THE ROLE OF PREVENTION
and
EARLY INTERVENTION
in
Type 2 DIABETES

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Questions

- Is there a pre-diabetic state?
- How is it defined?
- How does IGT progress to T2DM?
- Can we influence this progression?
- The Newcastle studies
- What does NICE say?
- Why is it not national policy?
- What we do in our practice

Is there a pre-diabetic state?

Alberti found 14 studies between 1968 and 1989

Study size 50-350

Duration 1-12 years

Rate of development of T2DM 1.7%-8.5% p.a.

Cumulative incidence 9-25% (5yrs), 15-62% (10yrs)

BMJ 1990; **301**: 397-402

DEFINITIONS for IGT

- FBS between 6.1 and 6.9 mmol/l (=IFG)
- 2 hour glucose between 7.8 and 11.1 mmol/l
- HbA_{1c} between 42 and 47 mmol/mol

2 Hour Glucose and FBG before diagnosis of T2DM

Whitehall 2 Study

>10,000 civil servants recruited (1985-88)

6058 ♂, 2758 ♀ tested (1991-94)

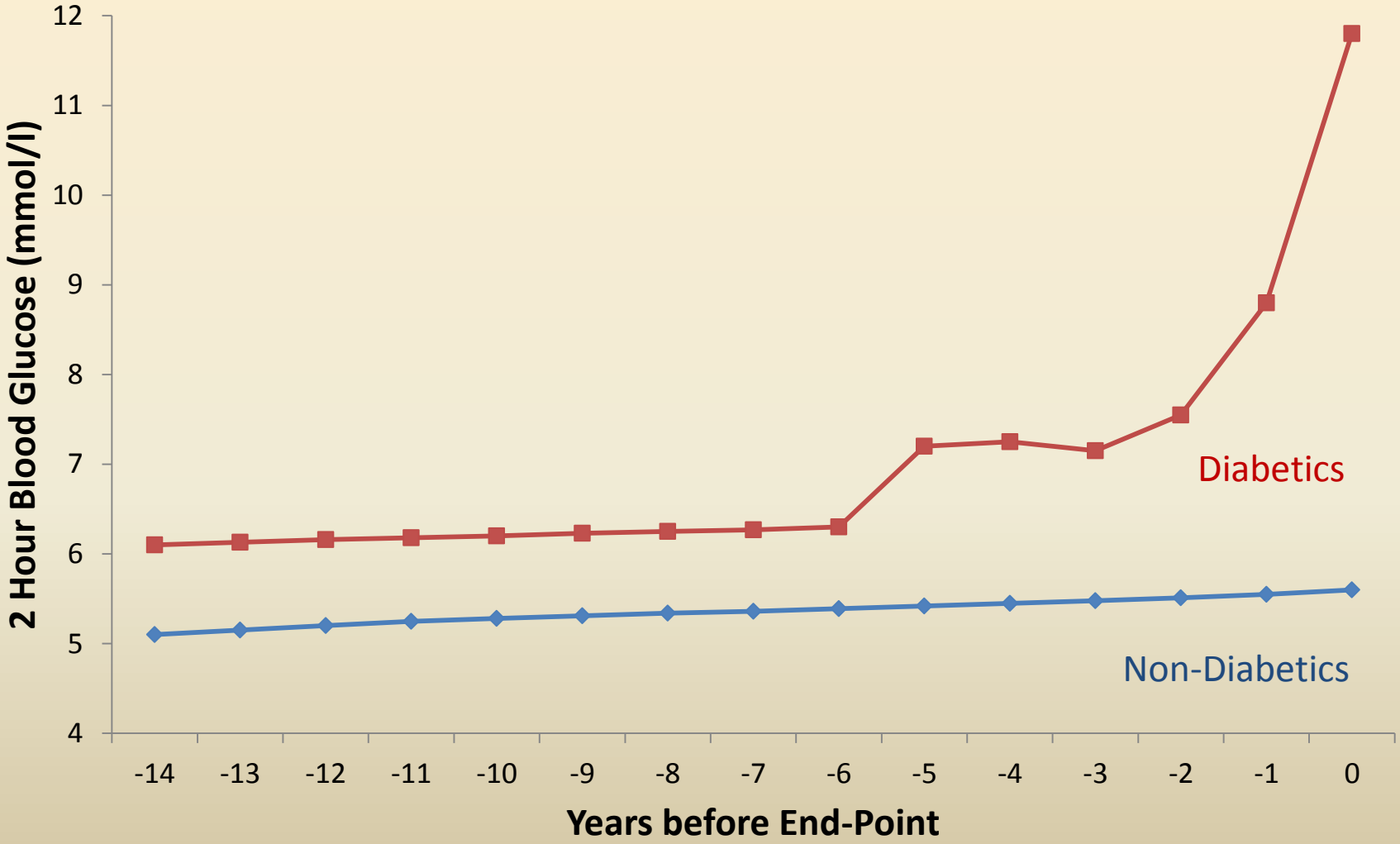
Diabetics excluded at baseline

Annual GTT thereafter (to 2007)

505 people developed T2DM

Lancet 2009; **373**:2215-21

Trajectory of 2 Hour Blood Glucose during development of T2DM



Lancet 2009; **373**:2215-21

HbA_{1c} and FBG before diagnosis of T2DM

Japanese study

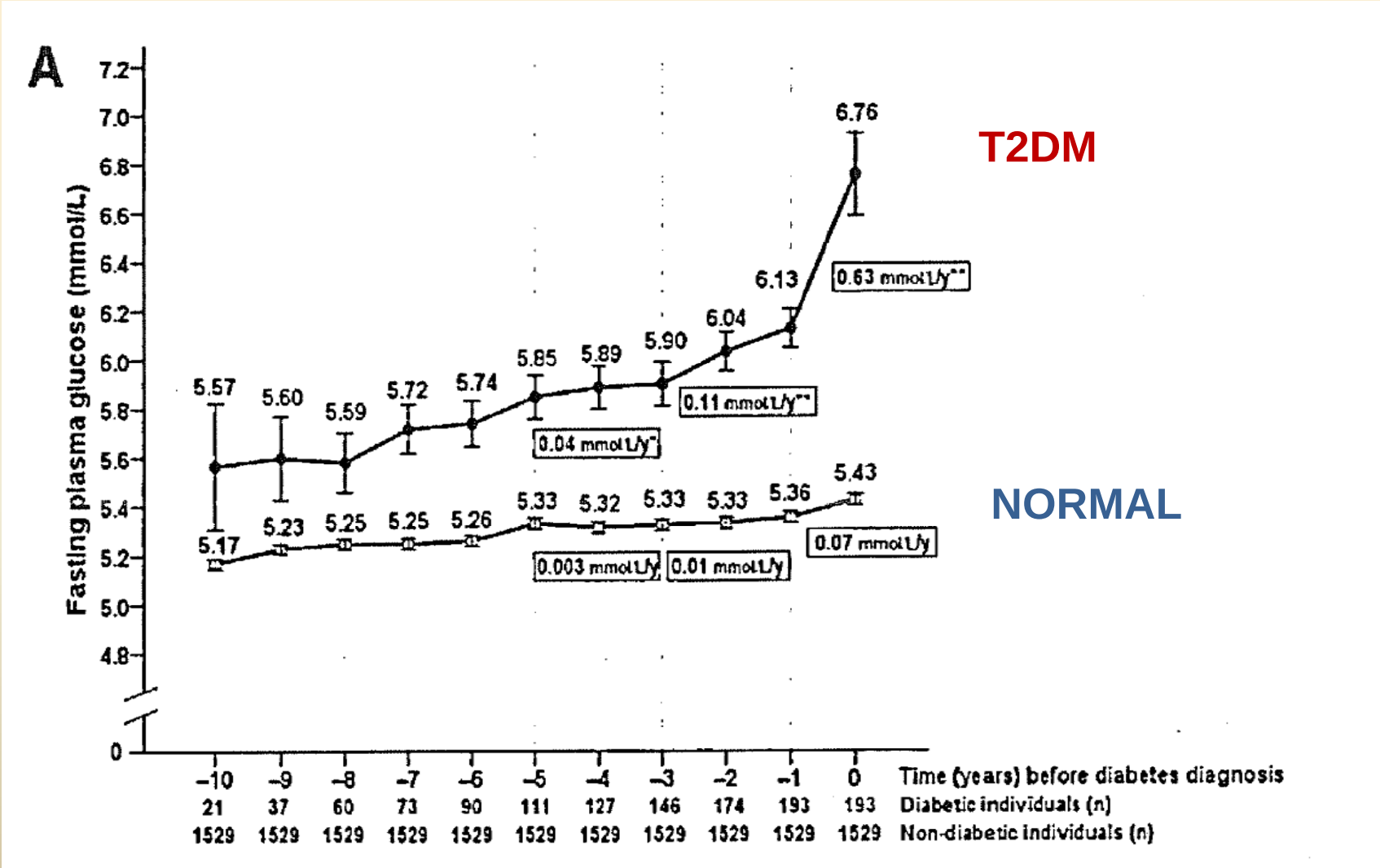
1795 healthy people followed for 10 years

Annual FBG and HbA_{1c} measurements

193 individuals developed T2DM over 10 years

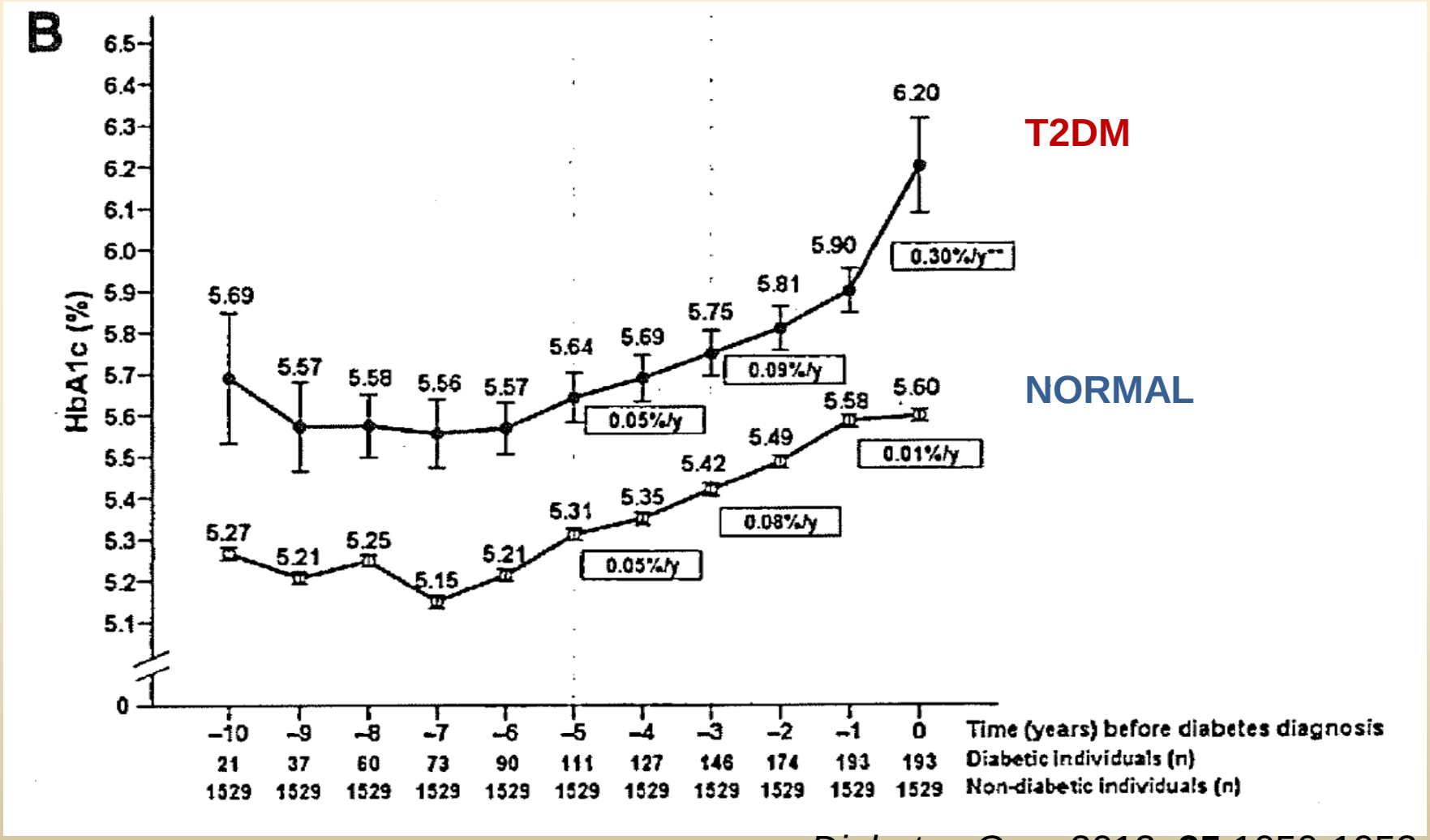
Diabetes Care 2012; 35:1050-102

Trajectory of FBG during development of T2DM



Diabetes Care 2012; 35:1050-1052

Trajectory of HbA_{1c} during development of T2DM



Diabetes Care 2012; **35**:1050-1052

Can we slow progression to T2DM? (Review) (1)

BMJ Review 2007

17 randomised controlled trials analysed

1979-2006

Over 8000 participants

Diet, Exercise, Diet & Exercise

Acarbose, Metformin, Orlistat

BMJ, doi:10.1136/bmj.39063.689375.55 (19 January 2007)

Can we slow progression to T2DM? (Review) (2)

"All the meta-analyses provided overwhelming evidence to support the benefit of interventions to prevent or delay type 2 diabetes"

Lifestyle	NNT 6.4
Oral R_x	NNT 10.8
Orlistat	NNT 5.4

BMJ, doi:10.1136/bmj.39063.689375.55 (19 January 2007)

Can we slow progression to T2DM? (DPS) (1)

Finnish Diabetes Prevention Study

- 522 subjects (172♂, 350♀) with IGT
- 5 study centres
- Age 55 (48-62)
- BMI 31 (26-36)
- Randomly assigned
- Annual GTT
- 3 year follow-up (average)

NEJM 2001:**344 (18)**; 1343-1350

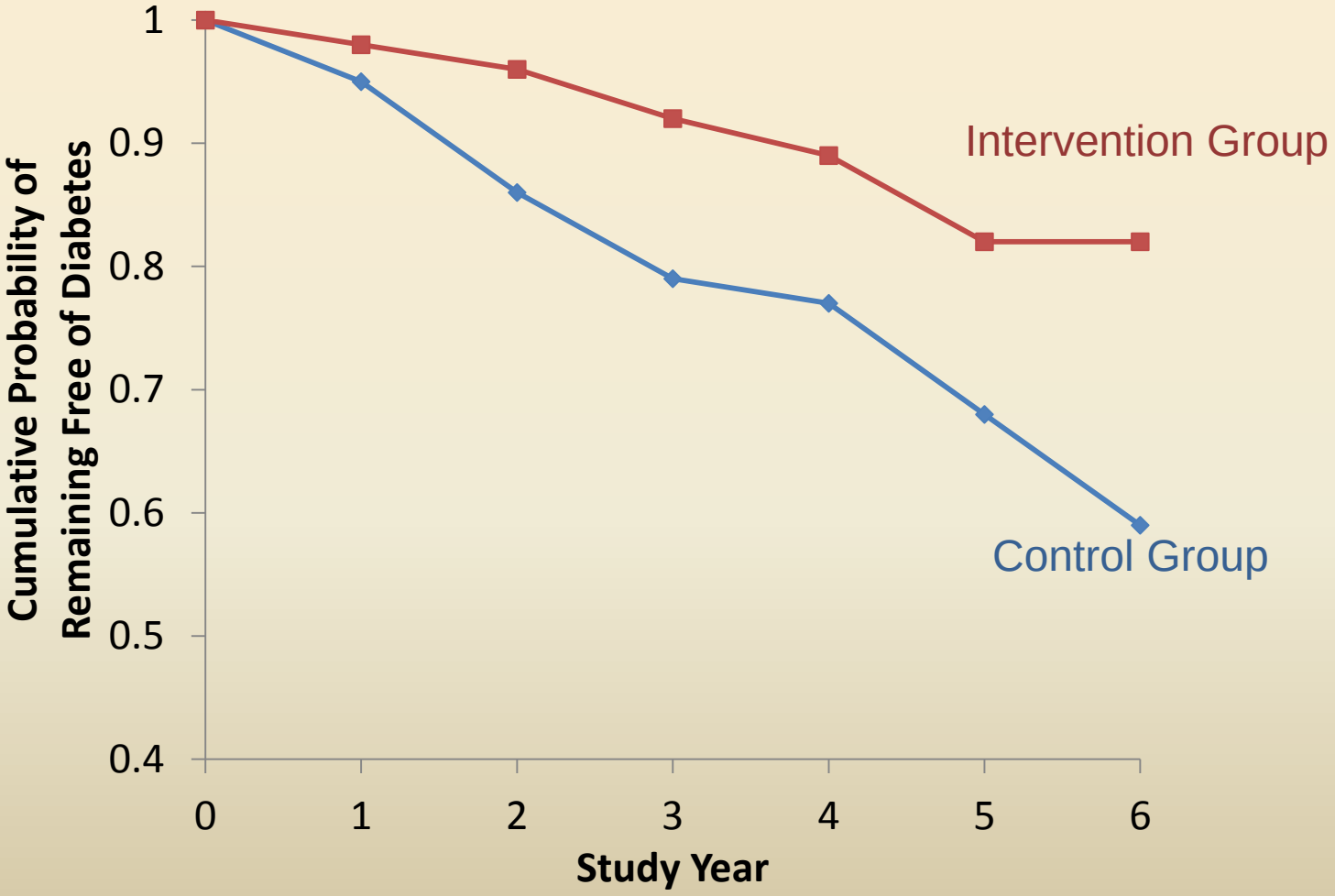
Can we slow progression to T2DM? (DPS) (2)

Intervention group:

- Individualised counselling
- Weight reduction
- Reduction total fat intake
- Reduction in saturated fat intake
- Increased intake of fibre
- Increased activity

NEJM 2001:**344 (18)**; 1343-1350

Can we slow progression to T2DM? (DPS) (3)



NEJM 2001:**344 (18)**; 1343-1350

Can we slow progression to T2DM? (DPS) (4)

The probability of progression was inversely related to the number of successful interventions.

NNT to prevent one case of T2DM

22 subjects with IGT for 1 year *or*

5 subjects with IGT for 5 years

NEJM 2001:**344 (18)**; 1343-1350

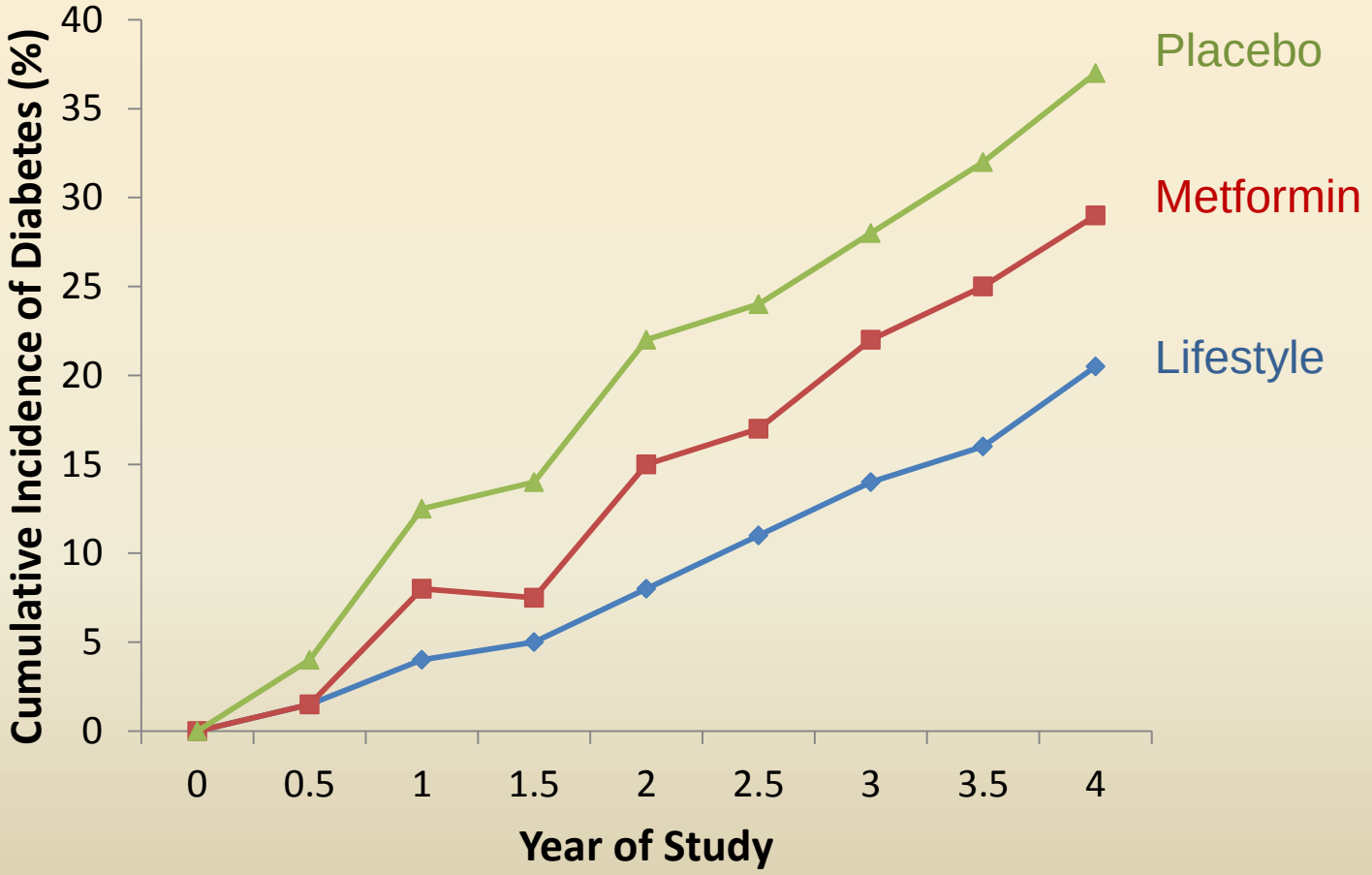
Can we slow progression to T2DM? (DPP) (1)

Diabetes Prevention Program (USA)

- 3235 subjects with IGT (32%♂, 68%♀)
- 27 centres
- 45% ethnic minorities
- Average age 51
- Average BMI 34
- Randomised to placebo or Metformin or Lifestyle modification
- Average 2.8 year follow-up

NEJM 2002;**346 (6)**:393-403

Can we slow progression to T2DM? (DPP) (2)



NEJM 2002;**346 (6)**:393-403

Can we slow progression to T2DM? (DPP) (3)

Incidence of diabetes (per 100 person years)

- Placebo 11
- Metformin 7.8
- Lifestyle 4.8

NNT to prevent one case of diabetes over 3 yrs

- Lifestyle intervention programme 7
- Metformin 14

NEJM 2002;**346 (6)**:393-403

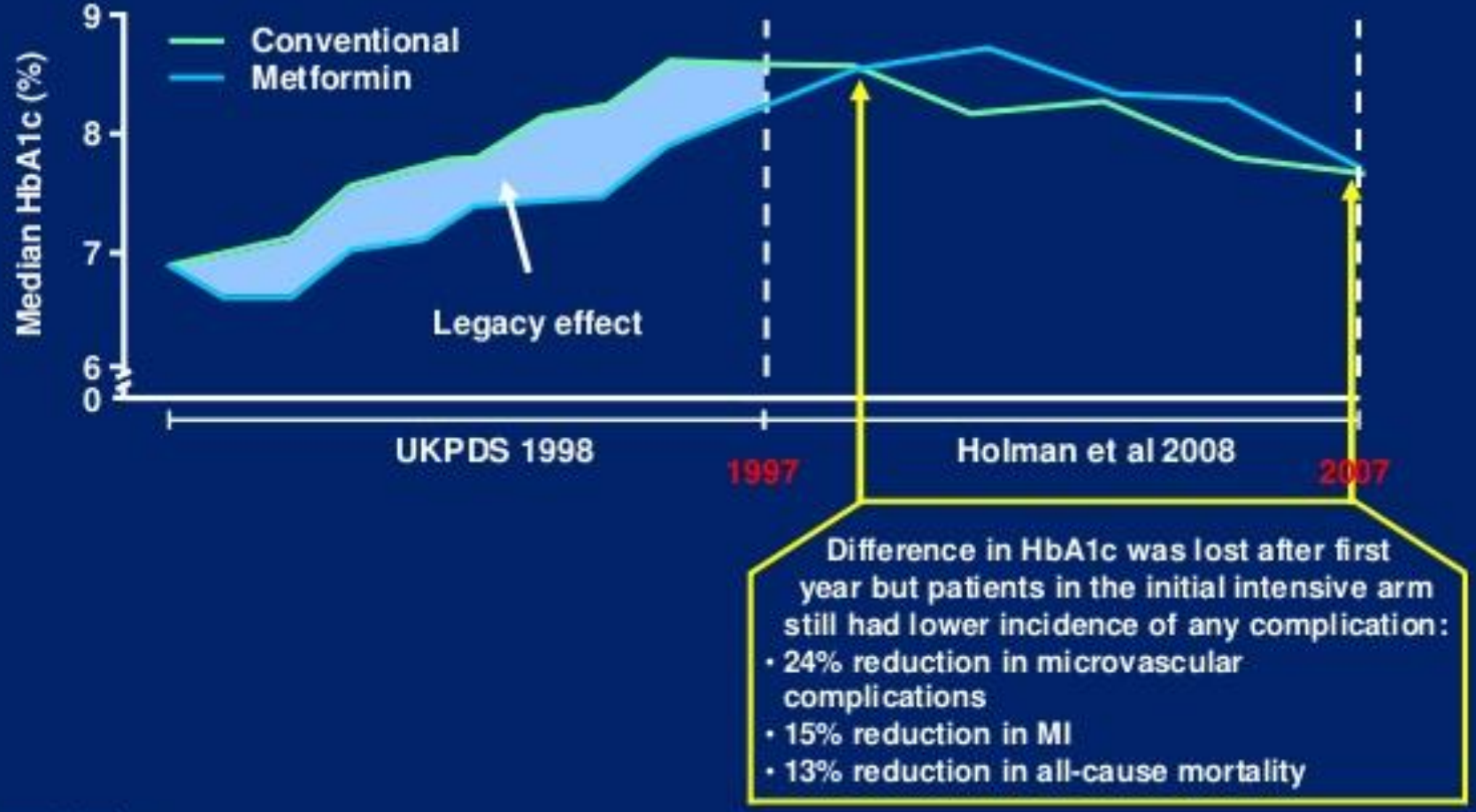
3 Principles

- Early Intervention gives lasting benefits
- Outcomes related to managing multiple risks
- True thresholds for treatment are rare

The Legacy Effect (1)

- 10 year follow up of UKPDS
- Initially in UKPDS clinics, then by GPs
- Difference in HbA_{1c} rapidly disappeared
- BUT: benefits persisted
  - 24% reduction in microvascular complications
  - 15% reduction in MI
  - 13% reduction in all cause mortality

Acheiving early glycaemic control may generate a good legacy effect



HbA1c=haemoglobin A1c.

Diabetes Trials Unit. UKPDS Post Trial Monitoring. UKPDS 80 Slide Set. Available at: http://www.dtu.ox.ac.uk/index.php?maindoc=/ukpds/. Accessed 12 September, 2008; Holman RR, et al. *N Engl J Med.* 2008; 359: 1577–1589; UKPDS 33. *Lancet.* 1998; 352: 837–853.

The Legacy Effect (2)

Diabetes Prevention Program Outcomes Study (DPPOS) USA

- 2766 participants
- 5.7 further years of follow-up
- Placebo→lifestyle intervention
- Metformin →lifestyle intervention + Metformin
- Lifestyle →additional lifestyle support

Lancet 2009;**374**:1677-86

Long-term Follow-up of DPP

Results:

- Incidence rates similar in all three groups
  - 5-6 per 100 person-years
- Over 10 years the cumulative incidence of diabetes was still reduced by 34% in lifestyle group and by 18% in Metformin group

Early benefits of lifestyle or Metformin persist for at least 10 years

(Compare with EDIC)

Lancet 2009;**374**:1677-86

Newcastle Diabetes Studies

BS falls within days of gastric bypass surgery

BS falls long before wt. reduction occurs

Anecdotal reports of normalisation of BS after massive weight loss

Newcastle Diabetes Study 2011 (1)

15 subjects with T2DM

9 controls

11 completed study

Medication discontinued

8 weeks of 600 kcal diet

Diabetologia DOI 10.1007/s00125-011-2204-7

Newcastle Diabetes Study 2011 (2)

FBS normalised within a week

Insulin sensitivity restored

Fall in hepatic and pancreatic fats

Diabetologia DOI 10.1007/s00125-011-2204-7

Newcastle Diabetes Study 2015 (1)

15 T2DM <4 yrs

14 T2DM >8 yrs

8 weeks of 625-700 kcal diet

All diab Rx stopped before starting diet

Diabet. Med. 32, 1149–1155 (2015)

Newcastle Diabetes Study 2015 (2)

BS normalised in all those Dx <4yrs

BS normalised in 50% of those Dx >8yrs

Significant correlation between FBS achieved at 8 weeks and duration of diagnosis

Diabet. Med. 32, 1149–1155 (2015)

Rationale of Identifying IGT

May enable us to influence progression to T2DM

Enables us to identify T2DM at earliest opportunity

Any lifestyle changes achieved (wt loss, improved diet, better fitness levels) will also benefit the psyche, the heart, and the m/skeletal system

Disadvantages of Identifying IGT ?

No stigma

No medication

No insurance implications

Management of IGT in our practice

Identify Individuals with IFG/IGT

Enter them on the Database

Give lifestyle advice

Annual/biennial testing

FBS, GTT or HbA_{1c}

Advice for People with IGT

Lose weight

Exercise at least 3 times a week

Avoid ‘obvious’ sugar

Cook ‘back to basics’

Avoid big sugar loads

Summary

Progression to T2DM can be slowed

Early T2DM is potentially reversible

Implications

Aim to identify IGT and early T2DM because this gives the best chance of real treatment

Intervention is most potent if it is about lifestyle modification (not drugs)

Continuity and 1:1 is best