RESIST

Dietary strategies to improve insulin sensitivity in overweight adolescents

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Childhood obesity Australia

One of the most common chronic diseases in children and adolescence

1:4 school aged children are overweight or obese

Consequences of childhood obesity

Pulmonary disease
sleep apnea
asthma

Idiopathic intracranial hypertension

Nonalcoholic fatty liver disease / steatosis

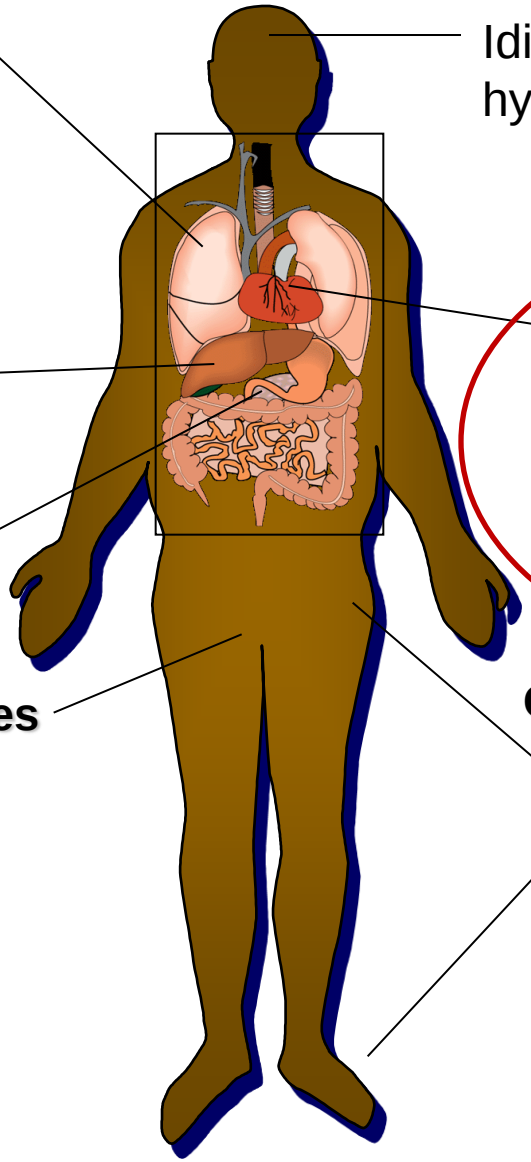
Coronary heart disease
Insulin resistance
Type 2 diabetes
Dyslipidemia
Hypertension

Gall bladder disease

Gynecologic abnormalities
abnormal menses
polycystic ovarian syndrome

Orthopedic
slipped capital epiphyses
flat feet
increased risk of fractures

Psychological
depression
poor quality of life
social Isolation



Type 2 diabetes

- costly & burdensome chronic disease in Australia (~$10.3 billion 2005)
- significant health problem in children
  - ~11% of children presenting with diabetes
  - higher indigenous & migrant populations
  - Mean BMI z-score 2.2 at presentation
  - 90% had BMI >85th%
- increased risk of complications compared to T1D
  - microalbuminuria, hypertension, dyslipideamia
  - present at diagnosis or appear early

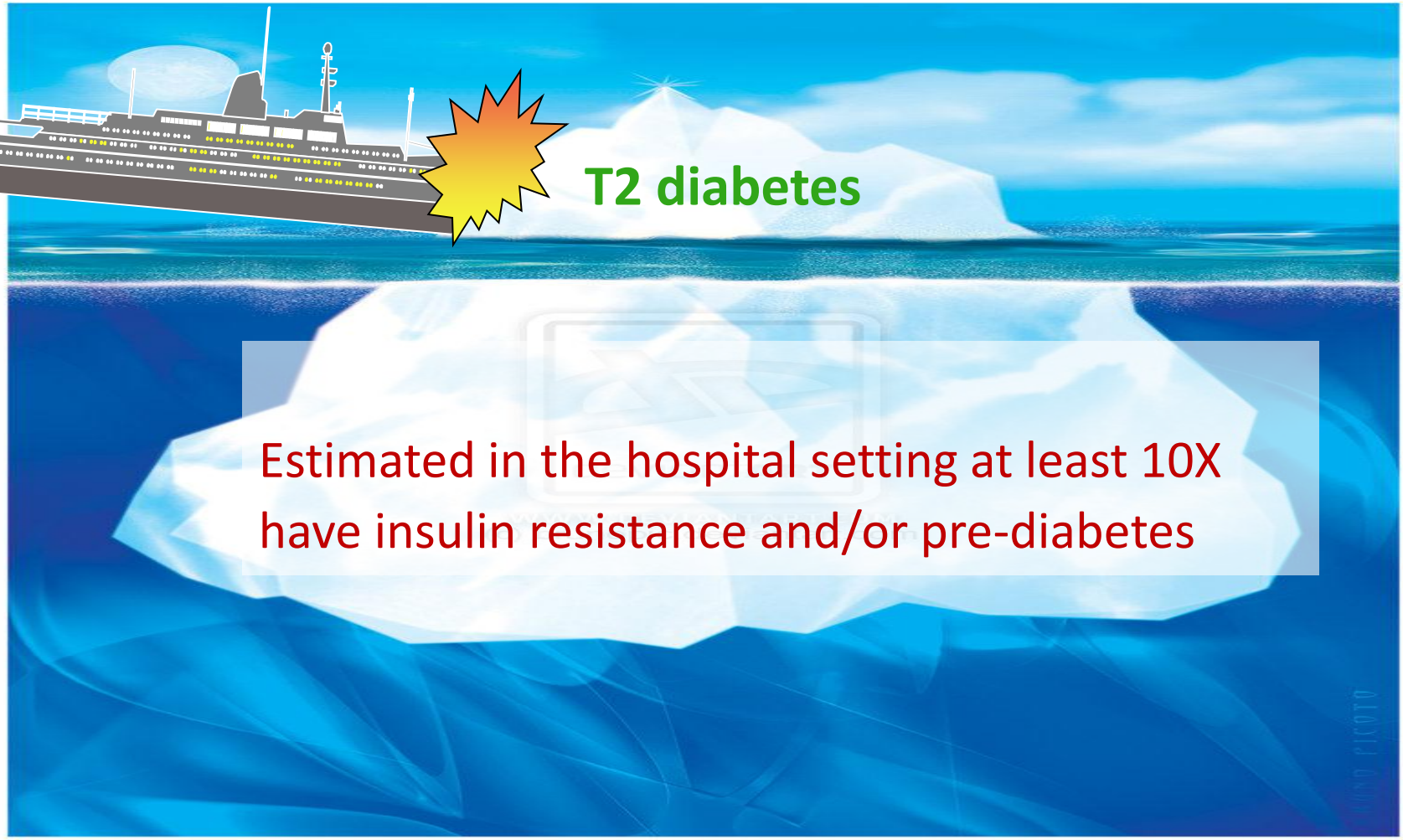
Craig ME et al, MJA 2007

Type 2 diabetes

- complications highlight the severity of T2D in the young
- 164 Canadians with early-onset T2D
  - 69 were followed into adulthood (mean age 23 years)
    - 9% mortality
    - 35% had microalbuminuria
    - 6% required dialysis
    - 45% had hypertension
    - 67% had poor glucose control.

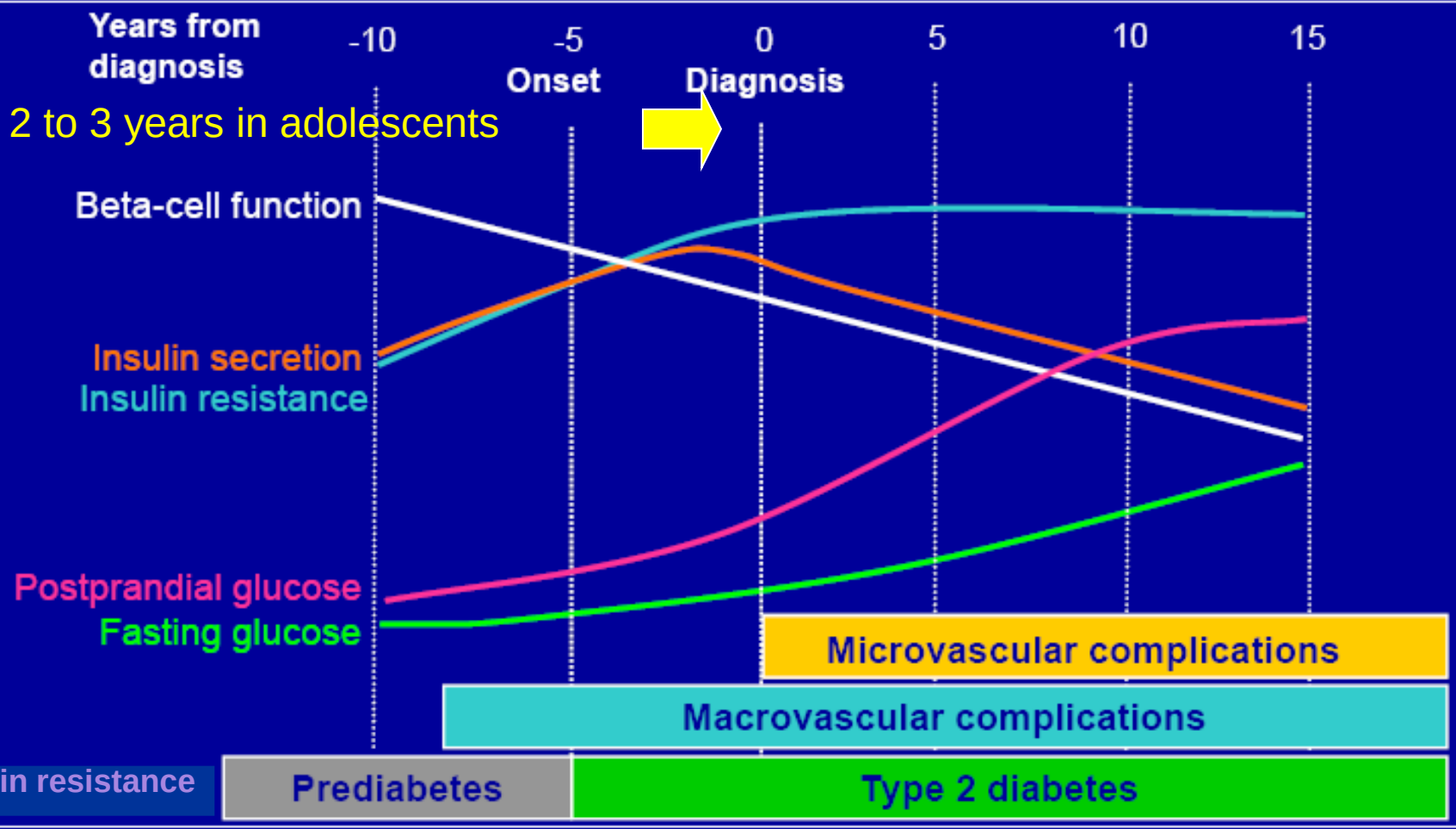
Dean HJ, Flett B. Diabetes 2002; 51

Type 2 diabetes



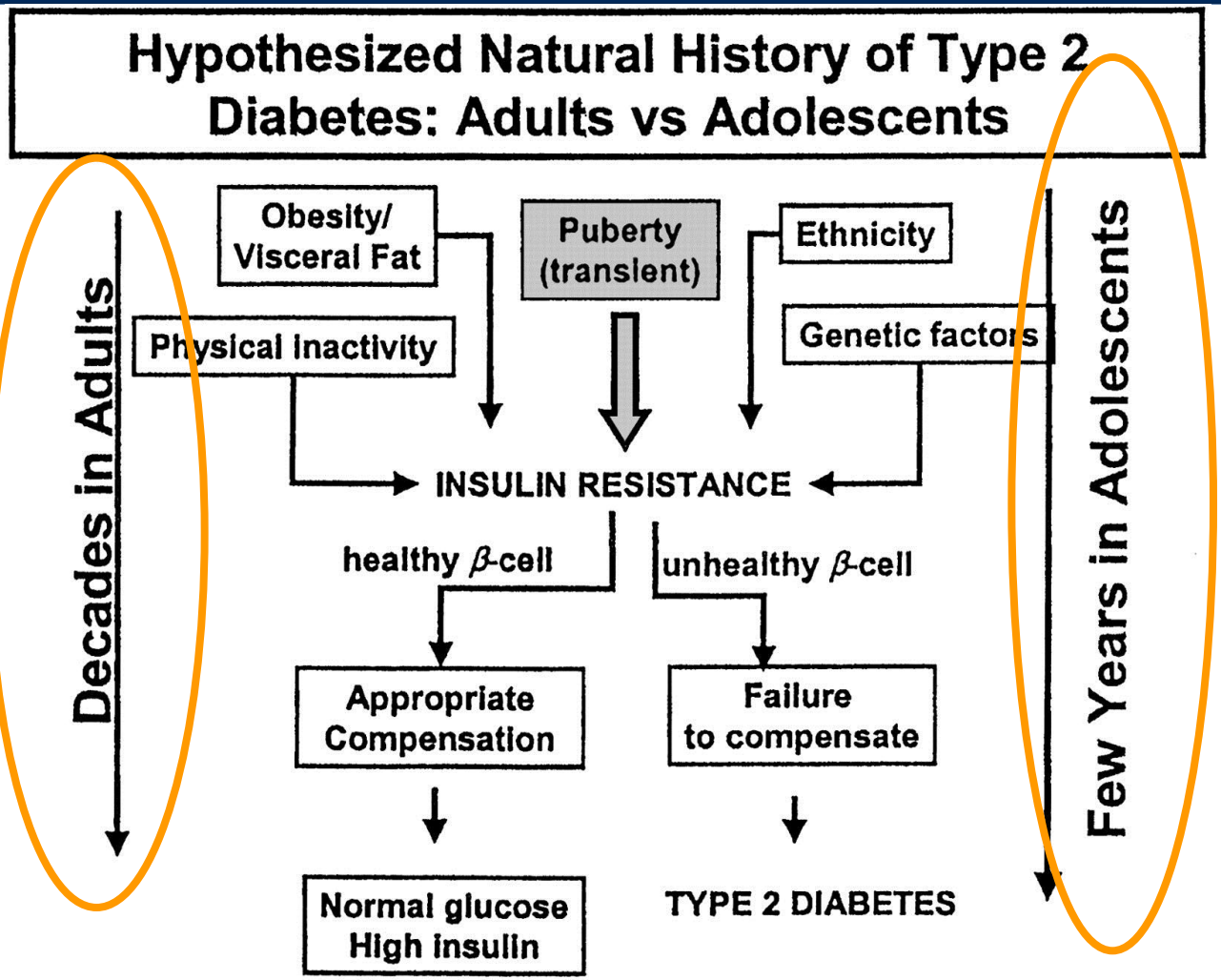
http://brunopic.deviantart.com/art/Iceberg-175070537

Natural History of T2DM in Adults



Data extrapolated.

Adapted from Holman RR. *Diabetes Res Clin Pract.* 1998;40(Suppl):S21–S25; Ramlo-Halsted BA, et al. *Prim Care.* 1999;26:771–789; Nathan DM. *N Engl J Med.* 2002;347:1342–1349.

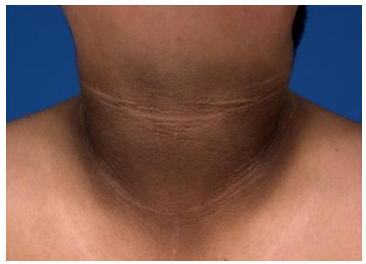


Goran, M. I. et al. J Clin Endocrinol Metab 2003;88:1417-1427

Presentation: Clinical insulin resistance & pre-diabetes

- ❑ Overweight or obese
  - elevated insulin to glucose ratio

- With one or more of the following
  - acanthosis nigricans
  - polycystic ovarian syndrome
    - Oligomenorrhoea
    - hyperandrogenism
      - +/- polycystic ovaries on USS
  - hypertension
  - dyslidaemia
  - non alcoholic fatty liver disease



Young people at risk

Family History

- ❑ T2D, gestational diabetes
- ❑ Obesity (central obesity)
- ❑ Premature heart disease
- ❑ Dyslipidaemia
- ❑ Hypertension
- ❑ Sleep apnoea

Ethnicity

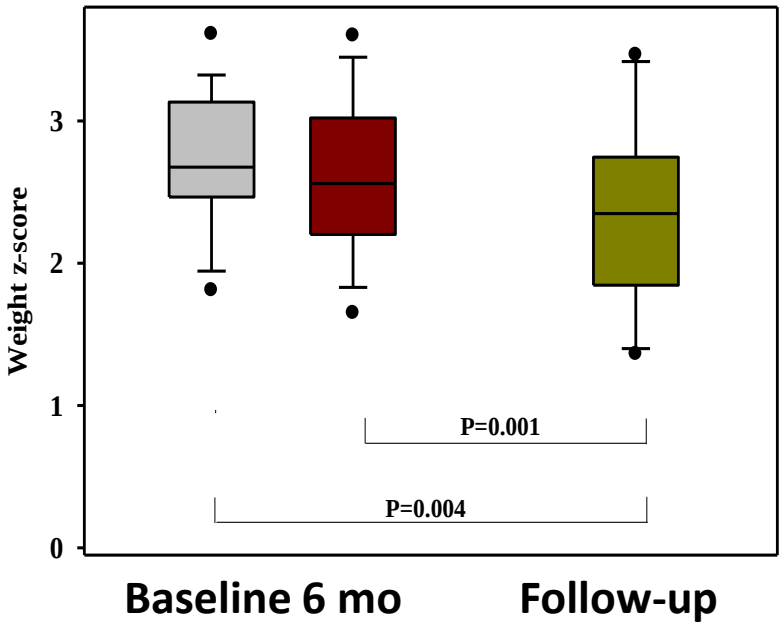
- ❑ Maoris & Pacific Islanders
- ❑ Indigenous Australians
- ❑ Middle-Eastern/Mediterranean
- ❑ Indian sub-continent
- ❑ Native Americans

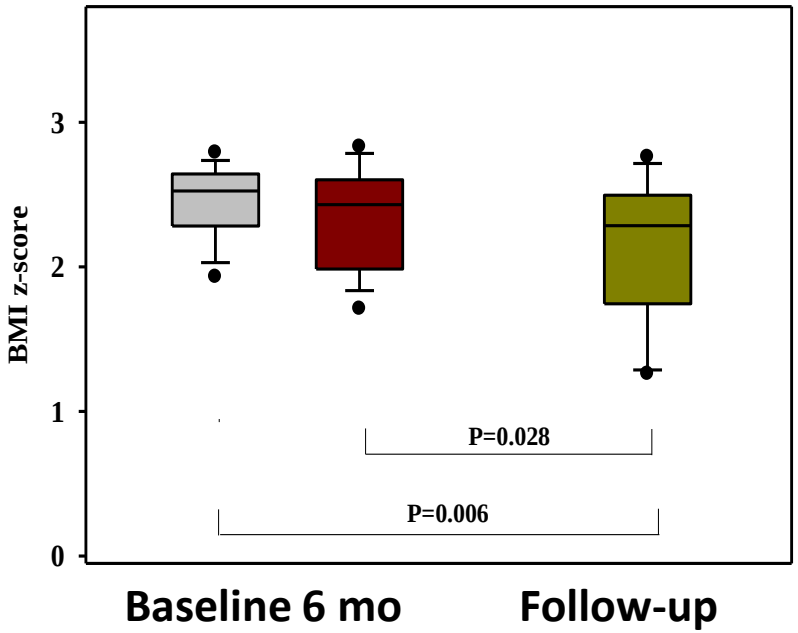
Management: Clinical insulin resistance & pre-diabetes

- Limited Evidence
  - Metformin
  - Diet
  - Exercise

Metformin Insulin sensitiser

- Five RCTs: beneficial effects on weight, body composition, insulin, glucose
  Quinn SM, Baur LA, Garnett SP, Cowell CT. Treatment of clinical insulin resistance in children: a systematic review Obes Rev 2009.
  - ↓ hepatic glucose & intestinal absorption of glucose
  - ↑ peripheral glucose uptake & utilisation
  - ↓ the feeling of hunger & reduces food intake





S Srinivasan, GR Ambler, LA Baur, SP Garnett, J Clin Endocrinol Metab 2006;91:2074

Diet: Clinical insulin resistance & pre-diabetes

- Intensive diet interventions can achieve weight loss
- No evidence based recommendations
- Consensus: national nutrition guidelines

- Recent systematic review (wt loss): Mandy Ho (PhD Student)
  - 6 RCTs macronutrients, small sample & length of study. Generally interested in low CHO diets <40grams

Diet: Clinical insulin resistance & pre-diabetes

- Increased protein, moderate CHO diet
  - ↑ satiety & thermogenesis
  - preserves fat free mass & ↓ fat mass
  - easier to achieve RDI for micronutrients (calcium, B12)
  - anecdotal evidence (Weight Management Services, CHW)
  - adults moderate carbohydrate, increased protein diets for both weight loss & improved metabolic profile

RESIST

The Children's Hospital at Westmead

Researching **E**ffective **S**trategies to improve **I**nsulin **S**ensitivity in children and **T**eenagers

ACTRN 12608000524392

Multicentred, randomised control trial

(CHW, Campbelltown Hospital)

SP Garnett et al: *Researching Effective Strategies to Improve Insulin Sensitivity in Children and Teenagers - RESIST. BMC Public Health 2010;10:575 doi 10.1186/1471-2458-10-575*

AIM

Establish an evidence based management plan for adolescents at risk of type 2 diabetes by examining the role of dietary protein in improving insulin sensitivity.

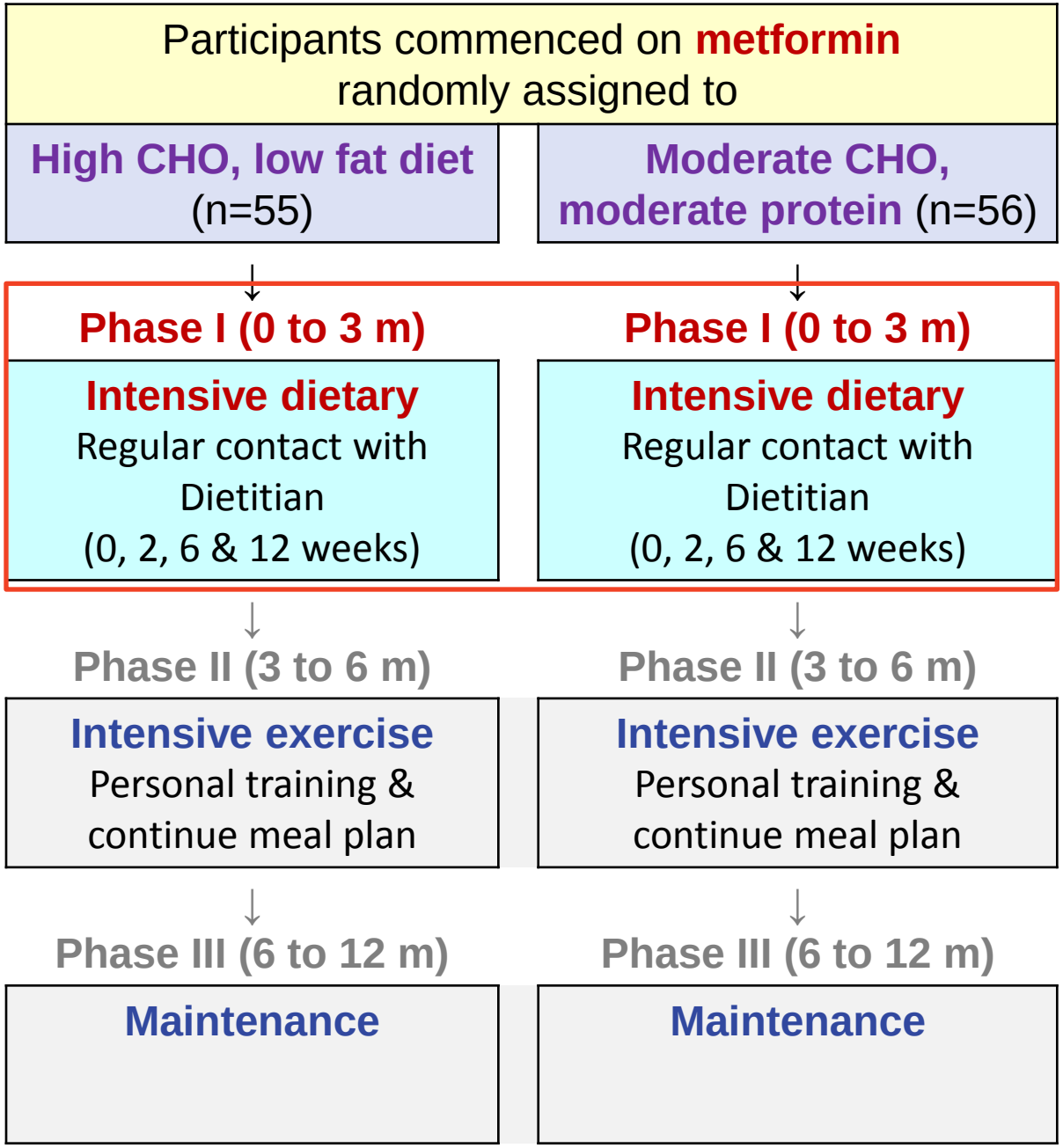
Target group: Young people with insulin resistance

Inclusion criteria

- 10 to 17 years of age
- Overweight or obese
- Pre diabetic and/or fasting insulin/glucose >20
- with one or more of the following
  - acanthosis nigricans
  - polycystic ovarian syndrome
  - hypertension
  - dyslidaemia

RESIST Overview

(ACTRN12608000416392)



24 months: Follow up

Repeat outcome measures

RESIST Dietary Intervention

- Diet 1: high CHO
  55-60% CHO, 30% fat (≤ 10% saturated fat), 15% protein

- Diet 2: moderate CHO, increased protein
  40-45 % CHO, 30% fat (≤ 10% saturated fat), 25-30% protein

- All participants receive metformin and the same lifestyle intervention
- Both diets are structured

Outcome measures

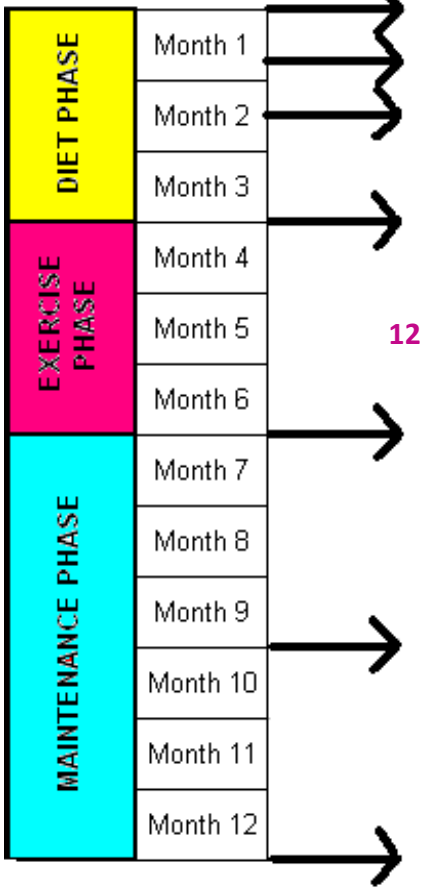
- Insulin sensitivity index: 2hr OGTT

  10 000/√ ((fasting insulin x fasting glu) x (mean 2hr glu x mean 2hr insulin))#

- Weight and %fat change (DXA)
- Cardiometabolic and clinical indicators

Yeckel CW, Weiss R, Dziura J et al. J.Clin.Endocrinol.Metab 2004;89:1096-101

RESIST Overview



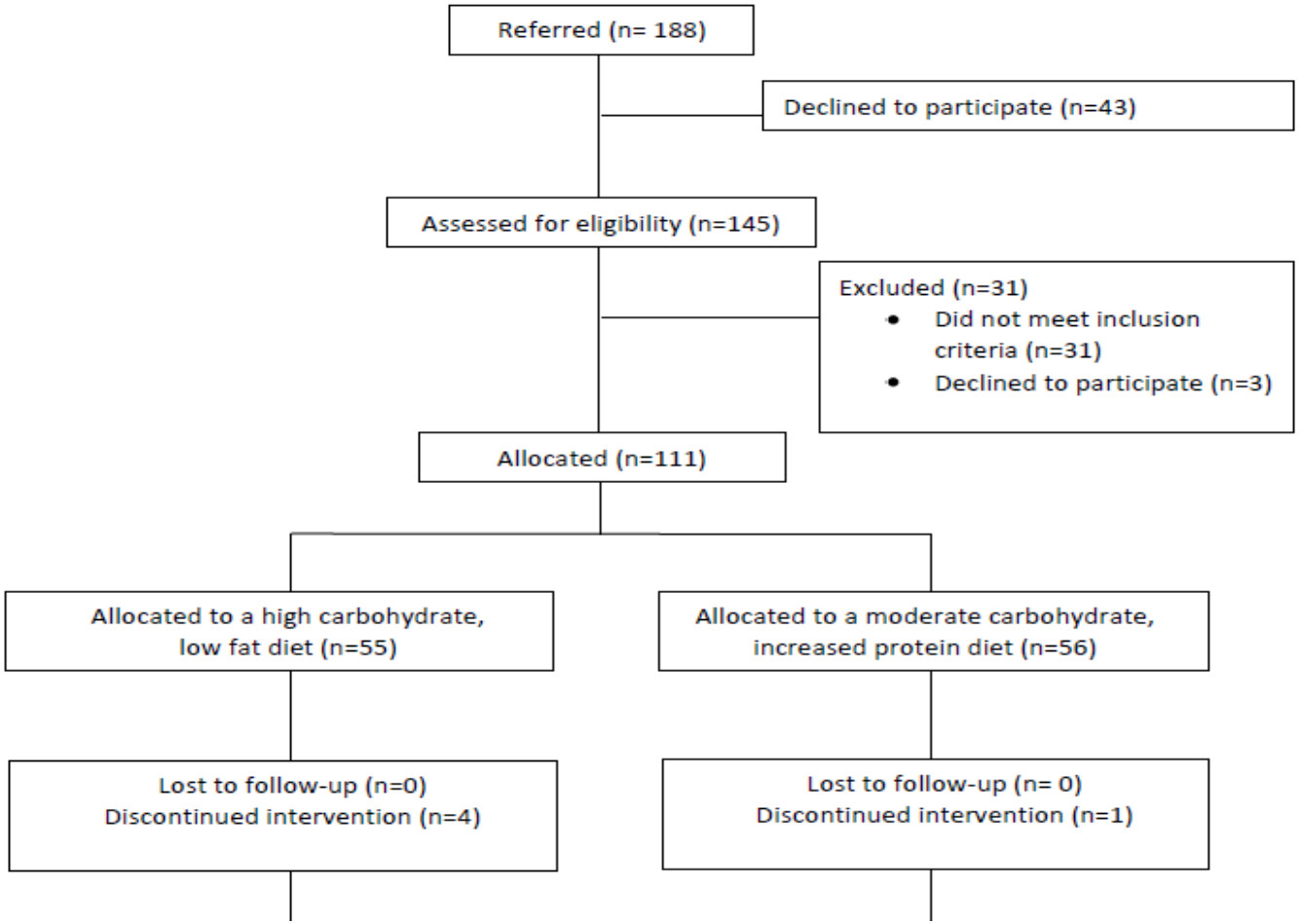
Appointment	Appointment Includes:
Week 0	OGTT, Clinical Review, DXA, VO2 peak test, CHISM Doctor, Diet
Week 2	Diet
Week 6	Diet
3 Month	OGTT, Clinical Review, DXA, Diet
6 Month	Bloods, Clinical Review, VO2 peak test, Diet
9 Month	Clinical Review
12 Month	OGTT, Clinical review, DXA, VO2 peak, diet review

Food hamper

12 – 14 weeks Fitness First gym sessions 2 x per week (PLUS 1 session at home)

Plus Dietitan support at weeks 4, 9, 16, 20, 24, 32, 38 and 44

Recruitment and progress



Phase 1: completed