Training course: Pharmacotherapy in Older People

Tight glycaemic control is necessary - PRO

Prof. Dr. Heinz Drexel, MD, FESC, FAHA, FRCP (Ed.)
Feldkirch, A; Bern, CH; Triesen, FL; Philadelphia, PA, USA
Chair, ESC-Working Group on Cardiovascular Pharmacotherapy

ESC Working Group Cardiovascular Pharmacotherapy

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x I have no potential conflict of interest to report

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Tight glycemic control is necessary: Three Questions

1. **Is tight glycemic control beneficial?**
2. **Is tight glycemic control dangerous?**
3. **How tight is necessary?**

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Type 2 DM

UKPDS

- >4000 pts with newly diagnosed T2DM
- Various interventions, including
  - intensified vs. conventional glucose lowering
- Median age 54 years (IQR 48-60 years)
- Follow-up: 10 years

Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33).

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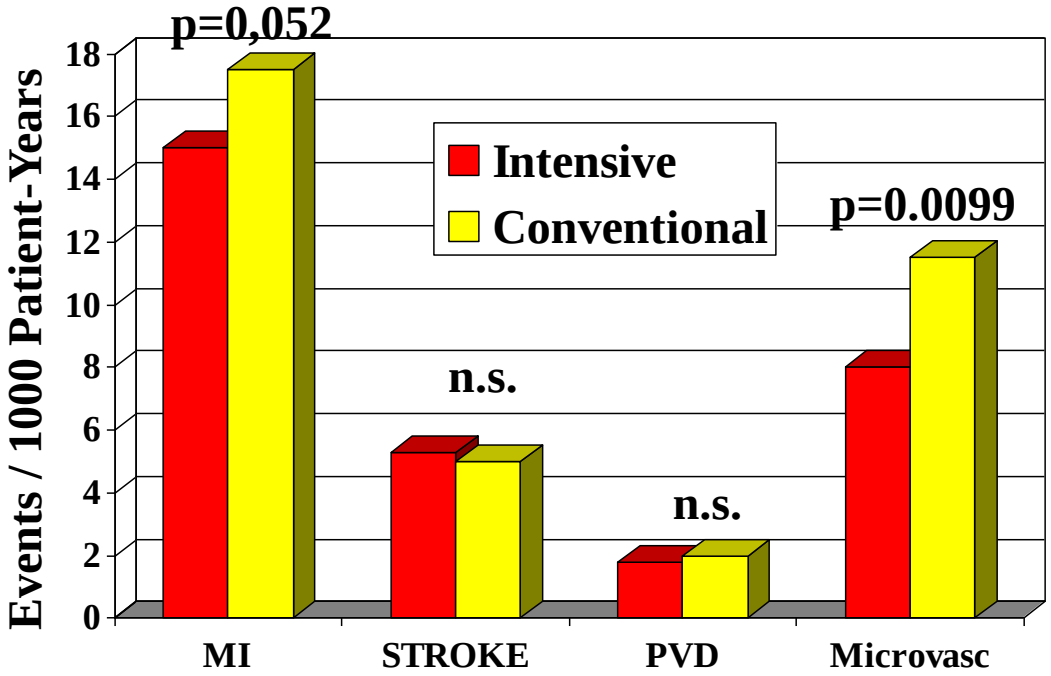
UKPDS Study Group Lancet 1998;352: 837

Diabetes-Related Events
UKPDS 33 – Glucose Intervention



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UKPDS Study Group. Lancet 1998; 352: 837.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes

Rury R. Holman, F.R.C.P., Sanjoy K. Paul, Ph.D., M. Angelyn Bethel, M.D., David R. Matthews, F.R.C.P., and H. Andrew W. Neil, F.R.C.P.

ABSTRACT

BACKGROUND

During the United Kingdom Prospective Diabetes Study (UKPDS), patients with type 2 diabetes mellitus who received intensive glucose therapy had a lower risk of microvascular complications than did those receiving conventional dietary therapy. We conducted post-trial monitoring to determine whether this improved glucose control persisted and whether such therapy had a long-term effect on macrovascular outcomes.

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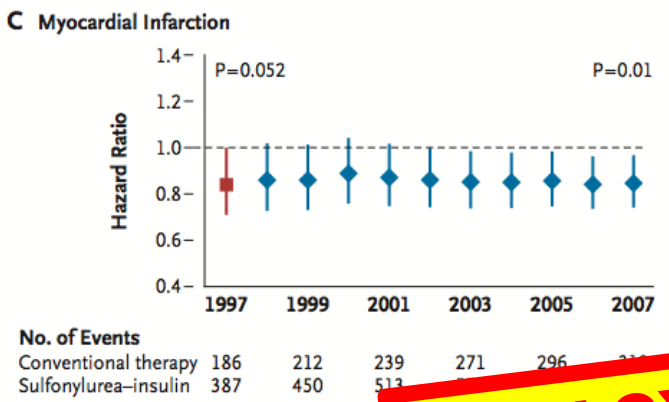
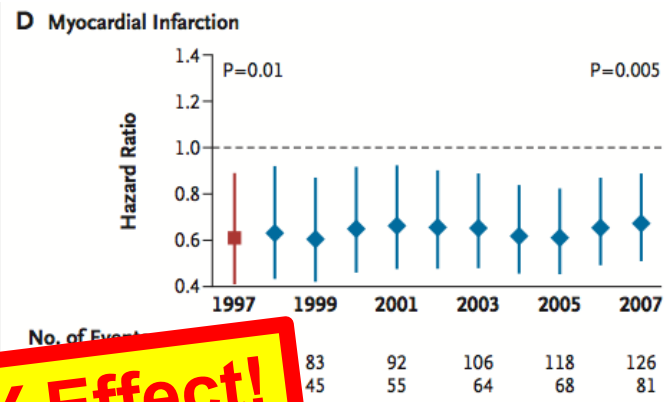
UKPDS – Long term follow-up





LEGACY Effect!
Patient patients & physicians!

Holman RR et al. N Engl J Med 2008;359:1577-89.

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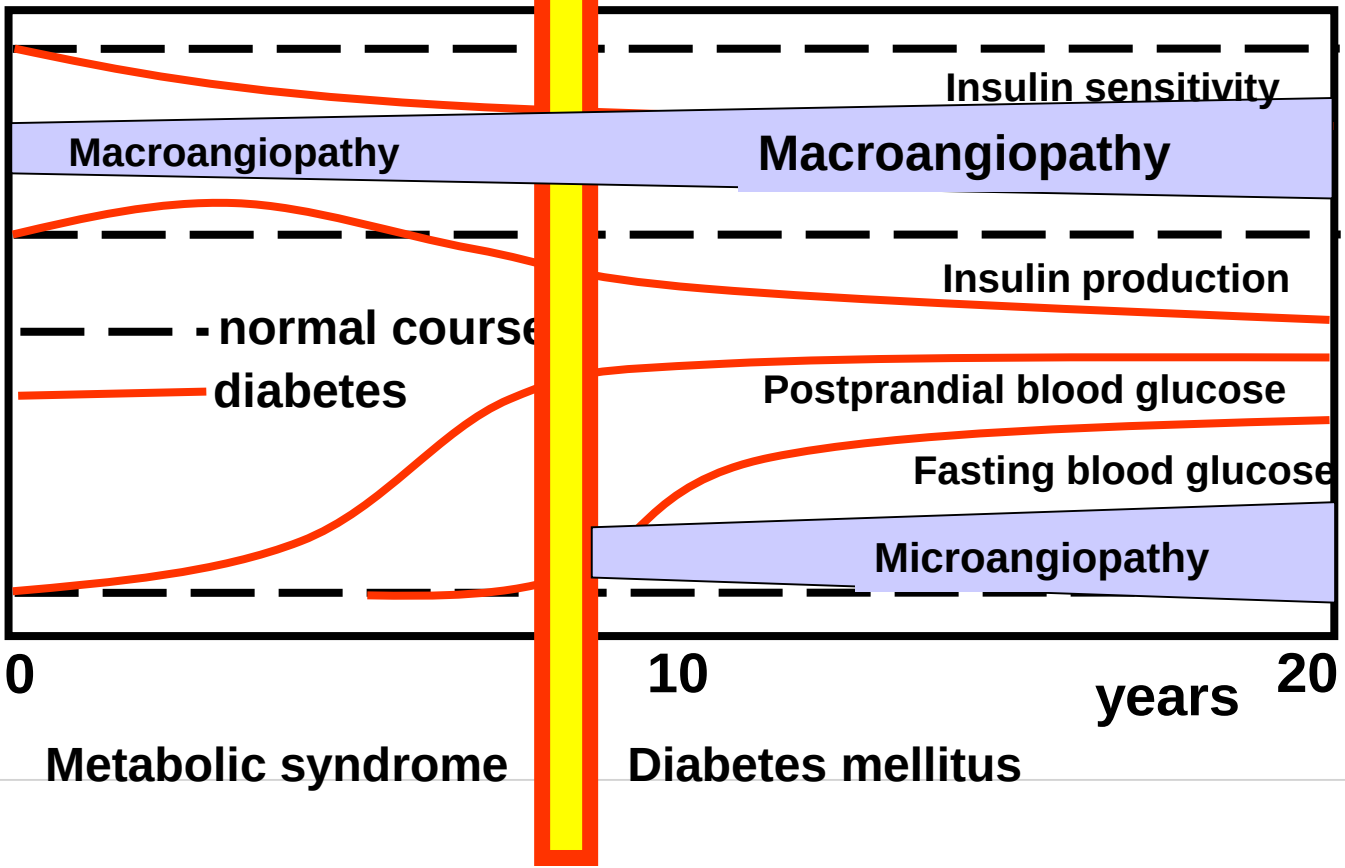
Risks for Macro- and Microangiopathy



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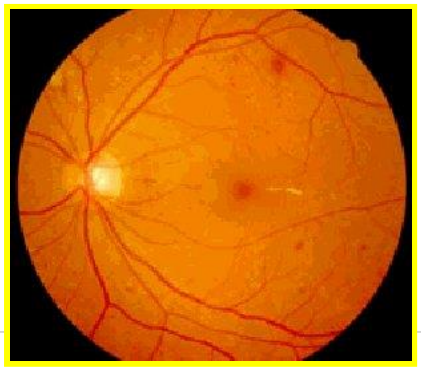
Complications in Diabetes

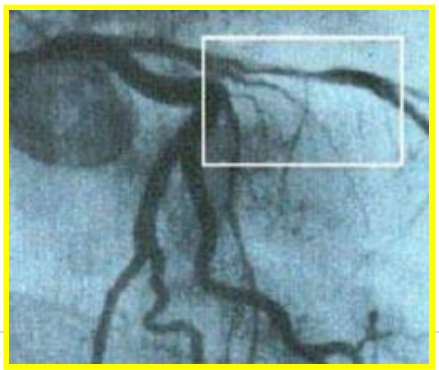
Microangiopathy

Specific for diabetes



Macroangiopathy

Not specific for diabetes,
but 3-fold risk



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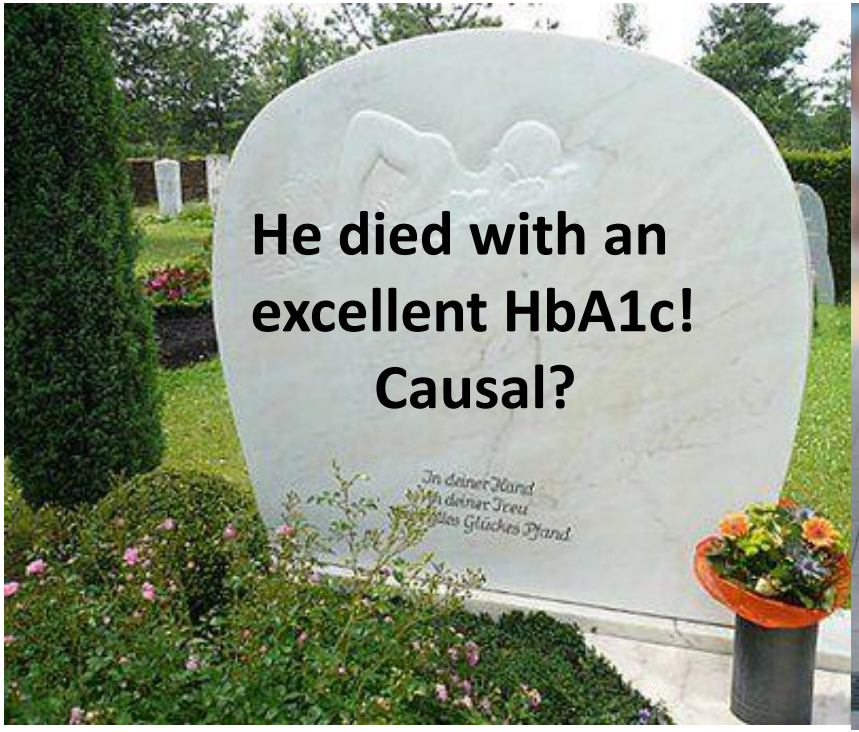
Two Identical Twins



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Our cases today: Two Identical Twins, age 65, British

Harold: only diabetes matters

Type 2 Diabetes over 20 yrs
HbA1c 7%
LDL-C 4 mmol/l, untreated
Blood pressure 180/105, tx
Smoker 40 PY
Dies of MI at age 68
No microangiopathy

David: only the heart matters

Type 2 Diabetes over 20 yrs
HbA1c 10%
LDL-C 4 mmol/l, Atorva + Ezetimib
Blood pressure 130/85, treated
Non-Smoker
Blind at age 60,
eGFR 40 ml/min
Terrible gastroparesis

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Type 1 DM:
It is the same glucose!

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 22, 2005 VOL. 353 NO. 25

Intensive Diabetes Treatment and Cardiovascular Disease in Patients with Type 1 Diabetes

The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group*

Nathan DM et al. NEJM 2005; 353: 2643-2653.

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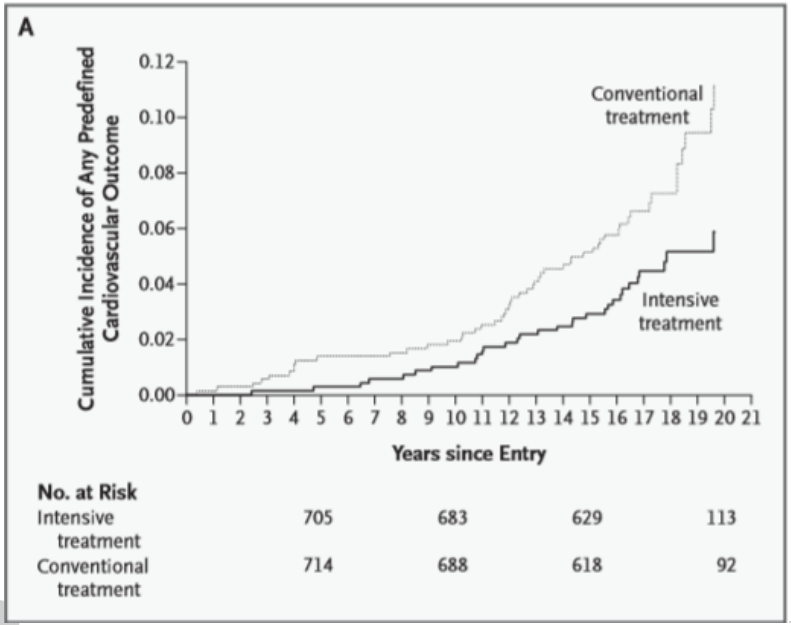
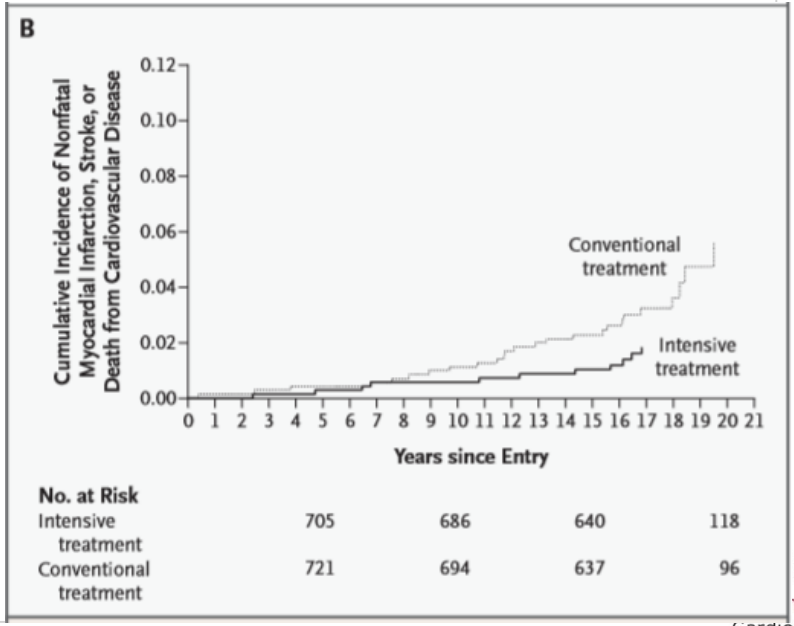
Cumulative Incidence of the First Occurrence of Predefined CV Disease Outcomes

First of Any of the Predefined CV Disease Outcomes



First Occurrence of Nonfatal Myocardial Infarction, Stroke, or Death from CV Disease



Nathan DM et al. NEJM 2005; 353: 2643-2653.

DCCT / EDIC-Trial: Conclusion

Intensive diabetes therapy has long-term beneficial effects on the risk of cardiovascular disease in patients with type 1 diabetes.

Nathan DM et al. NEJM 2005; 353: 2643-2653.

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Tight glycemic control is necessary: Three Questions

1. Is tight glycemic control beneficial?
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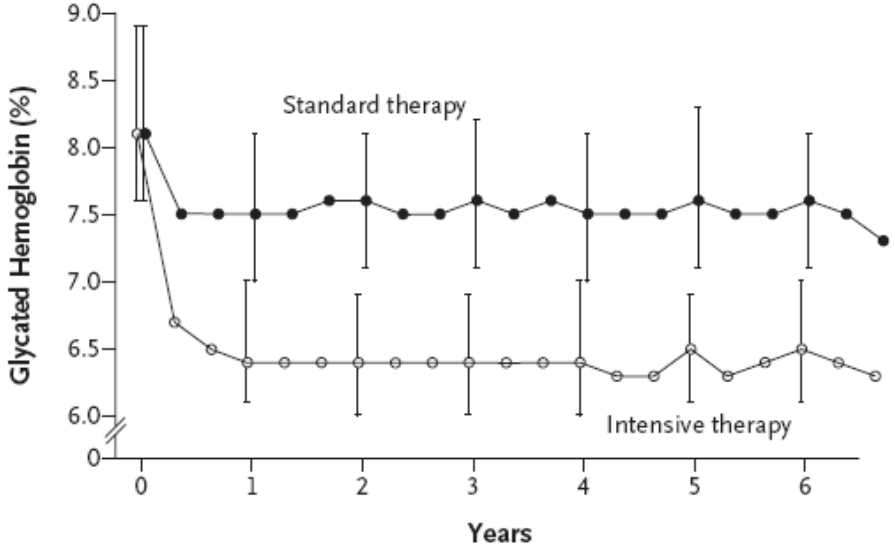
ACCORD: HbA1c lowering



No. at Risk

Standard therapy	5109	4774	4588	3186	1744	455	436
Intensive therapy	5119	4768	4585	3165	1706	476	471

N Engl J Med 2008; 358: 2545.

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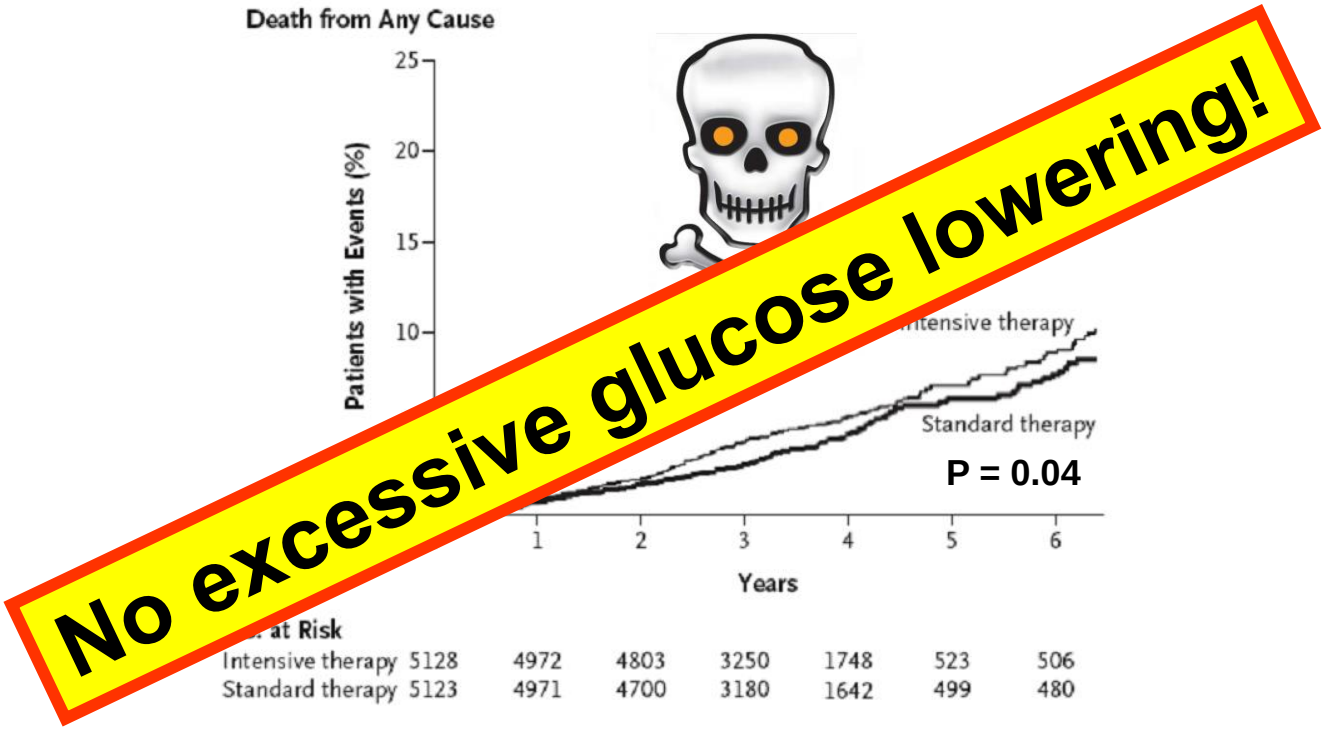
ACCORD: Total mortality



No excessive glucose lowering!

N Engl J Med 2008; 358: 2545.

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Explanation for the Failure of ACCORD and VADT

1. Up to 5 hypoglycemic drugs!
2. Hypoglycemia?
3. Weight gain?

Tight glycemic control is necessary: Three Questions

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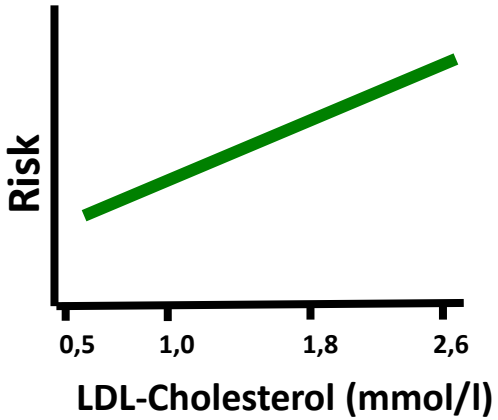
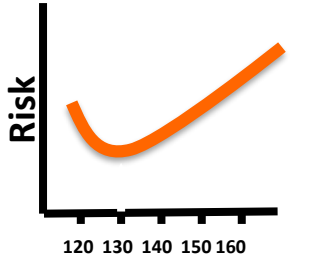
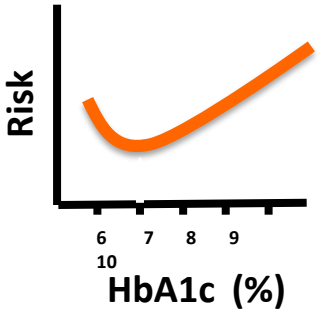
The Core Clinical Question: Infraphysiological Goals

No CAVEAT:
→ No J,
→ Goals





CAVEAT:
Hypotension
→ Goals



CAVEAT:
Hypoglycaemia
→ Goals

A final remark

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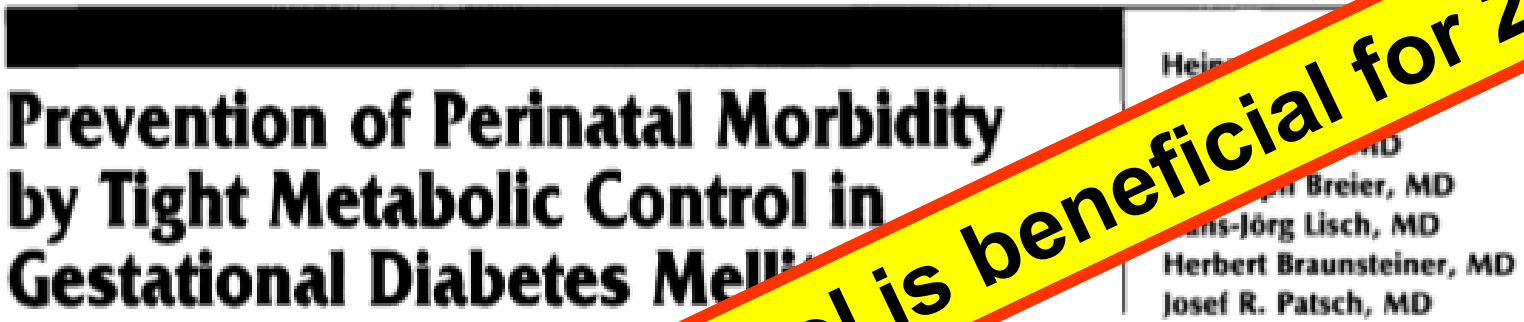

Tight glycemic control is beneficial for 2!

Drexel et al. 1988; 11: 761-768.

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Conclusions and Summary

1. Tight glycemic control is beneficial for microangiopathy.
2. Tight glycemic control is beneficial for macroangiopathy only on the long-term.
3. Type I and II diabetes share same hyperglycemia!
4. Too tight is dangerous: hypoglycemia, J curve
5. J curve also for blood pressure, but not for LDL-C

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Pharmacotherapy in Older People

Thank you!

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