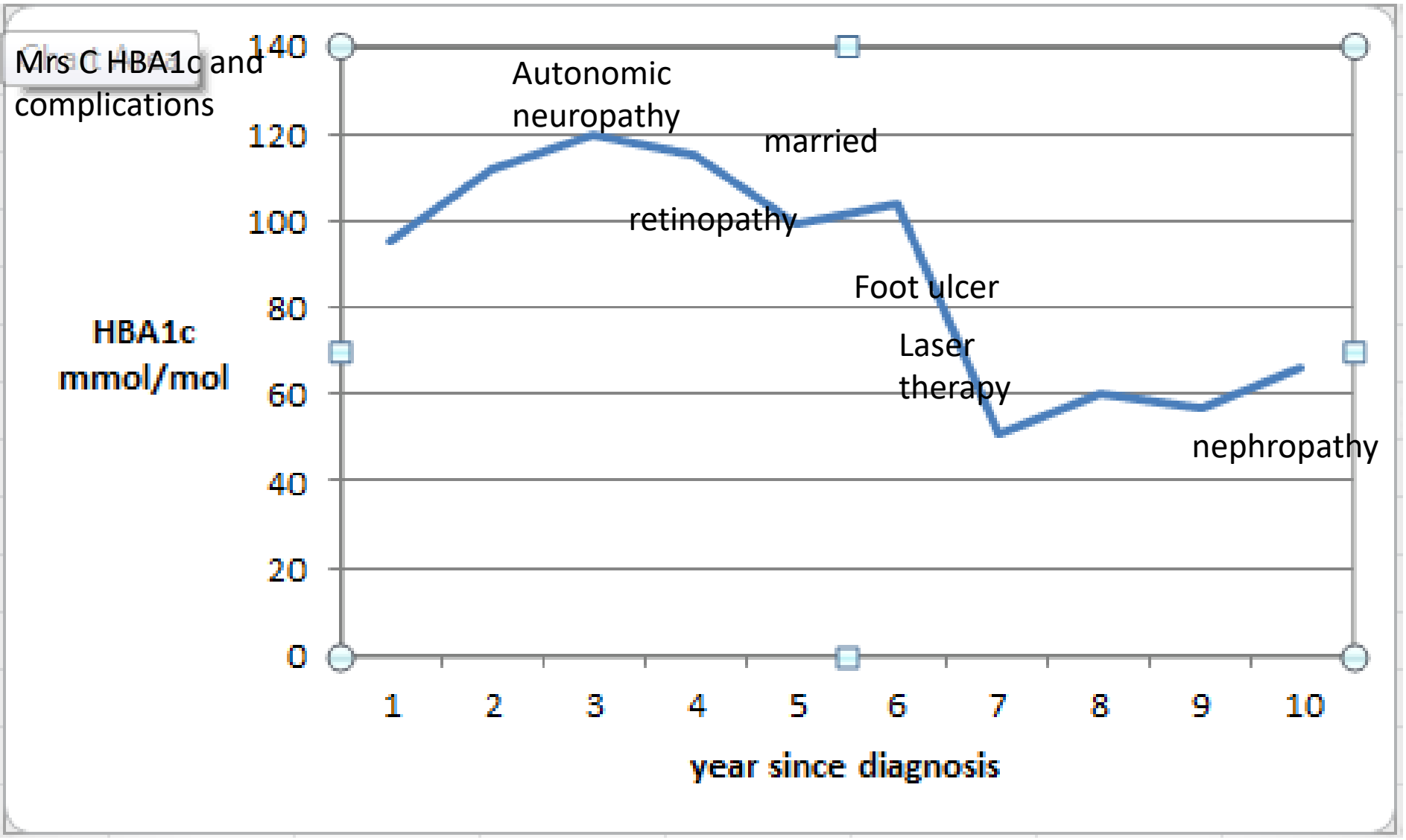
Mrs C

- Type 1 DM
- Diagnosed late 20s.
- Poor diabetes control: fear of weight gain, depression
- Psychologist: was slim and poor repour
- HBA1c 90-100 mmol/mol

- 34yo: evidence of autonomic neuropathy: nocturnal diarrhoea and postural hypotension
- 36yo retinopathy: mild
- 36 yo marries, more consistent with insulin, talk of pregnancy
- 37yo: admitted with foot ulcer: infected left heal and toe blister. Required grafting
- Finally checking BSLs (sometimes)

- On going heel break down
- Adhering to “off-loading”
- 38yo progression of retinopathy/ laser therapy
- 40yo nephropathy

- Medications:
  - Insulin :basal /bolus
  - metformin

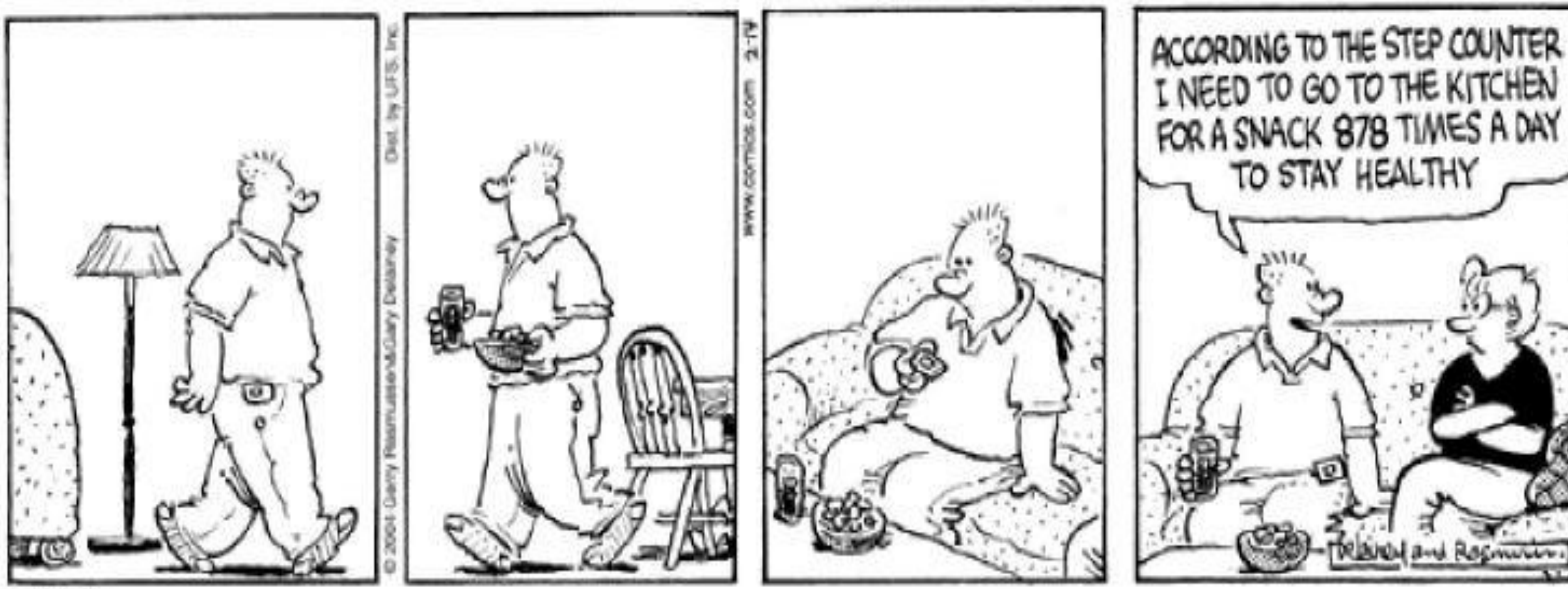

Mrs C HBA1c and complications
140
120
100
80
60
40
20
0
HBA1c mmol/mol
Autonomic neuropathy
married
retinopathy
Foot ulcer
Laser therapy
nephropathy
1
2
3
4
5
6
7
8
9
10
year since diagnosis

Mrs C
MDT

- Her and her husband
- GP
- DNS
- Psychology
- Foot clinic
- Ophthalmology
- Nephrology
- Gastro

Diabetes and Depression

- People with diabetes are twice as likely to experience depression as those without
- Depression is closely associated with development of diabetes complications ?due to stress response and resulting hyperglycaemia
- risk of developing diabetes 23% higher in people with a history of depression
- Close connection between mood and level of glycaemic control


ACCORDING TO THE STEP COUNTER I NEED TO GO TO THE KITCHEN FOR A SNACK 878 TIMES A DAY TO STAY HEALTHY

Mr L W

- 65 yo
- Type 2 DM 55yo
- Obesity 137kg, BMI 44
- Hypertension
- Dyslipidaemia

- GP Calls:
- Ankle swollen and red
- Recurrent cellulitis
- Neuropathy

Meds

- Aspirin
- Metformin
- Glicazide
- Simvastatin
- Ezetamibe
- Cilazapril
- Felodipine
- Bendrofluazide
- Metoprolol
- Voltaren

PMH

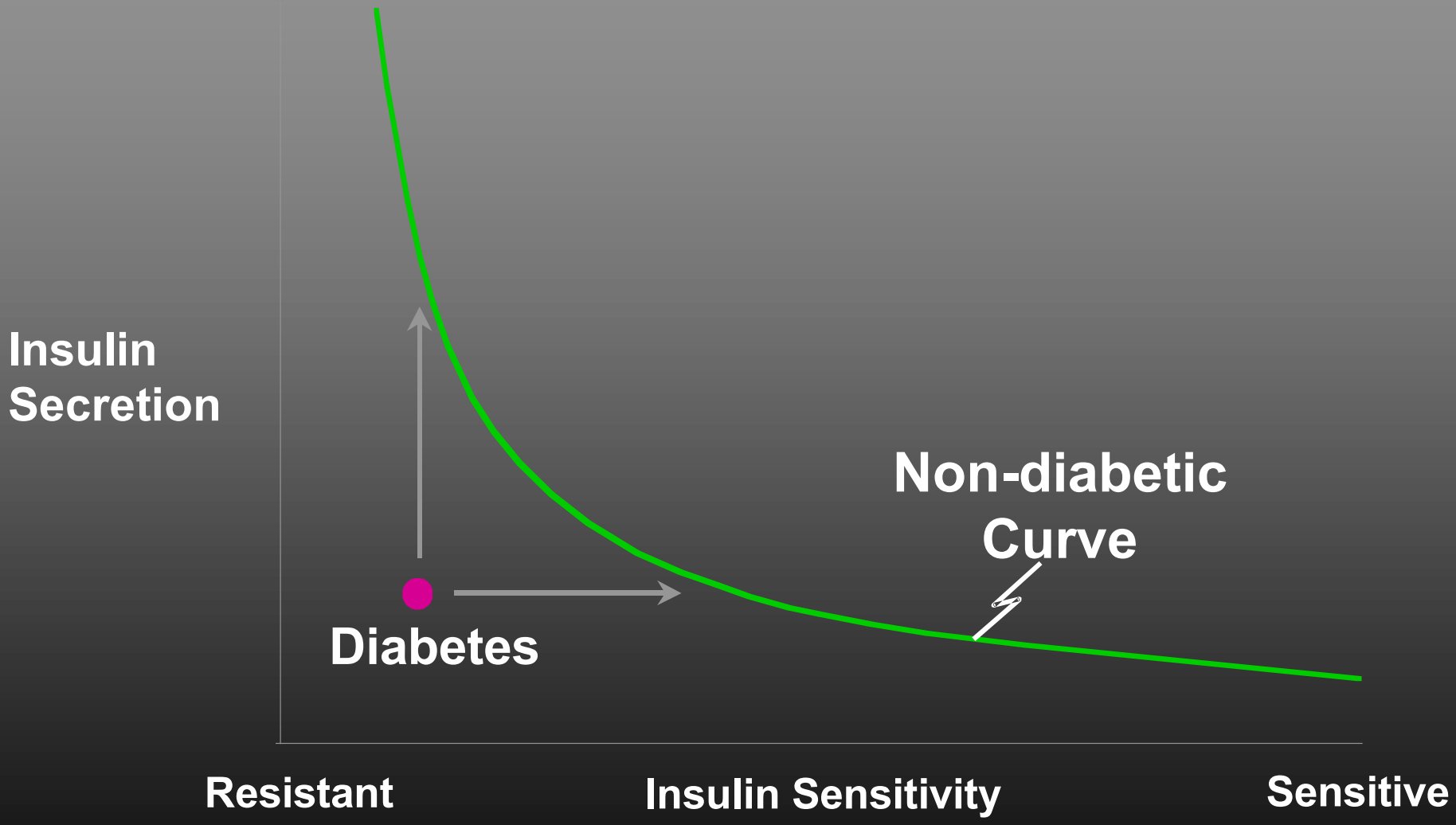
- Angina
- Hypertension
- Chronic renal impairment

What to do!

- Prevention
- Education
- Lifestyle
- Targets: HbA1c, BP, lipids. Evidence re control is bountiful! (UKPDS, 4S…)
- Screening. (retinal, renal, feet)
- **Address ALL risk factors collectively**

NEJM 2003,348(5)383-

Treatment of Type 2 Diabetes
"Getting Back on the Curve"

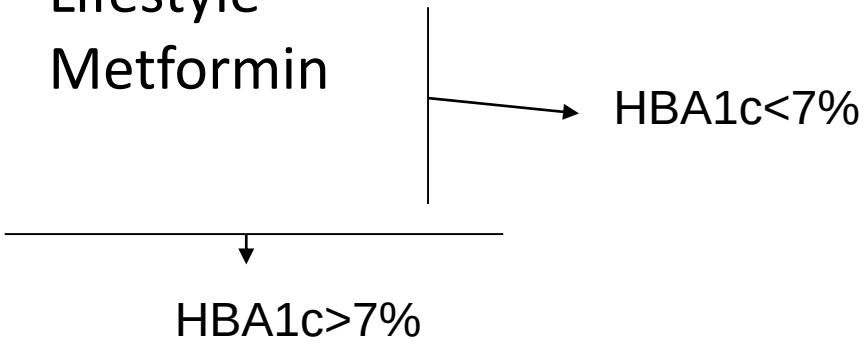


Therapeutic options for type 2 diabetes (blood sugar control)

- **Metformin**
- Sulphonylureas
- PPaγ (peroxisome-proliferator-activated receptor γ)
- Acabose
- Repaglinide
- **Insulin**
- GLP-1/DDP-IV
- GLT2 antagonists
- Surgery

What treatment then?

- Lifestyle
- Metformin



- Then add sulphonylurea or insulin-well established…tier 1.
- Or add pioglitazone, or GLP-1…tier 2.
- Target HBA1c <7.0% but…..use common sense, gain in elderly minimal with significant risk with hypo, gain in young greater….

Surgical treatment of obesity

- Bariatric surgery is the fastest growing surgical subspecialty
- Diabetes may disappear in days to weeks after surgery before weight loss!! Roux-en-Y. Increase in GLP-1, reduction in Ghrelin. JCEM.July 2008,93(7);2479-2485
- Weight loss of 10-25% (at 10 yrs) v/s 2% in controls, death reduction from all causes of 40%....diabetes, cancer, coronary artery disease
- LABS-1 study.,. perioperative safety 1%-7.8% adverse complications NEJM 2009 July 361;5 445-454
- Reduction in life expectancy is 20 years in young obese!

Mr LW

- Lost 40 kgs over 8 years.
- Swims for 1-2 hours each day
- Meds
  - Insulin ; reducing doses and Metformin
  - Metoprolol
  - Cilazapril
  - Aspirin
  - Simvastatin
- What about the foot/cellulitis…??

The Charcots joint

- Destructive arthropathy with bone and joint distruction.
- Peripheral neuropathy
- Usually no peripheral vascular disease.
- Difficult to diagnose? differential osteomyelitis….MRI

- Palmidronate infusion.
- On going care in the foot clinic in remission

Human Costs

- reduce the quality of life.
- Loss of mobility results in severe restrictions in the activities of daily living including employment, recreation, shopping and home maintenance.
- problems with social and interpersonal relationships and suffer emotional distress

What can this clinic do?

Weekly assessments of these high risk people by MDT may prevent 50% to 85% of diabetic foot amputations

"This new diet drug takes fat from the food you eat and moves it to your ear canal so you can't hear snacks calling you from the kitchen."

Mr W

- 56 yo
- Type 2 DM
- Schizophrenia, in supported accommodation
- Hypertension
- Obesity
- OSA
- dyslipidaemia
- Referred by GP to foot clinic.

Mr W

- Recurrent right foot cellulitis.

- Seen in Foot clinic
- No BSL, No recent labs, no real understanding of link between DM and other issues

THIS CLINIC IS THE HIGH RISK FOOT CLINIC

- You are attending this clinic because you have a significant foot problem as a consequence of your diabetes.
- To give yourself the best chance of recovery you should be focusing on
- Foot care and blood sugar control. .
- If you are a smoker you need to QUIT! Please ask for help if this is a problem for you.

Medication List

Tablet	Dosage	Number of tablets	Times per day

Blood Glucose Monitoring

Please fill in the following table with your blood glucose levels.

	Date	Breakfast	2 hours after breakfast	Lunch	2 hours after lunch	Evening Meal	2 hours after evening meal
Day 1							
Day 2							
Day 3							
Day 4							
Day 5							
Day 6							
Day 7							

Mr W

- HBA1c **70**mmol/mol (8.6%)
- Albumin/Creatinine ration 30ng/mmol (<2.5)
- Lipids : terrible, elevated triglycerides
- LFTs suggestive of Etoh plus NAFLD

Mr W

- Continued input and seen in Diabetes clinic
- HBA1c **47**mmol/mol! (6.5%)
- LFTs improving and lipids improving
- No decline in alb/creat ratio
- Medications rationalised
- To see ophthalmology.

- Foot improving

Diabetes and Schizophrenia

- Prevalence of diabetes in patients with schizophrenia found to be higher than in general population before widespread use of antipsychotic medications

- Insulin resistance noted in patients with schizophrenia >50years ago

- Mechanisms underlying link remain unknown

(Proietto 2004)

Mr W

- Impact of education, positive reinforcement and follow-up

- Essential patients with any complication of DM also assessed for other associated disease processes.

Diabetes Types