Pharmacological approaches in prevention of diabetes

- Michel Marre, Paris, France
Interactions between diabetes and vascular diseases

- CV disease
- μvasc disease
- Normal glucose tolerance
- Pre-diabetes
- diabetes
Pharmacological prevention of type 2 diabetes

• Prevention of What?
  • High Glucose: thirst, polyuria
  • CV disease
  • μvasc 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

Pharmacological prevention of type 2 diabetes

End points:

T2D onset
CV disease
µvasc 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

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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 µvasc disease not demonstrated)
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
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)
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)
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)
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: ?
Pharmacological prevention of type 2 diabetes; anti-obesity agents: SIBUTRAMINE

- Prevention of type 2 diabetes: ?
- Prevention of CV/μ disease: HARMFUL (NEJM, 2010)
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)
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**)
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); µvasc yes (FIELD, ACCORD)
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

Stepwise screening tests in the general practice

- Random capillary blood glucose
  - ≥11.1 mmol/L
  - 5.5–11.0 mmol/L
  - <5.5 mmol/L

- Fasting capillary blood glucose
  - ≥6.1 mmol/L
  - 5.5–6.0 mmol/L and capillary HbA1c ≥6.1%

- Capillary HbA1c also measured at this stage
  - <5.5 mmol/L

Confirmatory tests in outpatient clinical research facility

- ≥6.1 mmol/L
- 5.5–6.0 mmol/L and capillary HbA1c ≥6.1%

- Standard 75g oral glucose tolerance test

No diabetes

Simmons RK. Lancet 2012
Pharmacological approaches in prevention of diabetes

• A strategy which is not firmly established

• Put non pharmacological approaches on first line