

A simple model-based test for insulin sensitivity compares well with the euglycaemic hyperinsulinaemic clamp

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Introduction

Type 2 Diabetes affects more than **230 million people** worldwide and is responsible for **3.5 million deaths** annually [1]. About **215 000 New Zealanders** are estimated to have type 2 Diabetes and an equal number are insulin resistant, prior to developing the disease [2]. Costs for the NZ public health system: **\$540 million** in 2006, expected to rise over **\$1.8 billion by 2021** [2].



Early diagnosis of insulin resistance can reduce the burden of further complications and save lives and cost. Current diagnostic methods are too expensive and complicated to be useful in widespread population screening (euglycaemic clamp, IVGTT), or not accurate enough to give more than a high/low result (HOMA, OGTT).

Insulin resistance rises up to 10 years prior to diagnosis

Test design

Provide complete diagnostic information about:

- Insulin sensitivity
- β -cell function

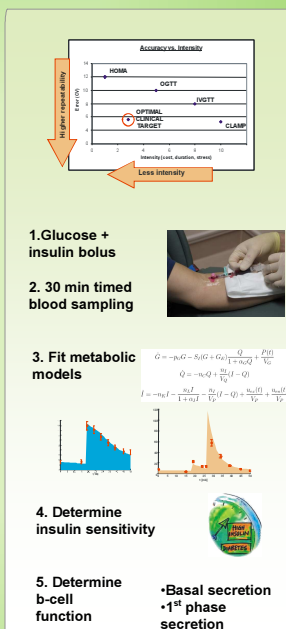
The test is designed to **measure the same metabolic effect as the gold standard euglycaemic hyperinsulinaemic clamp**.

Design goals:

Simple, low intensity, high accuracy, low cost, physiological dosing

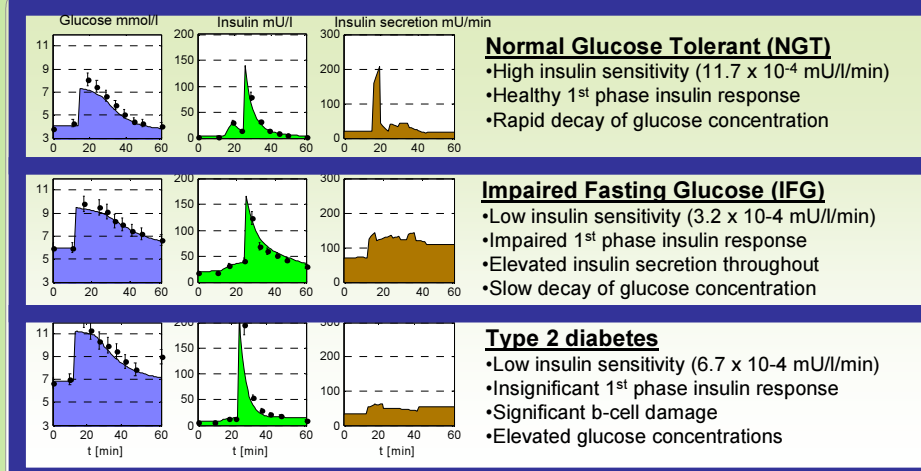
The protocol:

1. **Low dose bolus of glucose (10g) and insulin (1U)**
 - ➔ Reduce endogenous regulatory effects
 - ➔ Improve clinical practicability and safety
2. **30 min timed sampling of glucose, insulin and C-peptide**
3. **Fit metabolic models**
 - ➔ Only transient data from 10 - 30 minutes post bolus
 - ➔ Identification requires only few samples
4. **Determine insulin sensitivity from model parameter S_1**
5. **Determine β -cell function from C-peptide data**



Diagnostic outcome

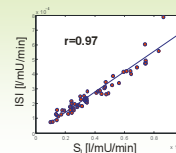
Test outcome on 3 exemplary subjects spanning the range from NGT to Type 2 Diabetes



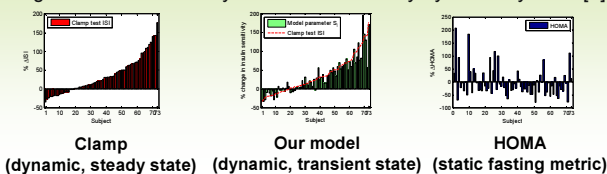
Performance

1. Model validation on euglycemic clamp data [3]

a) Correlation clamp ISI vs. model S_1 , $r=0.97$



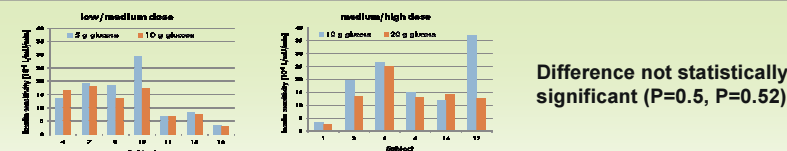
b) Change in insulin sensitivity in intervention study by McAuley et al. [4]



2. Clinical Pilot study: 17 subjects, 43 tests

Part 1: Effect of dose on outcome

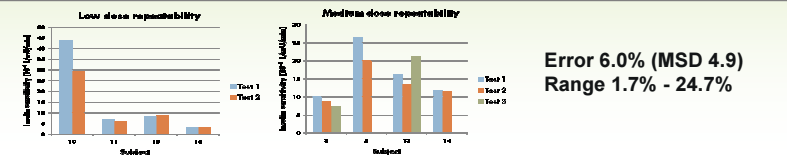
- Low dose: 5g glucose / 0.5U insulin
- Medium dose: 10g glucose / 1U insulin
- High dose: 20g glucose / 2U insulin



Difference not statistically significant (P=0.5, P=0.52)

Part 2: Repeatability

- Same dose on same individual on a different day



Error 6.0% (MSD 4.9)
Range 1.7% - 24.7%

[1] International Diabetes Federation (www.idf.org)

[2] PWC for Diabetes New Zealand (2007), "Type 2 Diabetes - Outcome model update"

[3] Lotz T, Chase JG, et al. (2006), "Transient and steady state euglycaemic clamp validation of a model for glycemic control & insulin sensitivity testing", DT&T 8(3)

[4] McAuley K, et al. (2002), "Intensive Lifestyle Changes Are Necessary to Improve Insulin Sensitivity", Diabetes Care 25(3)

[5] McAuley K, et al. (2007), "Point: Homeostasis Model Assessment", Diabetes Care 30(9)