

Pharmacological approaches in prevention of diabetes

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Interactions between diabetes and vascular diseases

CV disease

μ vasc
disease

Normal
glucose
tolerance

Pre-
diabetes

diabetes

Pharmacological prevention of type 2 diabetes

- **Prevention of What?**
- -High Glucose: thirst, polyuria
- -CV disease
- - μ vasc disease

Pharmacological prevention of type 2 diabetes

- ***Primary prevention:***
- normal glucose tolerance->pre-diabetes;
diabetes

Secondary prevention:
pre-diabetes-> diabetes

**Most of studies in the secondary
prevention setting**

STARLING 's PHENOMENON applied to the ENDOCRINE PANCREAS

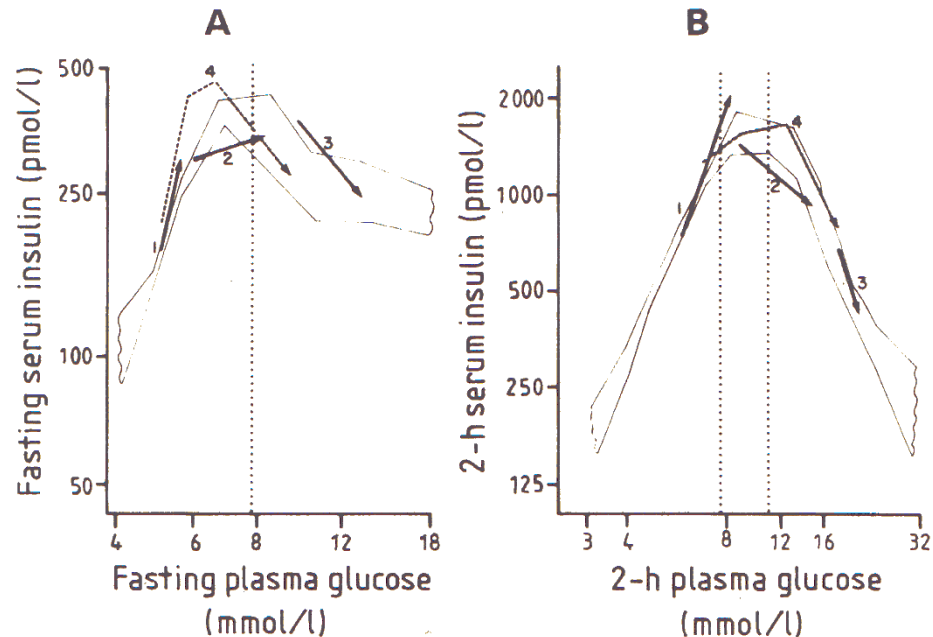


Fig 1—Changes in median fasting (A) and 2-h (B) serum insulin concentrations by corresponding plasma glucose concentrations for groups 1-4.

from M. SAAD et al: Sequential changes in serum insulin concentration during development of non-insulin-dependent diabetes. *Lancet*, 1989, i: 1356-1359

Pharmacological prevention of type 2 diabetes

End points:

T2D onset

CV disease

μ vasc disease

Pharmacological prevention of type 2 diabetes

- **Remarks on study designs:**
- *Pharmacological prevention of type 2 diabetes:* women>men
 - High BMI
 - young>mature
- *Prevention of CV/ μ disease:* men>women
 - lower BMI
 - mature>young

Pharmacological prevention of type 2 diabetes

Antidiabetic agents

- *Metformin*
- *TZDs (trogli-, rosi-, pio-)*
- *α -glucosidase inhib (acarbose)*
- *Glinides (nate-)*
- *Insulin (glargine)*

Other agents

- ***Anti-obesity:***
 - *orlistat*
 - *sibutramine*
- ***Renin blockers (ACEIs, ARBs)***
- ***Lipid lowering drugs:***
 - *fibrates*
 - *statins*
- ***ASPIRIN***

Pharmacological prevention of type 2 diabetes; antidiabetic agents: METFORMIN

- *Prevention of type 2 diabetes: : yes 31%*
RRR (*DPP study, NEJM, 2002*)
- *Prevention of CV/ μ disease: yes (UKPDS
34 – but μ vasc disease not demonstrated)*
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Pharmacological prevention of type 2 diabetes; antidiabetic agents: METFORMIN

- METFORMIN for prevention of T2D: an ADA 2013 recommendation (D Care, Suppl 1, 2013)
- *« may be considered , especially if BMI>35 kg/m², age<60 years, women with previous gestational diabetes »*

Pharmacological prevention of type 2 diabetes; antidiabetic agents: TZDs

- ***Prevention of type 2 diabetes:*** : **yes** trogli- 75% RRR (*TRIPOD study, DPP study interrupted*), **yes** rosi- 60% (*DREAM study, Lancet 2006*), **yes** pio- 55% (*NEJM, 2011*)
- ***Prevention of CV disease:*** **controversial** (*PROACTIVE ≠ RECORD*); ***/μalb: YES***
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Pharmacological prevention of type 2 diabetes; antidiabetic agents: ACARBOSE

- ***Prevention of type 2 diabetes: : yes 36%***
RRR (*STOP-NIDDM, Lancet, 2002*)
- ***Prevention of CV/ μ disease: yes 50%***
RRR (*STOP-NIDDM, JAMA, 2003*)

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Pharmacological prevention of type 2 diabetes; antidiabetic agents: nateglinide

- ***Prevention of type 2 diabetes: : no***
(NAVIGATOR study, NEJM, 2010)
- ***Prevention of CV/ μ disease: no***
(NAVIGATOR study, NEJM, 2010)

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Pharmacological prevention of type 2 diabetes; antidiabetic agents: insulin glargine

- ***Prevention of type 2 diabetes: : yes 28%***
RRR (*ORIGIN study, NEJM, 2012*)
- ***Prevention of CV/ μ disease: no*** (*ORIGIN
study, NEJM, 2012*)

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Pharmacological prevention of type 2 diabetes; anti- obesity agents: ORLISTAT

- *Prevention of type 2 diabetes: : yes 37%
RRR, but in IGT only (XENDOS study, D
Care, 2004)*
- *Prevention of CV/ μ disease: ?*
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Pharmacological prevention of type 2 diabetes; anti- obesity agents: SIBUTRAMINE

- *Prevention of type 2 diabetes: : ?*
- *Prevention of CV/ μ disease: HARMFUL*
(NEJM, 2010)

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Pharmacological prevention of type 2 diabetes; anti- obesity agents: RIMONABANT

- *Prevention of type 2 diabetes: : disputable*
- *Prevention of CV/ μ disease: **NOT SHOWN**
(*CRESCENDO interrupted, Lancet,2010*)*

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Pharmacological prevention of type 2 diabetes; cardioprotective agents: RENIN blockers

- ***Prevention of type 2 diabetes:*** : ambiguous
(ramipril, DREAM study, NEJM, 2006)
- ***Prevention of CV/ μ disease:*** **HIGH level of evidence** (HOPE, EUROPA)

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Pharmacological prevention of type 2 diabetes; lipid lowering agents: fibrates

- ***Prevention of type 2 diabetes: : maybe***
(old studies)
- ***Prevention of CV/ μ disease: CV no***
(FIELD, Lancet 2004); ***μ vasc yes*** (FIELD,
ACCORD)
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Pharmacological prevention of type 2 diabetes; lipid lowering agents: statin

- ***Prevention of type 2 diabetes:*** :favours dysglycaemia (*but is it worth being considered?*)
- ***Prevention of CV/ μ disease:*** ***high level of evidence*** (CARDS, *Lancet 2004*)

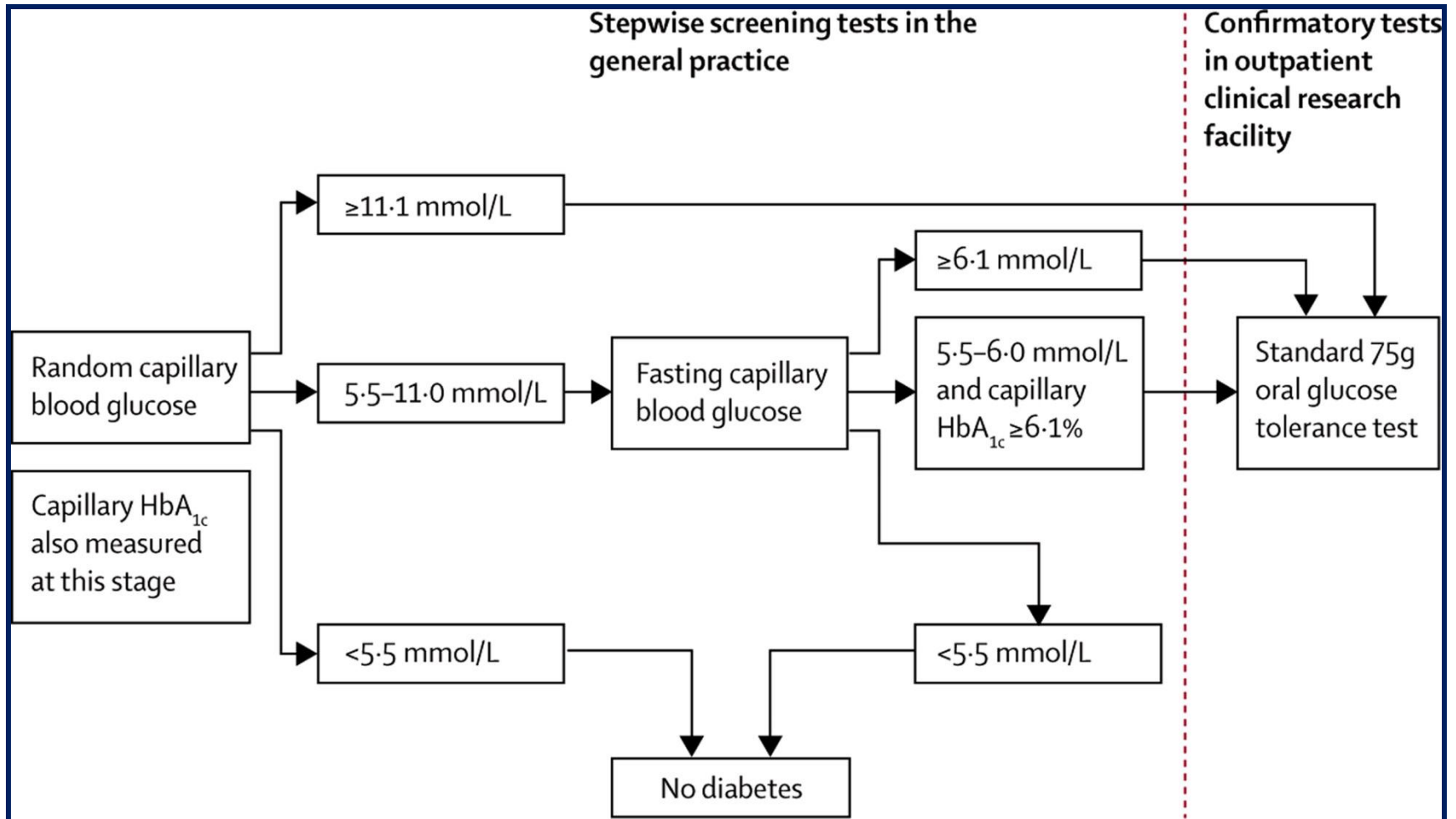
Pharmacological prevention of type 2 diabetes; cardioprotective agents: ASPIRIN

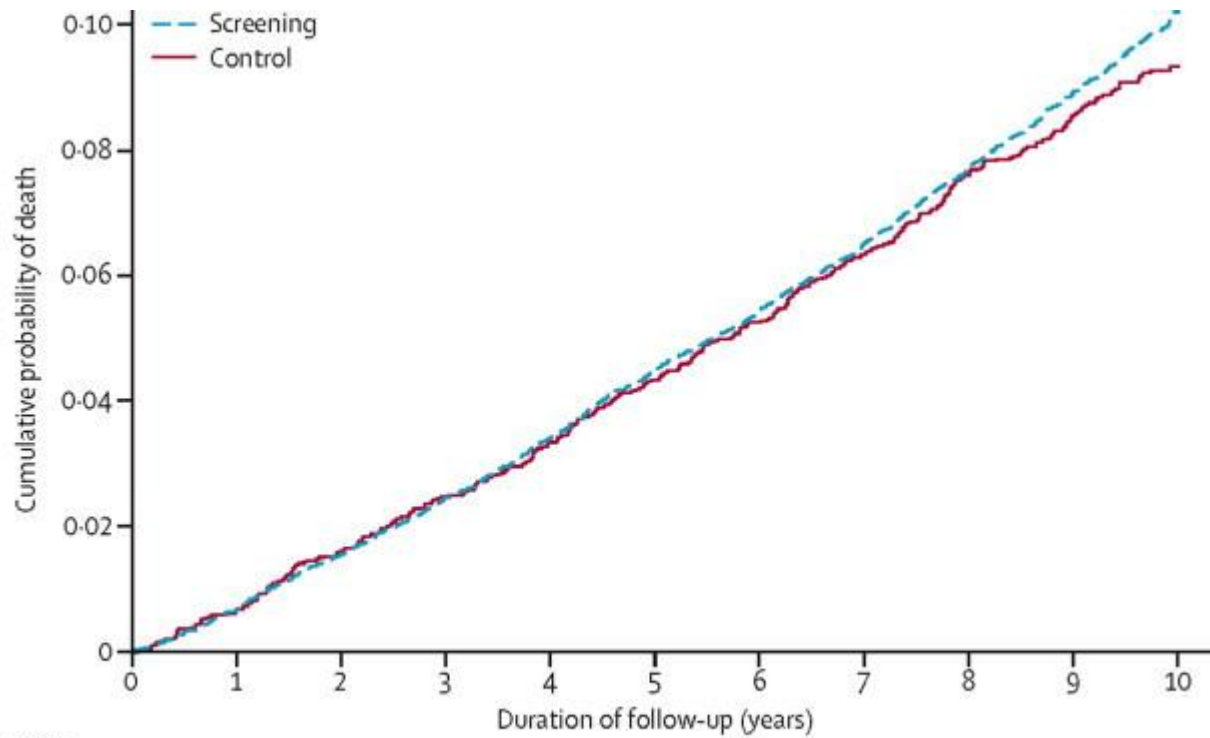
- *Prevention of type 2 diabetes*: **yes**, but very high doses
- *Prevention of CV/ μ disease*: **yes**, but no study specific for diabetes; active on retinopathy (DAMAD study)

Prevention vs early detection of diabetes

- *Screening for type 2 diabetes and population mortality over 10 years (ADDITION-Cambridge): a cluster-randomised controlled trial*
- ***Simmons RK et al, Lancet 2012 Nov 17, 380: 1741-8***

Usefulness of screening campaigns





Number at risk

Screening	16047	15798	15501	15173	14814	2619
Control	4137	4071	3999	3920	3822	422

Pharmacological approaches in prevention of diabetes

- ***A strategy which is not firmly established***
- ***Put non pharmacological approaches on first line***