# Diabetes Mellitus

## *Maandthema 2015*

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# Maandthema

- De ernst van diabetes
- Revival van het nut van glucoseverlaging
- Nieuws rondom medicatie

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Glycemic Control and Excess Mortality in Type 1 Diabetes

Marcus Lind, M.D., Ph.D., Ann-Marie Svensson, Ph.D., Mikhail Kosiborod, M.D., Soffia Gudbjörnsdottir, M.D., Ph.D., Aldina Pivodic, M.Sc., Hans Wedel, Ph.D., Sofia Dahlqvist, Mark Clements, M.D., Ph.D., and Annika Rosengren, M.D., Ph.D.

N Engl J Med 2014;371:1972-82.

# Kans op sterfte – instelling

| Variable | Hazard Ratio | |
|---|---|---|
| | Death from Any Cause | Death from Cardiovascular Disease |
| Time-updated mean glycated hemoglobin level — no. of events/total no. | 7386/200,539 | 2326/200,539 |
| Reference group (controls) | 1.00 | 1.00 |
| ≤6.9% | 2.36 (1.97–2.83) | 2.92 (2.07–4.13) |
| 7.0–7.8% | 2.38 (2.02–2.80) | 3.39 (2.49–4.61) |
| 7.9–8.7% | 3.11 (2.66–3.62) | 4.44 (3.32–5.96) |
| 8.8–9.6% | 3.65 (3.11–4.30) | 5.35 (3.94–7.26) |
| ≥9.7% | 8.51 (7.24–10.01) | 10.46 (7.62–14.37) |

Lind M ea. N Engl J Med 2014;371:1971-82.

Original Investigation

# Association Between 7 Years of Intensive Treatment of Type 1 Diabetes and Long-term Mortality

Writing Group for the DCCT/EDIC Research Group

JAMA 2015;313:45-53.

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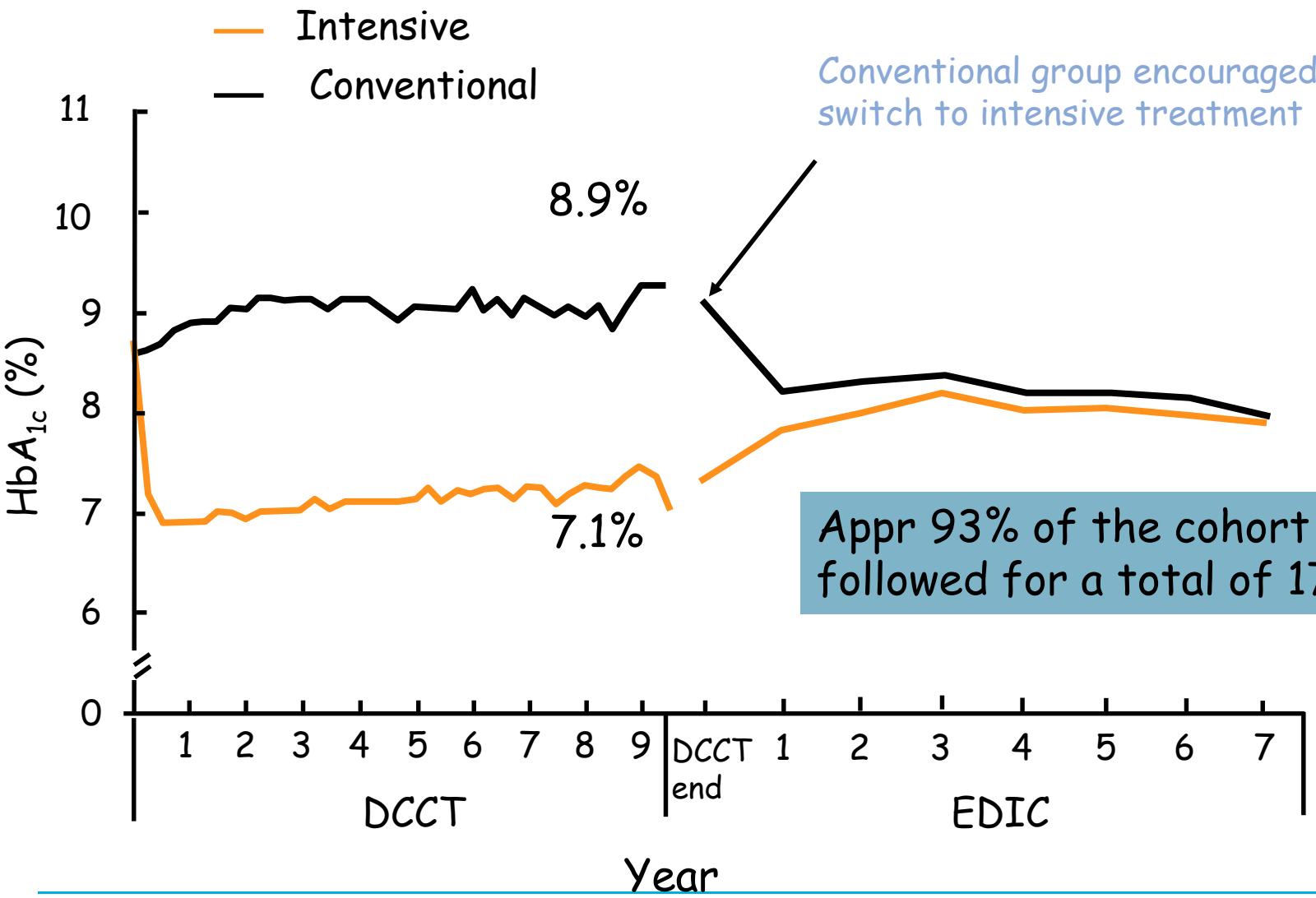
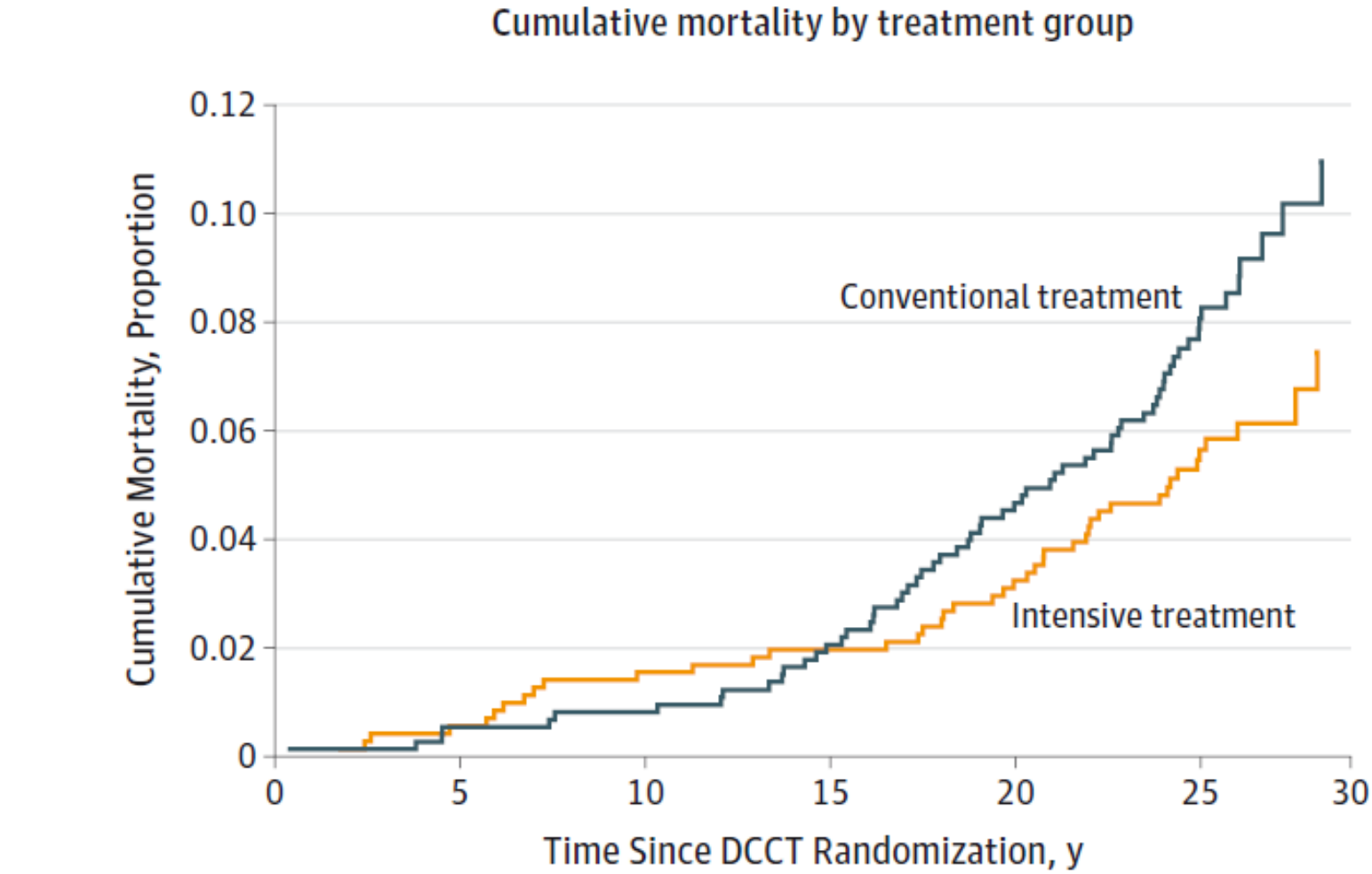
# EDIC: Follow up (observation) of DCCT




Appr 93% of the cohort was followed for a total of 17 years

Adapted from: N Engl J Med 1993;329:977-86,




| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| Conventional | 730 | 726 | 721 | 712 | 693 | 476 |
| Intensive | 711 | 706 | 697 | 694 | 685 | 501 |

JAMA 2015;313:45-53.

# Kan cardiovasculaire ziekte bij **type 2 diabetes** worden voorkomen door optimale glucoseregulatie?

# Na glucosetrials 2008-9

- Twijfel nut glucoseverlaging
- Target HbA1c niet verder omlaag (eerder omhoog)
- Nieuwe richtlijnen
- Is de hypothese niet juist of ligt het aan de geneesmiddelen:
  - Hypoglycemie
  - Gewichtstoename
  - "middel" specifieke bijwerkingen

# Is tight glycemic control in type 2 diabetes really worthwhile?

YES

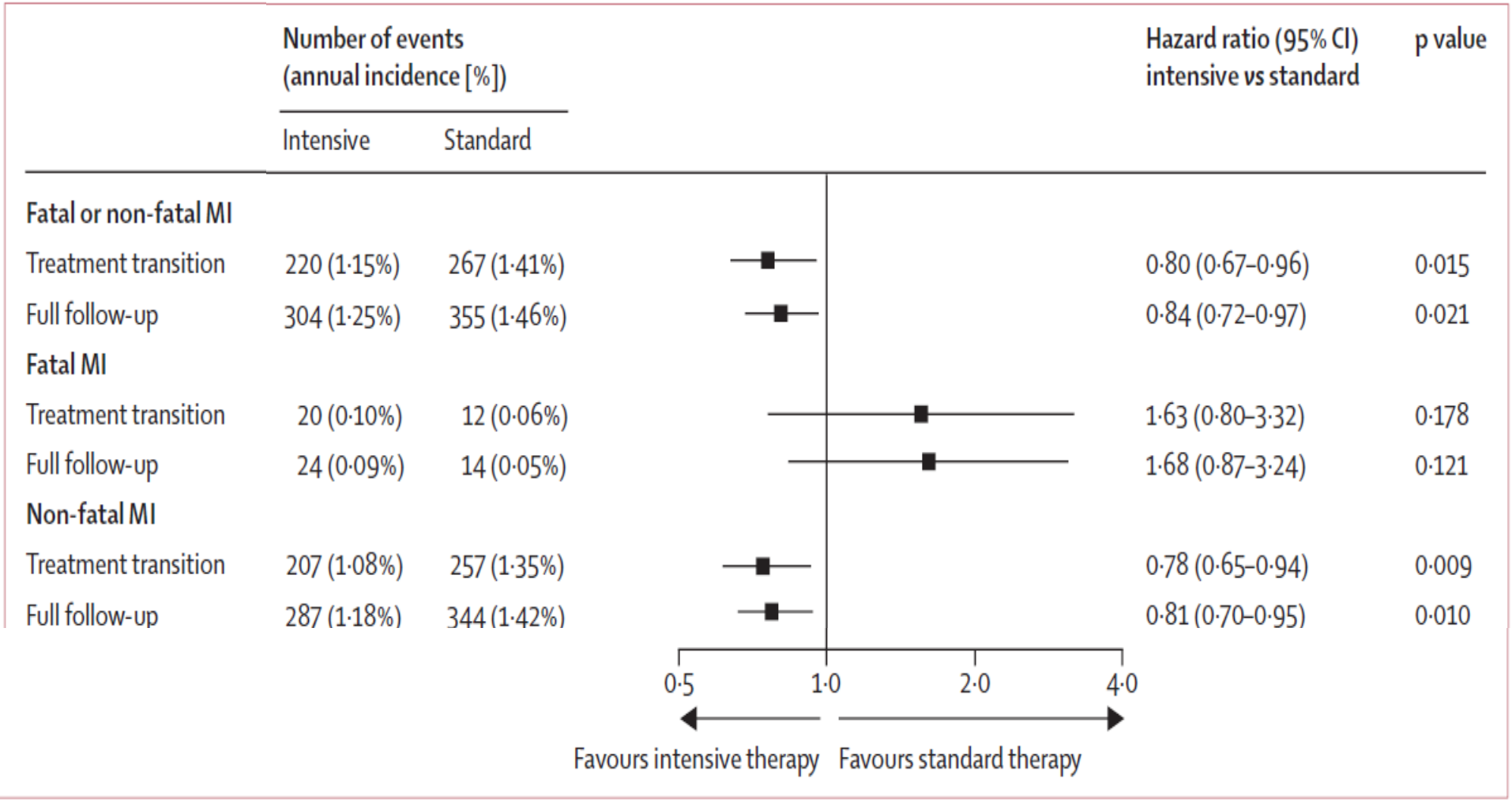
Maureen Clement MD CCFP  Onil Bhattacharyya MD PhD CCFP  J. Robin Conway MD

Woodcut by Thomas Murner, circa 1500.

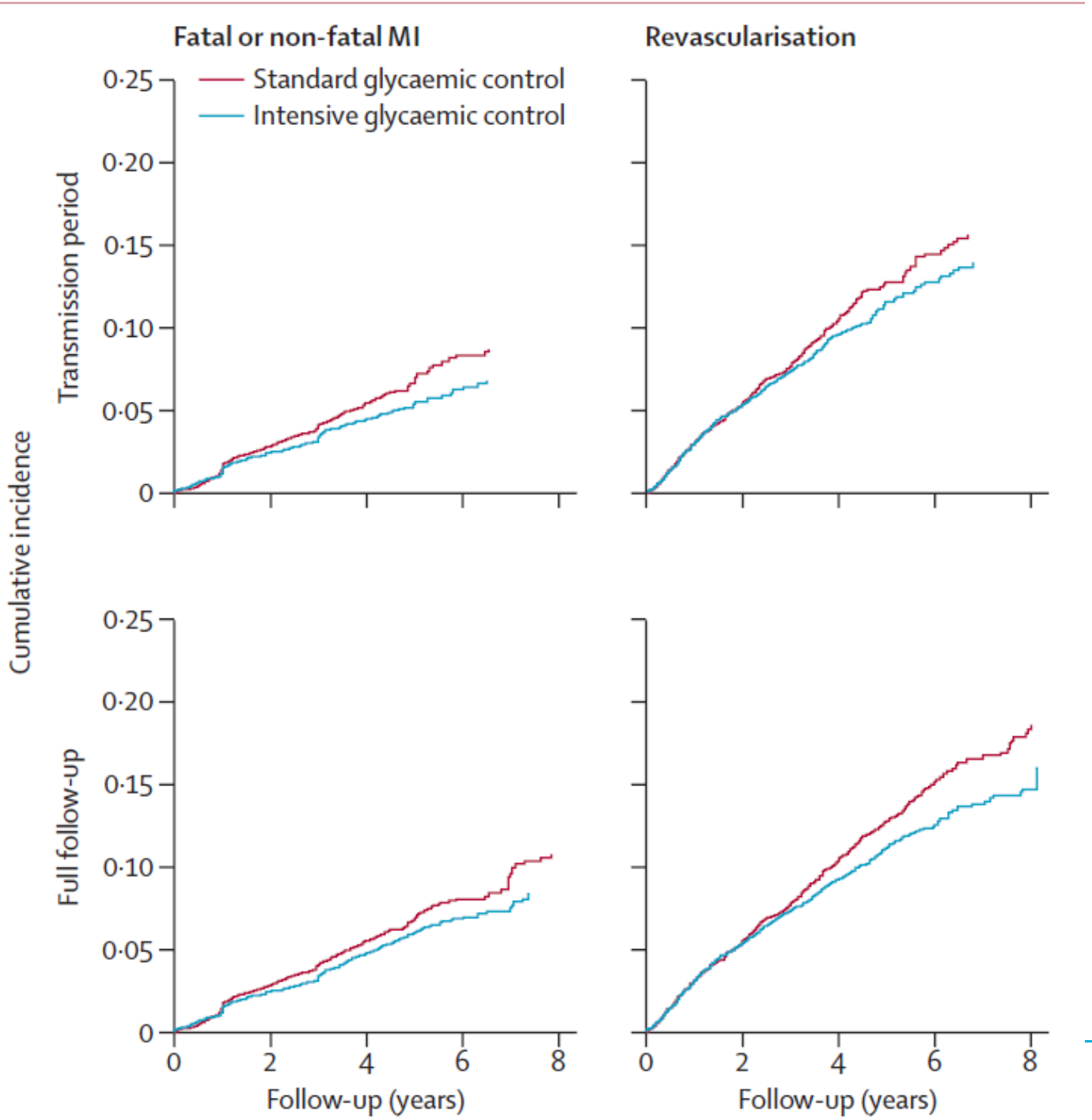
# Effects of intensive glycaemic control on ischaemic heart disease: analysis of data from the randomised, controlled ACCORD trial

*Hertzel C Gerstein, Michael E Miller, Faramarz Ismail-Beigi, Joe Largay, Charlotte McDonald, Heather A Lochnan, Gillian L Booth, for the ACCORD Study Group*

- Diabetes arm discontinued after 3.7 yrs "de-intensified"
- Additional follow up for 1.2 year
- Events:
  - 1263 during active period
  - 1619 for entire period




Gernstein HC ea. Lancet 2014; 384:1936-41.




Gernstein HC ea. Lancet 2014; 384:1936-41.

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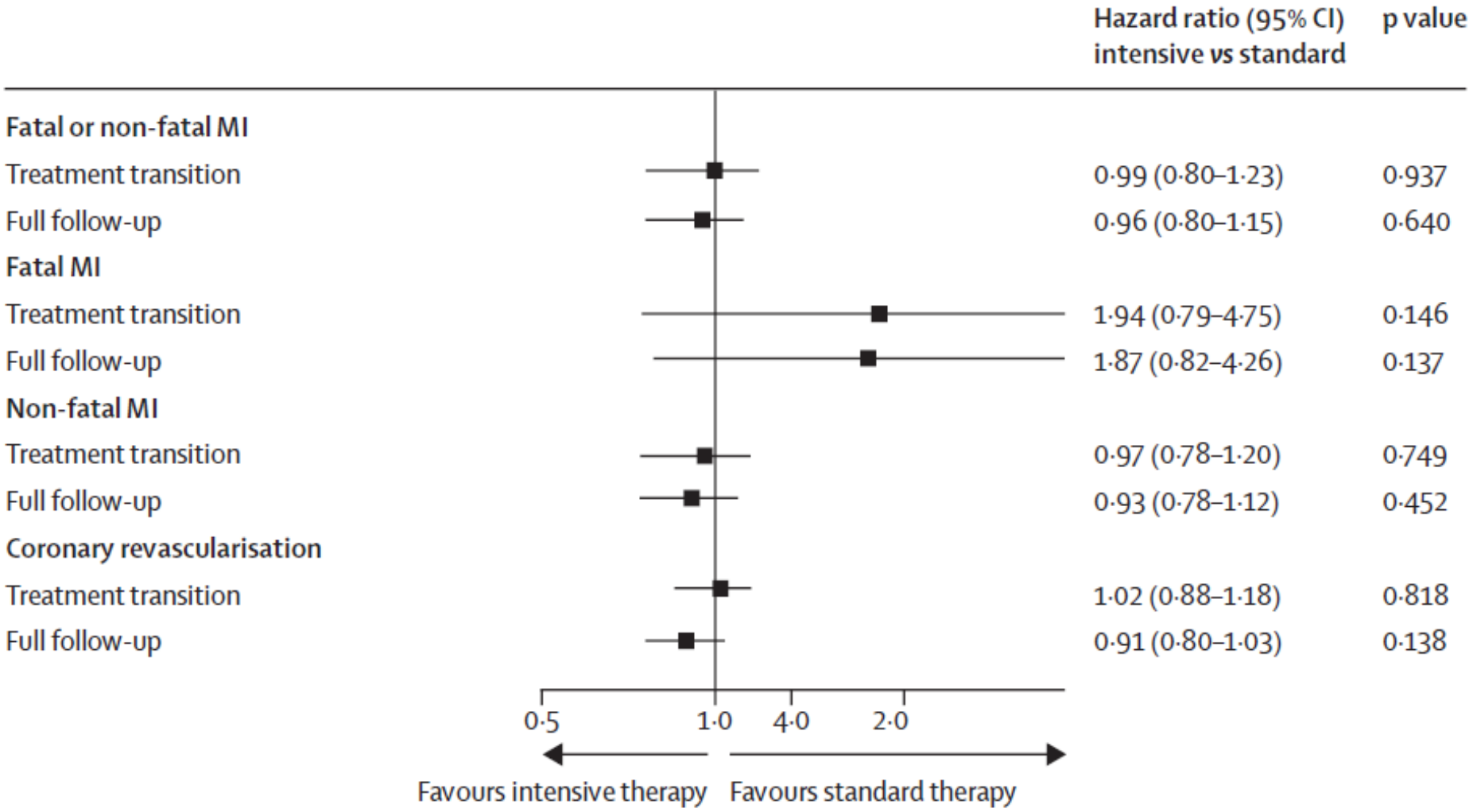
# Na "correctie" voor glucose

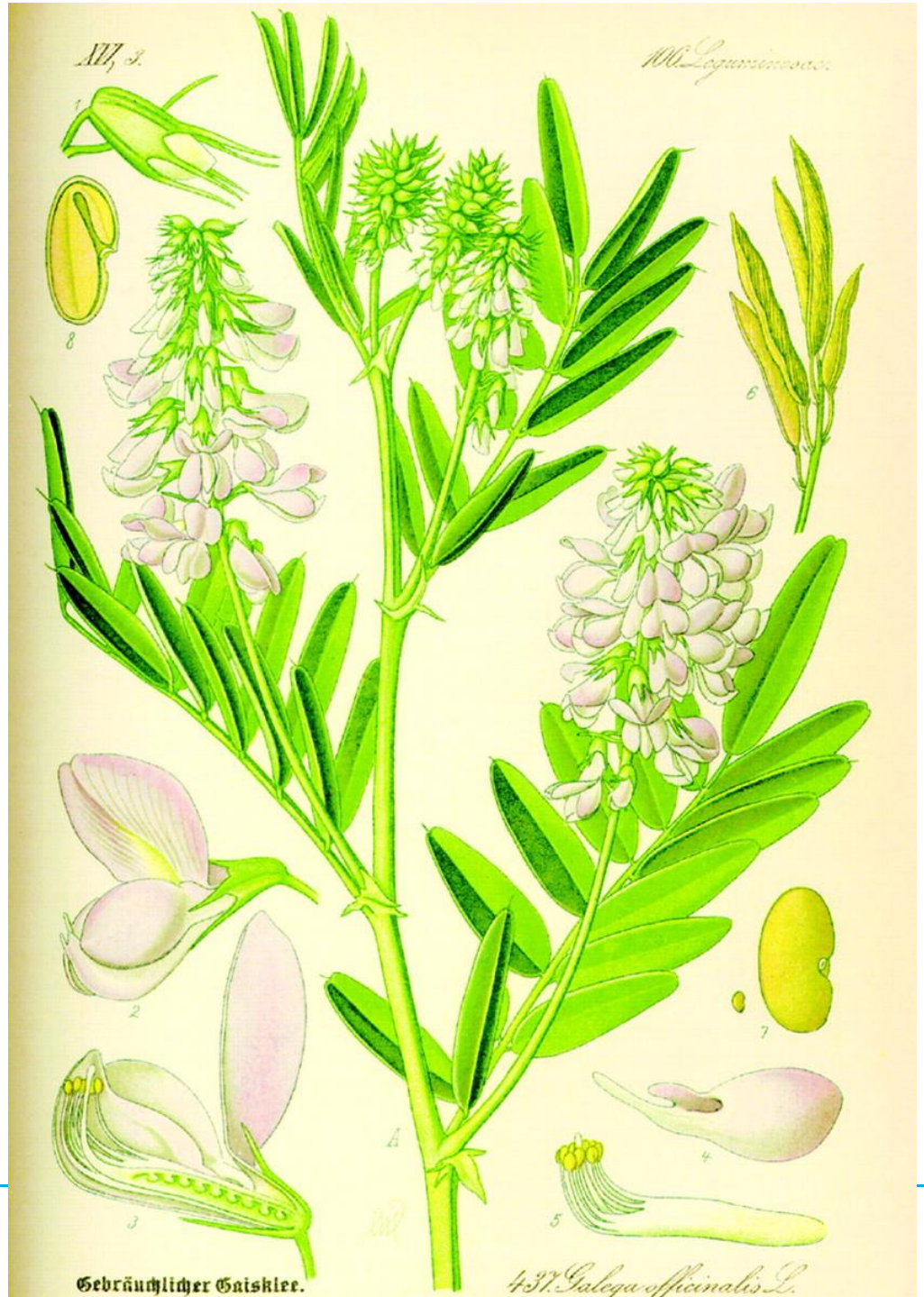



Gernstein HC ea. Lancet 2014; 384:1936-41.

# Interpretatie

- Verhoogde glucose is een "modifiable risk factor" voor ischemische hartziekte bij mensen met type 2 diabetes en andere CV risicofactoren
- Effect kost tijd, maar blijft lang bestaan → glycemic **memory**
- Therapiekeuze weer terug op agenda

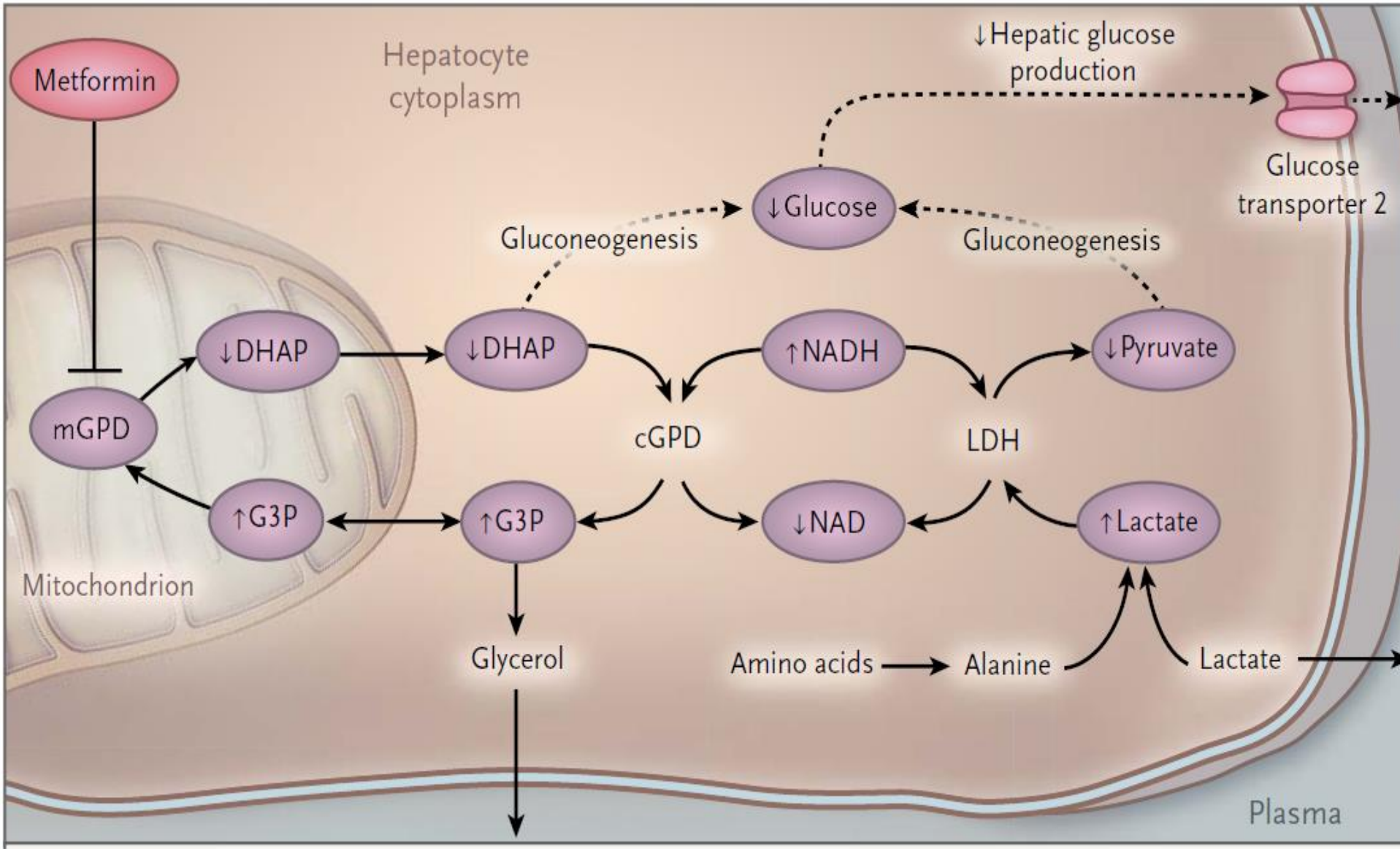
galega officinalis




french Lilac

# Werking biguaniden

- Metformine remt glucoseproductie lever, weinig effect op spier- en vetweefsel
- Werkingsmechanisme lange tijd onduidelijk
- 2014: metformine remt de mitochondriele isovorm van glycerofosfaat dehydrogenase (mGPD): omzetting in dihydroxyaceton fosfaat (DHAP) = transfer electronenpaar geremd.




Ferranninni E. NEJM 2014; 371:1547

# Werking metformine

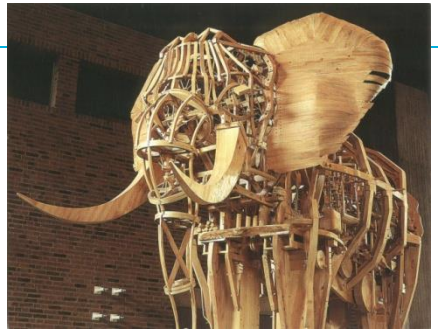
“Dokter, hoe werkt deze pil?”

“Het blokkeert een enzym in de lever waardoor die minder glucose aan het bloed afgeeft”

# The Effect of Liraglutide on insulin-associated wEight GAiN in patients with Type 2 diabetes (ELEGANT trial)

Heleen de Wit

Gerald Vervoort, Henry Jansen, Bastiaan de Galan, Cees Tack



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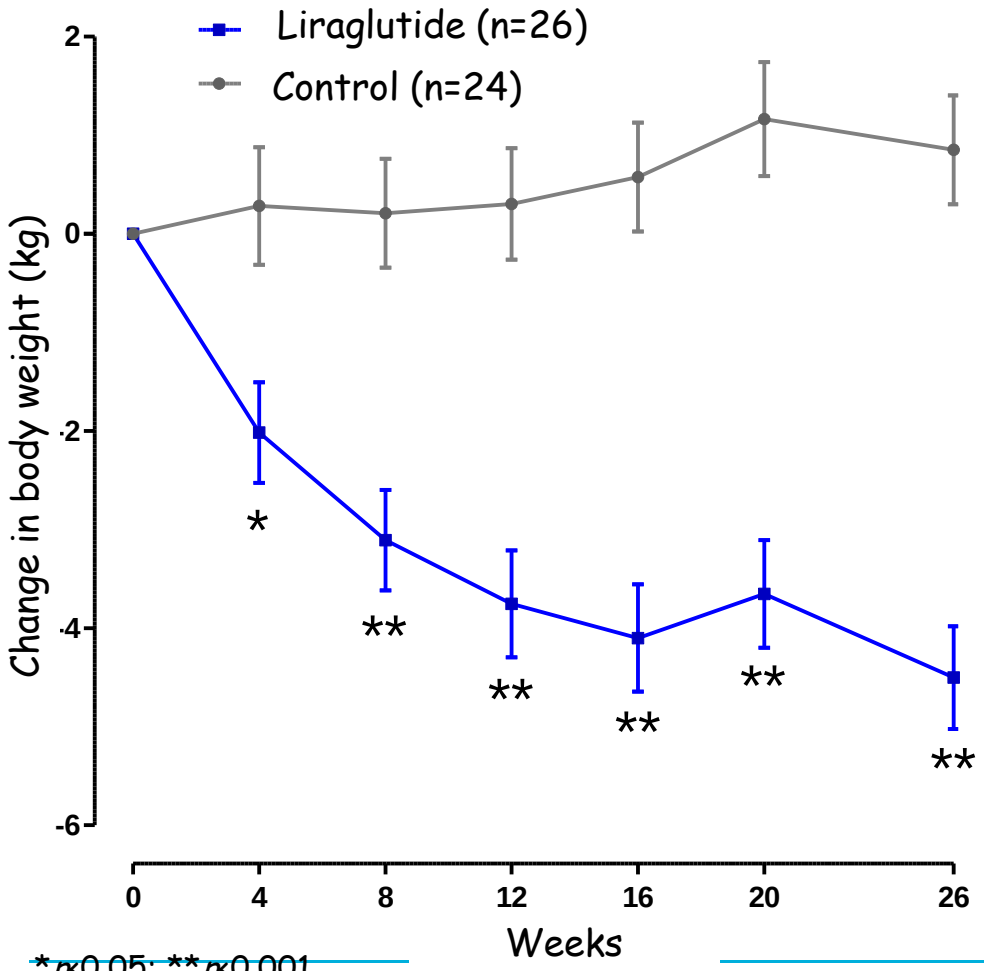
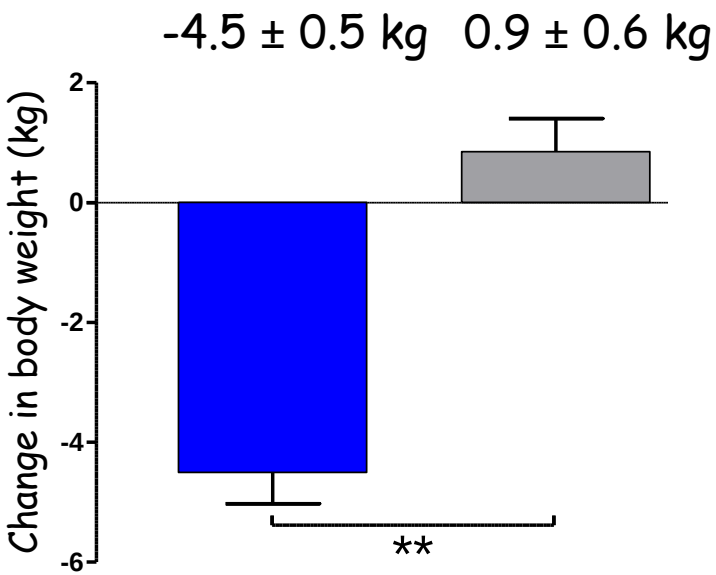
# The *E*ffect of *L*iraglutide on Insulin-associated w*E*ight *GAiN* in Patients With *T*ype 2 Diabetes Mellitus (ELEGANT Trial)

- Hypothesis: patients who develop a large weight gain with insulin treatment may specifically benefit from addition of GLP-1ra

# Effect on body weight




*$p$<0.05; **$p$<0.001

de Wit HM et al. *Diabetologia* 2014;57:1812-1819

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