Insulinresistenz, Metabolisches Syndrom und die Prävention des Typ 2-Diabetes

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Insulinresistenz, Metabolisches Syndrom und die Prävention des Typ 2-Diabetes

1. Epidemiologie: Metabolisches Syndrom, Typ 2 – Diabetes und KHK
2. Pathophysiologie der Insulinresistenz: Risikofaktor für KHK
3. Screening auf erhöhtes Diabetes-Risiko: praxistaugliche Methoden
4. Einfluss von Lebensstil-Faktoren: Ernährung und körperliche Aktivität
5. Medikamente in Prävention und Therapie

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"Es gibt vermutlich bereits mehr als eine halbe Million Diabetiker in den USA. Deshalb sollte die Aufmerksamkeit nicht nur auf die Therapie, sondern ... auf die Prävention gelenkt werden.

Die Ergebnisse werden nicht so schnell zu sehen sein, aber sie kommen sicher und werden eine große Bedeutung haben."

Joslin, Elliott P., JAMA 1921; 76(2)

The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

Vol. 76, No. 2 — Chicago, Illinois — January 8, 1921

THE PREVENTION OF DIABETES MELLITUS

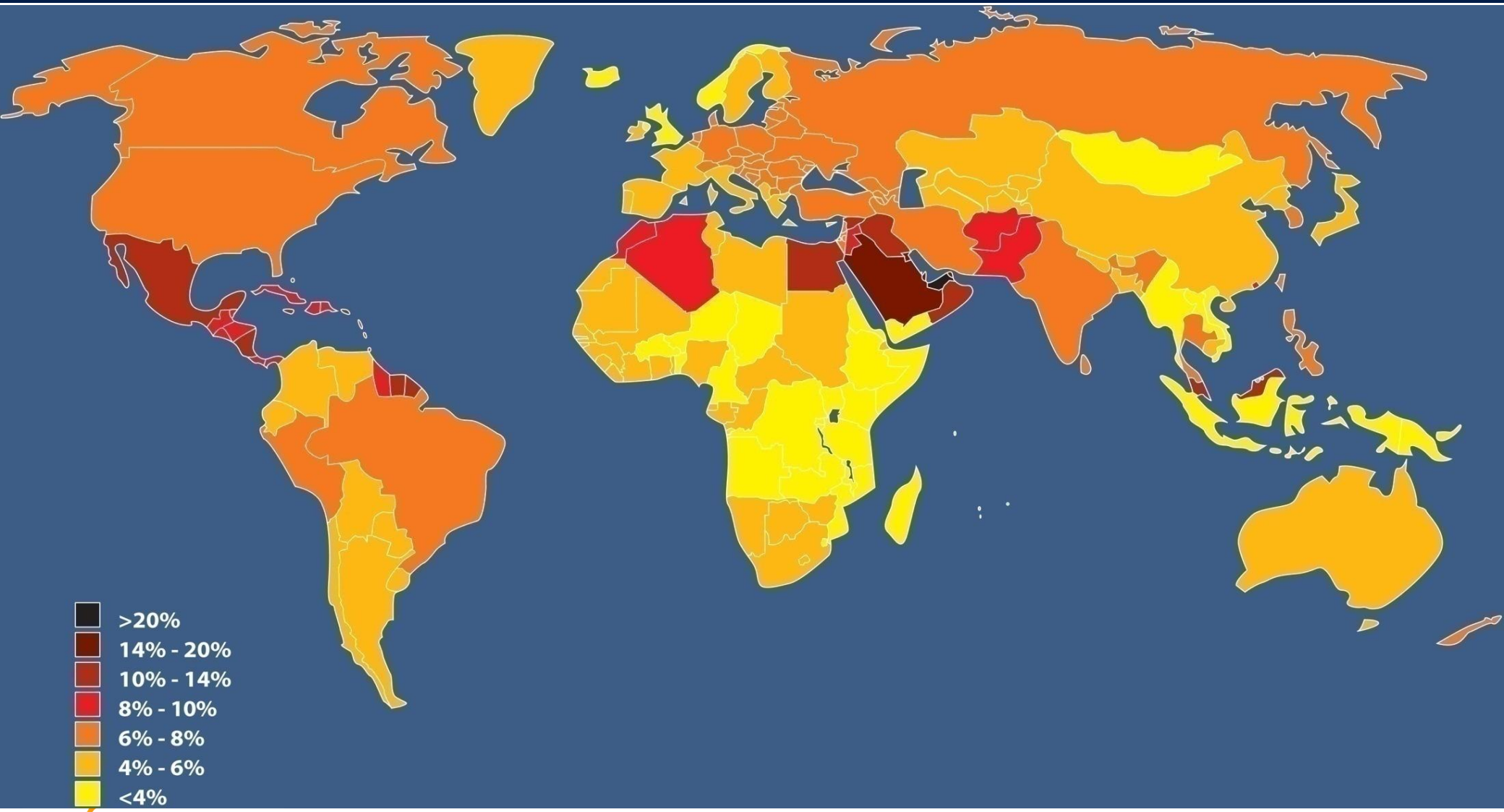
ELLIOTT P. JOSLIN, M.D.

BOSTON

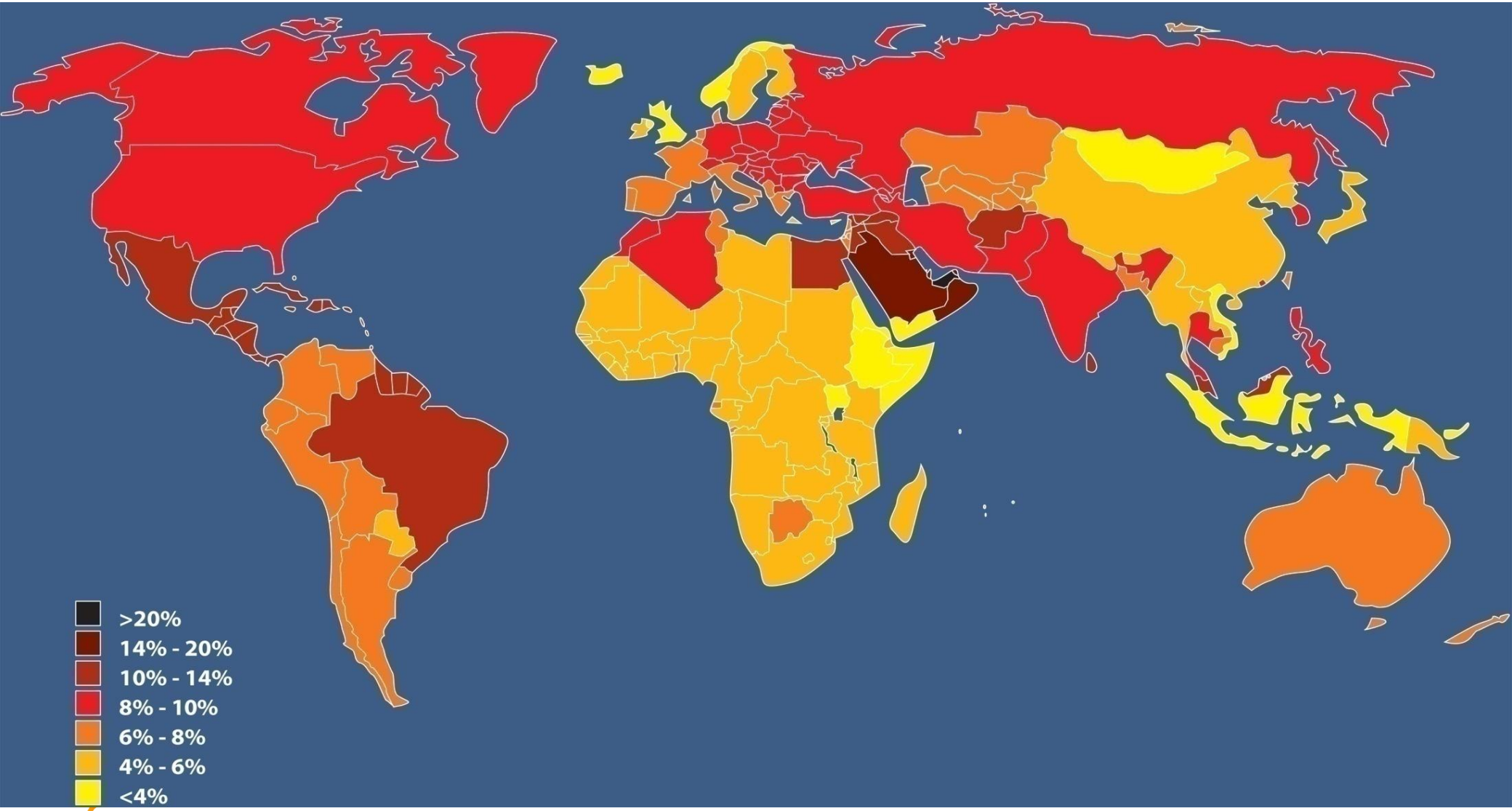
On the broad street of a certain peaceful New England village there once stood three houses side by side, as commodious and attractive as any in the town. Into these three houses moved in succession four women

of the United States was 10 per hundred thousand, and in 1915, 18 per hundred thousand. In the same period in Boston, it rose from 14 to 26 on the same basis. There are probably more than half a million diabetics in the United States. Therefore, it is proper at the present time to devote attention not alone to treatment, but still more, as in the campaign against typhoid fever, to prevention. The results may not be quite so striking or as immediate, but they are sure to come and to be important.

PREVALENCE ESTIMATES OF DIABETES, 2007

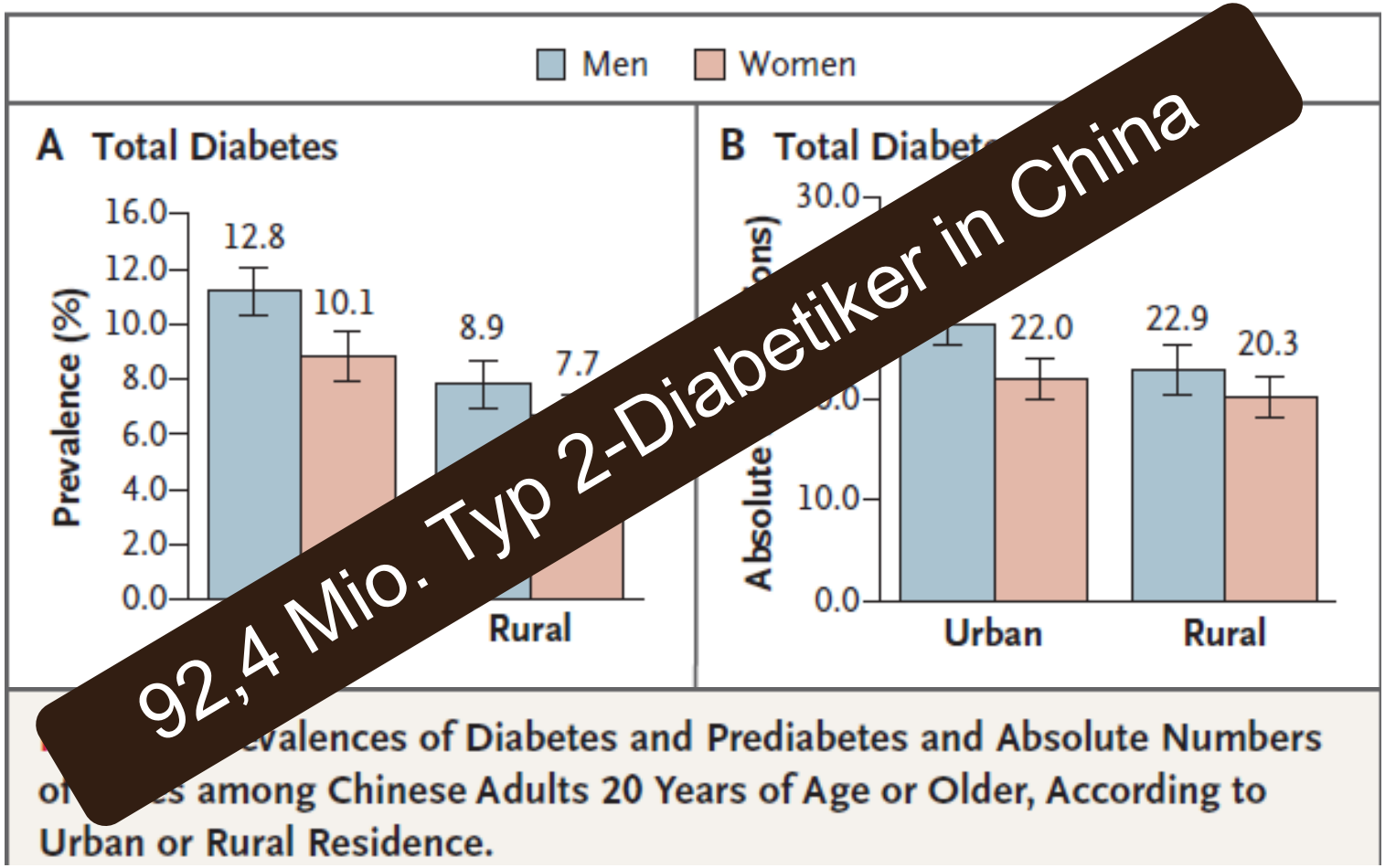


PREVALENCE ESTIMATES OF DIABETES, 2025



Diabetes-Prävalenz in China: höher als erwartet!

Yang W et al., N Engl J Med. 2010; 362; 1095-1101



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Diabetes-Prävalenz in China: höher als erwartet!

Yang W et al., N Engl J Med. 2010; 362; 1095-1101

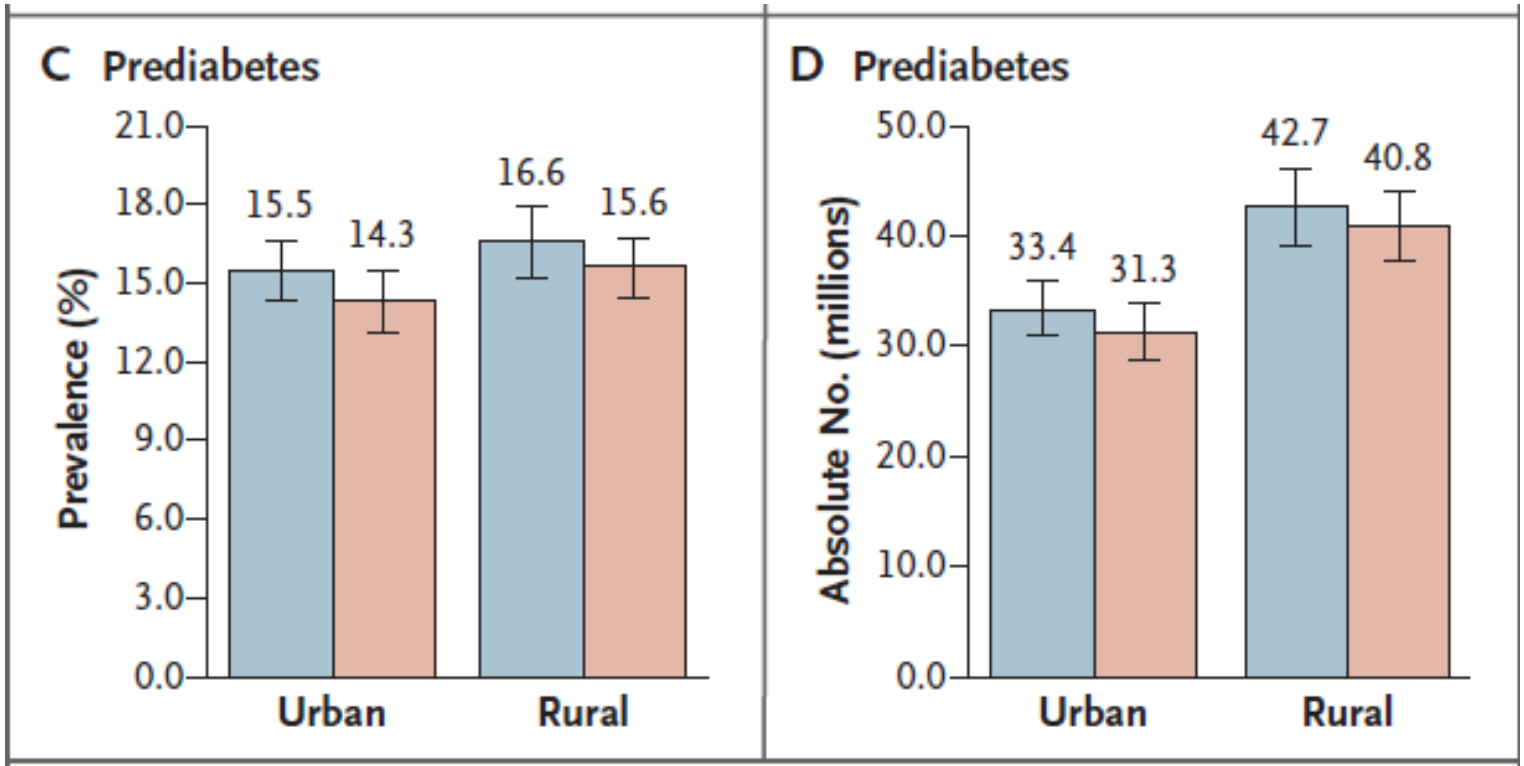

Figure 2. Prevalences of Diabetes and Prediabetes and Absolute Numbers of Cases among Chinese Adults 20 Years of Age or Older, According to Urban or Rural Residence.

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Diabetes-Prävalenz in China: höher als erwartet!

Yang W et al., N Engl J Med. 2010; 362; 1095-1101

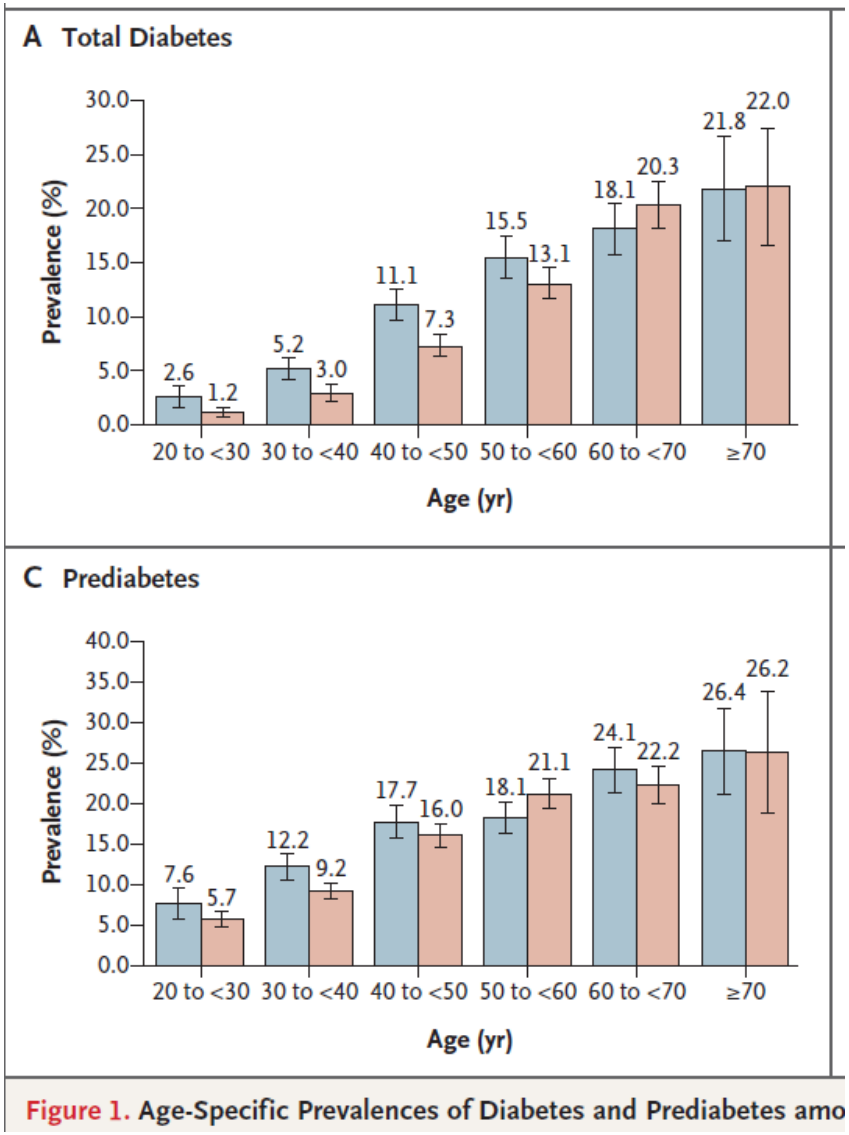

Figure 1. Age-Specific Prevalences of Diabetes and Prediabetes amo

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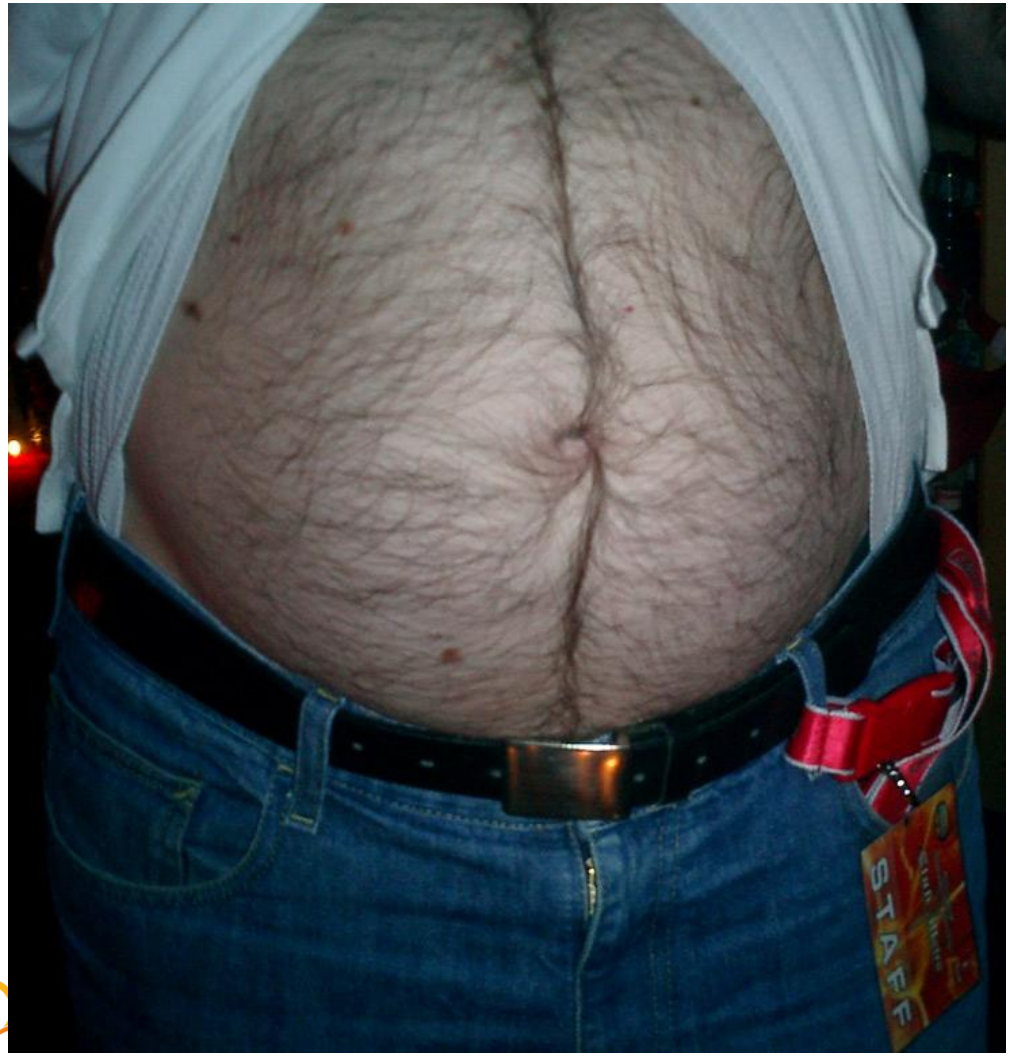
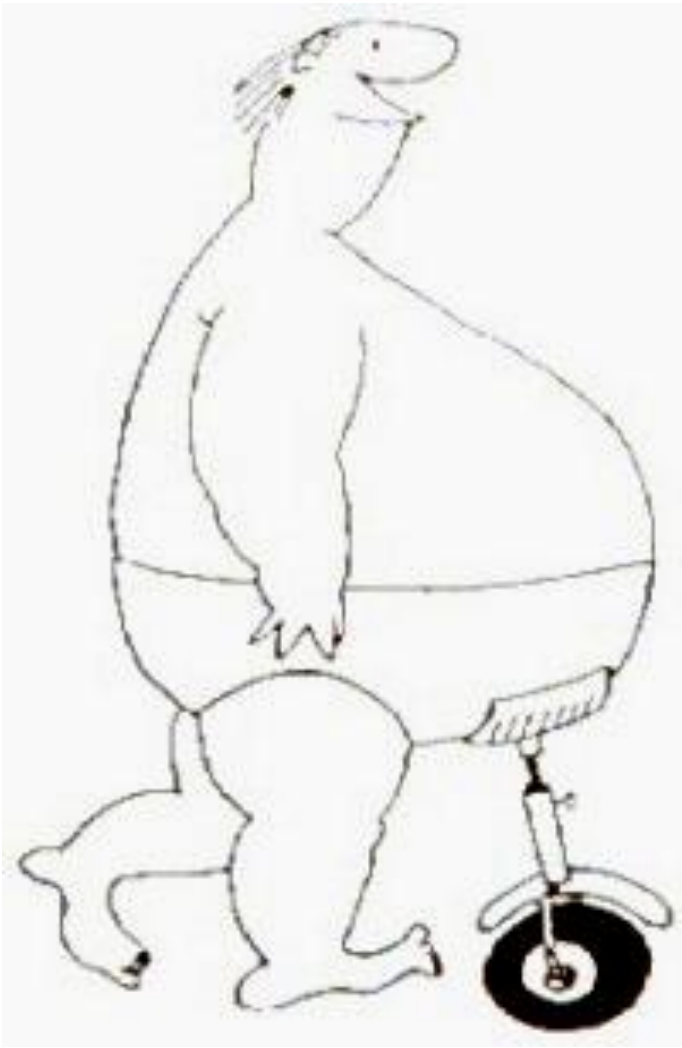
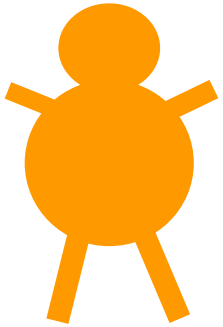
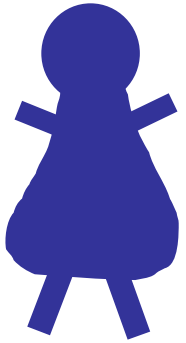
Schon Cäsar sagte auf Latein:
"Lasst dicke Männer um mich sein"

Bauchumfang: Risikofaktor für KHK !





viszerale Fettzelle	subkutane Fettzelle
	
Adiponectin ⇓, Leptin ⇓, TNF- α⇑, IL-6 ⇑, Resistin ⇑	geringere endokrine / parakrine Aktivität (TNF- α, IL-6, Resistin)
verstärkte Lipolyse (α2-Rezeptoren = β-Rezeptoren)	geringere Lipolyse (α2-Rezeptoren > β-Rezeptoren)
geringe Insulinsensitivität ⇒ geringere Lipolyse-Hemmung	verstärkte Insulin-vermittelte Anti-Lipolyse
steigert Gluconeogenese in Leber, VLDL -Synthese⇑, HDL⇓	geringerer Einfluss auf die Gluconeogenese

Lafontan M, Berlan M. Trends Pharm Sci 2003; 24: 276-283

Yusuf S et al., Lancet 2005; 366: 1640-1649

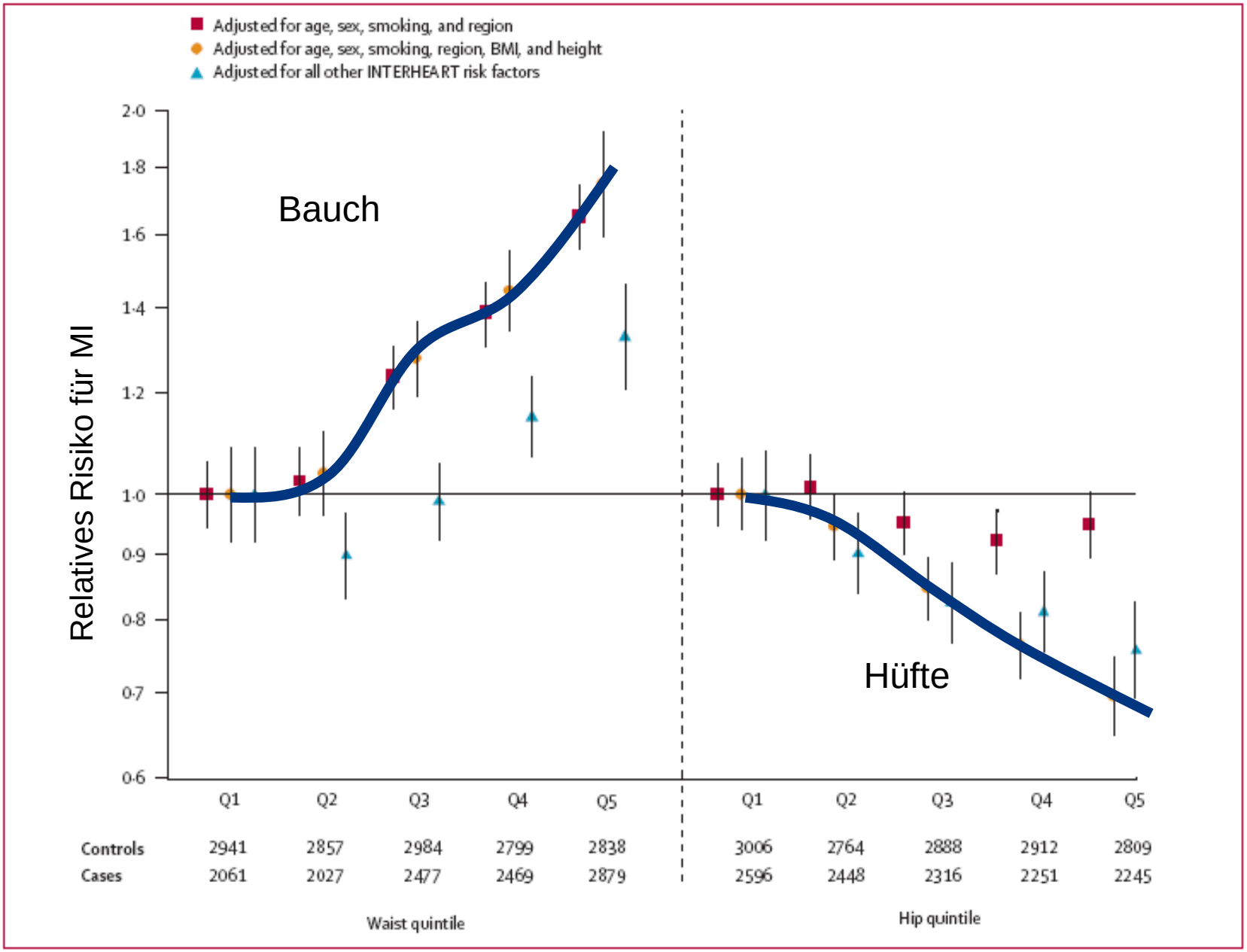


Figure 4: Risk of MI associated with increasing waist circumference and hip circumference
Vertical bars=95% CIs.

Yusuf S et al., Lancet 2005; 366: 1640-1649

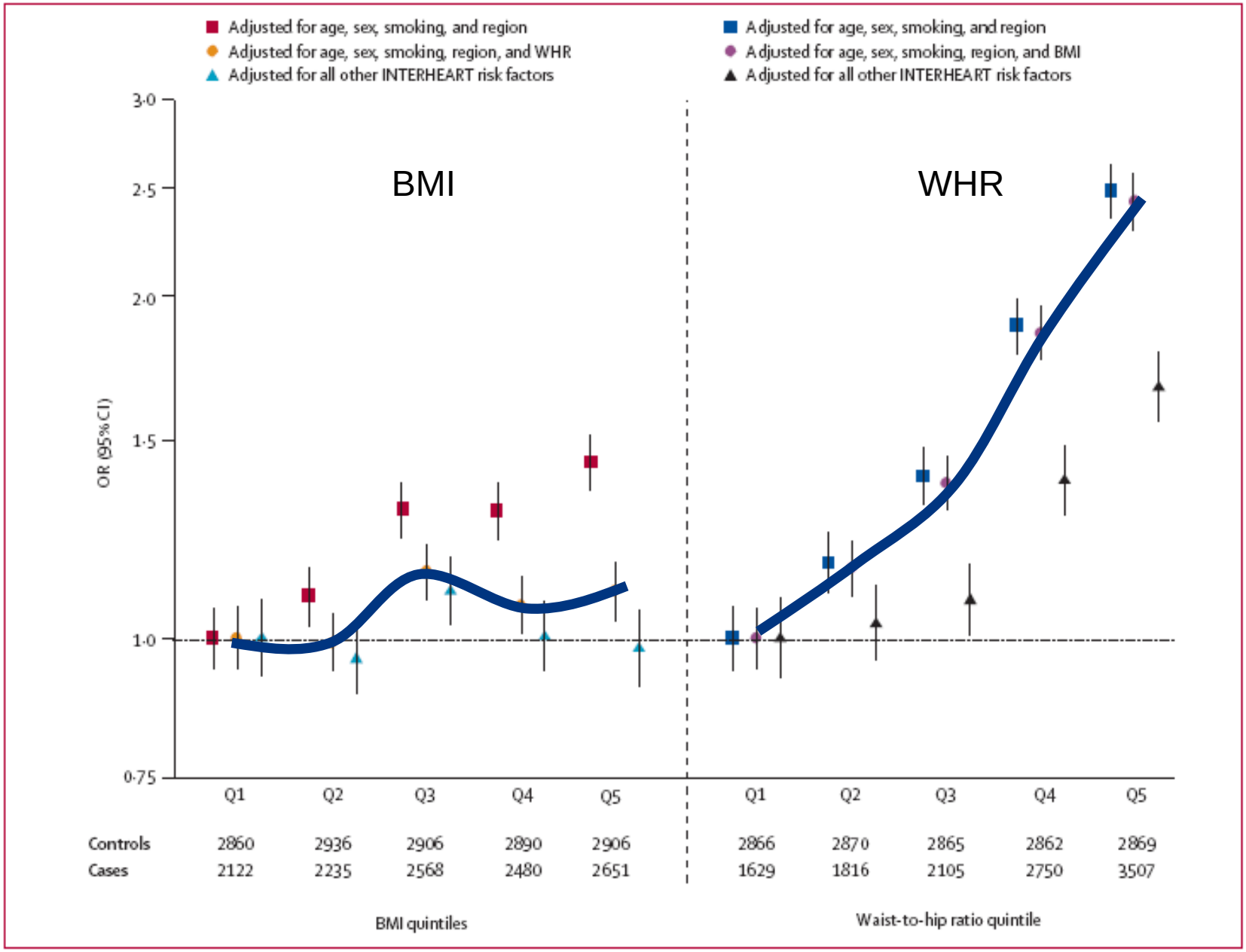


Figure 3: Association of BMI and waist-to-hip ratio with myocardial infarction risk
Vertical bars=95% CIs.

Diabetische Dyslipoproteinämie und Atherosklerose

Mazzone T et al., Lancet 2008; 371: 1800-1809

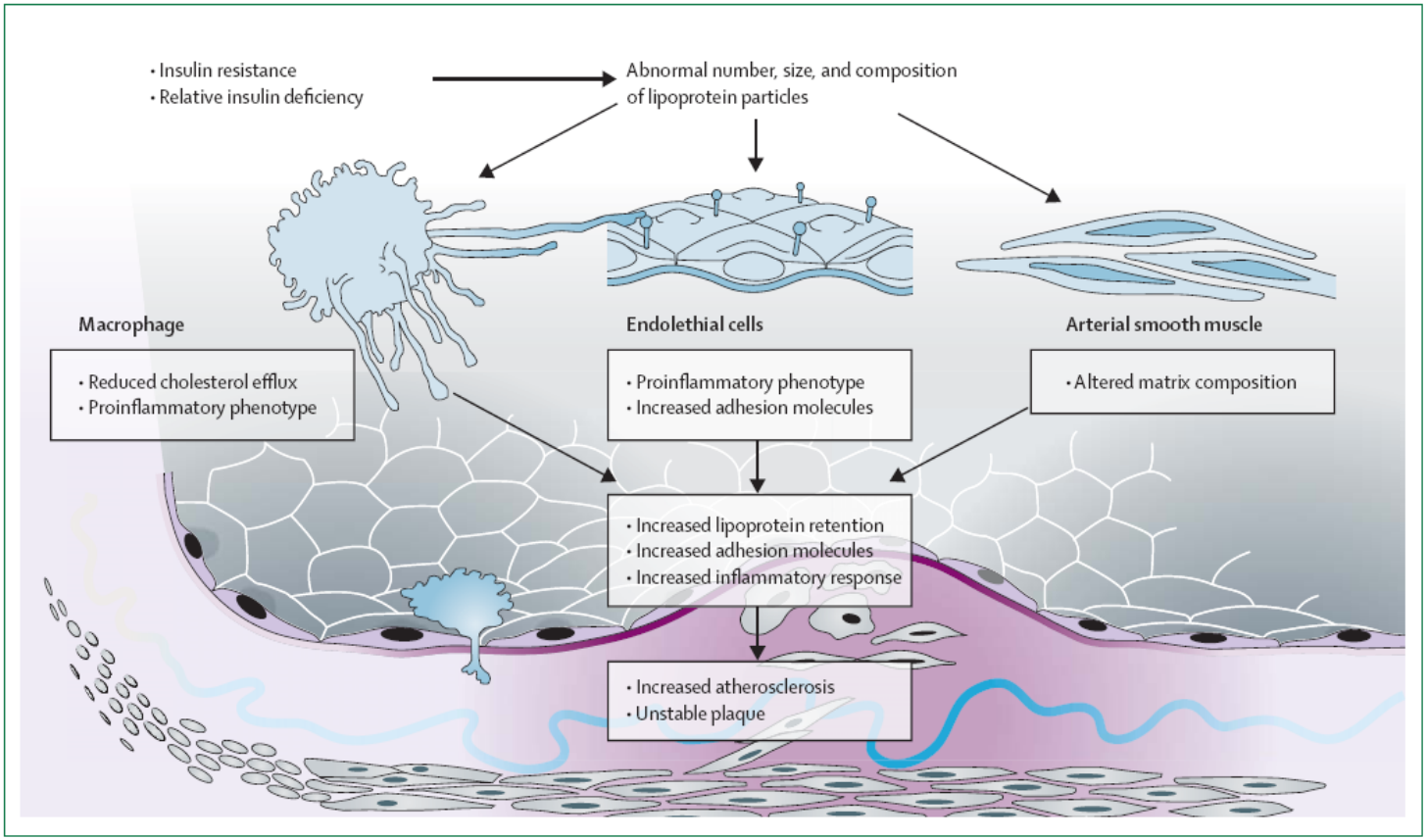


Figure 2: Diabetic dyslipidaemia and the vessel wall

<u>Lipide beim Diabetiker</u>:

- ApoB ⇑
- sd-LDL ⇑
- TG⇑ + VLDL⇑
  (besonders postprandial)
- ApoA1⇓
- HDL⇓
- reverse-cholesterol-transport ⇓

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Glukose, AGEs und Atherosklerose

Mazzone T et al., Lancet 2008; 371: 1800-1809

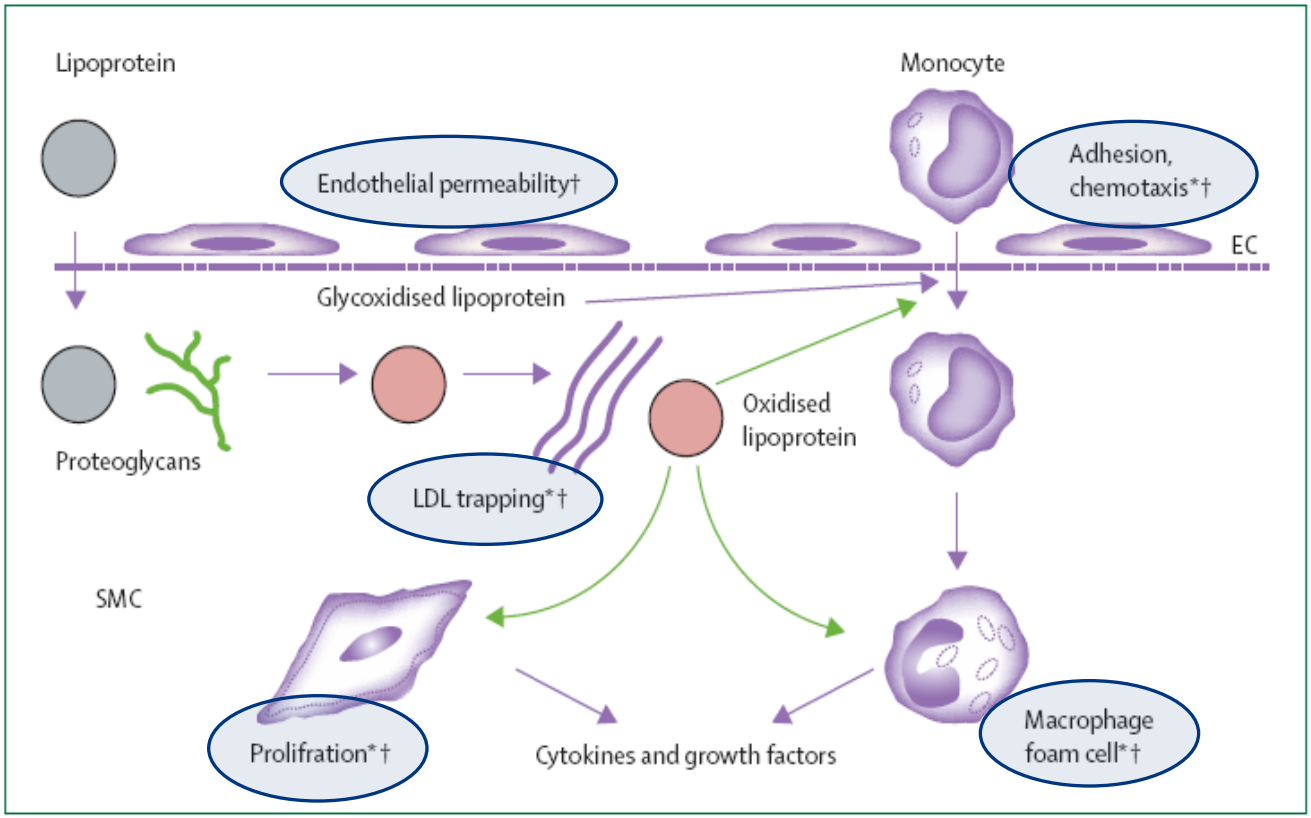

Figure 1: **Possible mechanisms by which glucose and advanced glycation end-products (AGEs) can affect atherogenesis in diabetes**

EC=endothelial cell. SMC=smooth-muscle cell. *Glucose and †AGEs have been proven to affect various steps in these pathways.

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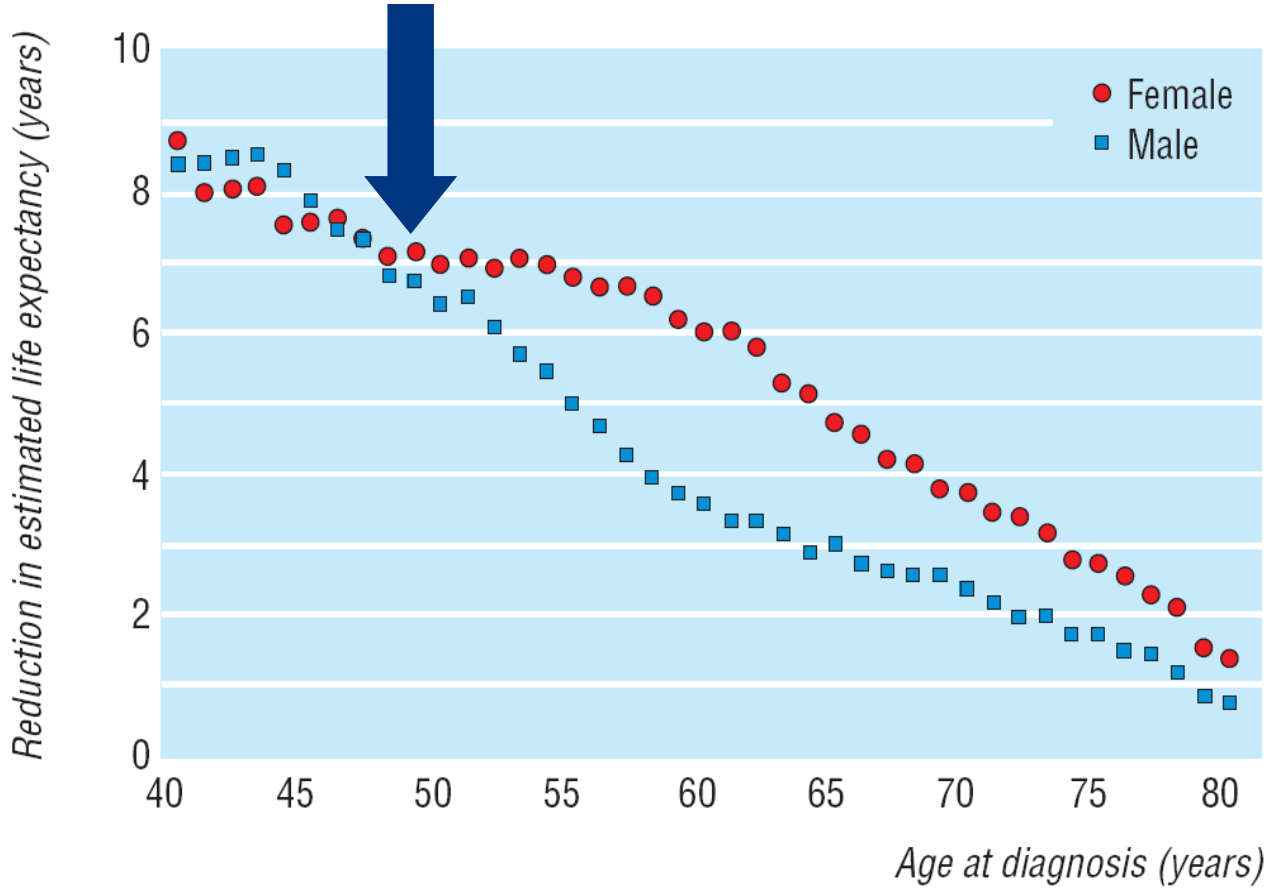
Verkürzung der Lebenserwartung durch Typ 2-Diabetes

Roper NA et al., BMJ 2001; 322: 1389-1393



Reductions in estimated life expectancy, by age at diagnosis of type 2 diabetes

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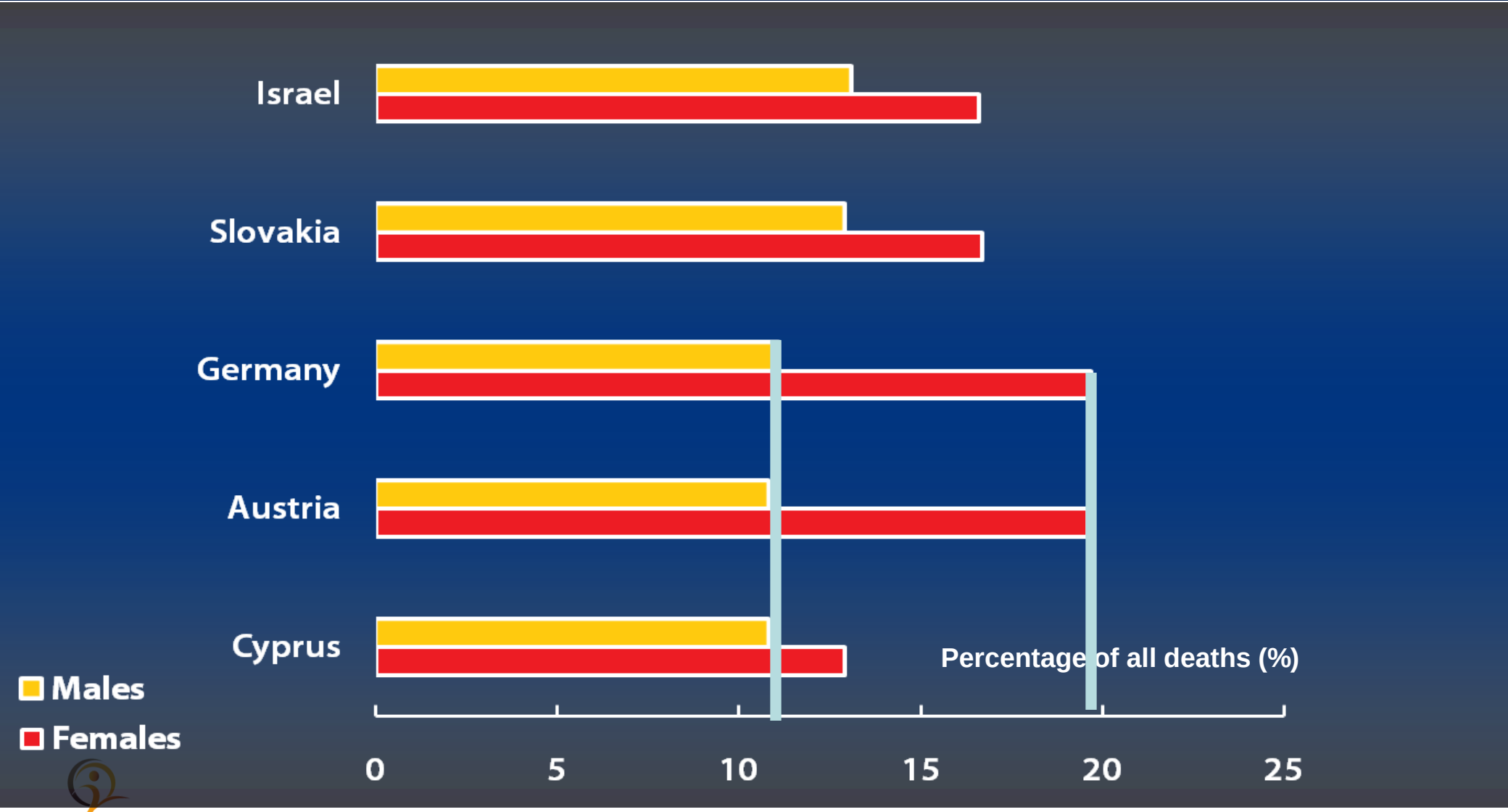
MORTALITY ATTRIBUTABLE TO DIABETES AS A PERCENTAGE OF ALL DEATHS IN SELECTED COUNTRIES, EUROPEAN REGION, 2007



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IDF Diabetes Atlas 2006

Wie viele **Patienten mit Myokardinfarkt** haben einen **normalen** Glucosestoffwechsel (4 Wochen nach dem Infarkt)

A: 82%

C: 32%

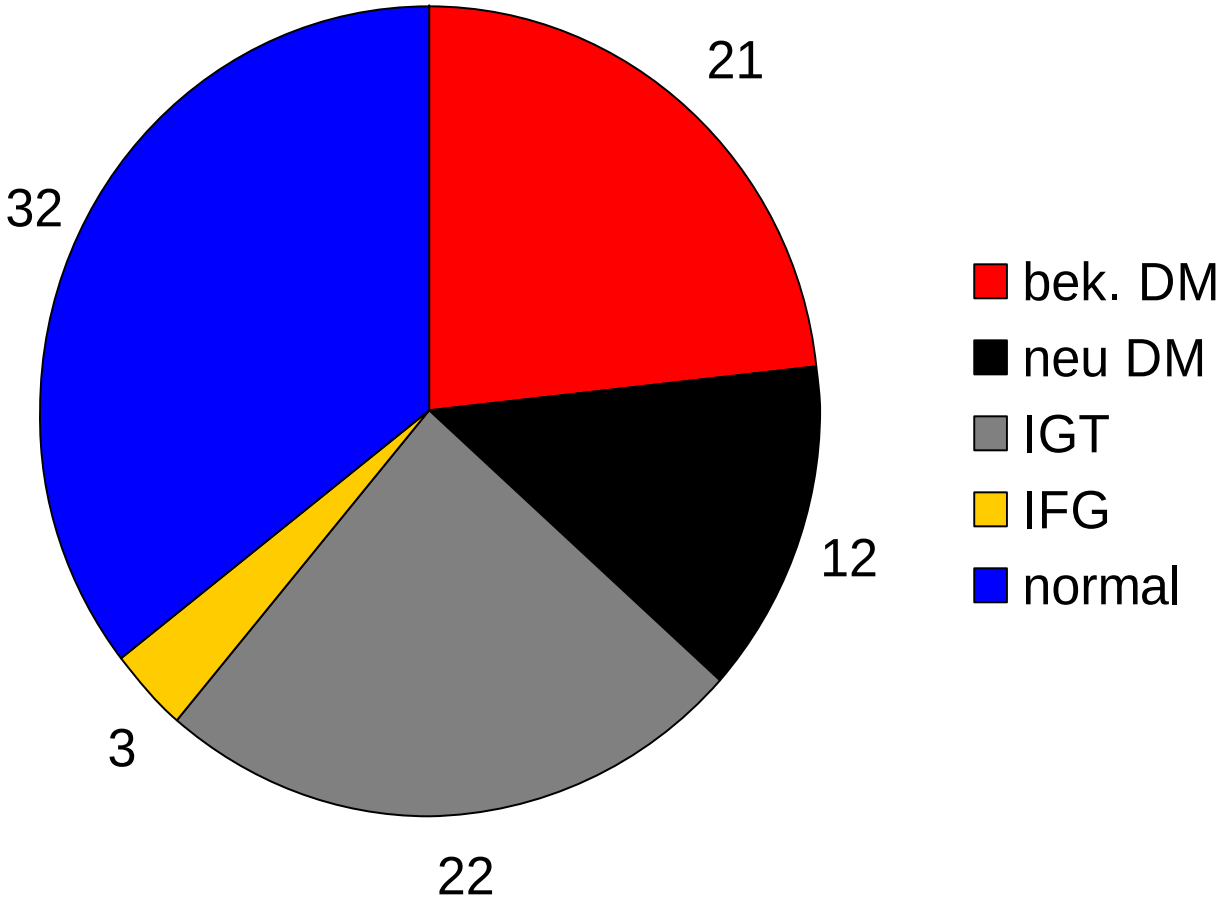
B: 65%

D: 16%

Euro Heart Survey – Diabetes and the Heart

Bartnik et al., Eur Heart J 2004; 25: 1880

n=4961 Patienten mit akutem Myokardinfarkt



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www.StrangeCosmos.com

Davis JN et al., Am J Clin Nutr 2005;82: 1004-1010

The relation of sugar intake to β cell function in overweight Latino children[1–3]

Jaimie N Davis, Emily E Ventura, Marc J Weigensberg, Geoff DC Ball, Martha L Cruz, Gabriel Q Shaibi, and Michael I Goran

ABSTRACT

Background: Few studies have investigated the association between sugar intake and insulin dynamics in children, and none have examined this association in overweight Latino youth.

Objective: We aimed to examine the relation between dietary components, especially sugar intake, and insulin dynamics in overweight Latino youth.

Design: We examined 63 overweight Latino children aged 9–13 y.

among certain ethnic groups, including Latinos (2). If left untreated, these risk factors could have disastrous consequences for minority health and the health care costs of future generations.

On the basis of findings in previous studies in adults, the progression of type 2 diabetes is linked to increased adiposity, insulin resistance (3), and the inability of β cells to compensate adequately for insulin resistance (4). Although, to date, very limited research has examined the etiology of type 2 diabetes in

Conclusions: In overweight Latino children, higher intakes of sugar and sugar-sweetened beverages were associated with lower AIR and disposition index, which suggested that these children already have early signs of poor β cell function. These results emphasize the need for early nutritional interventions to reduce daily sugar intake in overweight Latino children and potentially reduce their risk for type 2 diabetes. *Am J Clin Nutr* 2005;82:1004–10.


BOSSE, PALLE
und die Köche des Königs
Das Kochbuch
Tre Torri

OBSTFONDUE

Die Melone aushöhlen. Das Obst putzen, schälen, in mundgerechte Stücke schneiden und jeweils in kleinen Schälchen anrichten.

Speisequark, Milch, Zitronensaft, Honig und Haferflocken vermischen und in die ausgehöhlte Melone füllen. Die Zartbitterschokolade mit einem Sparschäler in grobe Raspel hobeln.

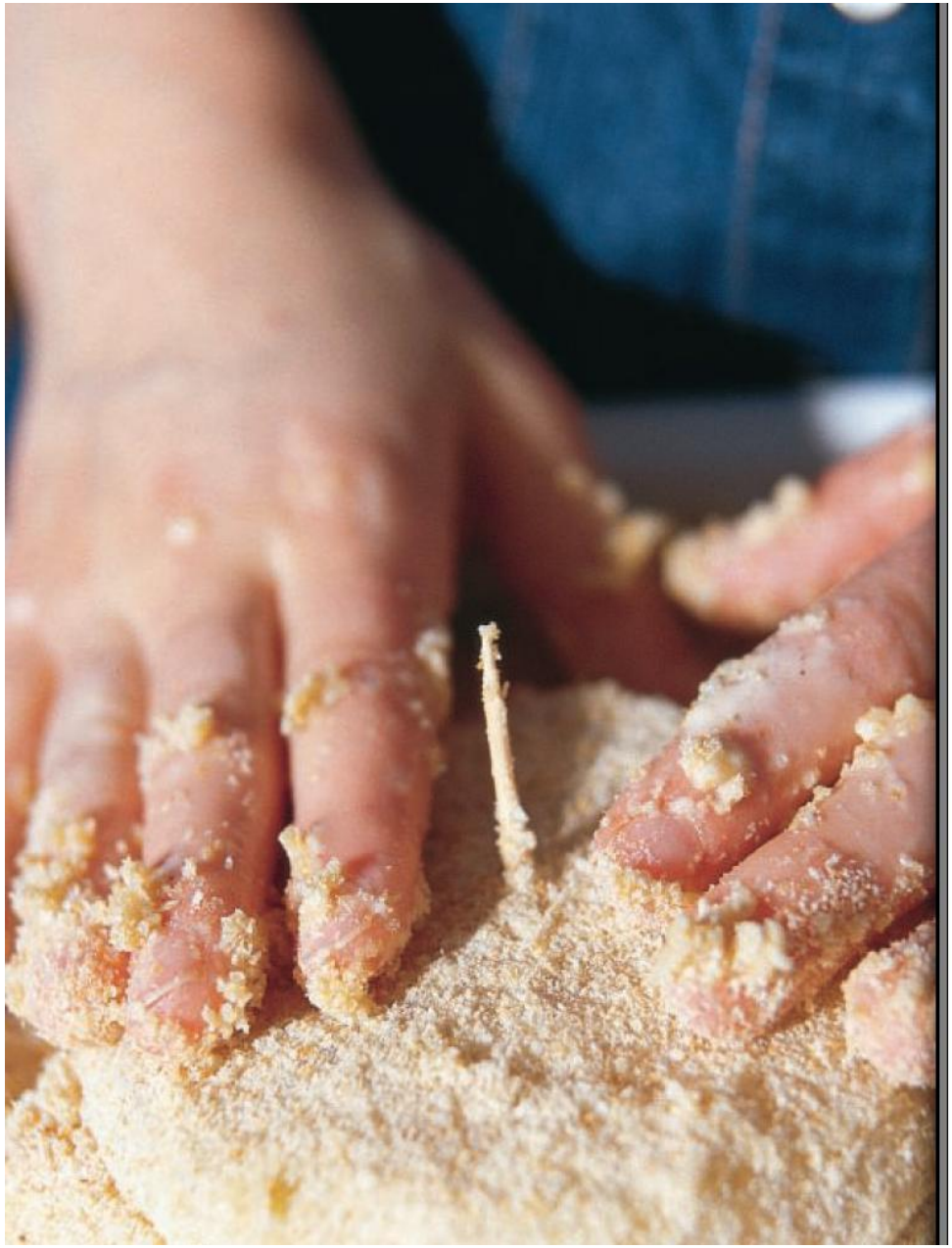
Haselnüsse, Mandeln und Sckokoladenraspel ebenfalls auf kleine Schälchen verteilen.

Die Obststücke auf Fonduespieße stecken, in die Quarkcreme dippen und anschließend in die Schälchen tunken.

Für 6 Personen

1/2 Melone
1,5 kg Obst (Apfel, Banane, Weintrauben, Ananas aus der Dose)
250 g Speisequark
125 ml Vollmilch
1 Zitrone
3 EL Honig
3-4 EL feine Vollkornhaferflocken
1/2 Tafel Zartbitter-Schokolade
gehackte Haselnüsse
gehobelte Mandeln



KOHLRABI-CORDON-BLEU

Die Kohlrabi schälen und in kochendem Wasser blanchieren. Herausnehmen, etwas abkühlen lassen und in 8 Scheiben schneiden. Die Schinkenscheiben halbieren und die Käsescheiben vierteln.

In einem Suppenteller die Eier mit der Milch verquirlen. Mehl und Paniermehl in jeweils einen flachen Teller geben.

Für die Cordons bleus je eine Scheibe Kohlrabi mit gekochtem Schinken, mit Käse und wieder mit gekochtem Schinken belegen. Darauf eine weitere Kohlrabischeibe legen und mit Zahnstochern feststecken. Die Cordons bleus zuerst in Mehl, dann in verquirltem Ei und zum Schluss in Paniermehl wenden.

In einer Pfanne das Öl erhitzen und die Kohlrabi-Cordons-bleus darin von beiden Seiten etwa 3 Minuten goldbraun braten.

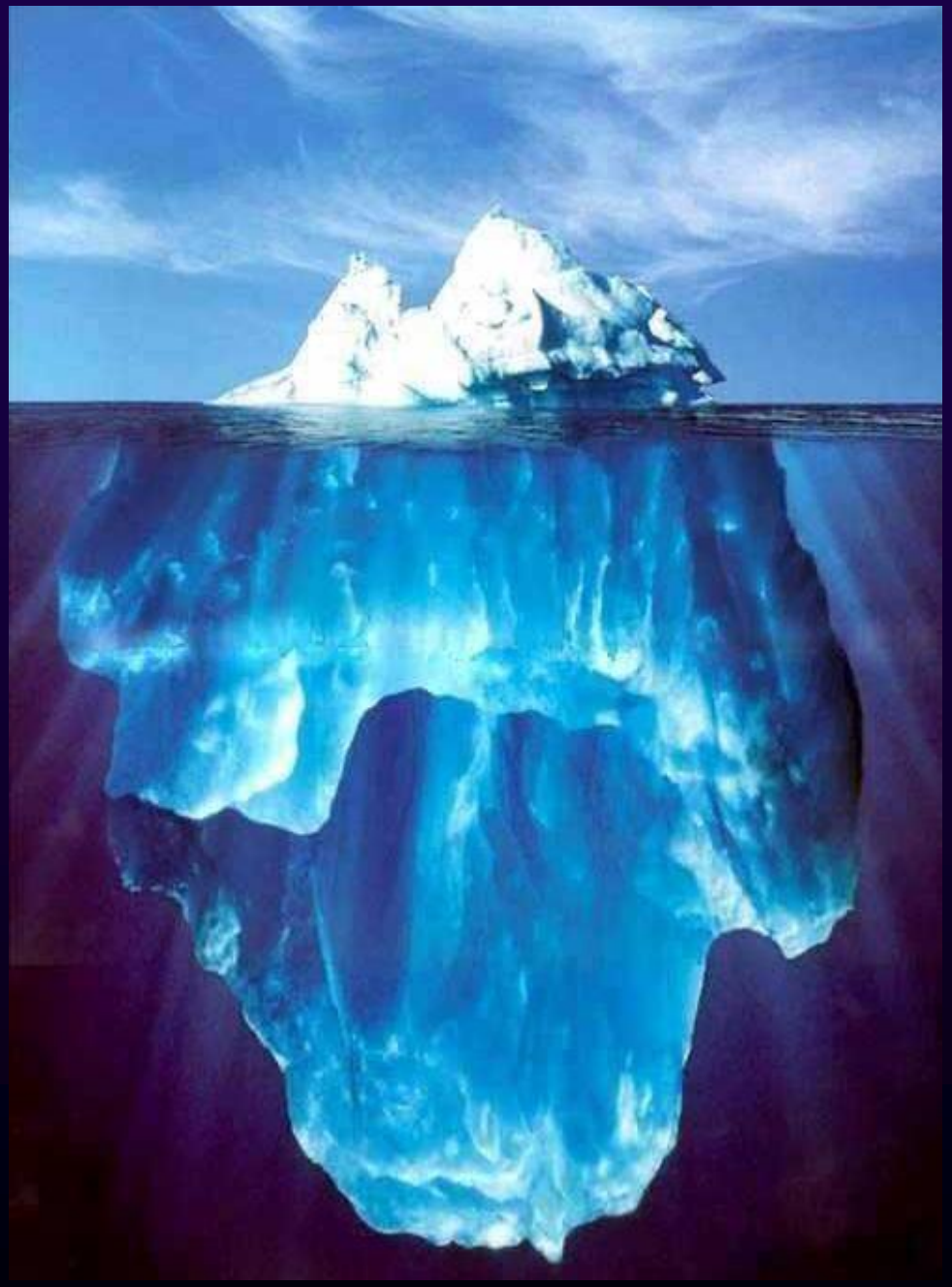
Für 4 Personen

2 dicke Kohlrabi
4 Scheiben gekochter Schinken
2 Scheiben Käse (z. B. Gouda)

Für die Panade

2 Eier
50 ml Milch
3 EL Mehl
3 EL Paniermehl

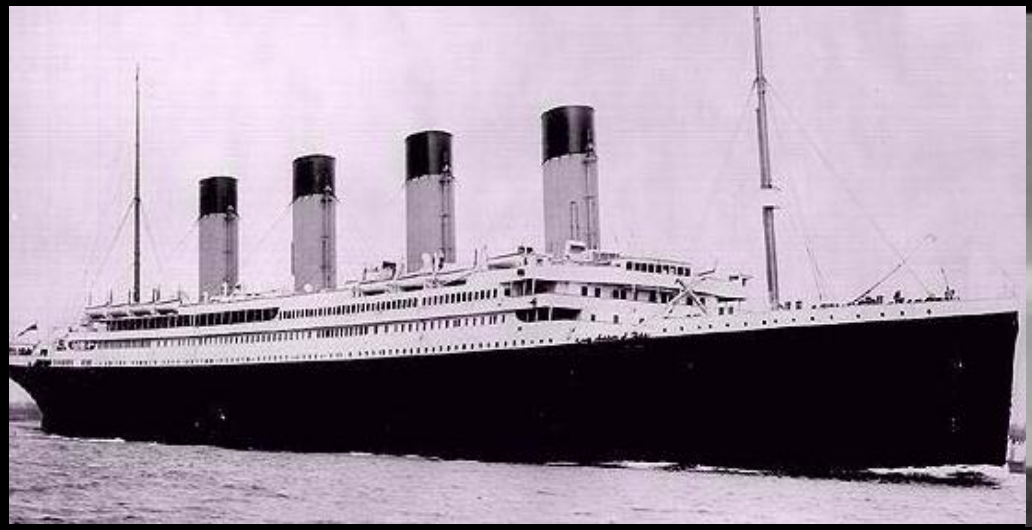
2 EL Rapsöl



Deutschland 2009:

ca. 9 000 000
Diabetiker

ca. 20 000 000
Metabolisches
Syndrom



„What modern cardiology does with diabetics is nothing, but re-arranging the deck-chairs on the Titanic.“

Prof. John E. Deanfield, London, Cardiology-Update, Februar 2003, Davos

IDF-Definition 2005: Metabolisches Syndrom

International Diabetes Federation 2005

Zentrale Adipositas:

- **Bauchumfang** ≥ 94 cm Männer, ≥ 80 cm Frauen

  + 2 der folgenden 4 Faktoren:

- Triglyzeride ≥ 150 mg/dl
- HDL-Cholesterin < 40 mg/dl Männer, < 50 mg/dl Frauen
- Blutdruck ≥ 130 mm Hg syst. und/oder ≥ 85 mm Hg diast.
- Nüchtern-Blutzucker ≥ 100 mg/dl

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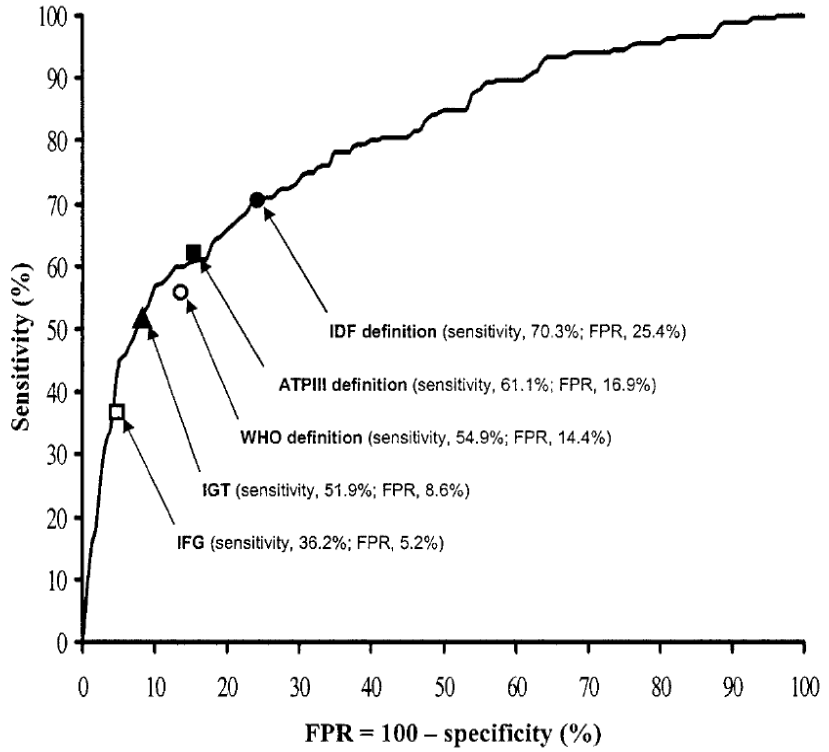
Sensitivität und Spezifität der MS-Definitionen

Lorenzo C et al., Diab Care 2007; 30: 8-13

San Antonio Heart Study, Texas/USA,
n=2559 Pat., Alter ~44 Jahre, Follow-up 7,4 Jahre



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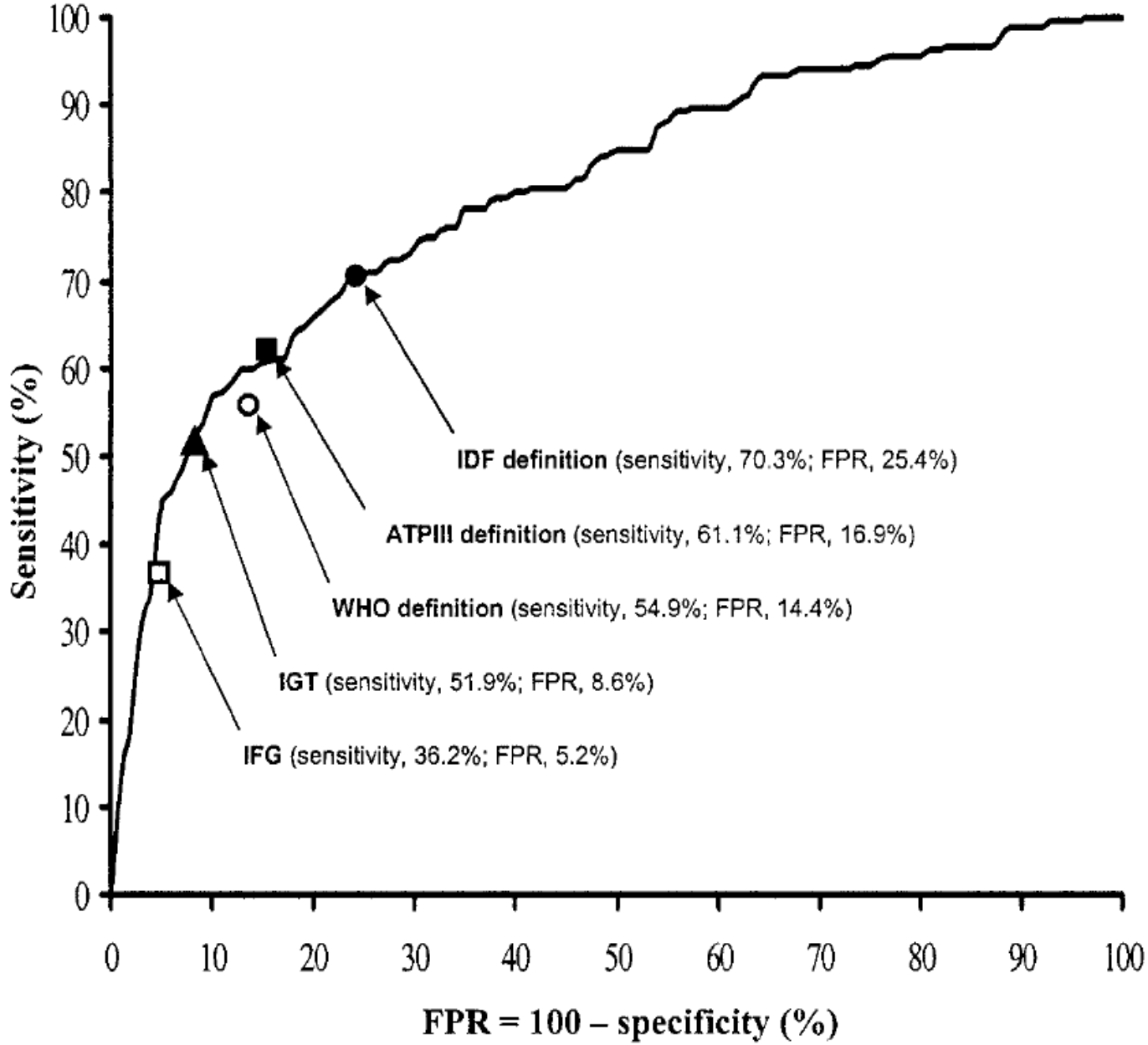
Lorenzo C et al., Diab Care 2007; 30: 8-13



Metabolisches Syndrom – IDF-Definition 2005

Country/Ethnic group		Waist circumference*
Europids *In the USA, the ATP III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes*	Male	≥ 94 cm
	Female	≥ 80 cm
South Asians *Based on a Chinese, Malay and Asian-Indian population*	Male	≥ 90 cm
	Female	≥ 80 cm
Chinese	Male	≥ 90 cm
	Female	≥ 80 cm
Japanese	Male	≥ 85 cm
	Female	≥ 90 cm
Ethnic South and Central Americans	*Use South Asian recommendations until more specific data are available*	
Sub-Saharan Africans	*Use European data until more specific data are available*	
Eastern Mediterranean and Middle East (Arab) populations	*Use European data until more specific data are available*	

* *In future epidemiological studies of populations of Europid origin, prevalence should be given using both European and North American cut-points to allow better comparisons.*

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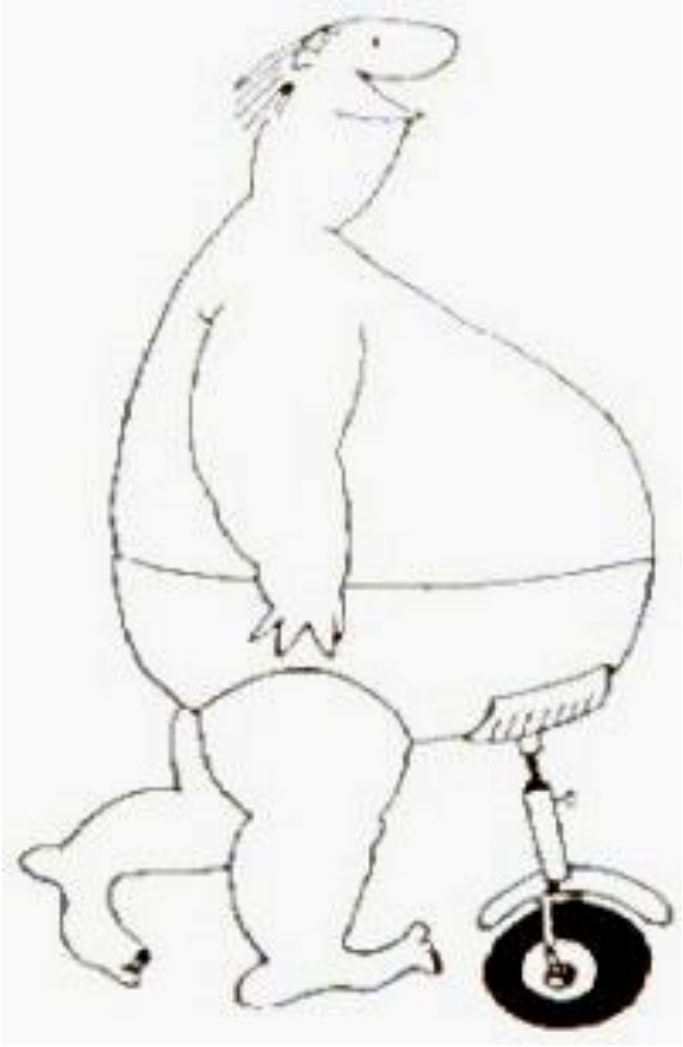
Messung des Bauchumfangs - Verfahrensanweisung



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Wieviele Patienten > 55 Jahre
in Ihrer Praxis haben ein
Metabolisches Syndrom nach IDF?

A: 12%

C: 37%

B: 25%

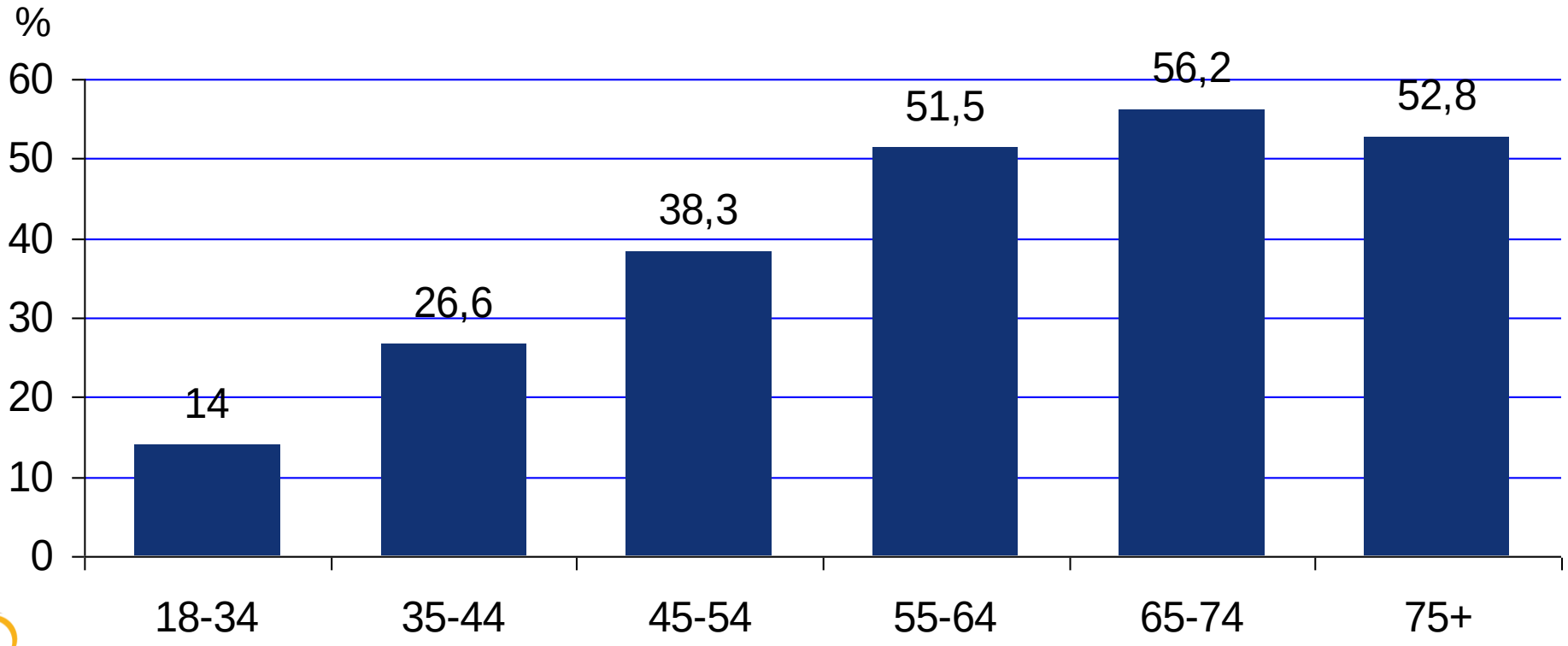
D: >50%

Prävalenz des Metabolischen Syndroms in Deutschland nach IDF-Kriterien

Stridde E et al., Abstract 330, 42. Jahrestagung der DDG, 2007

DETECT-Studie, 3188 Hausarztpraxen, Prävalenz des Typ 2-Diabetes 15%

15 345 Patienten ohne Typ 2-Diabetes, Metab. Syndrom nach IDF-Kriterien



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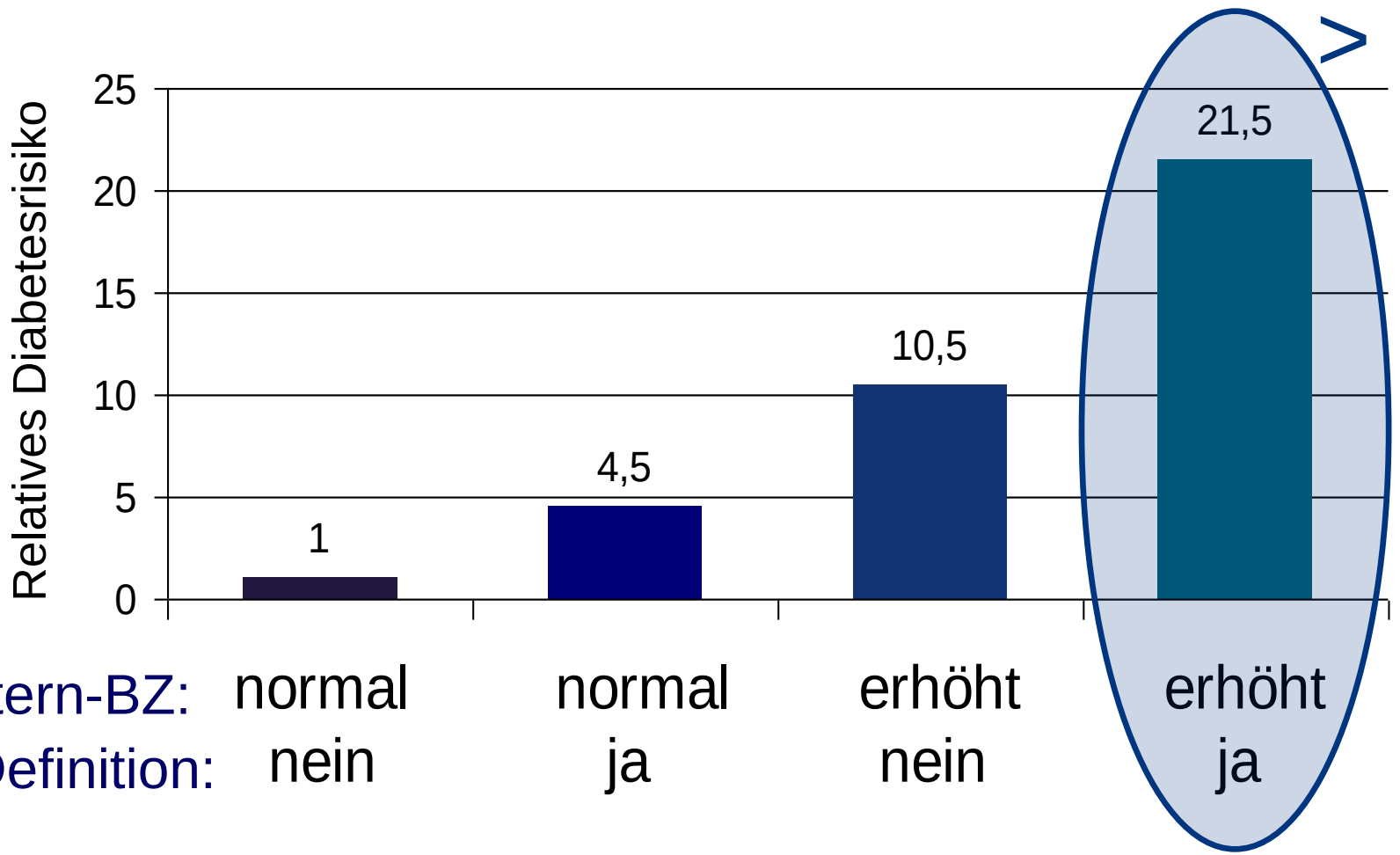
Diabetes-Risiko nach Nüchtern-Blutzucker und IDF-Definition des Metabolischen Syndroms

Lorenzo C et al., Diab Care 2007; 30: 8-13



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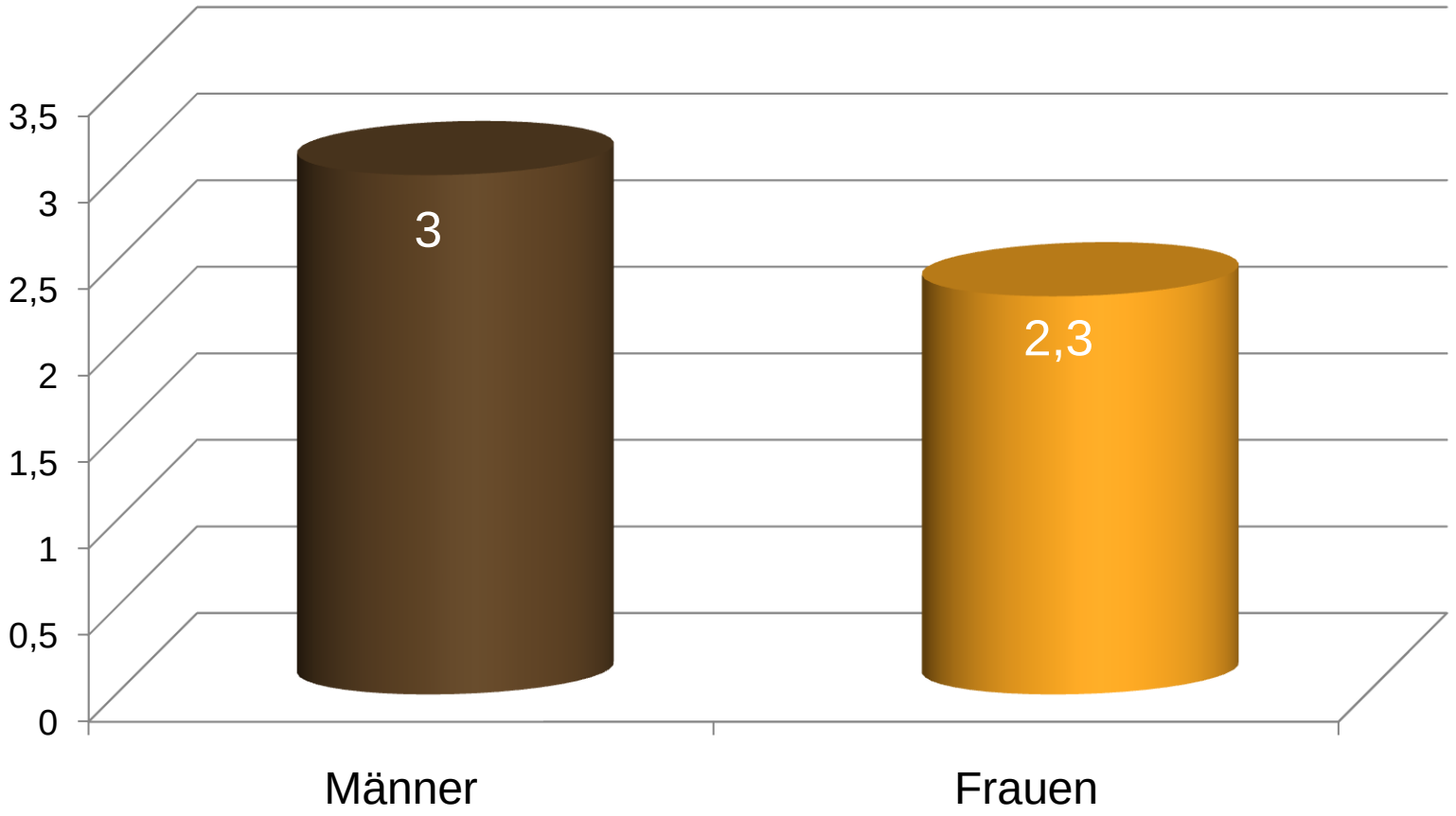
IDF-Definition 2010: Metabolisches Syndrom

International Diabetes Federation und AHA 2010

3 von 5 der folgenden Faktoren:

- Bauchumfang ≥ 94 cm Männer, ≥ 80 cm Frauen
- Triglyzeride ≥ 150 mg/dl
- HDL-Cholesterin < 40 mg/dl Männer, < 50 mg/dl Frauen
- Blutdruck ≥ 130 mm Hg syst. und/oder ≥ 85 mm Hg diast.
- Nüchtern-Blutzucker ≥ 100 mg/dl

Anteil von Untersuchten mit Typ 2-Diabetes bei Prevention First



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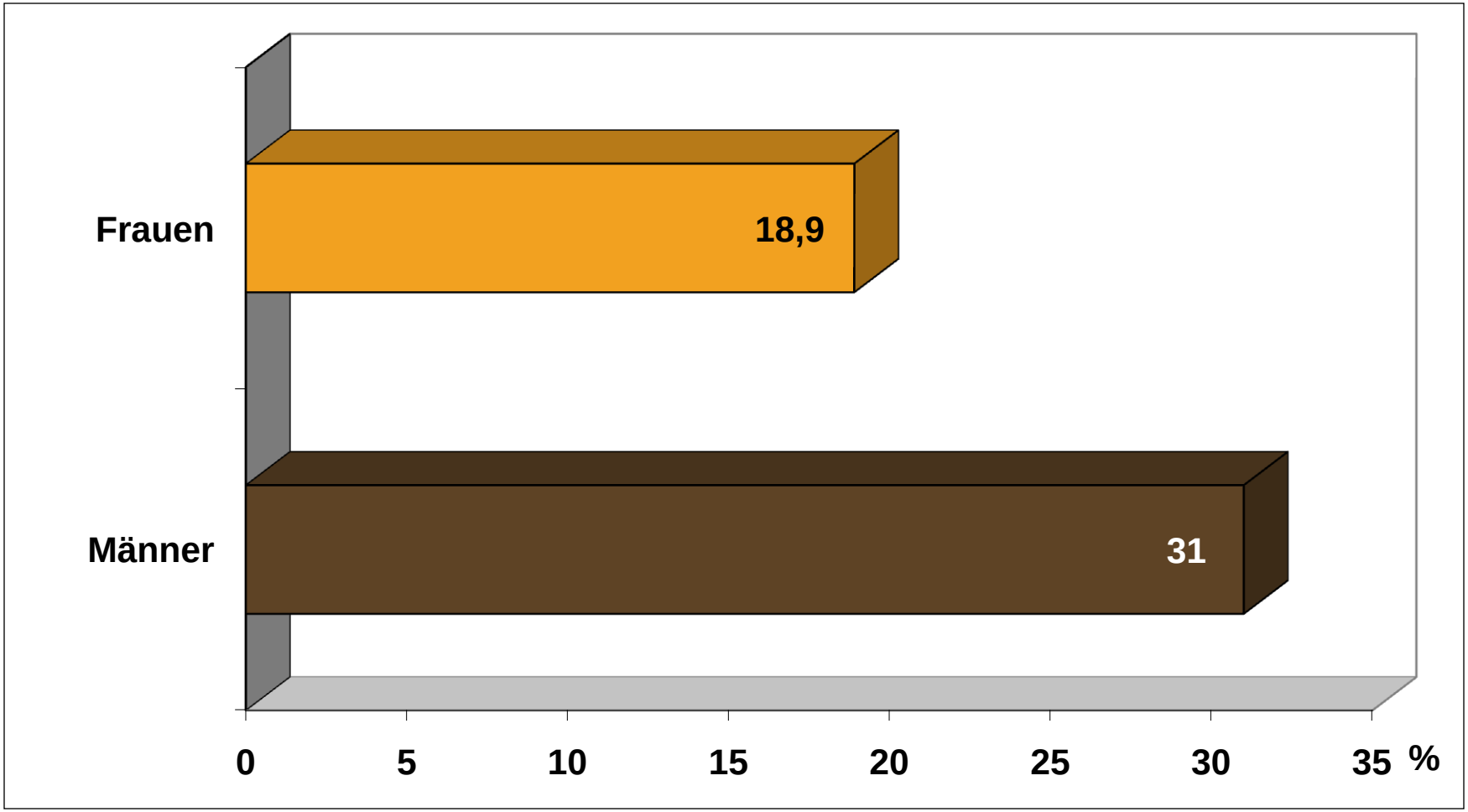
Prevention First: Häufigkeit des Metabolischen Syndroms (IDF 2010)
n=5780, mittleres Alter 46 Jahre



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Metaanalyse Metabolisches Syndrom und kardiovaskuläre Erkrankungen

Gami AS et al., J Am Coll Cardiol 2007;49:403–14)

37 Kohorten, 43 Studien, n = 172 573 Teilnehmer

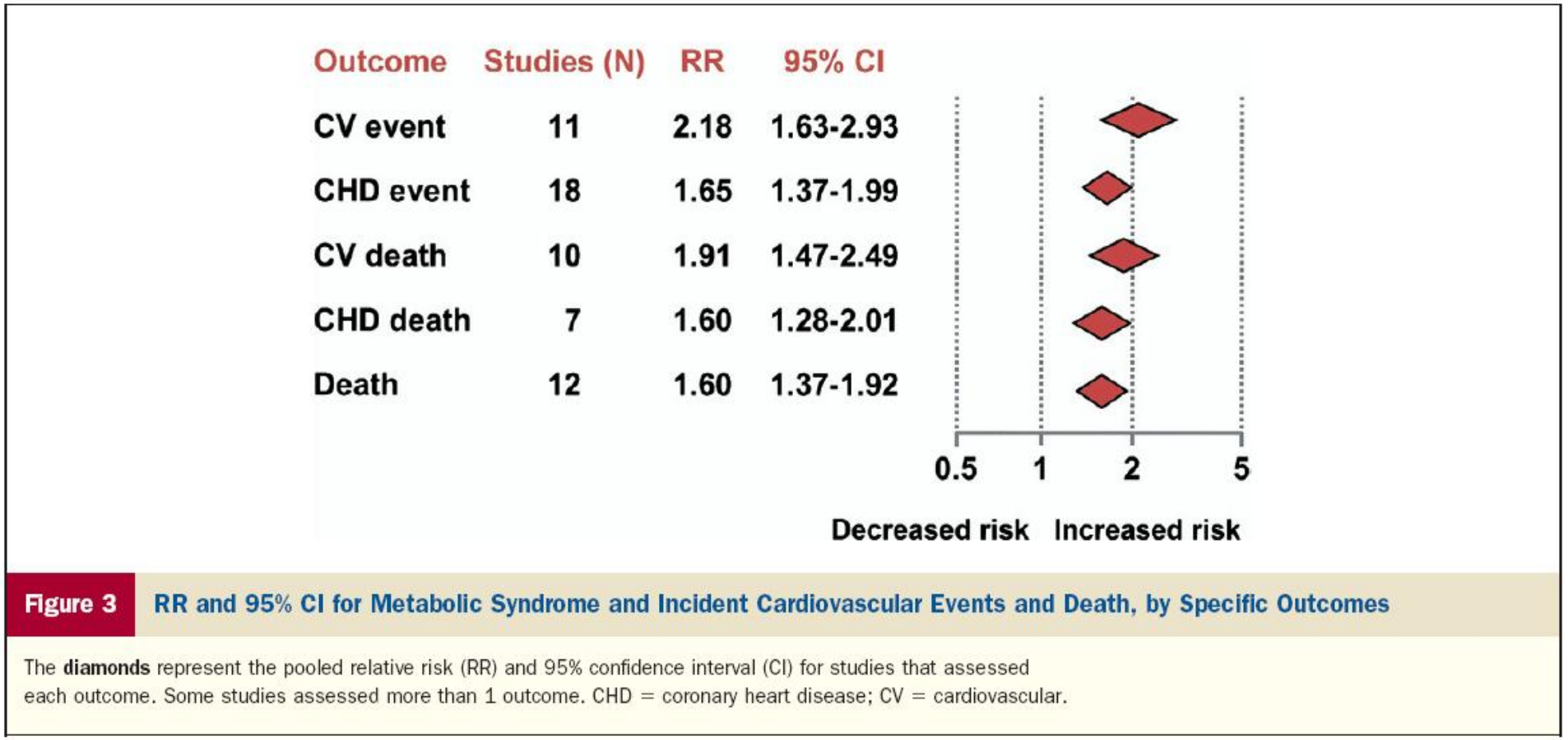
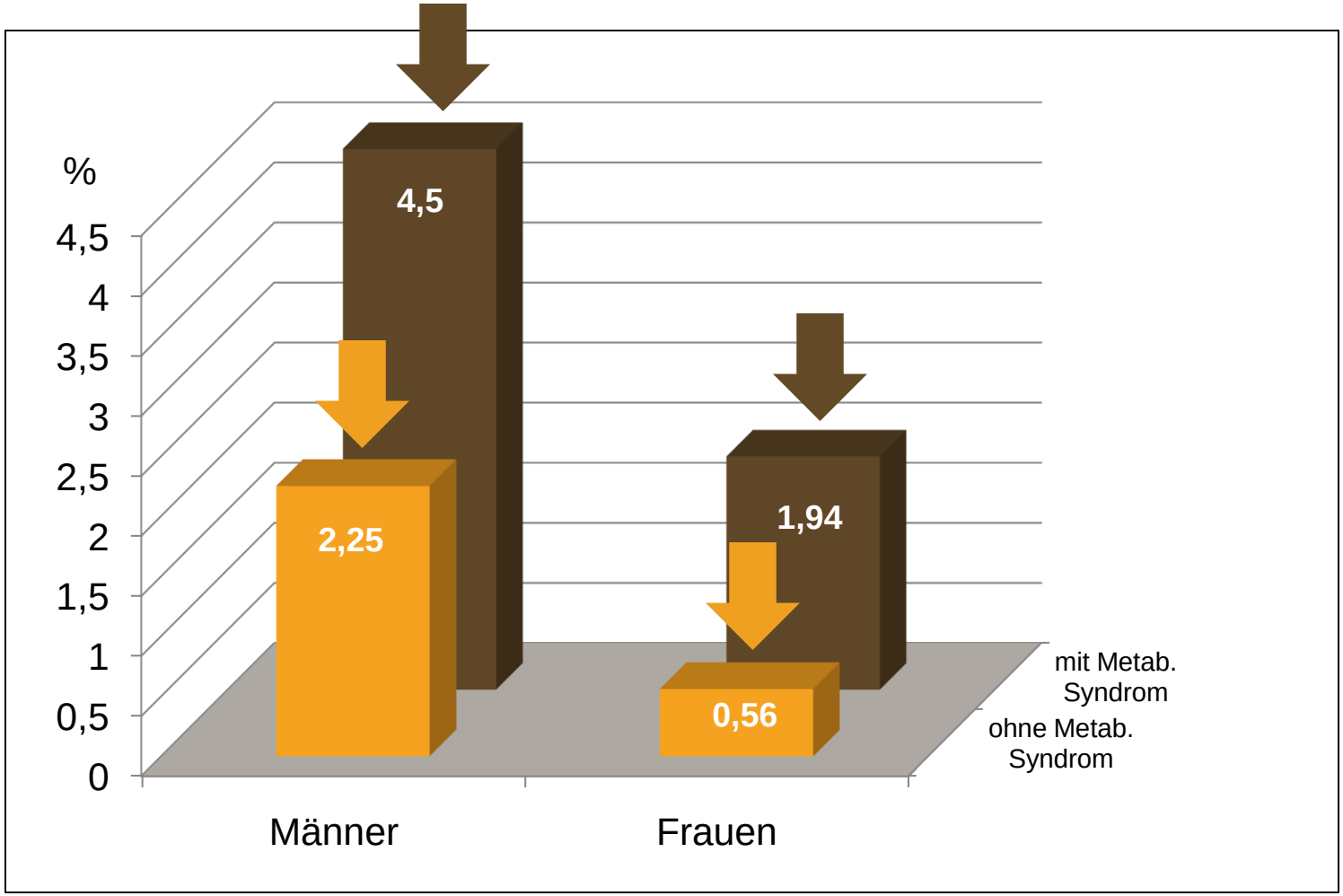


Figure 3 RR and 95% CI for Metabolic Syndrome and Incident Cardiovascular Events and Death, by Specific Outcomes

The **diamonds** represent the pooled relative risk (RR) and 95% confidence interval (CI) for studies that assessed each outcome. Some studies assessed more than 1 outcome. CHD = coronary heart disease; CV = cardiovascular.

Besonderheiten bei Metabolischem Syndrom: Erhöhtes 10-Jahres-Risiko für Herzinfarkt und Schlaganfall



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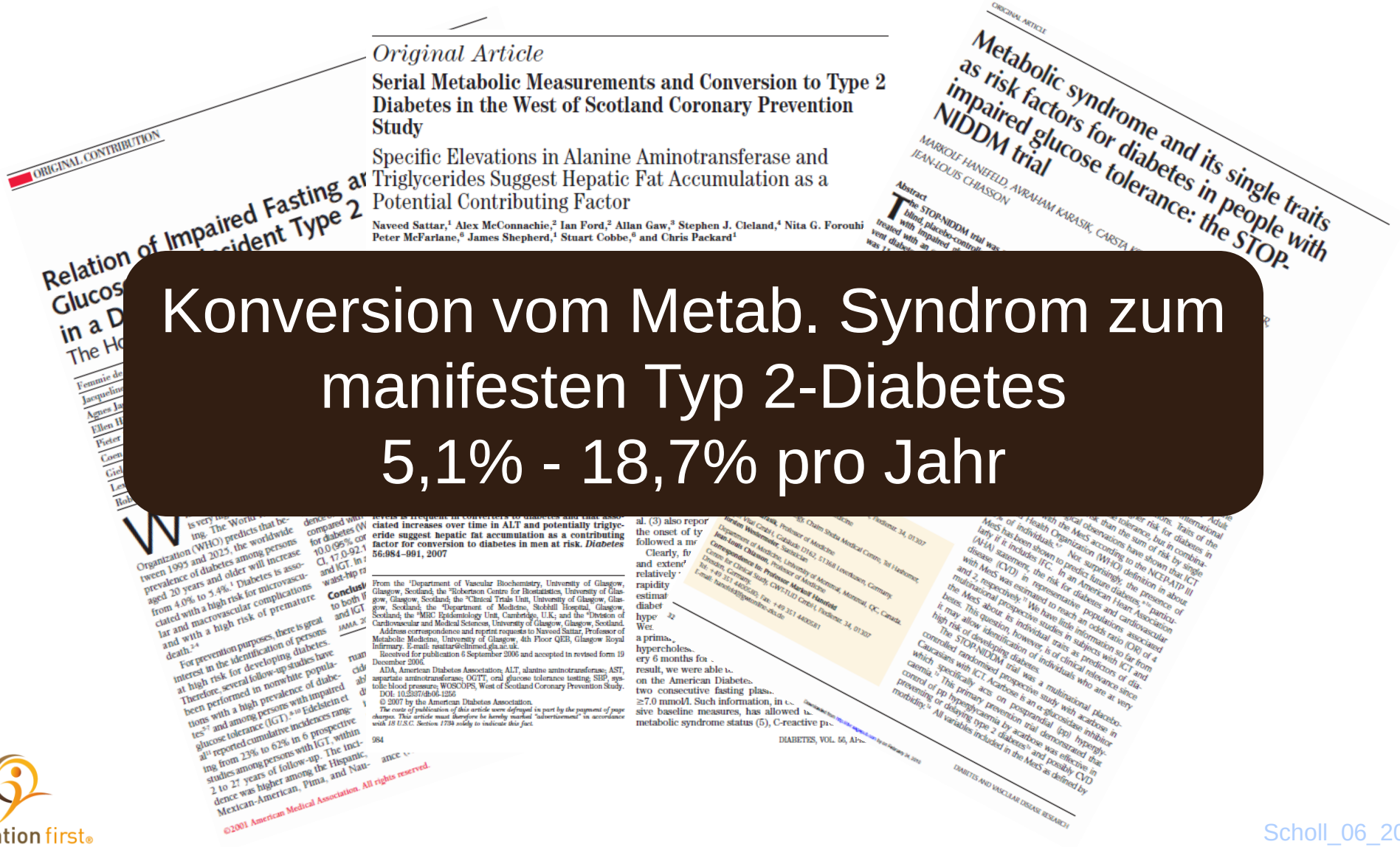
Prognose des Anteils von Typ 2-Diabetikern unter den untersuchten Männern und Frauen bis zum Jahr 2020



Konversion vom Metab. Syndrom zum manifesten Typ 2-Diabetes

5,1% - 18,7% pro Jahr

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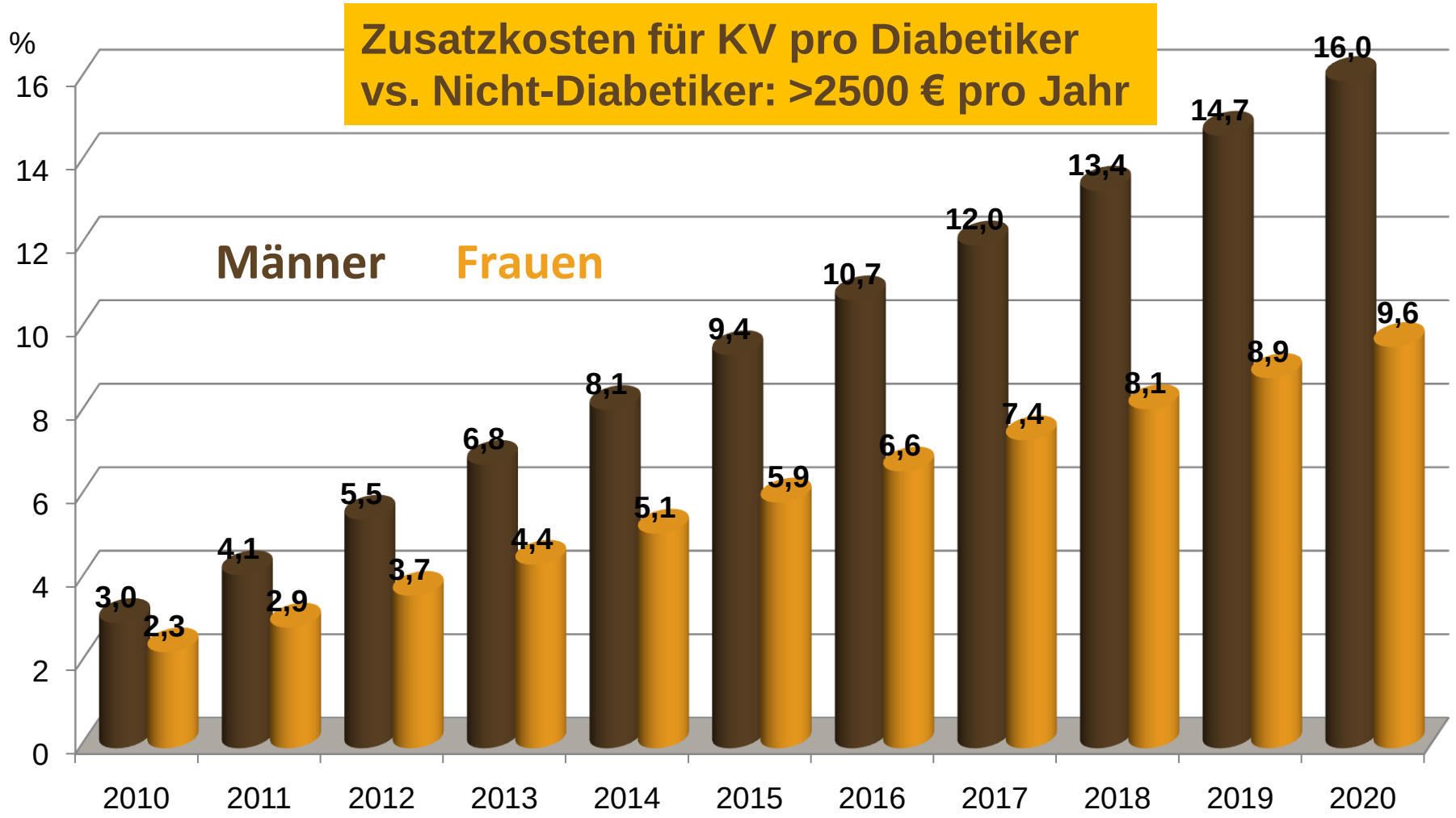
Prognose des Anteils von Typ 2-Diabetikern unter den untersuchten Männern und Frauen bis zum Jahr 2020



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Insulinresistenz, Metabolisches Syndrom und die Prävention des Typ 2-Diabetes

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4. Einfluss von Lebensstil-Faktoren: Ernährung und körperliche Aktivität
5. Medikamente in Prävention und Therapie

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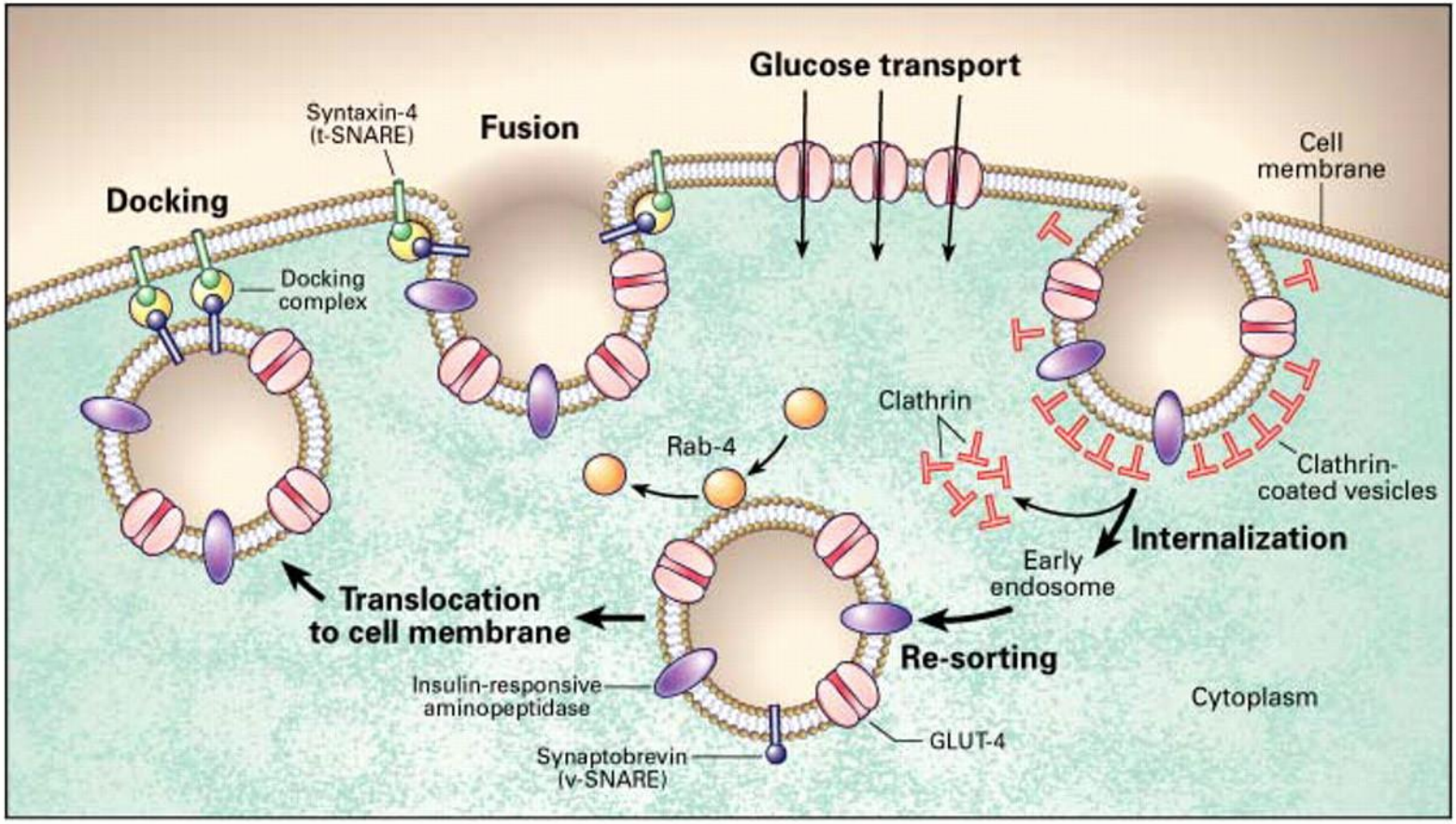
Pathophysiologie der Insulinresistenz



Shepherd, PR; Kahn, BB. N Engl J Med 1999; 341: 248-257

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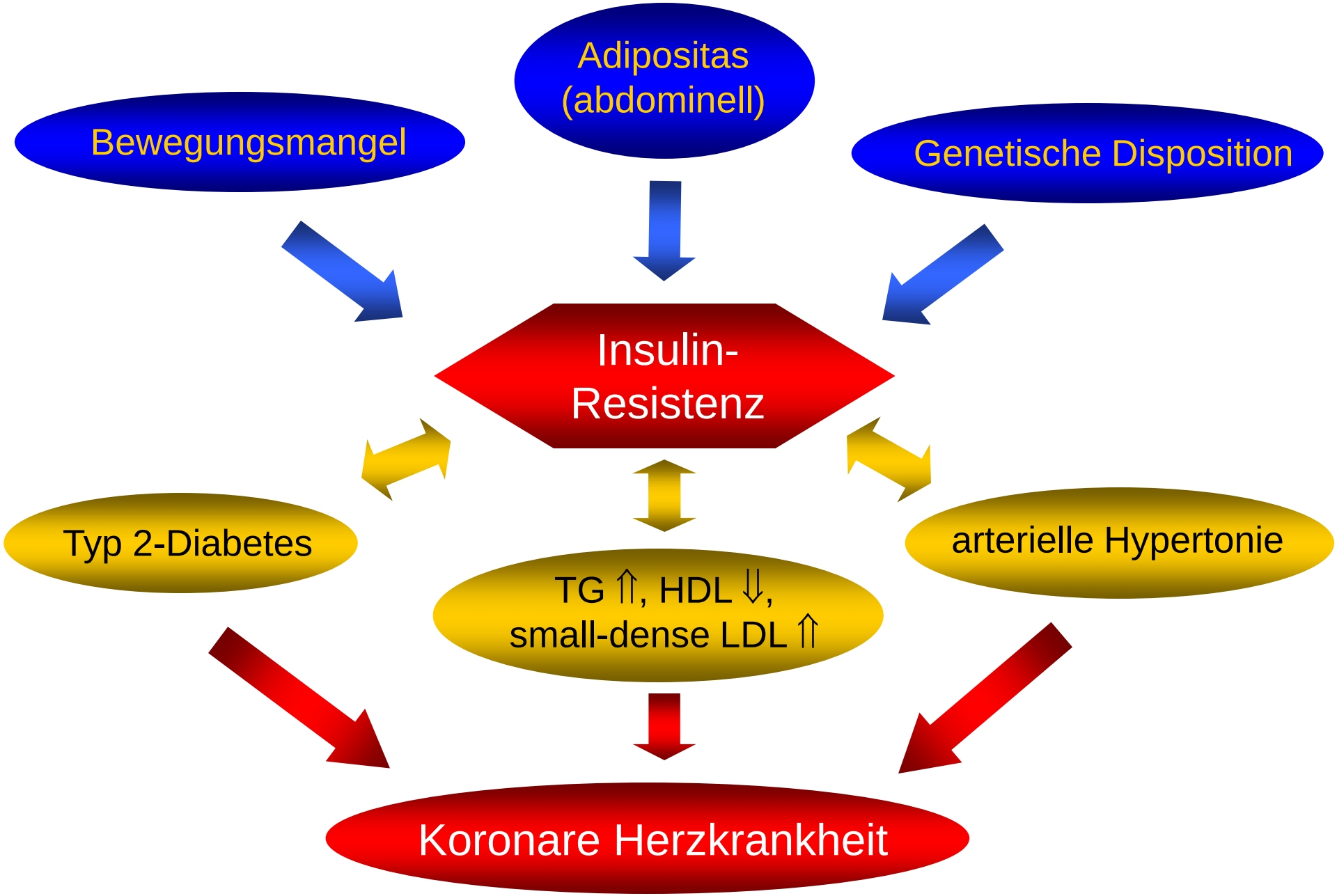
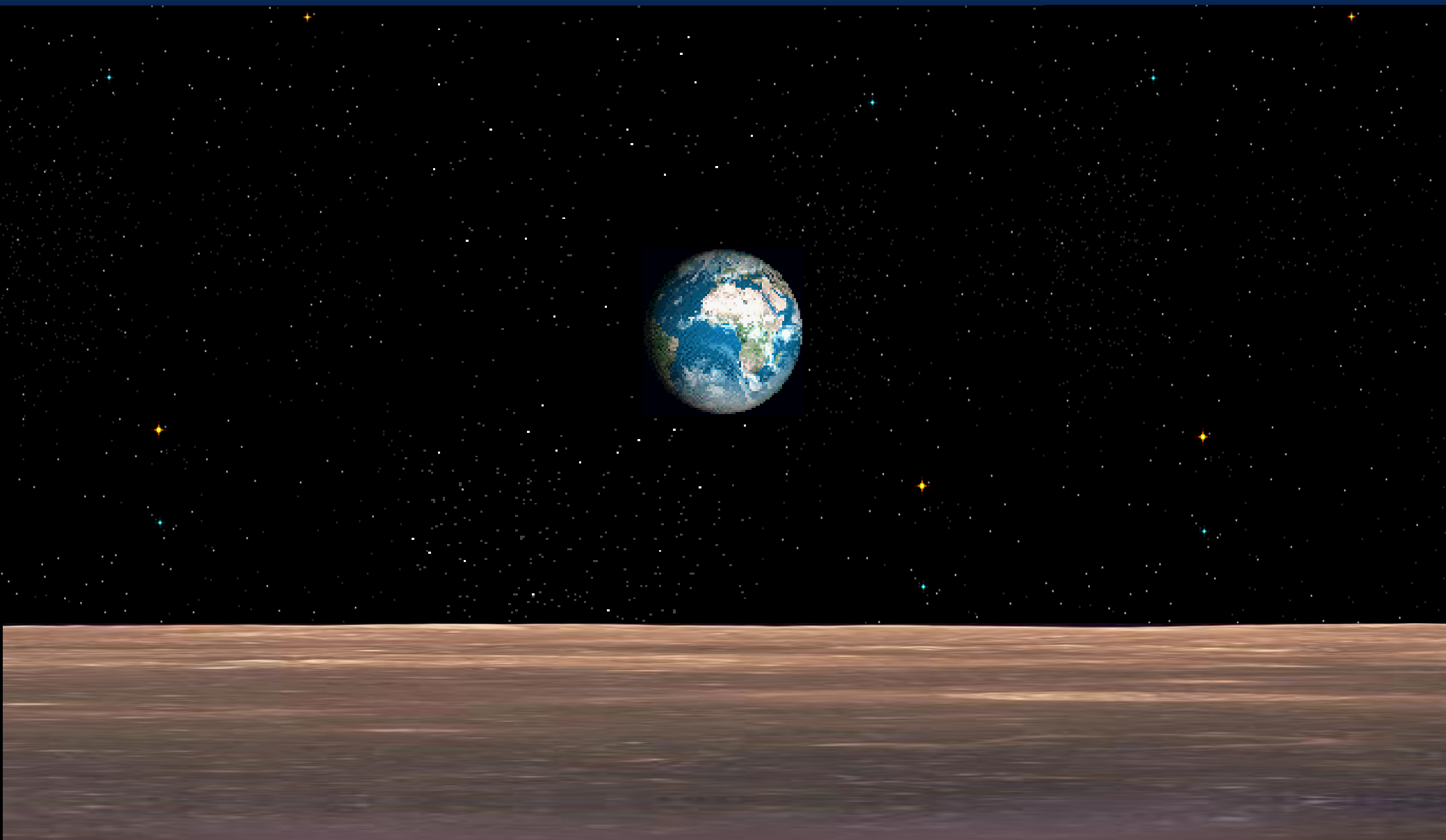
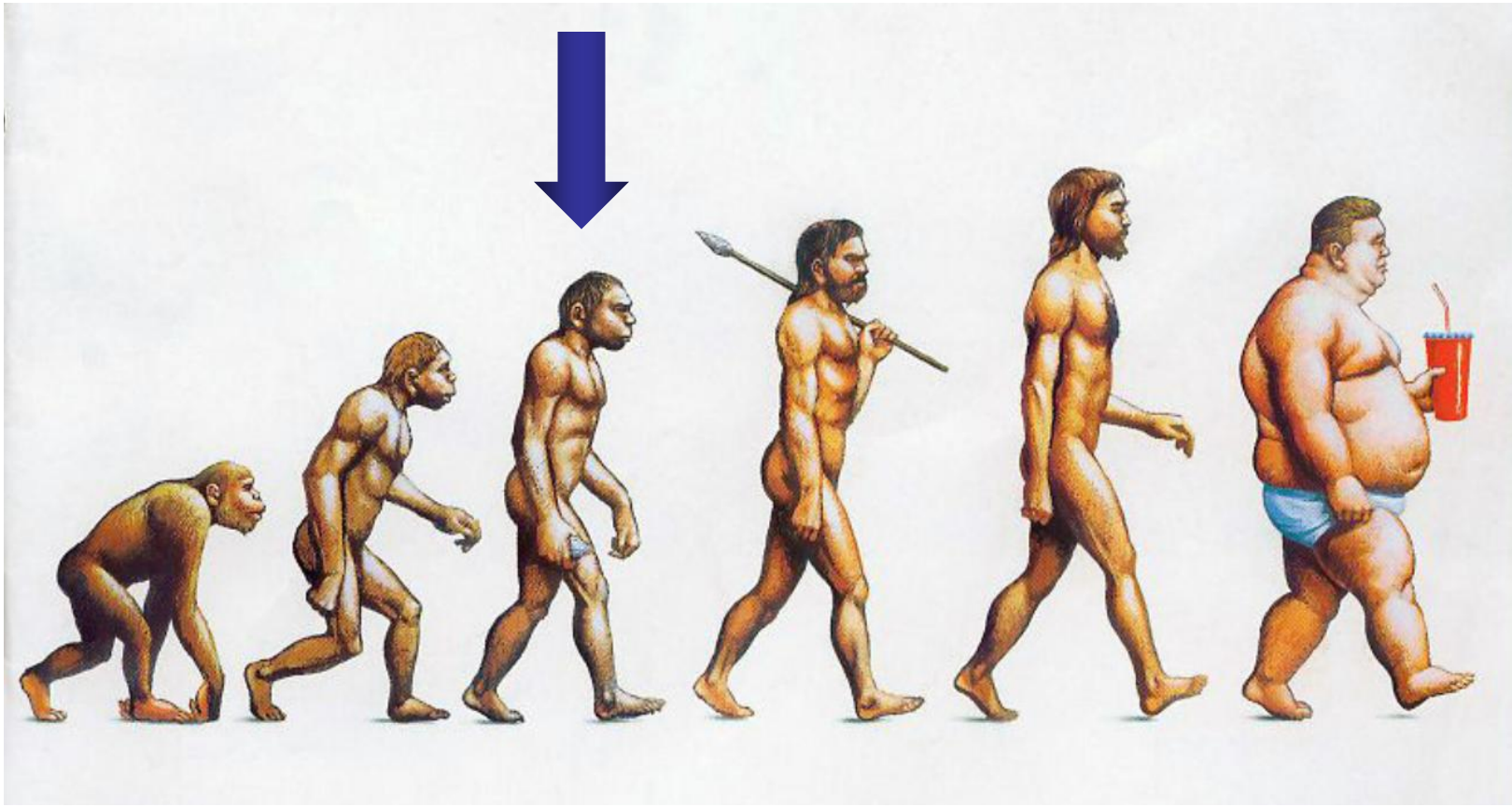

Adipositas (abdominell)
Bewegungsmangel
Genetische Disposition
Insulin-Resistenz
Typ 2-Diabetes
arterielle Hypertonie
TG ⇑, HDL ⇓, small-dense LDL ⇑
Koronare Herzkrankheit

Insulinresistenz: Die evolutionäre Perspektive



Woher stammen unsere Gene?



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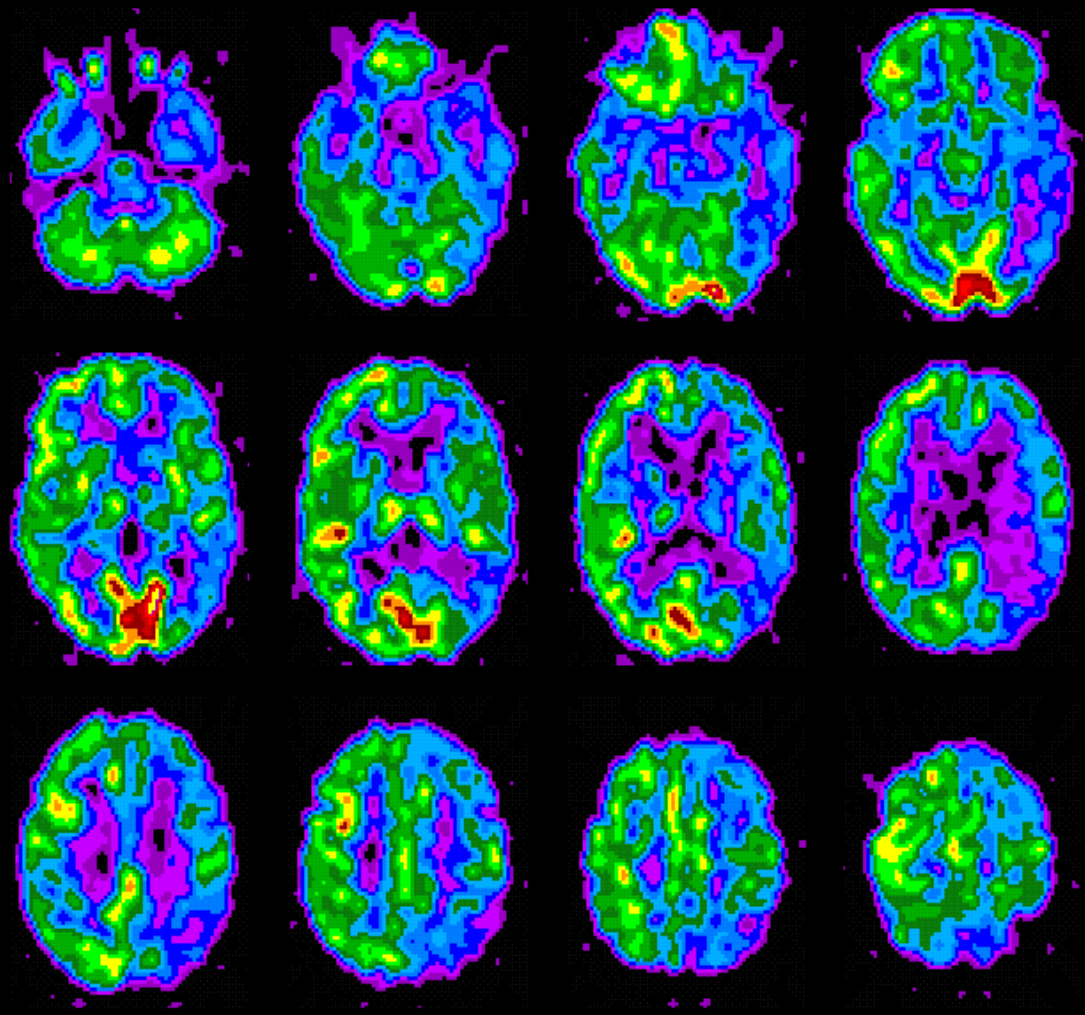
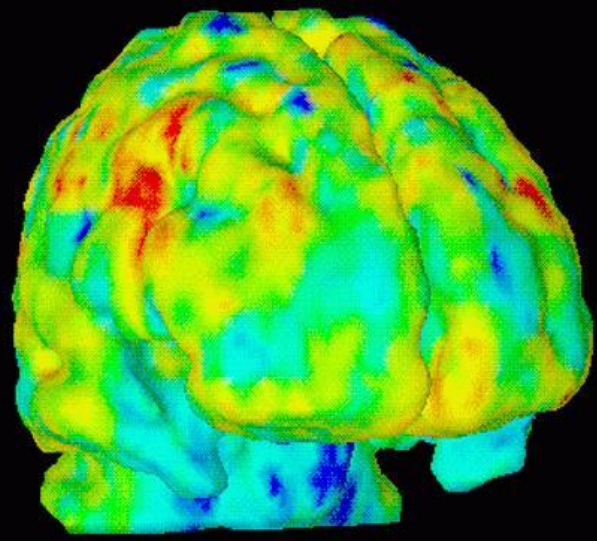
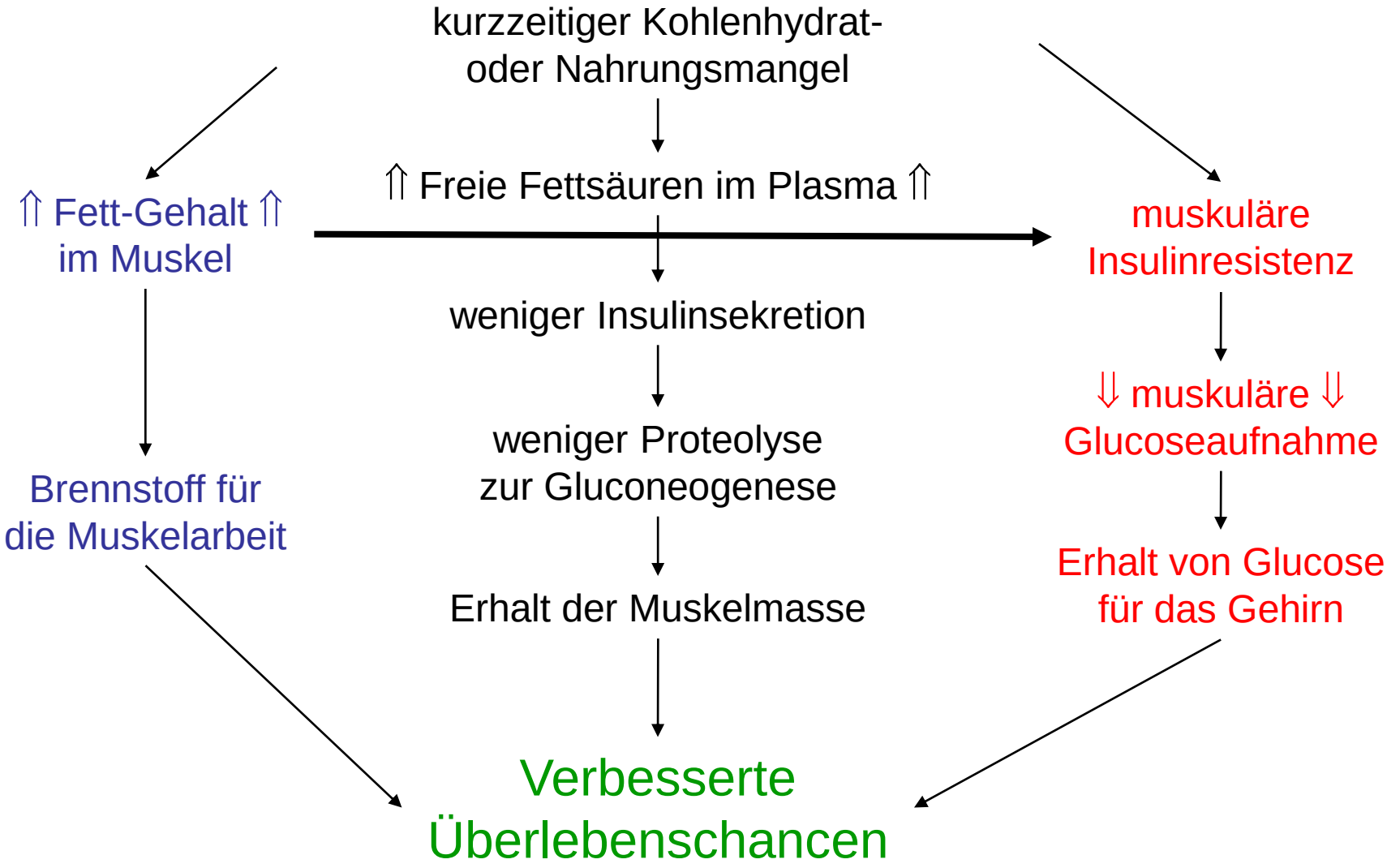
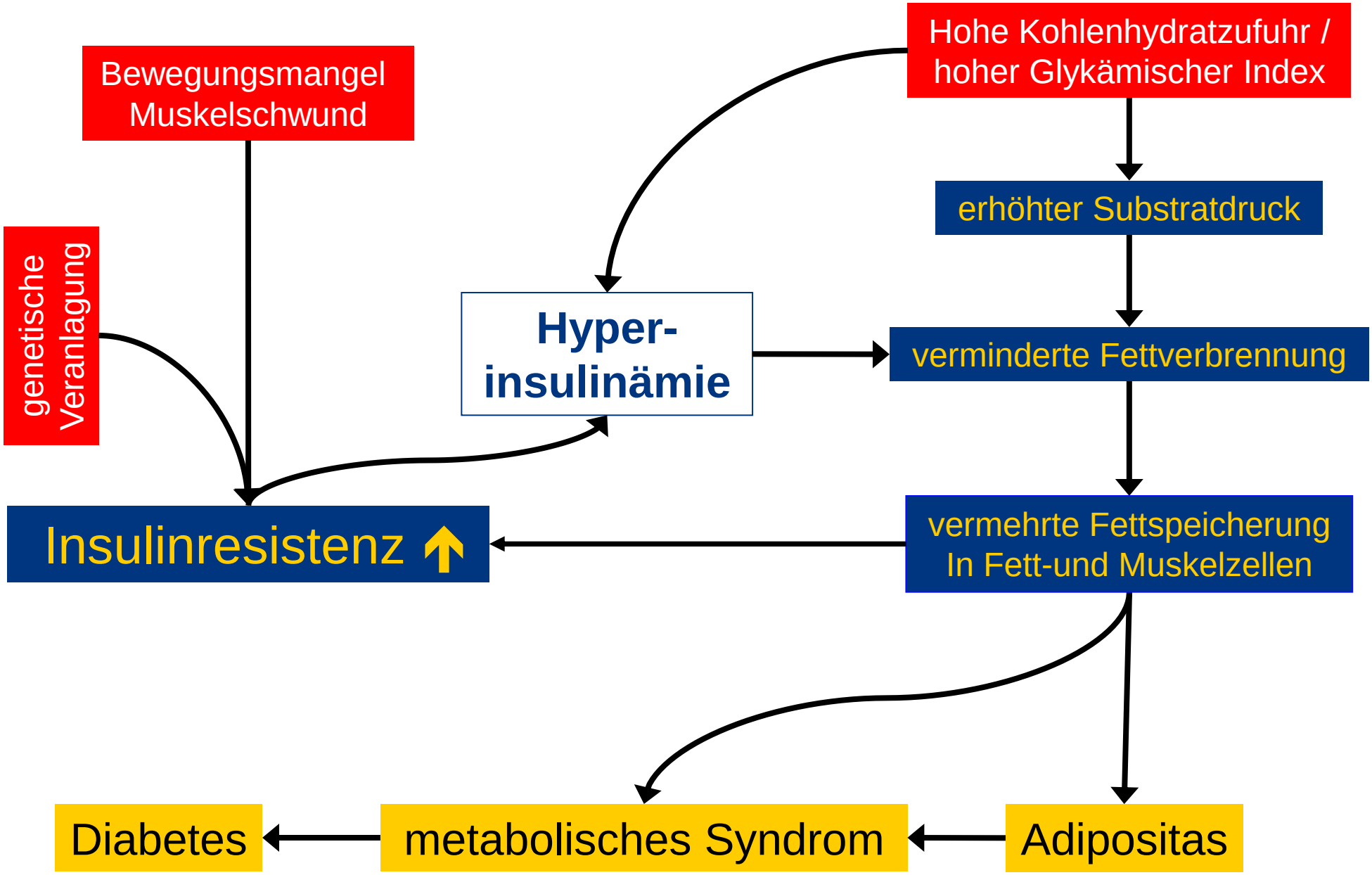




Überlebensvorteil Insulinresistenz ?

Stannard SR, Johnson NA, J Physiol 2003; 554.3: 595-607




Hohe Kohlenhydratzufuhr / hoher Glykämischer Index
Bewegungsmangel Muskelschwund
erhöhter Substratdruck
genetische Veranlagung
Hyper-insulinämie
verminderte Fettverbrennung
Insulinresistenz
vermehrte Fettspeicherung In Fett-und Muskelzellen
Diabetes
metabolisches Syndrom
Adipositas

Nahrungsspezifische Empfehlungen: DGE

Getreide, Getreideerzeugnisse:

- 4-6 Scheiben Brot
- 200-250 g Kartoffeln oder Nudeln oder Reis 150-180 g

Gemüse/ Salat:

Insgesamt 400 g und mehr

Obst:

2-3 Portionen und mehr

Milch und Milchprodukte (fettarme Produkte bevorzugen):

- Milch/ Joghurt 200-250 g
- Käse 50-60 g

Fette, Öle:

- Butter, Margarine: 15-30 g; Öl: 10-15 g

Fleisch, Wurst, Fisch, Ei: (pro Woche)

300-600 g Fleisch und Wurst, 2-3 Eier, 80-150 g fettarmer Fisch und 70 g fettreicher Fisch

Die Kohlenhydratfalle

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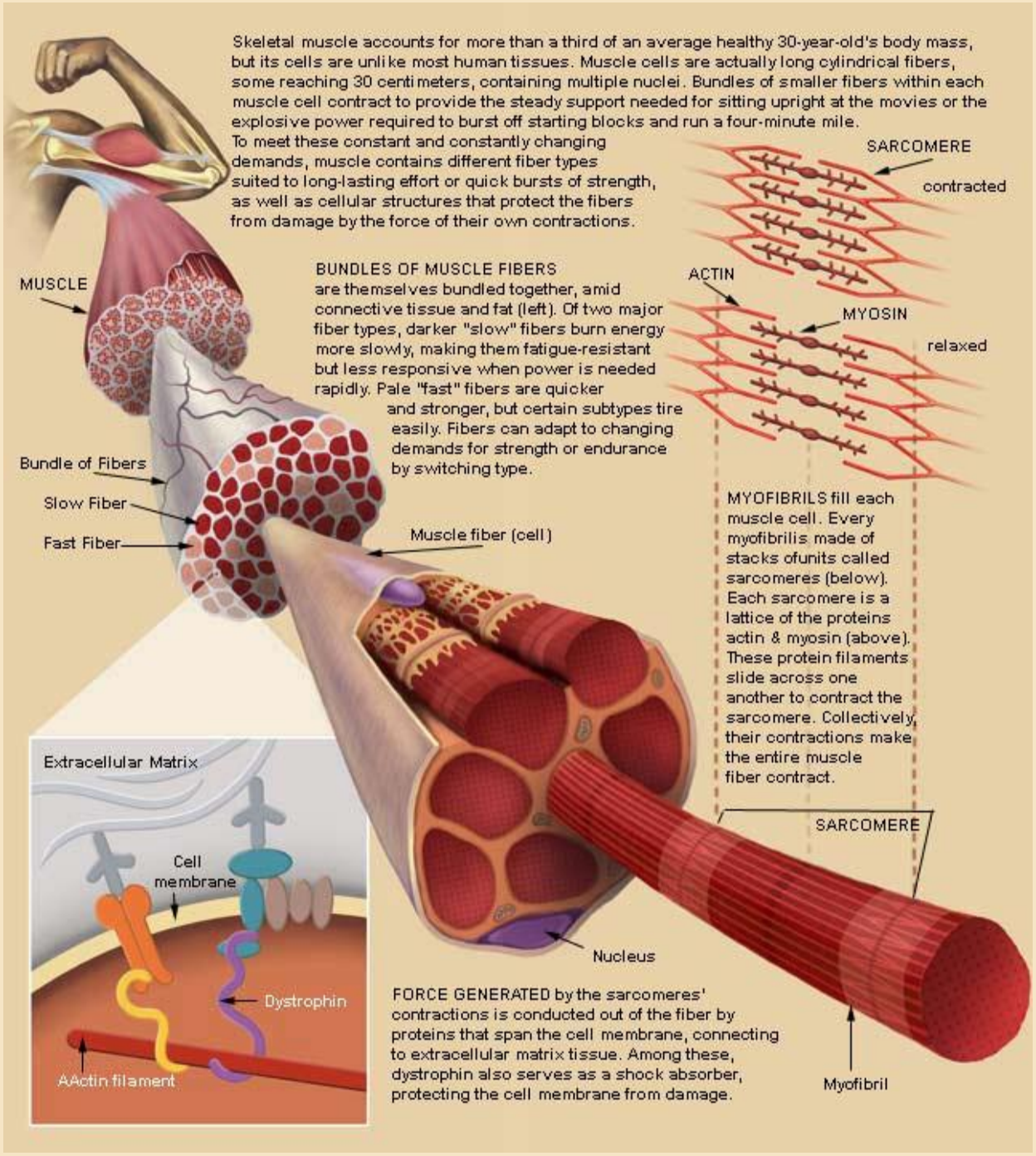

Skeletal muscle accounts for more than a third of an average healthy 30-year-old's body mass, but its cells are unlike most human tissues. Muscle cells are actually long cylindrical fibers, some reaching 30 centimeters, containing multiple nuclei. Bundles of smaller fibers within each muscle cell contract to provide the steady support needed for sitting upright at the movies or the explosive power required to burst off starting blocks and run a four-minute mile.
To meet these constant and constantly changing demands, muscle contains different fiber types suited to long-lasting effort or quick bursts of strength, as well as cellular structures that protect the fibers from damage by the force of their own contractions.
SARCOMERE
contracted
ACTIN
MYOSIN
relaxed
MUSCLE
BUNDLES OF MUSCLE FIBERS are themselves bundled together, amid connective tissue and fat (left). Of two major fiber types, darker "slow" fibers burn energy more slowly, making them fatigue-resistant but less responsive when power is needed rapidly. Pale "fast" fibers are quicker and stronger, but certain subtypes tire easily. Fibers can adapt to changing demands for strength or endurance by switching type.
Bundle of Fibers
Slow Fiber
Fast Fiber
Muscle fiber (cell)
MYOFIBRILS fill each muscle cell. Every myofibrilis made of stacks ofunits called sarcomeres (below). Each sarcomere is a lattice of the proteins actin & myosin (above). These protein filaments slide across one another to contract the sarcomere. Collectively, their contractions make the entire muscle fiber contract.
SARCOMERE
Extracellular Matrix
Cell membrane
Dystrophin
AActin filament
Nucleus
FORCE GENERATED by the sarcomeres' contractions is conducted out of the fiber by proteins that span the cell membrane, connecting to extracellular matrix tissue. Among these, dystrophin also serves as a shock absorber, protecting the cell membrane from damage.
Myofibril

Petersen KF et al., PNAS 2007; 104: 12587-12594

PNAS

INAUGURAL ARTICLE

The role of skeletal muscle insulin resistance in the pathogenesis of the metabolic syndrome

Kitt Falk Petersen*, Sylvie Dufour†, David B. Savage*, Stefan Bilz*, Gina Solomon*, Shin Yonemitsu*, Gary W. Cline*, Douglas Befroy*, Laura Zemany‡, Barbara B. Kahn‡, Xenophon Papademetris§, Douglas L. Rothman§, and Gerald I. Shulman*†§¶‖

Departments of *Internal Medicine; §Diagnostic Radiology and Biomedical Engineering; ¶Cellular and Molecular Physiology, and †Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, CT 06536; and ‡Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215

This contribution is part of the special series of Inaugural Articles by members of the National Academy of Sciences elected on May 1, 2007.

Contributed by Gerald I. Shulman, June 8, 2007 (sent for review May 25, 2007)

Die Rolle der muskulären Insulinresistenz in der Pathogenese des Metabolischen Syndroms

Petersen KF et al., PNAS 2007; 104: 12587-12594

- Studientyp: experimentelle Ernährungs-Interventionsstudie
- Rekrutierung der Probanden: ~ 400 x OGTT + Insulin bei schlanken Nichtsportlern
- Studienteilnehmer:
  - 12 Probanden mit Insulinresistenz (ISI in unterster Quartile)
  - 12 insulinsensitive Probanden (ISI in oberster Quartile)
- Intervention:
  - zwei kohlenhydratreiche Mahlzeiten um 10 Uhr und 14:30 Uhr
- Untersuchungen:
  - ^{1}H Magnetresonanzspektroskopie (Triglyceridsynthese in Muskel und Leber)
  - 13C Magnetresonanzspektroskopie (Glykogensynthese in Muskel und Leber)
  - Deuterium-Inkorporation in Plasma-TG (hepatische *de novo*-Lipogenese)

Die Rolle der muskulären Insulinresistenz in der Pathogenese des Metabolischen Syndroms

Petersen KF et al., PNAS 2007; 104: 12587-12594

Table 3. Fasting plasma adipocytokine concentrations

	HMW adiponectin, μg/ml	IL-6, pg/ml	Resistin, ng/ml	TNF-α, pg/ml	PAI-1, ng/ml	RBP-4, μg/ml	TTR, μg/ml
Insulin-sensitive	5.8 ± 2.5	0.91 ± 0.20	11.0 ± 1.1	1.49 ± 0.12	13.8 ± 3.9	29.5 ± 3.3	134 ± 8
Insulin-resistant	3.5 ± 0.7	1.31 ± 0.23	12.5 ± 0.9	1.49 ± 0.17	13.2 ± 2.5	28.1 ± 3.1	149 ± 11
P value	NS	NS	NS	NS	NS	NS	NS

PAI-1, plasminogen activator inhibitor-1; TTR, transthyretin; NS, not significant.

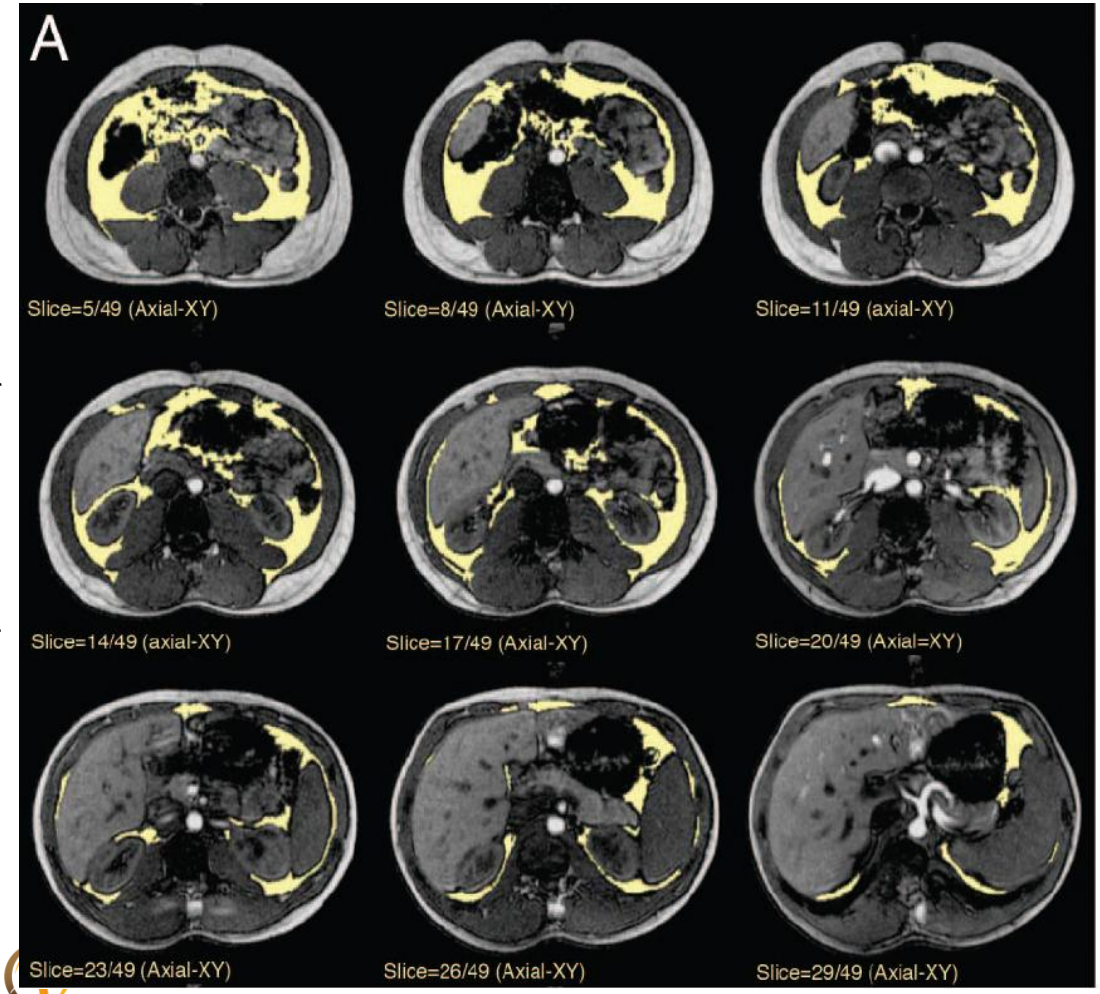
diastolic blood pressure; NS, not significant.

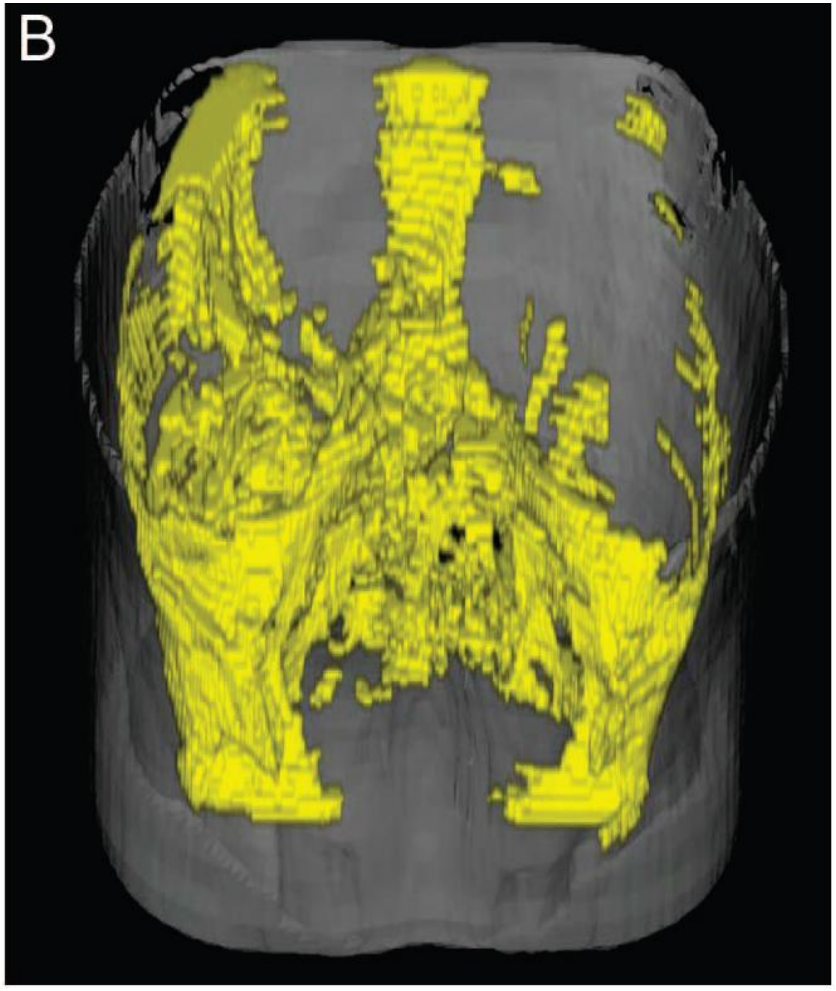
Table 2. Fasting plasma metabolite and hormone concentrations

	Glucose, mg/dl	Insulin, microunits/ml	Triglyceride, mg/dl	Total cholesterol, mg/dl	LDL, mg/dl	HDL, mg/dl	VLDL SP, nmol/liter	LDL LP, nmol/liter	Uric acid, mg/dl	CRP, mg/liter
Insulin-sensitive	84.1 ± 1.7	7.6 ± 0.6	53 ± 7	182 ± 12	93 ± 9	78 ± 5	38.6 ± 4.0	446.4 ± 34.2	3.9 ± 0.3	0.47 ± 0.16
Insulin-resistant	90.6 ± 1.5	12.1 ± 1.2	86 ± 13	157 ± 5	77 ± 6	62 ± 3	23.8 ± 2.9	311.9 ± 46.0	5.2 ± 0.5	1.02 ± 0.24
P value	0.009	0.003	0.03	NS	NS	0.01	0.007	0.03	0.04	0.07

SP, small particles; LP, large particles; CRP, C-reactive protein; NS, not significant.

Messung des intraabdominellen Fettgehaltes im NMR





Petersen KF et al., PNAS 2007; 104: 12587-12594

Petersen KF et al., PNAS 2007; 104: 12587-12594

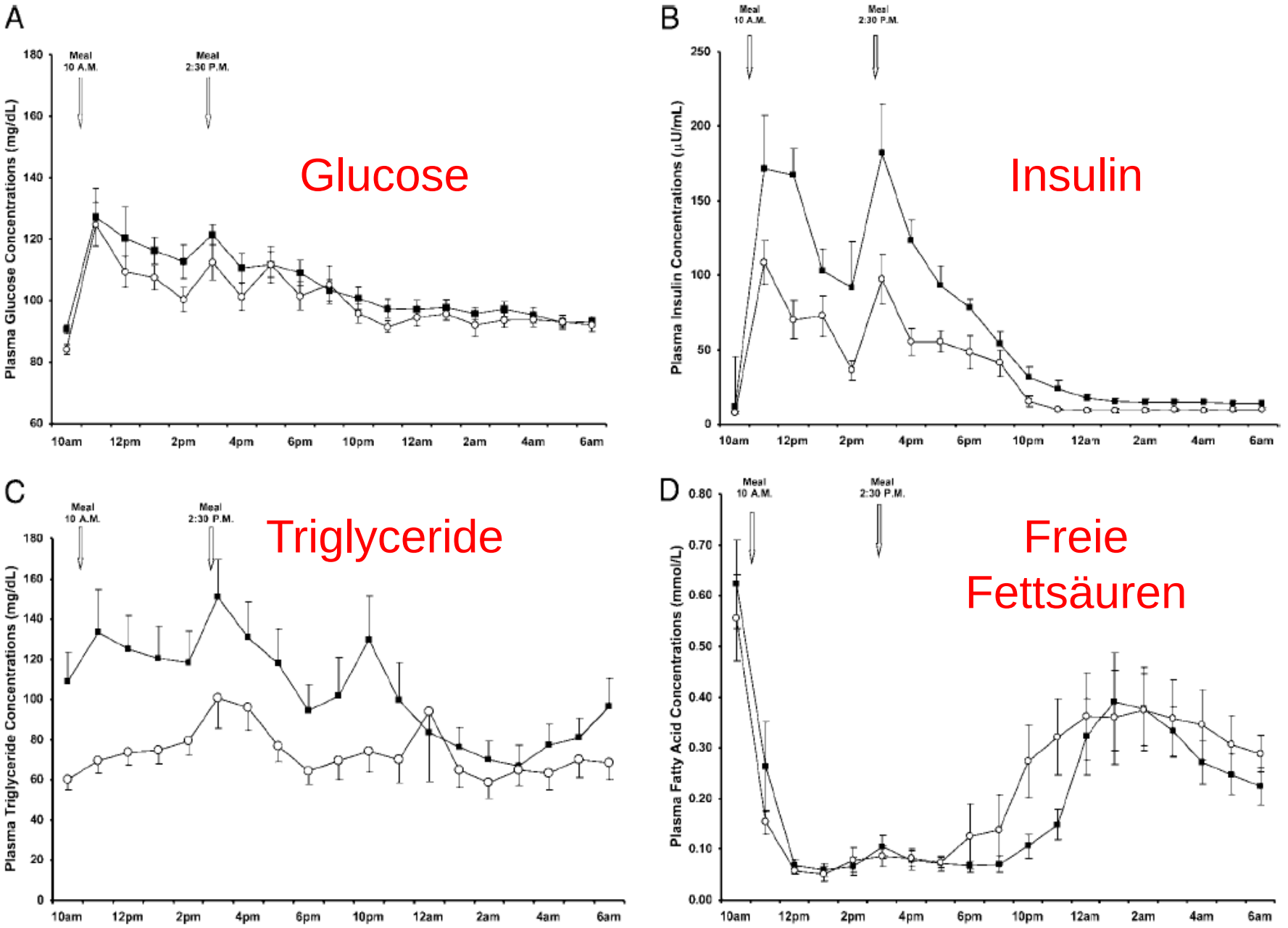
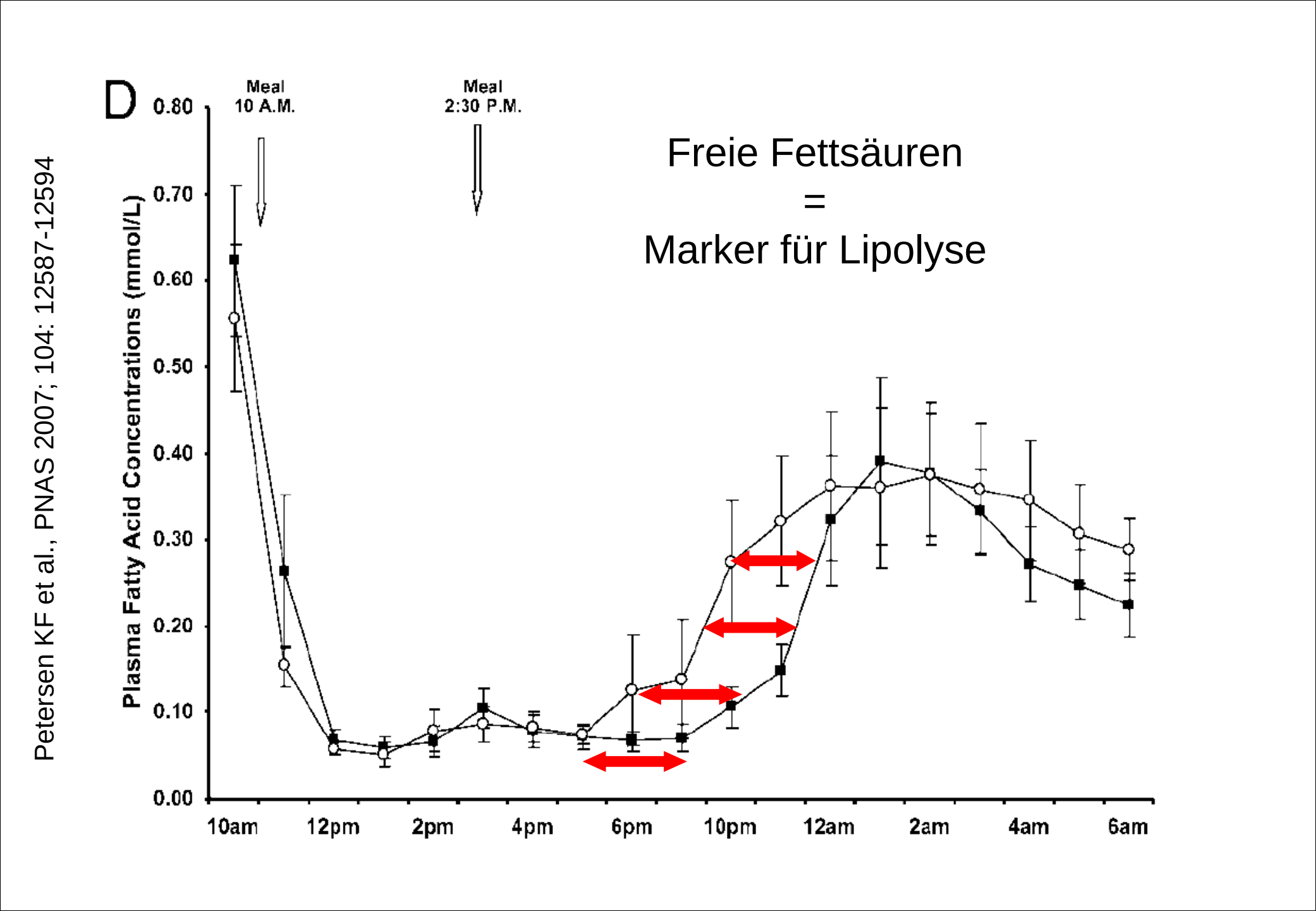


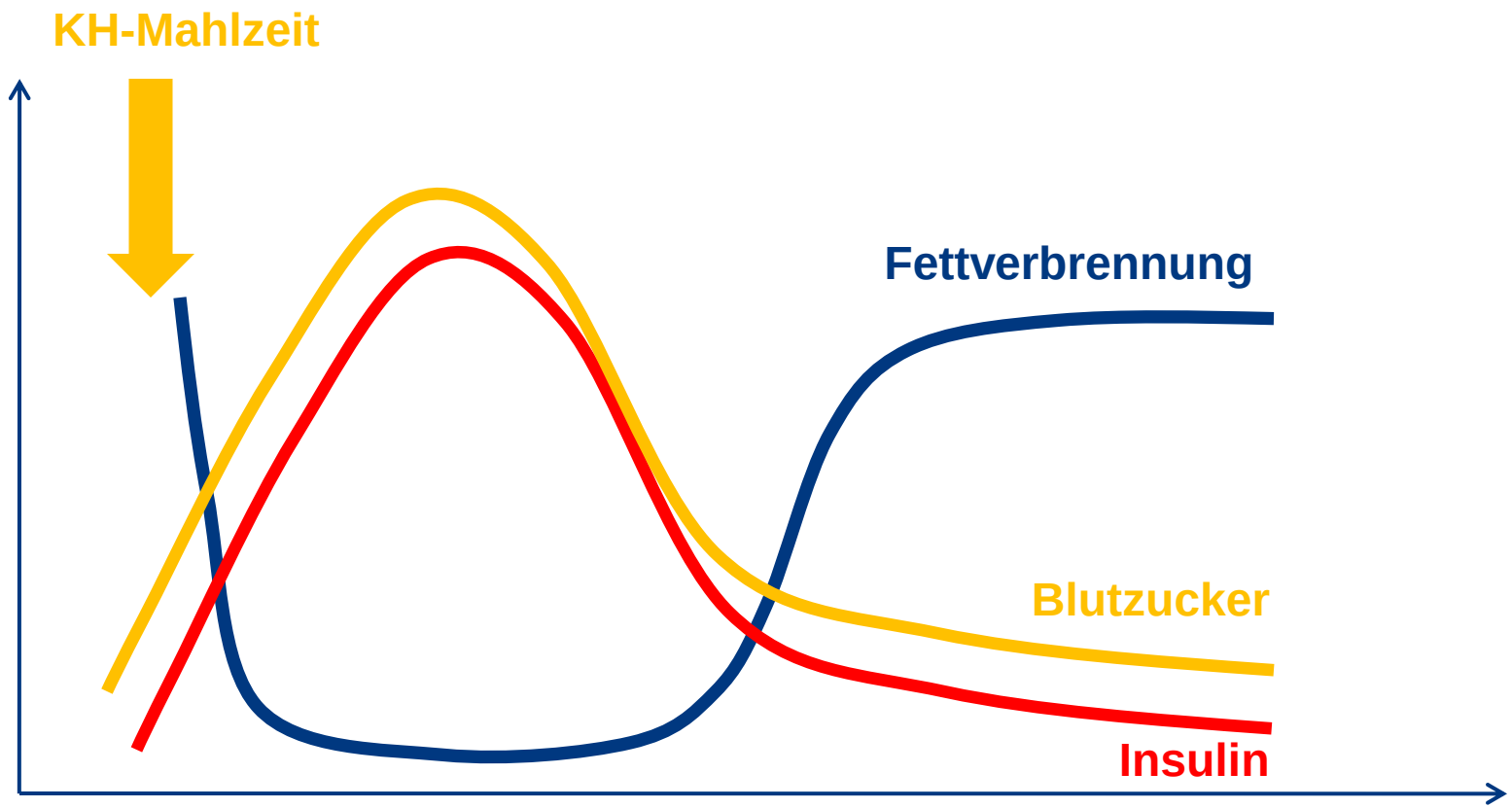
Fig. 1. Plasma concentrations of glucose (*A*), insulin (*B*), triglyceride (*C*), and fatty acids (*D*) in insulin-sensitive (○) and insulin-resistant (■) participants before and after the mixed meals.



Petersen KF et al., PNAS 2007; 104: 12587-12594

Kohlenhydratmahlzeiten belasten die Bauchspeicheldrüse und hemmen den Fettabbau

Petersen KF et al., PNAS 2007; 104: 12587-12594



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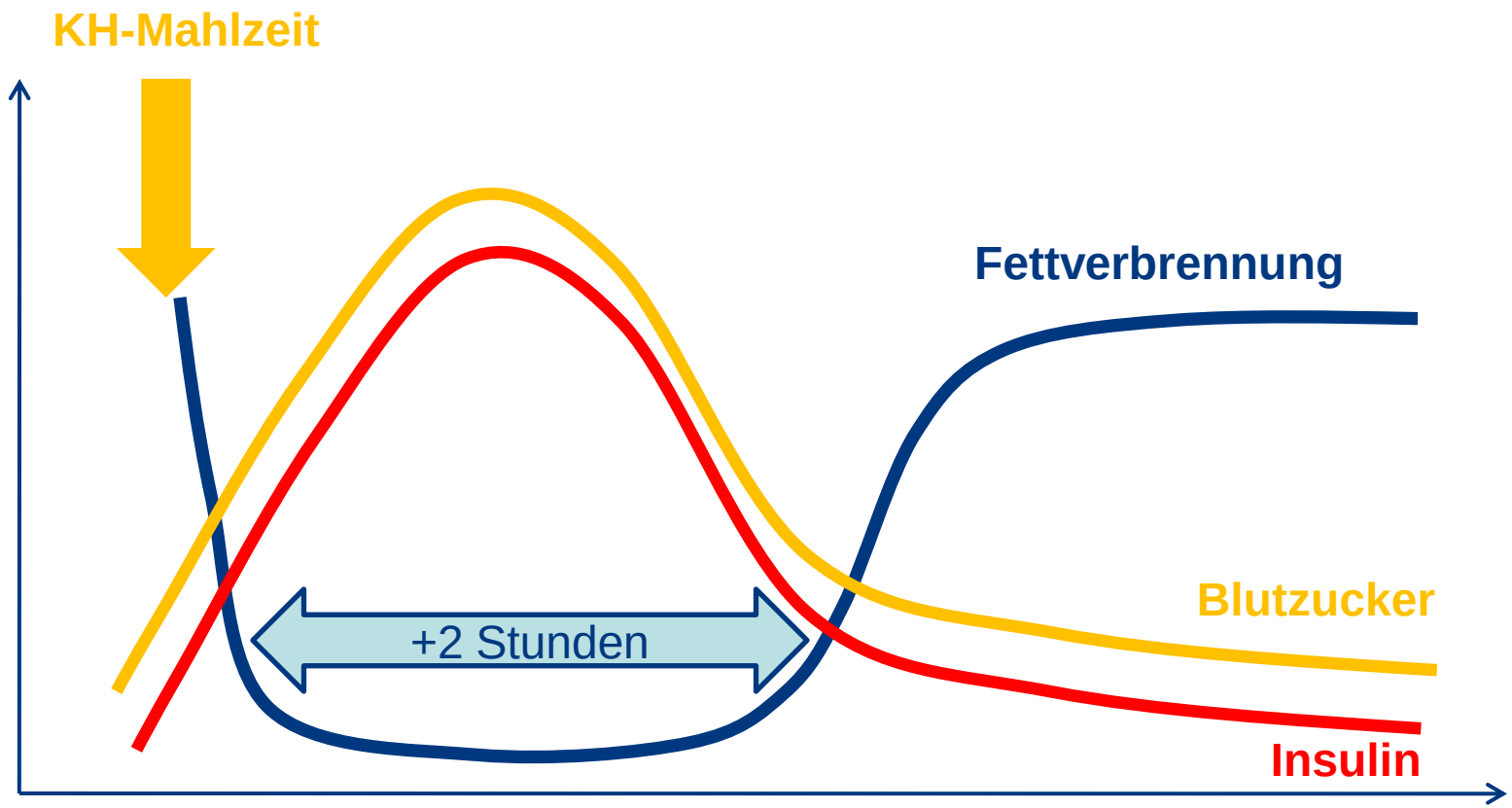
Kohlenhydratmahlzeiten hemmen den Fettabbau

besonders lange bei Menschen mit Veranlagung zum Typ 2-Diabetes!

Petersen KF et al., PNAS 2007; 104: 12587-12594



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Petersen KF et al., PNAS 2007; 104: 12587-12594

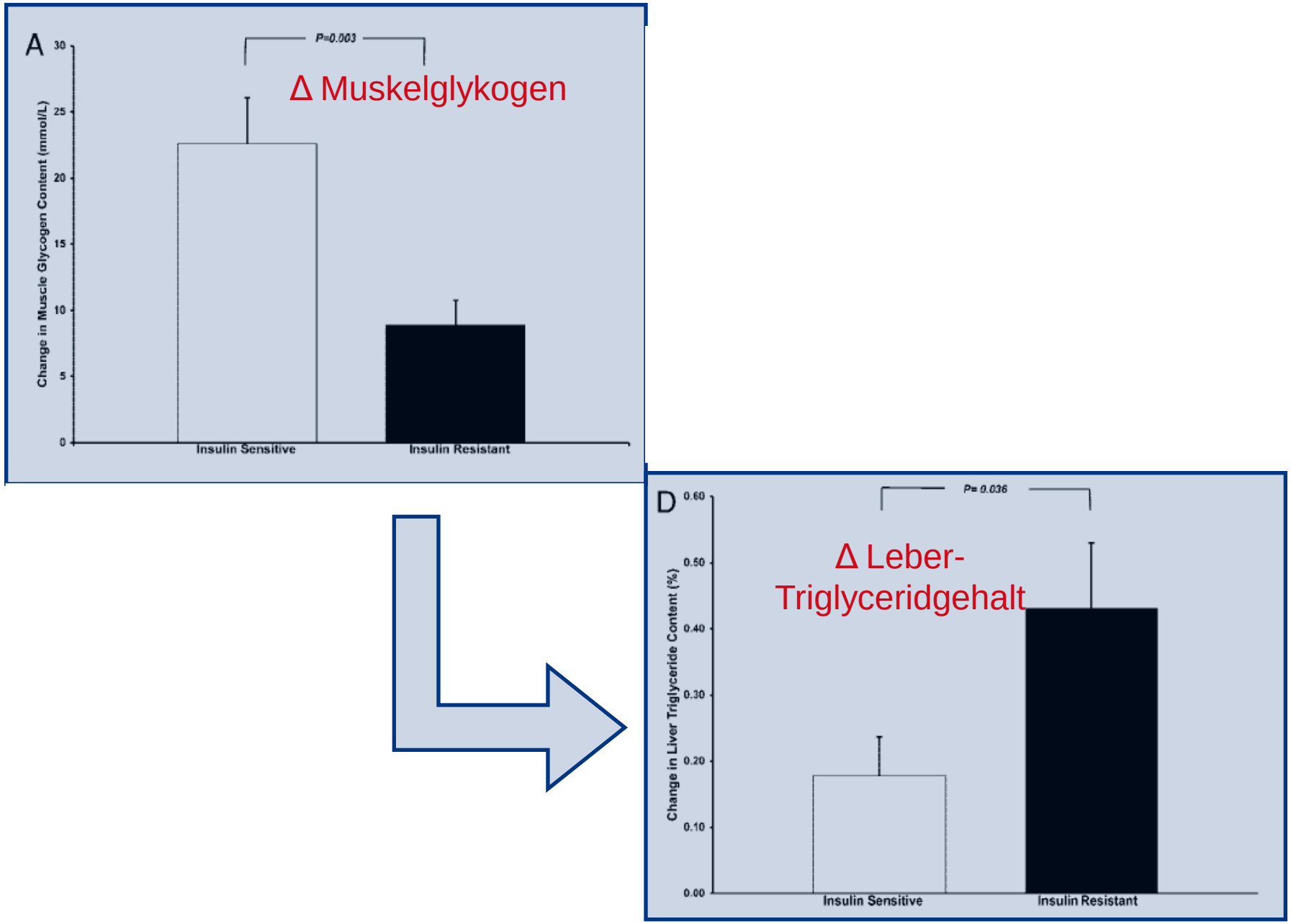

Fig. 2. ^{13}C MRS measurements of changes in muscle (*A*) and liver (*B*) glycogen concentrations and ^{1}H MRS measurements of changes in intramyocellular triglyceride (*C*) and hepatic triglyceride (*D*) content in insulin-sensitive and insulin-resistant subjects after the mixed meals.

Die *de novo*-Lipogenese nach kohlenhydratreicher Mahlzeit ist bei Insulinresistenten 2,2fach erhöht

Petersen KF et al., PNAS 2007; 104: 12587-12594

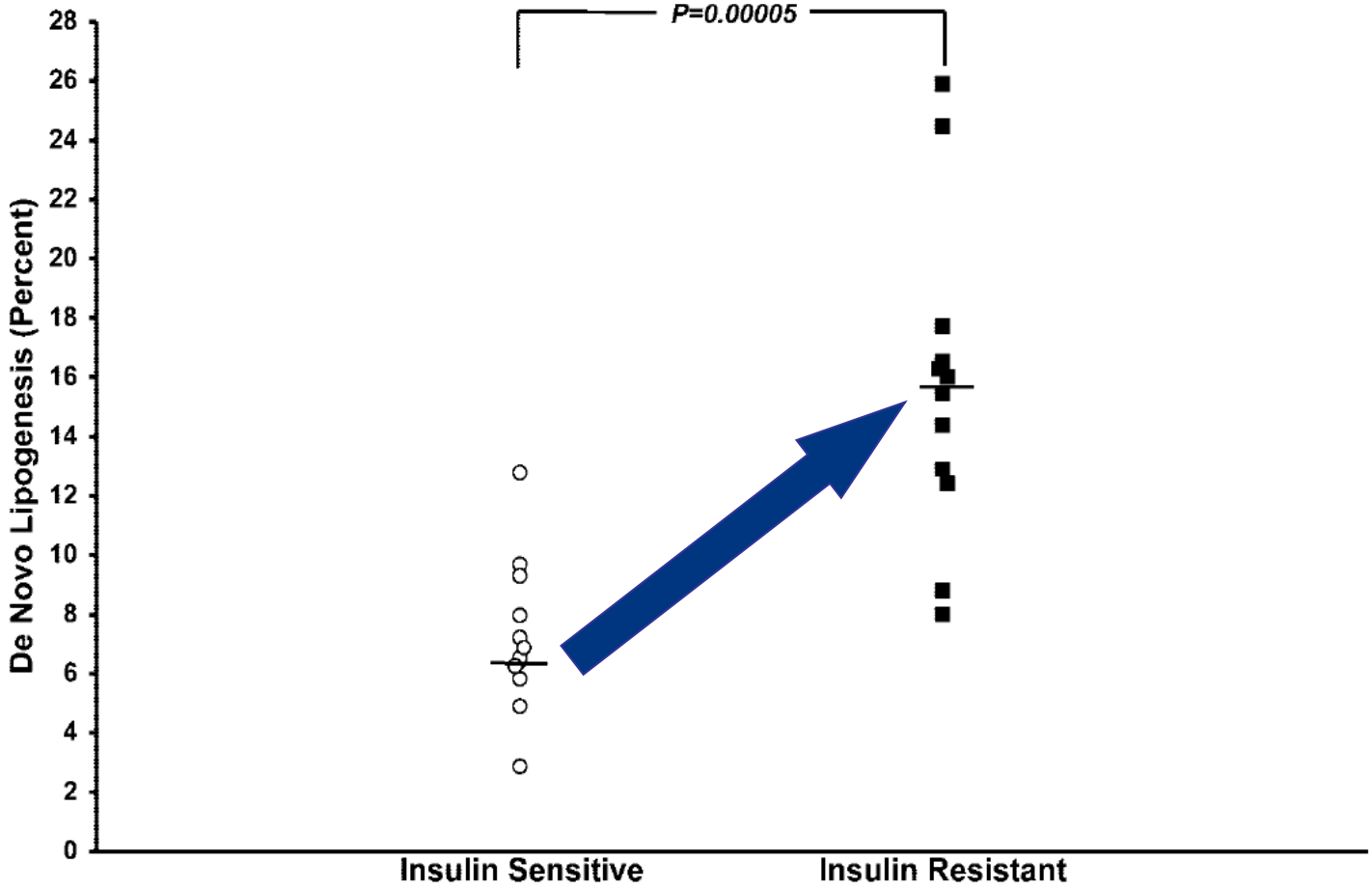

Fig. 4. Fractional *de novo* lipogenesis in insulin-sensitive and insulin-resistant subjects after the two high-carbohydrate mixed meals.

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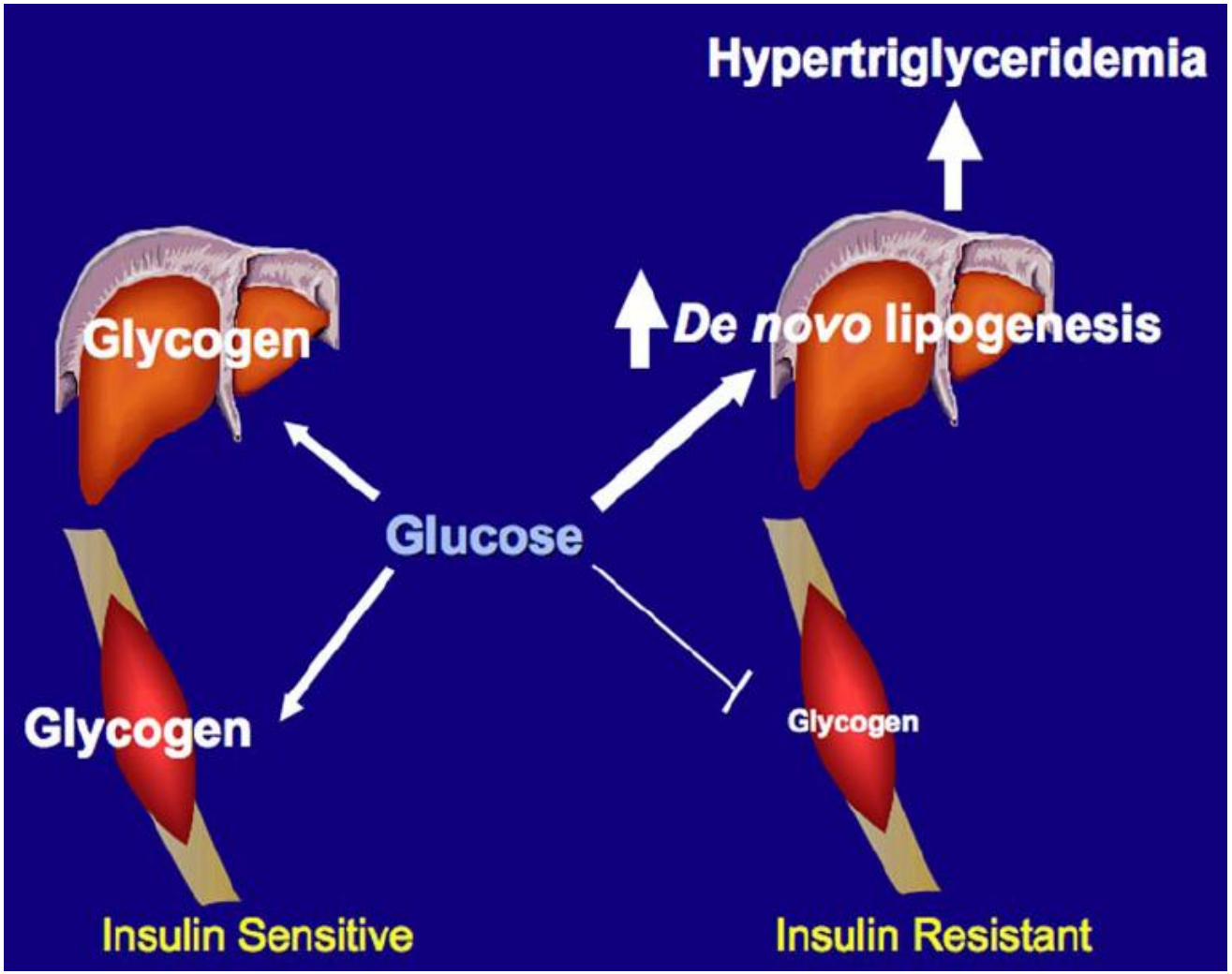
Der Energiefluss nach kohlenhydratreicher Mahlzeit ist abhängig von der Insulinsensitivität der Muskeln



Petersen KF et al., PNAS 2007; 104: 12587-12594

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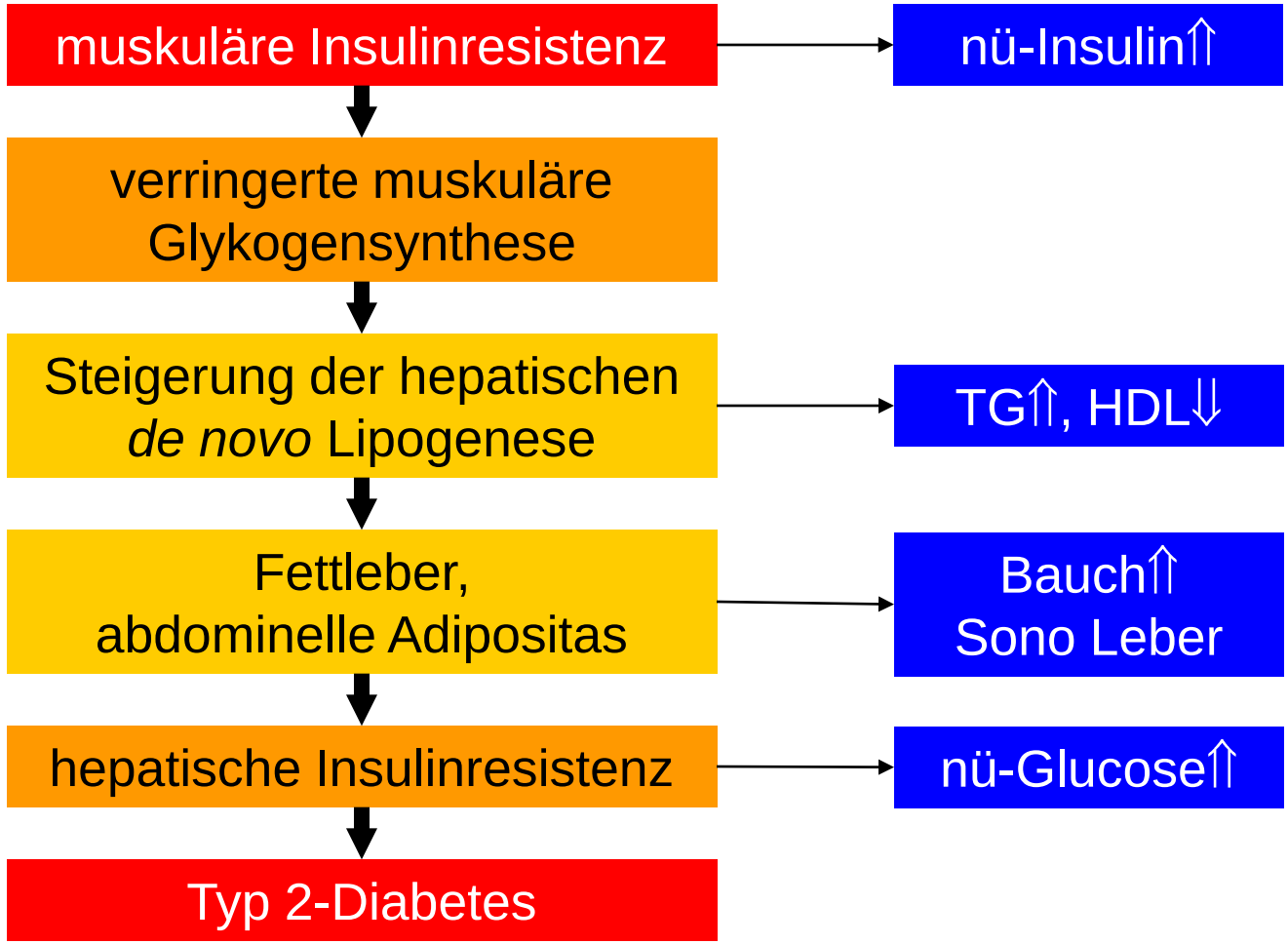
Fazit: Der insulinresistente Muskel ist der erste Schritt in Richtung metabolisches Syndrom und Typ 2-Diabetes

Petersen KF et al., PNAS 2007; 104: 12587-12594



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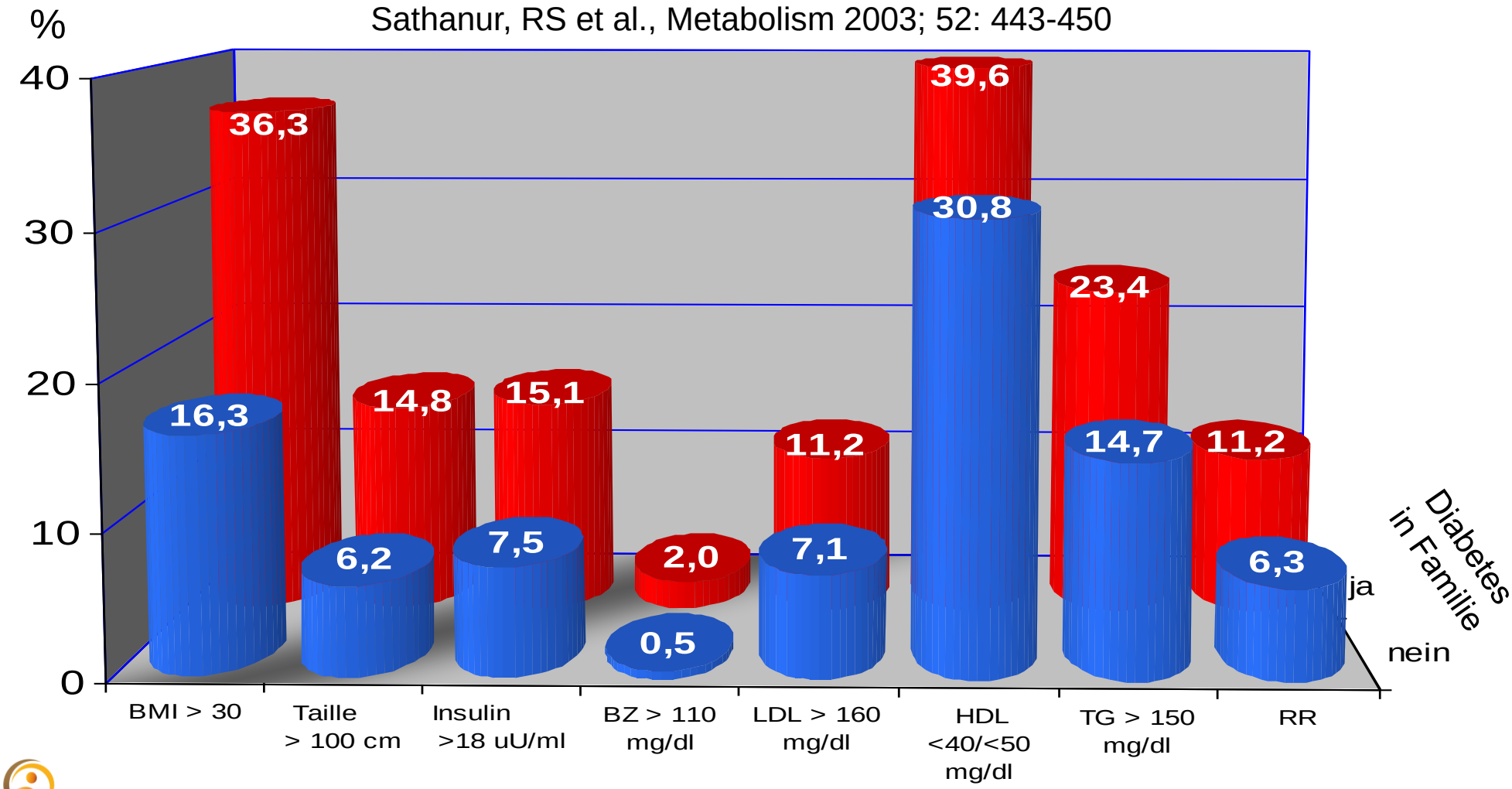
Familiäre Diabetes-Belastung und Risikofaktoren-Profil



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Florez JC et al., N Engl J Med 2006; 355: 241-250

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 20, 2006 VOL. 355 NO. 3

TCF7L2 Polymorphisms and Progression to Diabetes in the Diabetes Prevention Program

Jose C. Florez, M.D., Ph.D., Kathleen A. Jablonski, Ph.D., Nick Bayley, B.A., Toni I. Pollin, Ph.D., Paul I.W. de Bakker, Ph.D., Alan R. Shuldiner, M.D., William C. Knowler, M.D., Dr.P.H., David M. Nathan, M.D., and David Altshuler, M.D., Ph.D., for the Diabetes Prevention Program Research Group

ABSTRACT

BACKGROUND

Common polymorphisms of the transcription factor 7–like 2 gene (*TCF7L2*) have recently been associated with type 2 diabetes. We examined whether the two most strongly associated variants (rs12255372 and rs7903146) predict the progression to diabetes in persons with impaired glucose tolerance who were enrolled in the Diabetes Prevention Program, in which lifestyle intervention or treatment with metformin was compared with placebo.

METHODS

We genotyped these variants in 3548 participants and performed Cox regression analysis using genotype, intervention, and their interactions as predictors. We assessed

From the Diabetes Prevention Program Outcomes Study Coordinating Center, George Washington University, Rockville, Md. Address reprint requests to Dr. Florez at the Diabetes Prevention Program Coordinating Center, the Biostatistics Center, George Washington University, 6110 Executive Blvd., Suite 750, Rockville, MD 20852, or at dppmail@biostat.bsc.gwu.edu.

N Engl J Med 2006;355:241-50.

Genetische Varianten der Insulinsekretion

Florez JC et al., N Engl J Med 2006; 355: 241-250

- Genetische Variante rs7903146 des TCF7L2-Faktors
- ca. 10% der Bevölkerung sind homozygot für TT-Variante
- TT-Variante ist mit schlechterer Insulinsekretion assoziiert
  - bedeutet insgesamt ein RR von 2,41 für T2DM
- Risiko für T2DM in der Placebo-Gruppe + 80%
- Risiko für T2DM in der Lifestyle-Gruppe + 15% (n.s.)

Florez JC et al., N Engl J Med 2006; 355: 241-250

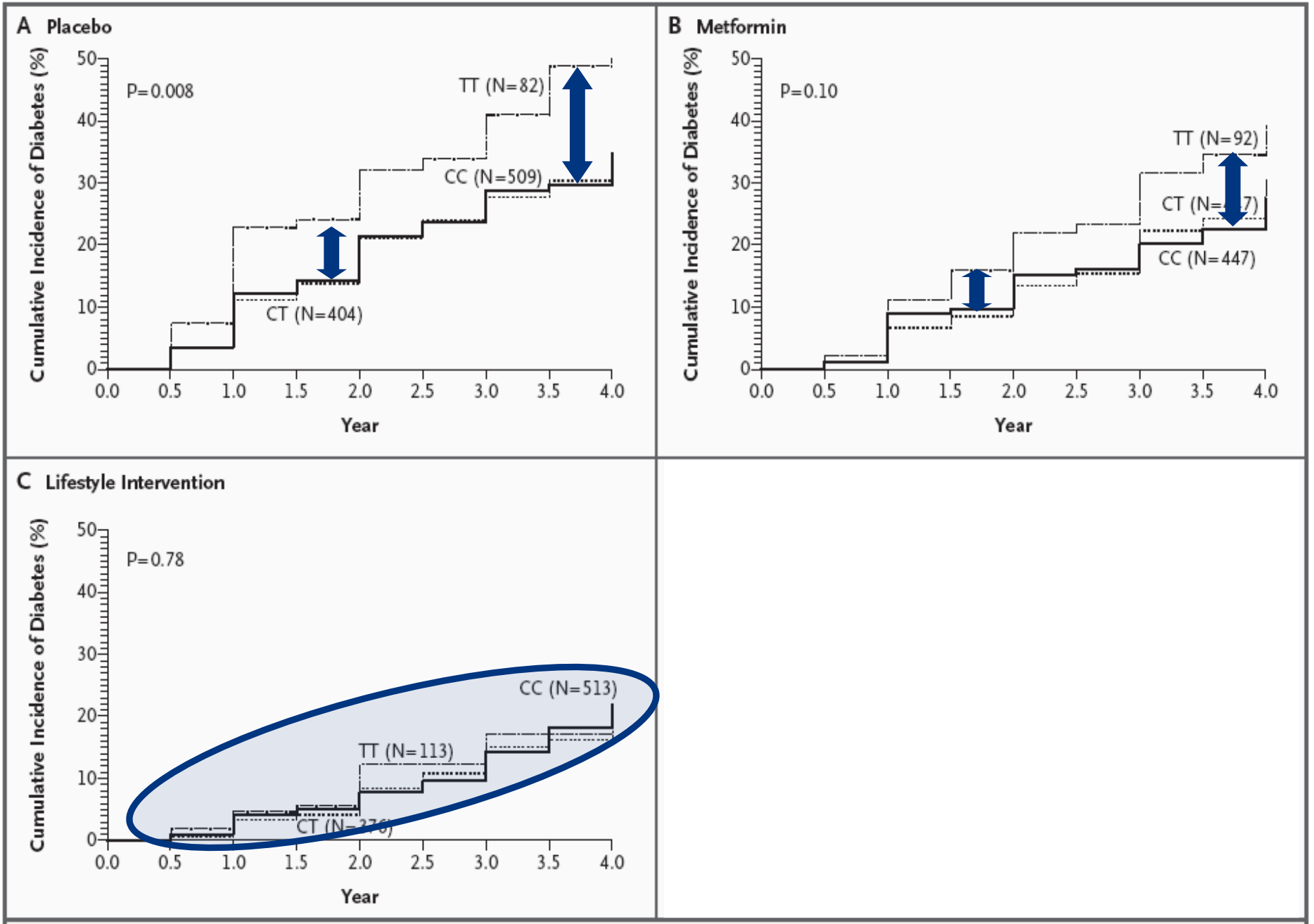

Figure 1. Incidence of Diabetes According to Treatment Group and Genotype at Variant rs7903146.

The P values were determined by the log-rank test.

Vom Normalzustand zum Typ 2-Diabetes

Faerch K et al., Diab Care 2009; 32: 439-444

Pathophysiology/Complications
ORIGINAL ARTICLE

Natural History of Insulin Sensitivity and Insulin Secretion in the Progression From Normal Glucose Tolerance to Impaired Fasting Glycemia and Impaired Glucose Tolerance: The Inter99 Study

KRISTINE FÆRCH, MSC[1]
ALLAN VAAG, DMSC[1]
JENS J. HOLST, DMSC[2]
TORBEN HANSEN, PHD[1]
TORBEN JØRGENSEN, DMSC[3]
KNUT BORCH-JOHNSEN, DMSC[4]

OBJECTIVE — The aim of this study was to describe the natural history of insulin secretion and insulin sensitivity in the development of isolated impaired fasting glycemia (i-IFG), isolated impaired glucose tolerance (i-IGT), and combined IFG/IGT.

RESEARCH DESIGN AND METHODS — Baseline and 5-year follow-up data from the Inter99 study were used. Individuals with normal glucose tolerance (NGT) at baseline and i-IFG, i-IGT, combined IFG/IGT, or NGT at the 5-year follow-up were examined with an oral glucose tolerance test (n = 3,145). Insulin sensitivity index (ISI), homeostasis model assessment of insulin sensitivity (HOMA-IS), early-phase insulin release (EPIR), and insulin secretion relative to insulin action (disposition index) were estimated.

abetes risk in individuals with i-IGT and IFG/IGT (9,10), but whether lifestyle interventions have the same preventive effects in individuals with i-IFG is not known. Indeed, a more profound insight into the pathogenesis of the disease is needed to optimize prevention and treatment of type 2 diabetes. In particular, focus on the initial defects responsible for hyperglycemia in the fasting and postprandial states is essential for interrupting the progression from normal to abnormal glucose metabolism.

Most previous studies have examined the pathophysiology of pre-diabetes in

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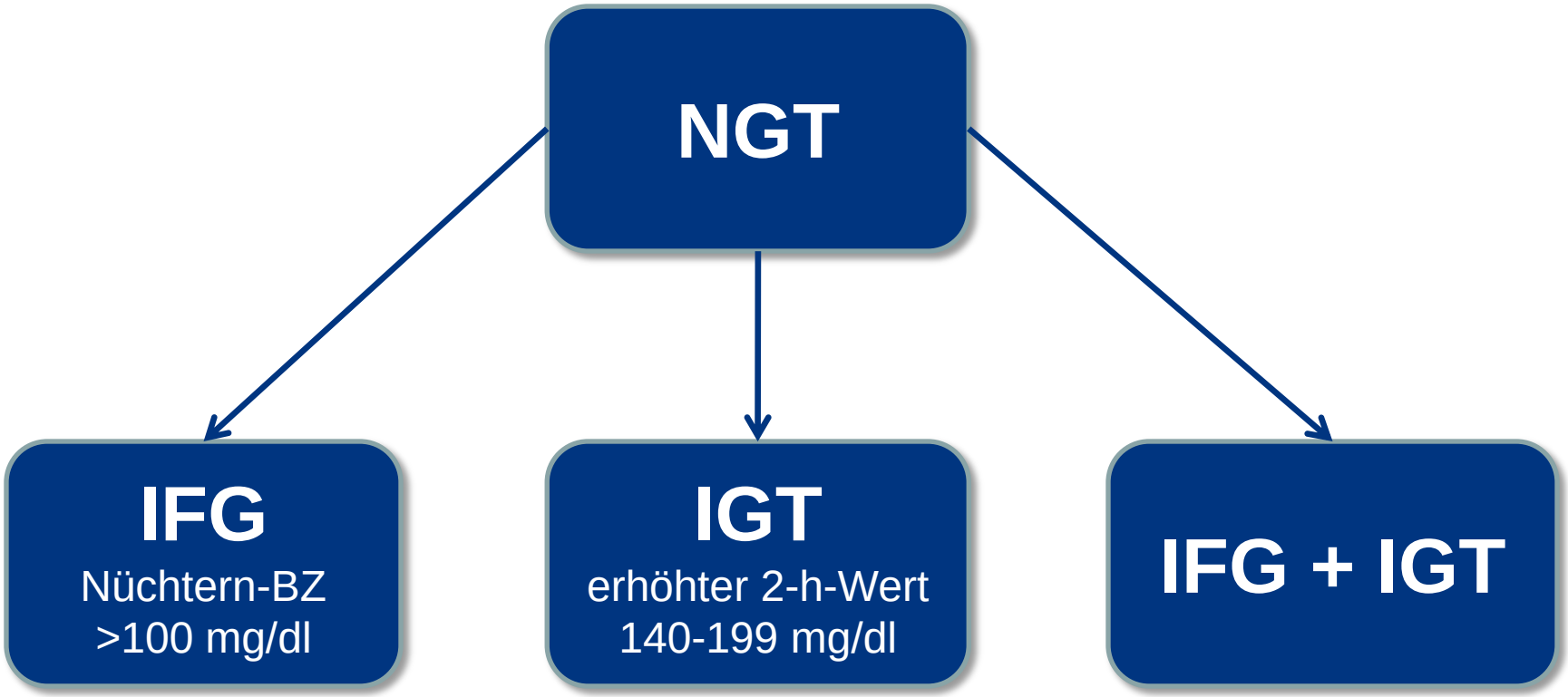
Inter99: Vom Normalzustand zum Typ 2-Diabetes

Faerch K et al., Diab Care 2009; 32: 439-444

- **Inter99-Studie**:
  - repräsentative Bevölkerungsstichprobe in Dänemark
  - Lebensstil-Intervention zur Diabetes- und KHK-Prävention
- **Teilnehmer**: n = 3145 Personen aus Inter99 mit normalem 2-h-Wert im OGTT = normale Glukosetoleranz (WHO) zum Start
- **Studiendesign**:
  - OGTT mit 75 g Glukose bei Basisuntersuchung und Follow-up
  - Bestimmung von Glukose und Insulin nach 0, 30 und 120 min
  - Follow-up 5 Jahre
- **Endpunkt**: Veränderung von Insulinsekretion und Insulinsensitivität

Inter99: Vom Normalzustand zum Typ 2-Diabetes

Faerch K et al., Diab Care 2009; 32: 439-444



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Inter99: Vom Normalzustand zum Typ 2-Diabetes

Faerch K et al., Diab Care 2009; 32: 439-444

IFG
Nüchtern-BZ
>100 mg/dl

IGT
erhöhter 2-h-Wert
140-199 mg/dl

5 Jahre vor Diagnose IFG:

- gestörte Insulinsekretion (EPIR)
- EPIR unverändert nach 5 Jahren
- aber: progressive Abnahme der hepatischen Insulinsensitivität
- häufiger: pos. Familienanamnese

5 Jahre vor Diagnose IGT:

- normale Insulinsekretion (EPIR)
- EPIR abnehmend über 5 Jahre
- Hauptproblem: bereits zu Beginn sehr geringe Insulinsensitivität
  → ß-Zell-Versagen ist sekundär

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Insulinresistenz, Metabolisches Syndrom und die Prävention des Typ 2-Diabetes

1. Epidemiologie: Metabolisches Syndrom, Typ 2 – Diabetes und KHK
2. Pathophysiologie der Insulinresistenz: Risikofaktor für KHK
3. Screening auf erhöhtes Diabetes-Risiko: praxistaugliche Methoden
4. Einfluss von Lebensstil-Faktoren: Ernährung und körperliche Aktivität
5. Medikamente in Prävention und Therapie

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Wen screenen auf Insulinresistenz ?

- Adipöse BMI > 30
- Übergewichtige mit „Bauch“
- Normalgewichtige mit „Bauch“
- inaktive Büromenschen?
- Z. n. Schwangerschafts-Diabetes
- familiäre Diabetes-Belastung

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Kosteneffektivität des Screenings auf Diabetes bzw. Diabetesvorstufen: ADDITION-Study, Leicester

- Kosteneffektivität pro QUALY (quality adjusted life-year saved)
- Vergleich:
  - abwarten und behandeln, wenn Diabetes auffällt = 1
  - Screenen auf Diabetes = 3,2 x
  - Screenen auf Diabetes-Vorstufe = 14,2 x
- Bester Zeitpunkt für Screening: mit 30 Jahren!

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Ist der OGTT zur Früherkennung geeignet?

- normaler nüchtern-BZ und normaler 2-h-Wert:

  bedeutet das einen normalen Glucose-Stoffwechsel?

- erhöhter nüchtern-BZ und normaler 2-h-Wert:

  bedeutet das einen normalen Glucose-Stoffwechsel?

- Hilft der 1-h-Wert?

Fallbeispiel: Winzer, 45 Jahre

- Familie: Typ-2-Diabetes bei allen Verwandten mütterlicherseits
- BMI 27,4; Taillenumfang 102 cm
- Triglyceride: 170 mg/dl; HDL-Cholesterin: 55 mg/dl
- keine arterielle Hypertonie
- erstmalig erhöhter Nüchtern-BZ von 114 mg/dl
- Nüchtern-Insulin: 14,5 uIU/ml, HOMA-Index 4,07 !!!
- **OGTT: 102 mg/dl nüchtern, (1 h: 206 mg/dl), 2 h: 136 mg/dl**

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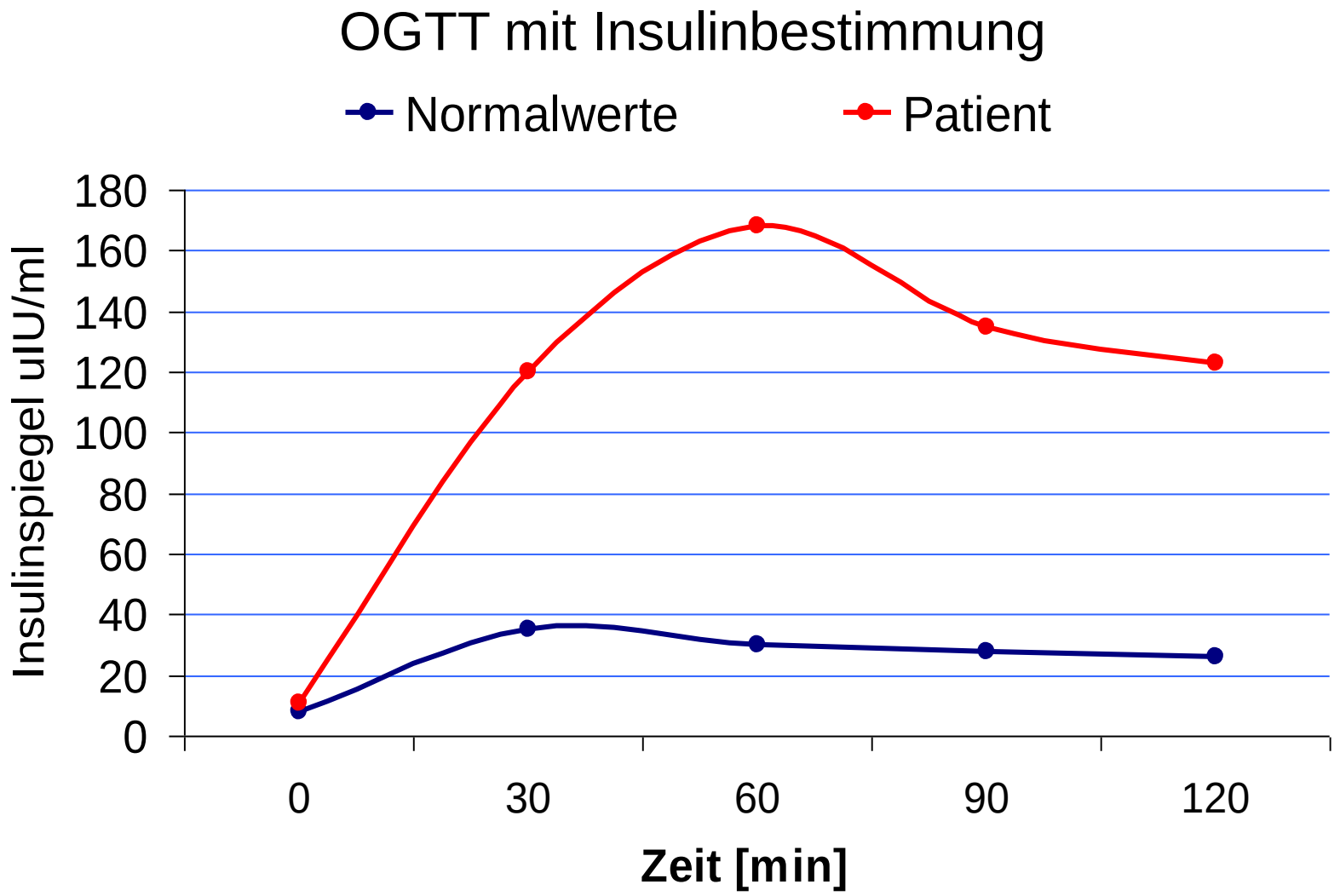
Fallbeispiel: Winzer, 45 Jahre



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Wie bestimmt man Insulinsensitivität bzw. Insulinresistenz?

Surrogatparameter HOMA:

- Grundannahme: Steady-State nach 12 h Nahrungskarenz
- Messung von Nüchtern-BZ und Nüchtern-Insulin
- reflektieren v.a. hepatische Insulinresistenz
- gilt nicht bei verminderter ß-Zell-Funktion in späteren Stadien eines T2DM (hier: intaktes Pro-Insulin)

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Nüchtern-Insulinbestimmung: praktikable Methode?

Zuverlässige Insulinbestimmung aus dem Serum:

- Abwarten der Gerinnung (ca. 10-15 min)
- dann zentrifugieren
- anschließend Serum abpipettieren
- im Cool-Pack oder tiefgefroren ins Labor

  (24 h stabil bei 2-8 ºC, tiefgefroren unbegrenzt)

HOMA-Index

HOMA = Glucose (mmol/l) x Insulin (μIU/ml) / 22,5

HOMA = Glucose (mg/dl) x 0,0555 x Insulin (μIU/ml) / 22,5

HOMA = Glucose (mg/dl) x Insulin (μIU/ml) / 405,40

HOMA = Glucose (mg/dl) x Insulin (μIU/ml) / 405

Korrelation mit euglykämischem Clamp: r=0,88

HOMA-Index: Rechenbeispiele

Nü-BZ = 90 mg/dl
Nü-Insulin = 4,5 µIU/ml
HOMA = 90 x 4,5/405 = 1,0

Nü-BZ = 90 mg/dl
Nü-Insulin = 14 µIU/ml
HOMA = 3,11

Nü-BZ = 105 mg/dl
Nü-Insulin = 20 µIU/ml
HOMA = 5,2

Surrogatparameter für die Insulinresistenz

McLaughlin T et al., Ann Int Med 2003; 139: 802-809, McAuley, K et al., Diabetes Care 2001; 24: 460-464
Stern SE et al., Diab Care 2005; 54: 333-339

Marker	Cut-off	Sensitivität	Spezifität	PPV
Triglycerid-HDL-Ratio	> 3,0	64%	68%	67%
nü-Insulin	> 15 µU/ml [>108 pmol/l)	57%	85%	80%
nü-Insulin + TG	> 12 µU/ml und > 130 mg/dl	65%	83%	80%
HOMA-Index	> 3,0	80%	74%	88%
Kombination HOMA und BMI	> 4,65 oder BMI >28,9 oder [>3,60 + BMI >27,5]	85%	78%	89%

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Petersen KF et al., PNAS 2007; 104: 12587-12594

PNAS

INAUGURAL ARTICLE

The role of skeletal muscle insulin resistance in the pathogenesis of the metabolic syndrome

Kitt Falk Petersen*, Sylvie Dufour†, David B. Savage*, Stefan Bilz*, Gina Solomon*, Shin Yonemitsu*, Gary W. Cline*, Douglas Befroy*, Laura Zemany‡, Barbara B. Kahn‡, Xenophon Papademetris§, Douglas L. Rothman§, and Gerald I. Shulman*†§¶‖

Departments of *Internal Medicine; §Diagnostic Radiology and Biomedical Engineering; ¶Cellular and Molecular Physiology, and †Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, CT 06536; and ‡Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215

This contribution is part of the special series of Inaugural Articles by members of the National Academy of Sciences elected on May 1, 2007.

Contributed by Gerald I. Shulman, June 8, 2007 (sent for review May 25, 2007)

Table 2. Fasting plasma metabolite and hormone concentrations

	Glucose, mg/dl	Insulin, microunits/ml
Insulin-sensitive	84.1 ± 1.7	7.6 ± 0.6
Insulin-resistant	90.6 ± 1.5	12.1 ± 1.2
P value	0.009	0.003

SP, small particles; LP, large particles; CRP, C-reactive protein; NS, not significant.

HOMA-Index

→ 1,64

→ 2,70

San Antonio Heart Study: HOMA und kardiovaskuläres Risiko

Hanley AJG et al., Diab Care 2002; 25: 1177-1184

prospektive Kohortenstudie, n=2569 Nicht-Diabetiker, Follow-up ~7,5 Jahre
187 kardiovaskuläre Ereignisse (KHK, Apoplex, Bypass, Tod)

Quintile	HOMA	Glucose (mg/dl)	Insulin (uIU/ml)	2-h-Glucose (mg/dl)
1	bis 1,03	81	3,2	92
2	1,1-1,6	83	6,3	95
3	1,7-2,5	85	9,7	102
4	2,6-4,8	87	14,6	107
5	4,9-41,7	93	31,8	121

San Antonio Heart Study: HOMA und kardiovaskuläres Risiko

Hanley AJG et al., Diab Care 2002; 25: 1177-1184

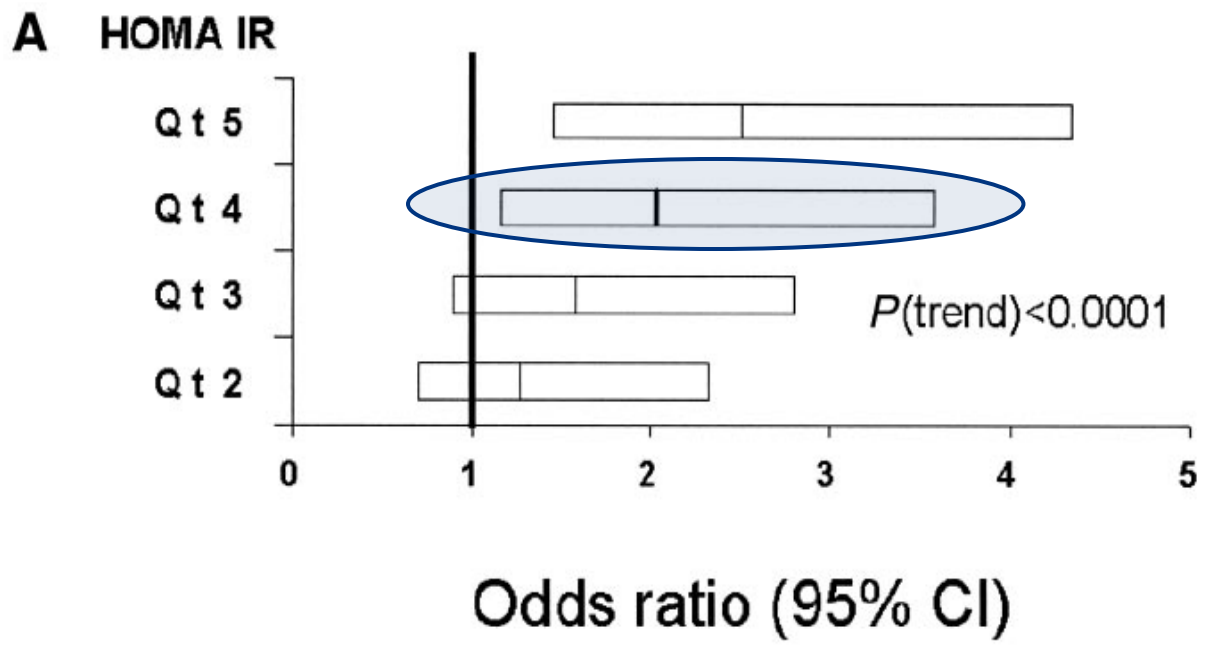

Figure 1—*Association between quintiles of HOMA-IR and 8-year risk of cardiovascular outcomes among subjects in the SAHS without diabetes and CVD at baseline. ORs were estimated using logistic regression and refer to risk in the given category relative to quintile 1. A: Quintiles of HOMA-IR (0–1.025, 1.026–1.626, 1.627–2.470, 2.471–4.802, and 4.803–41.700) adjusted for age, sex, and ethnicity. B: Quintiles of HOMA-IR adjusted for age, sex, ethnicity, LDL, triglyceride, HDL, systolic blood pressure, smoking, alcohol consumption, leisure time exercise, and waist circumference (median split). Qt, quintile.*

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Vorschlag für Patientenberatung

Ausgangsbasis:

- **IDF-Definition des Metabolischen Syndroms**
- *unterstützt durch:* **HOMA-Index ≥ 2,6 (3,0) oder BMI ≥ 29**
- *falls ein Kriterium oder mehrere positiv:*
  - Beratung wegen „erhöhter Diabetes-Gefährdung“
  - Erstellung eines Trainingsplans für Ausdauer + Kraft
  - Ernährungsumstellung nach LOGI

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Insulinresistenz, Metabolisches Syndrom und die Prävention des Typ 2-Diabetes

1. Epidemiologie: Metabolisches Syndrom, Typ 2 – Diabetes und KHK
2. Pathophysiologie der Insulinresistenz: Risikofaktor für KHK
3. Screening auf erhöhtes Diabetes-Risiko: praxistaugliche Methoden
4. Einfluss von Lebensstil-Faktoren: (Ernährung) und körperliche Aktivität
5. Medikamente in Prävention und Therapie

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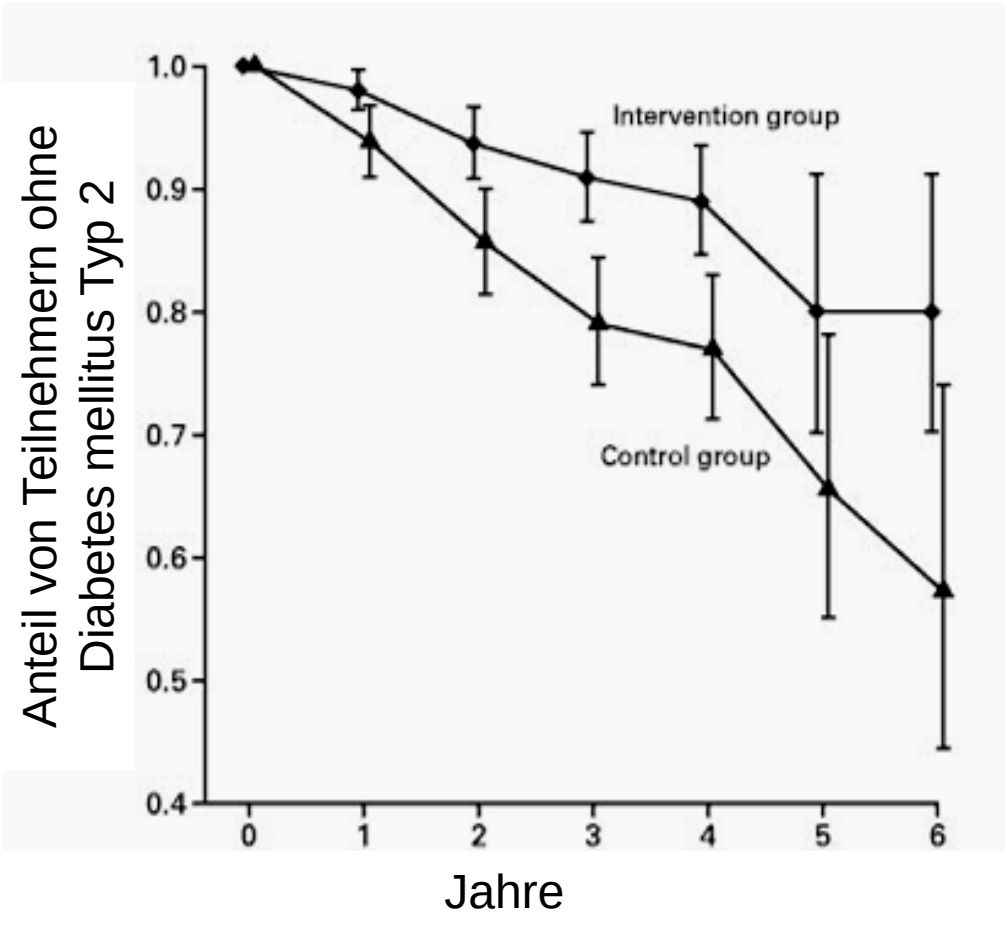
Die finnische Diabetes-Präventions-Studie

Tuomilehto, J et al.; N Engl J Med 2001; 344: 1343-1350



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Die finnische Diabetes-Präventions-Studie

Tuomilehto, J et al.; N Engl J Med 2001; 344: 1343-1350

Zielvorgaben der Interventionsgruppe:

- Gewichtsreduktion >= 5%
- Fettaufnahme < 30% der Gesamtkalorien
- Gesättigte Fettsäuren < 10% der Gesamtkalorien
- Ballaststoffe > 15 g pro 1000 kcal
- moderate Aktivität 30 min pro Tag

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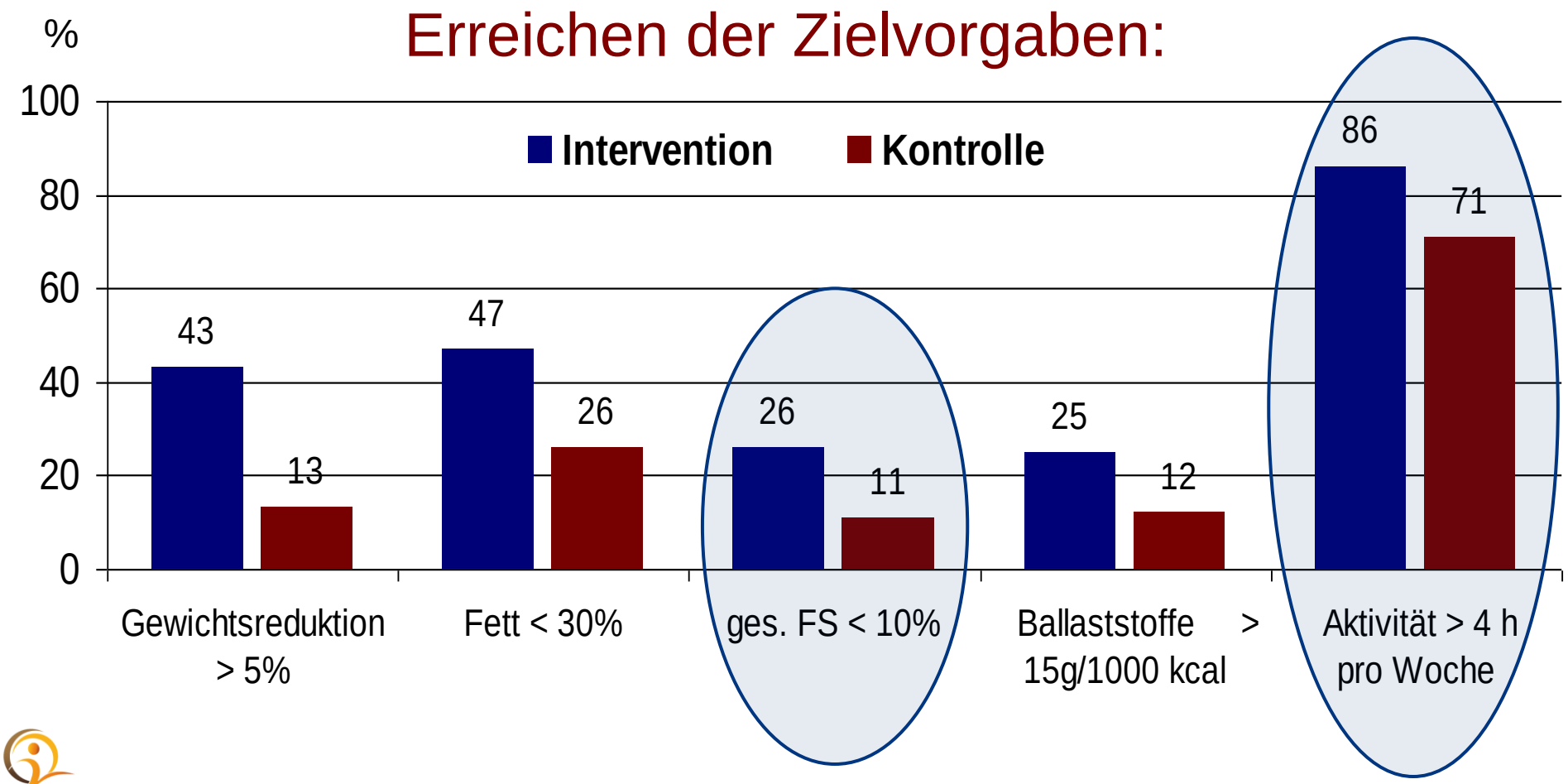
Die finnische Diabetes-Präventions-Studie

Tuomilehto, J et al.; N Engl J Med 2001; 344: 1343-1350



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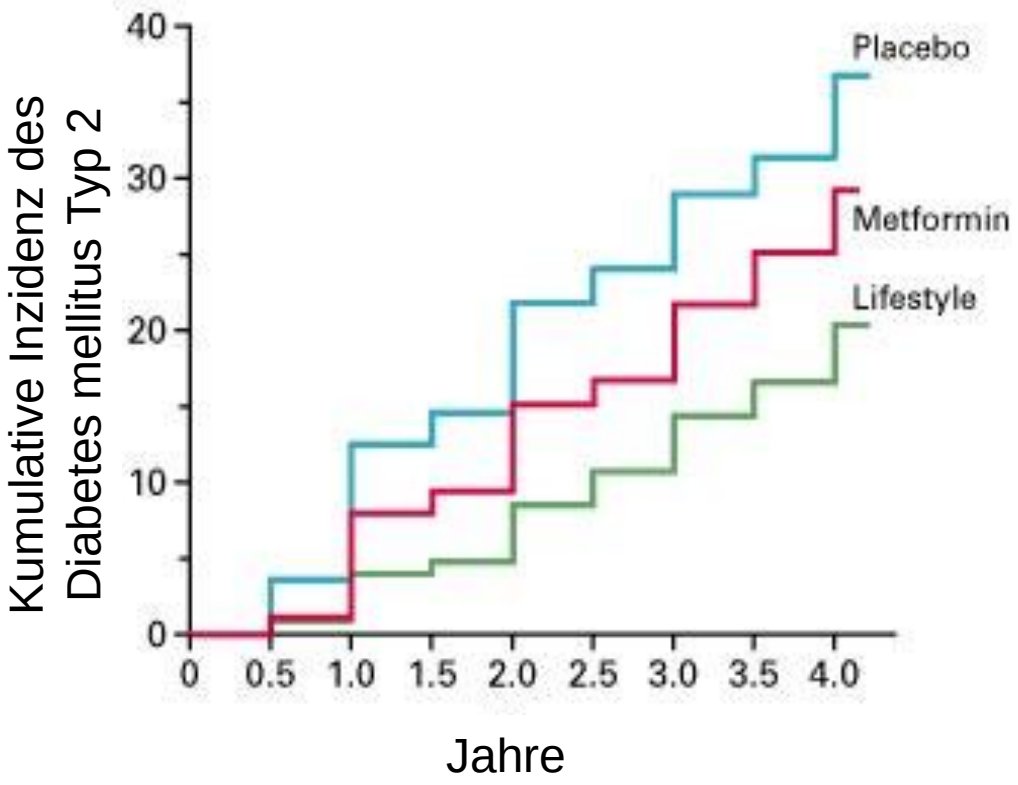
Die amerikanische Diabetes-Präventions-Studie Lebensstil-Änderung oder Metformin

The DPP Research Group, NEJM 346:393-403, 2002



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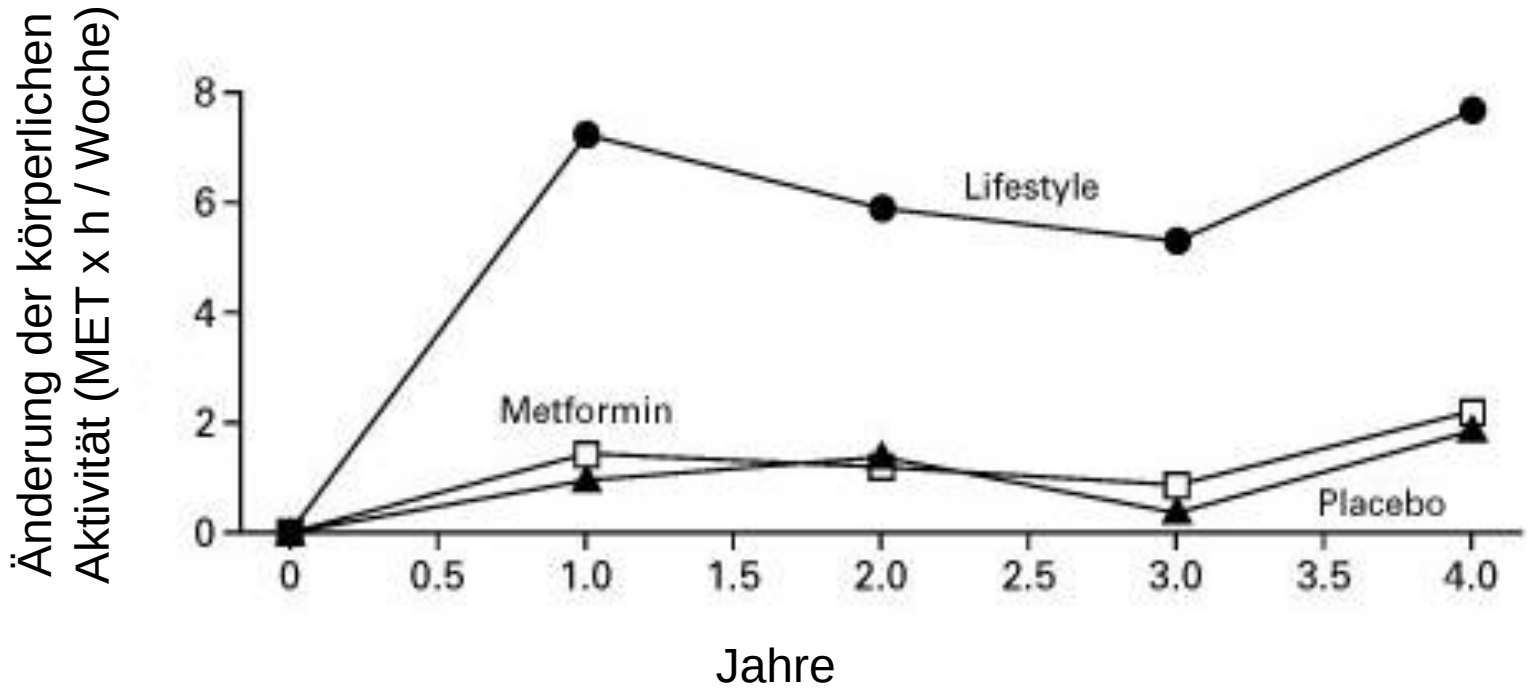
Die amerikanische Diabetes-Präventions-Studie Lebensstil-Änderung oder Metformin

The DPP Research Group, NEJM 346:393-403, 2002



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Persönliches Fazit: Die Fitness macht´s!

Regelmäßiges körperlichesTraining
und eine Gewichtsreduktion durch negative
Energiebilanz wirken Diabetes-präventiv,

selbst wenn die Ernährungsempfehlungen
nicht korrekt sind.

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Programme zur Diabetesprävention wirken

Results:

Mean age of participants was 42,3 years. The du
90 days. There were complete follow-up data for
did not complete the study due to workplace- and
up between baseline measurements and final visit
Significant improvements were seen for: weight
insulin, HOMA index, total cholesterol, and ldl-chol

Table 1:

Parameter	Unit	Baseline MW (95%CI)	Foll MW (
Weight	kg	83.6 (80.2-87.1)	80.2 (7
BMI	kg/cm²	28.1 (27.2-29.1)	26.7 (2
Waist circumference	cm	95.5 (92.5-98.4)	92.8 (9
Insulin	mU/l	11.02 (9.45-12.59)	8.42 (7
HOMA-Index	-	2.91 (2.51-3.30)	2.20 (1
Total Cholesterol	mg/dL	211.3 (203.8-218.9)	205.2 (1
LDL-Cholesterol	mg/dL	129.7 (123.1-136.3)	122.1 (1

Lifestyle Intervention in Bank Employees with Abdominal Obesity

J.G. Scholl[1], N. Worm[2], N. von Hentig[3], O. Albrecht[4];
[1]Prevention First Praxisverbund, Munich, Germany; [2]Nutritional Scientist, Munich, Germany; [3]University Clinics of Frankfurt, Zentrum für innere Medizin, [4]Praxis für Kardiologie und Angiologie, Bad Homburg, Germany; correspondence to: scholl@pf-arbeitsmedizin.de

Background:
Prevention First is one of the leading institutions performing health check-ups for employees of German companies. Our cross-sectional data show a high prevalence of abdominal obesity, insulin resistance, and the metabolic syndrome (MS) (> 30% according to the IDF definition of 2005). Therefore we planned a "real life intervention study" in employees of a large bank, who were at risk for diabetes. The study was conducted on the worksite of a bank in Frankfurt/Main, Germany, and was supported by a grant of the BKK Deutsche Bank (health insurance).

Recruitment:
In front of the cantine, we projected an entertaining PPT-presentation about the risks of abdominal obesity, including the results from INTERHEART. Nurses of the department of occupational medicine invited the employees to measure their waist circumference. Within three months we recruited 99 persons who fulfilled the IDF criterion of a waist circumference ≥94 cm in men or ≥80 cm in women. The employees gave informed consent to participate in a lifestyle intervention study. The data collection was done by the bank's department of occupational medicine (ärztl. TÜV Arbeitsmedizinische Dienste GmbH, Darmstadt; Head of department Dr. med. Ulrike Roth).

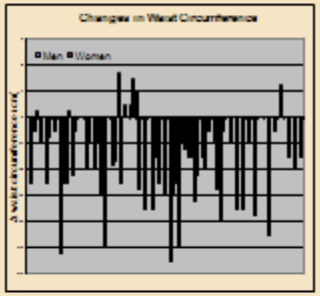
Intervention:
All participants received 6 hours of personal nutrition counselling, one hour every two weeks during the intervention period. The nutritional advice was based on the Joslin Diabetes Center's "Nutrition Guideline for overweight and obese adults with Type-2 Diabetes, Prediabetes or those at risk for developing Type-2 Diabetes", published in 2005.
Shortly, it aimed at reducing the glycemic load of the diet by reducing starchy foods like bread, rice, pasta, potatoes, sweets and sugared beverages. In exchange for an increase of non-starchy vegetables, legumes, fruits, protein from lean sources and of monounsaturated and n-3-polyunsaturated fatty acids (LoGI-Diet).
The aim of the personal trainer intervention was to facilitate the uptake of a physical activity programme (short "how to...") and then to maintain an active lifestyle. Participants were asked to perform 2x30 min of aerobic exercise per week and two sessions of intensive resistance training per week.

Study goals:
Reducing waist circumference, body weight, insulin resistance, and improving blood lipid values, thus lowering cardiovascular risk.

Results:
Mean age of participants was 42.3 years. The duration of the intervention period was 90 days. There were complete follow-up data for 76 of 99 participants. 12 participants did not complete the study due to workplace- and time-related reasons. Mean follow-up between baseline measurements and final visit was 120 days.
Significant improvements were seen for: weight, BMI, waist circumference, fasting insulin, HOMA index, total cholesterol, and ldl-cholesterol (Table 1).

Table 1.

Parameter	Unit	Baseline MW (95%CI)	Follow-up MW (95%CI)	Change from Baseline MW (95%CI)	p-value
Weight	kg	83.6 (80.2-87.1)	80.2 (76.8-83.6)	-3.45 (-4.32; -4.62)	< 0.001
BMI	kg/cm²	28.1 (27.2-29.1)	26.7 (25.8-27.7)	-1.40 (-1.62; -1.41)	0.001
Waist circumference	cm	95.5 (92.5-98.4)	92.8 (90.1-95.4)	-2.71 (-3.42; -2.02)	0.000
Insulin	mU/l	11.02 (9.45-12.59)	8.42 (7.09-9.75)	-2.60 (-3.56; -1.57)	0.000
HOMA Index	-	2.91 (2.51-3.30)	2.20 (1.89-2.51)	-0.71 (-0.96; -0.46)	0.000
Total Cholesterol	mg/dL	211.3 (203.8-218.9)	205.2 (197.8-212.5)	-6.11 (-9.32; -2.91)	0.000
LDL-Cholesterol	mg/dL	129.7 (123.1-136.3)	122.1 (115.8-128.4)	-7.60 (-10.62; -4.58)	0.001



Discussion:
Traditionally, dietary recommendations for overweight people at risk for diabetes focused on reducing fat intake and a high intake of carbohydrates. Recent controlled dietary intervention trials and a Cochrane meta-analysis of such trials showed the superiority of low-carb diets over low-fat diets, especially in insulin-resistant individuals. In our study, lowering the glycemic load of the participants diets resulted in marked improvements of main components of the MS, which is a strong risk factor for cardiovascular disease even before the manifestation of type 2-diabetes. A LoGI diet as suggested by the Joslin Diabetes Center is palatable and can be simply incorporated into a person's lifestyle.
Difficulties were seen with the realization of the physical activity programme, mainly due to organizational and time-related problems. Three hours of a personal trainer intervention may be too short for the maintenance of a physical activity programme in formerly sedentary individuals. To improve the compliance of the physical activity programme, a partial solution could be the construction of showers and changing rooms inside the bank building, thus facilitating cycling, walking or jogging to work for the employees.

Conclusion:
This study demonstrates the feasability of a lifestyle intervention programme in a "real life setting" at the workplace of bank employees.

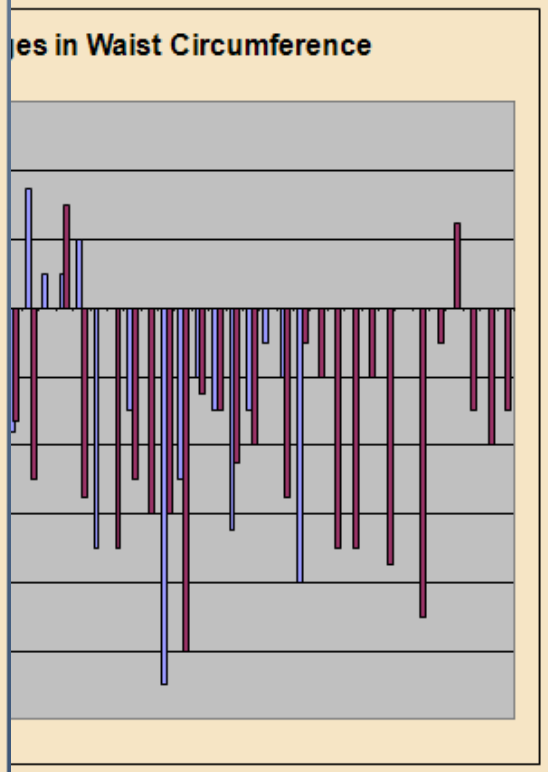


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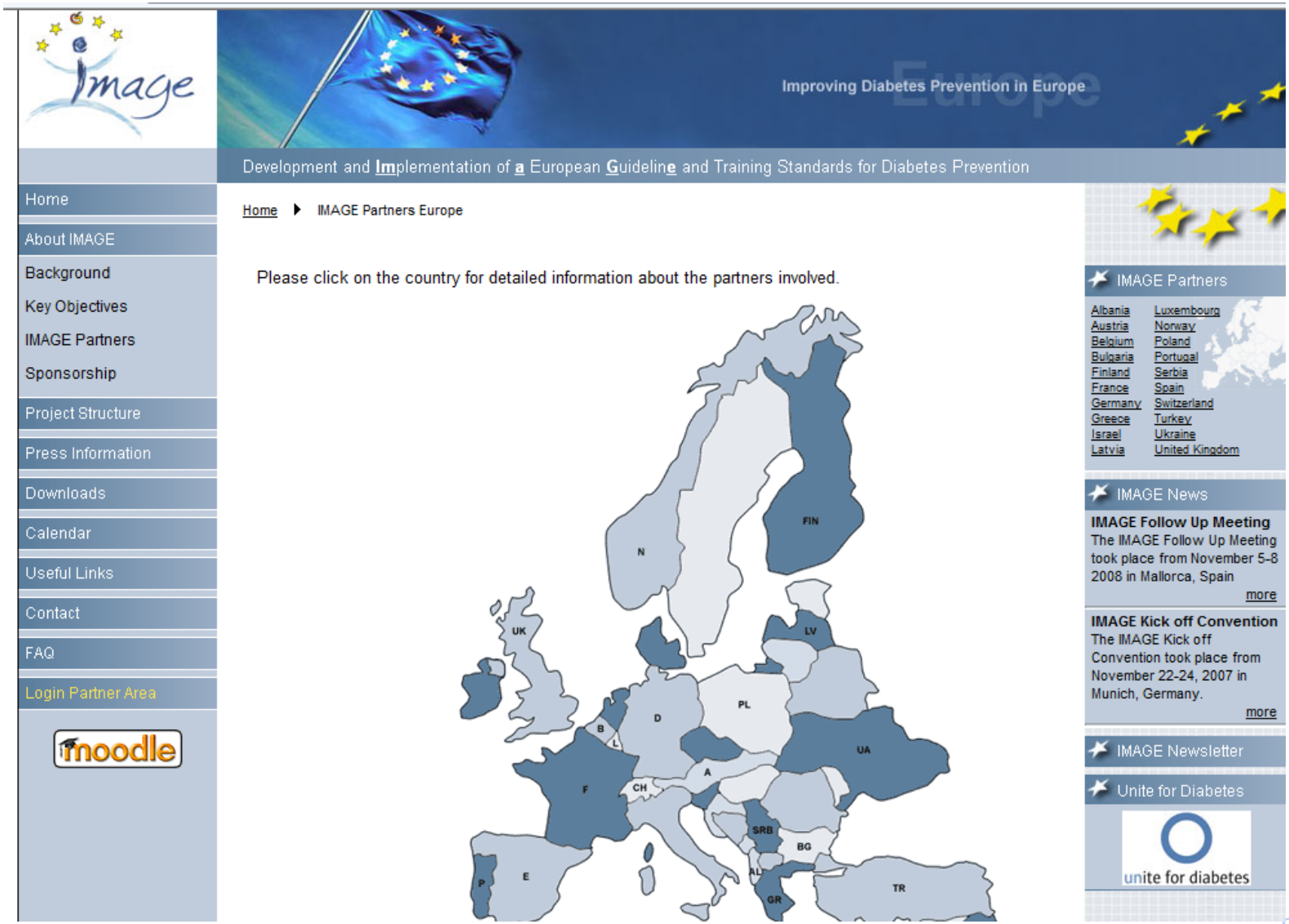
IMAGE
Improving Diabetes Prevention in Europe



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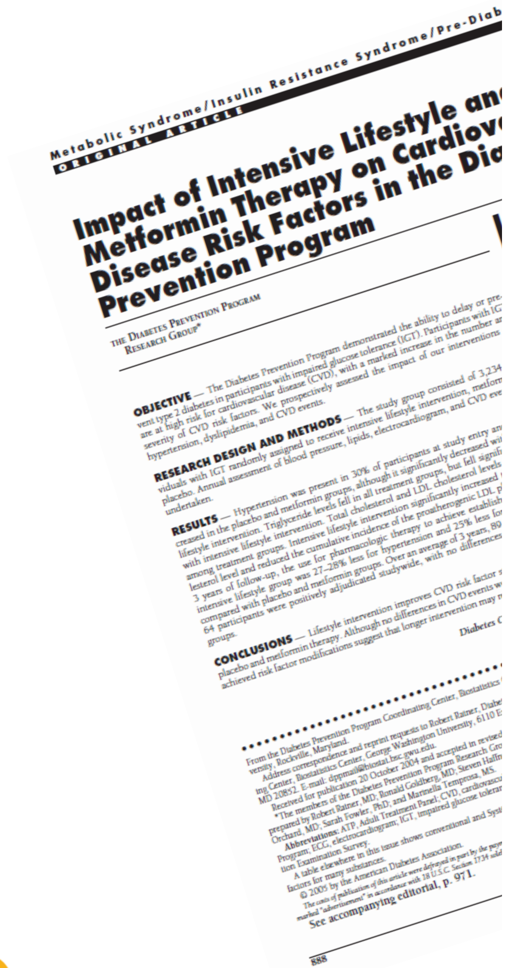
Programme zur Diabetesprävention wirken


Metabolic Syndrome/Insulin Resistance Syndrome/Pre-Diab
ORIGINAL ARTICLE

Impact of Intensive Lifestyle an
Metformin Therapy on Cardiov
Disease Risk Factors in the Dia
Prevention Program

THE DIABETES PREVENTION PROGRAM RESEARCH GROUP*

OBJECTIVE — The Diabetes Prevention Program demonstrated the ability to delay or pre-vent type 2 diabetes in participants with impaired glucose tolerance (IGT).

RESEARCH DESIGN AND METHODS — The study group consisted of 3,234

RESULTS — Hypertension was present in 30% of participants at study entry

CONCLUSIONS — Lifestyle intervention improves CVD risk factor

See accompanying editorial, p. 971.

TAKE ACTION
TO PREVENT DIABETES

A toolkit for the prevention of type 2 diabetes in Europe

Image Improving Diabetes Prevention

Executive Agency for Health and Consumers


The New England Journal of Medicine
Copyright © 2001 by the Massachusetts Medical Society
MAY 3, 2001
NUMBER 18

N OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE
NG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE

FOR THE FINNISH DIABETES PREVENTION STUDY GROUP

THE incidence of type 2 diabetes mellitus is increasing worldwide.

May 3, 2001 · www.nejm.org · 1343

Fallbeispiel: Gemüsehändlerin, 68 J.

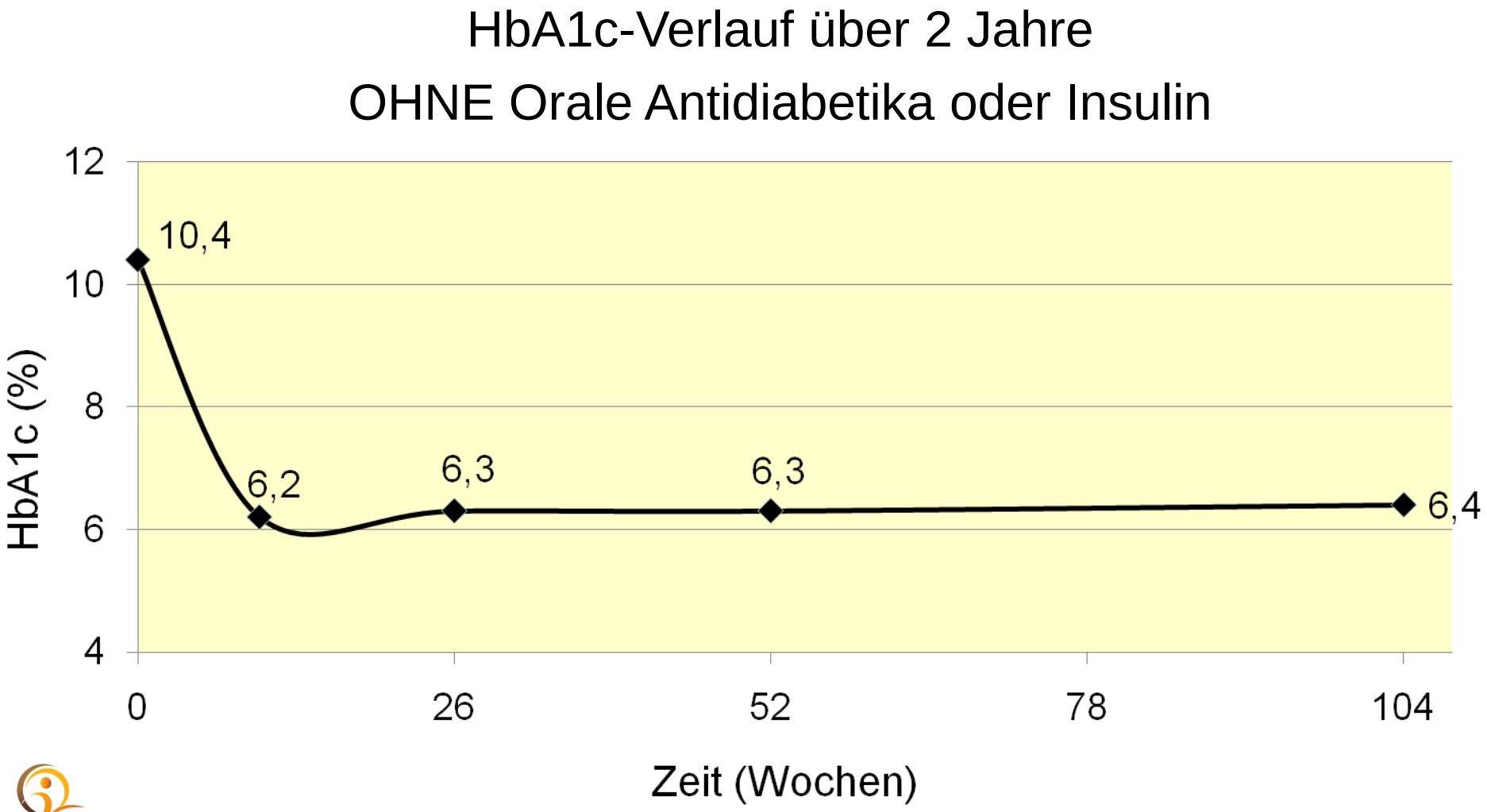
- 68 Jahre alte Gemüsehändlerin im Ruhestand
- Erstdiagnose Typ 2-Diabetes Anfang Oktober 2006: nüchtern BZ 260 mg/dl, HbA1c 12,1%
- Vorstellung beim Diabetologen:
  - Metformin 2x1000 mg
  - Ernährungsempfehlung: fettarm, kohlenhydratreich

Fallbeispiel: Gemüsehändlerin, 68 J.

Prevention First – Gesundheits-Checkup am 16.11.2006:

- BMI 28, HbA1c 10,4%, nü-BZ 120 mg/dl
- Leistungsdiagnostik mit Spiroergometrie und Laktatmessung
- Bestimmung GA-I-Bereich (Fettstoffwechseltraining)
- Ziel: täglich >45 min aktiv werden
- Personal Trainer
- Ernährungsumstellung nach LOGI

Fallbeispiel: Gemüsehändlerin, 68 J.



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For breakfast, at 9.0 A.M., I take five to six ounces of either beef, mutton, kidneys, broiled fish, bacon, or cold meat of any kind except pork or veal; a large cup of tea or coffee (without milk or sugar), a little biscuit, or one ounce of dry toast; making together six ounces solid, nine liquid.

For dinner, at 2.0 P.M., Five or six ounces of any fish except salmon, herrings, or eels, any meat except pork or veal, any vegetable except potato, parsnip, beetroot, turnip, or carrot, one ounce of dry toast, fruit out of a pudding not sweetened, any kind of poultry or game, and two or three glasses of good claret, sherry, or Madeira— Champagne, port, and beer forbidden; making together ten to twelve ounces solid, and ten liquid.

For tea, at 6.0 P.M., Two or three ounces of cooked fruit, a rusk or two, and a cup of tea without milk or sugar; making two to four ounces solid, nine liquid.

For supper, at 9.0 P.M. Three or four ounces of meat or fish, similar to dinner, with a glass or two of claret or sherry and water; making four ounces solid and seven liquid.

For nightcap, if required, A tumbler of grog—(gin, whisky, or brandy, without sugar)—or a glass or two of claret or sherry.

LETTER ON CORPULENCE,

Addressed to the Public

By WILLIAM BANTING.

FOURTH EDITION

WITH PREFATORY REMARKS BY THE AUTHOUR

COPIOUS INFORMATION FROM CORRESPONDENTS AND CONFIRMATORY EVIDENCE OF THE BENEFIT OF THE DIETARY SYSTEM WHICH HE RECOMMENDED TO PUBLIC NOTICE

LONDON

PUBLISHED BY HARRISON, 59, PALL MALL

Bookseller to the Queen and H.R.H. the Prince of Wales

1869

PRICE ONE SHILLING

Letter on CORPULENCE

OF all the parasites that affect humanity I do not know of, nor can I imagine, any more distressing than that of Obesity, and, having emerged from a very long probation in this affliction, I am desirous of circulating my humble knowledge and experience for the benefit of other sufferers, with an earnest hope that it may lead to the same comfort and happiness I now feel under the extraordinary change,—which might almost be termed miraculous had it not been accomplished by the most simple common-sense means.

William Banting (1797-1878):

- mit 65 Jahren: 152 cm, 91 kg, BMI 39
- mit 66 Jahren: 152 cm, 68 kg, BMI 29

LETTER ON CORPULENCE,

Addressed to the Public

By WILLIAM BANTING.

“The items from which I was advised to abstain as much as possible were: Bread, butter, milk, sugar, beer, and potatoes, which had been the main (and, I thought, innocent) elements of my subsistence, or at all events they had for many years been adopted freely.

These, said my excellent adviser [Dr. William Harvey, London], contain starch and saccharine matter, tending to create fat, and should be avoided altogether.”

Elliott TD, Naughton GA, Cochrane.Database.Syst.Rev., Vol. 3, 2006

Exercise for type 2 diabetes mellitus (Review)

Thomas D, Elliott EJ, Naughton GA

THE COCHRANE COLLABORATION®

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Glycated haemoglobin (%)	13	361	Mean Difference (IV, Fixed, 95% CI)	-0.62 [-0.91, -0.33]
2 Visceral adipose tissue (cm2)	2	40	Mean Difference (IV, Fixed, 95% CI)	-45.54 [-63.76, -27.31]
3 Subcutaneous adipose tissue (cm2)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4 Body Mass (kg)	10	248	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-3.83, 3.76]
5 Triglycerides (mmol/litre)	5	139	Mean Difference (IV, Fixed, 95% CI)	-0.25 [-0.48, -0.02]
6 Maximal exercise capacity (VO2max)(ml/(kg*min))	3	95	Mean Difference (IV, Fixed, 95% CI)	4.84 [2.55, 7.12]
7 Systolic blood pressure (mmHg)	4	127	Mean Difference (IV, Fixed, 95% CI)	-4.16 [-9.46, 1.14]
8 Diastolic blood pressure (mmHg)	3	78	Mean Difference (IV, Fixed, 95% CI)	-0.13 [-3.70, 3.45]
9 Fasting plasma glucose concentration (mmol/L)	9	238	Mean Difference (IV, Fixed, 95% CI)	-0.45 [-1.09, 0.18]
10 Insulin (fasting concentration (pmol/litre)	7	168	Mean Difference (IV, Fixed, 95% CI)	-0.71 [-4.13, 2.71]
11 Body Mass index (kg/m2)	7	216	Mean Difference (IV, Fixed, 95% CI)	-0.21 [-1.35, 0.93]
12 Total cholesterol (mmol/l)	5	139	Mean Difference (IV, Fixed, 95% CI)	-0.11 [-0.41, 0.18]
13 HDL-cholesterol (mmol/)	5	139	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.10, 0.06]
14 LDL-cholesterol (mmol/)	3	73	Mean Difference (IV, Fixed, 95% CI)	0.12 [-0.29, 0.53]

"Make Your Diabetic Patients Walk"

Di Loreto C et al. Diabetes Care 2005; 28: 1295-1302

- Studientyp: prospektive Interventionsstudie (Ernährungs-/Trainingsberatung)
- Studienteilnehmer: 179 Typ 2-Diabetiker, Alter ~62 J., BMI ~ 29
- Studiendesign:
  - Ernährungsempfehlungen gemäß American Diabetes Association
  - Trainingsempfehlungen zu moderater, täglicher Aktivität
  - Beratung durch Arzt: *Dauer 30 min*; *Follow-up-Telefonat* nach 1 Monat
  - danach *15 min Beratung alle 3 Monate*, Studiendauer: 2 Jahre
- Endpunkte: erreichte MET-hours/Woche, Gewicht, Bauchumfang, Ruhepuls, Blutzucker, Cholesterin, LDL, HDL und Veränderung der Medikamentenkosten

Trainingsberatung

Di Loreto C et al. Diabetes Care 2005; 28: 1295-1302

- Vorgabe: mindestens 30 min pro Tag aktiv werden
- Ermutigung: "je länger, umso besser für den Diabetes"
- moderate körperliche Aktivität: 3-6 MET = flottes Spazierengehen
- tägliches Aktivitätsprotokoll: *was, wie lange, wie intensiv?*
- Auswertung der "MET-hours per week"

Resultate: Trainingsumfang

Di Loreto C et al. Diabetes Care 2005; 28: 1295-1302

- post-hoc Randomisierung auf 6 Gruppen mit steigendem Trainingsumfang

Gruppe	n	mittlerer Trainingsumfang (MET-h/Woche)
Gruppe 0	28	0
Gruppe 1-10	27	6,8 0,3
Gruppe 11-20	31	17,1 0,4
Gruppe 21-30	27	27,0 0,5
Gruppe 31-40	32	37,5 0,5
Gruppe > 40	34	58,3 1,8

Resultate: Endpunkte nach Trainingsumfang

Di Loreto C et al. Diabetes Care 2005; 28: 1295-1302

Table 1— Effects of physical activity counseling on energy expenditure (METs per hour per week); body weight; BMI; waist circumference; FPG; HbA_{1c}; systolic and diastolic blood pressure; resting heart rate; serum total, LDL, and HDL cholesterol; serum triglycerides; and 10-year CHD risk in 179 type 2 diabetic subjects divided into six groups on the basis of different amounts of energy expenditure

	Group 0 (n = 28) A		Group 1–10 (*n* = 27) B		Group 11–20 (*n* = 31) C		Group 21–30 (*n* = 27) D		Group 31–40 (*n* = 32) E		Group >40 (n = 34) F		Between-group comparisons	
	Basal	Change	Basal	Change	Basal	Change	Basal	Change	Basal	Change	Basal	Change	*P*	Post hoc analysis
Energy expenditure (METs · h^{-1} · $week^{-1}$)	0.3 ± 0.2	0.6 ± 0.3 (0.0–1.1)	0.3 ± 0.2	6.30 ± 0.4 (5.7–7.2)*	0.4 ± 0.2	17.1 ± 0.4 (16–17.9)	0.7 ± 0.3	27.0 ± 0.5 (25.9–28)†	0.9 ± 0.4	37.5 ± 0.5 (36–38.5)†	0.8 ± 0.3	58.3 ± 1.8 (54.3–62)†	0.000	All groups differ
Weight (kg)	80.8 ± 2.0	0.8 ± 0.5 (–0.3 to 1.9)	82.0 ± 2.6	0.6 ± 0.7 (–0.8 to 1.9)	81.3 ± 2.9	0.1 ± 0.3 (–0.6 to 0.8)	81.9 ± 2.2	–2.2 ± 0.2 (–2.6 to –1.7)†	83.1 ± 1.7	–3.0 ± 0.3 (–3.6 to –2.4)	79.8 ± 2.0	–3.2 ± 0.3 (–3.7 to –2.7)†	0.268	—
BMI (kg/m^2)	29.5 ± 0.6	0.3 ± 0.2 (–0.1 to 0.7)	29.1 ± 0.6	0.3 ± 0.3 (–0.3 to 0.8)	28.9 ± 0.4	0.03 ± 0.1 (–0.2 to 0.3)	29.3 ± 0.4	–0.8 ± 0.1 (–0.9 to –0.6)†	29.4 ± 0.5	–1.0 ± 0.1 (–1.2 to –0.8)†	29.7 ± 0.4	–1.2 ± 0.1 (–1.4 to –1.0)†	0.256	—
Waist circumference (cm)	97.3 ± 1.6	1.0 ± 0.7 (–0.5 to 2.5)	99.7 ± 2.4	1.0 ± 0.9 (–0.8 to 2.9)	100.6 ± 1.8	–0.9 ± 0.4 (–1.7 to –0.1)	100.0 ± 2.2	–3.8 ± 0.3 (–4.4 to –3.1)†	100.1 ± 1.8	–5.5 ± 0.4 (–6.3 to –4.7)†	97.3 ± 1.6	–7.1 ± 0.5 (–8.1 to –6.2)†	0.000	ABC vs. F
FPG (mmol/l)	9.1 ± 0.4	1.6 ± 2.9 (–7.5 to 4.3)	9.4 ± 0.5	–0.02 ± 0.3 (–0.6 to 0.6)	9.2 ± 0.3	–0.39 ± 0.2 (–0.8 to 0.1)	9.1 ± 0.2	–1.2 ± 0.2 (–1.7 to –0.7)†	9.3 ± 0.3	–1.6 ± 0.3 (–2.0 to –1.2)†	8.8 ± 0.2	–1.5 ± 0.1 (–1.8 to –1.3)†	0.000	A vs. F, B vs. DEF, C vs. EF
HbA_{1c} (%)	7.3 ± 0.2	0.03 ± 0.01 (–0.1 to 0.2)	7.6 ± 0.3	–0.06 ± 0.09 (–0.2 to 0.1)	7.7 ± 0.2	–0.4 ± 0.1 (–0.6 to –0.3)†	7.6 ± 0.2	–0.9 ± 0.07 (–1.0 to –0.7)†	7.7 ± 0.2	–1.1 ± 0.1 (–1.3 to –0.9)†	7.6 ± 0.2	–1.0 ± 0.1 (–1.2 to –0.9)†	0.001	B vs. EF
Maximum blood pressure (mmHg)	147 ± 2	–1.8 ± 0.9 (–3.6 to 0.1)	145 ± 3	–1.5 ± 0.9 (–3.3 to 0.3)	143 ± 3	–6.4 ± 2.4 (–11 to –1.5)*	143 ± 3	–5.6 ± 2.7 (–11 to –0.1)*	142 ± 3	–6.6 ± 1.0 (–8.6 to –4.4)†	146 ± 3	–9.1 ± 0.6 (–10.3 to –8)†	0.061	—
Minimum blood pressure (mmHg)	91 ± 3	–4.6 ± 2.5 (–9.8 to 0.6)	87 ± 1	–2.4 ± 0.9 (–4.3 to –0.5)	85 ± 1	–2.9 ± 1.6 (–4.6 to –1.2)†	86 ± 1	–4.8 ± 1.8 (–8.5 to –1.1)*	84 ± 1	–5.3 ± 0.7 (–6.8 to –3.9)*	86 ± 1	–7.1 ± 1.0 (–9.1 to –5.0)†	0.000	A vs. EF, B vs. EF
Heart rate (bpm)	81 ± 1	1.1 ± 0.7 (–0.4 to 2.4)	79 ± 2	0.5 ± 0.9 (–1.4 to 2.4)	80 ± 1	–0.9 ± 0.4 (–1.7 to –0.1)	79 ± 2	–3.8 ± 0.3 (–4.4 to –3.1)†	79 ± 2	–5.6 ± 0.4 (–6.3 to –4.7)†	76 ± 2	–7.0 ± 0.5 (–8.1 to –6.2)†	0.000	A vs. EF, B vs. F, C vs. F
Total cholesterol (mmol/l)	5.7 ± 0.1	–0.1 ± 0.05 (–0.3 to 0.1)	5.5 ± 0.1	–0.1 ± 0.1 (–0.4 to 0.1)	5.6 ± 0.2	–0.3 ± 0.1 (–0.4 to –0.1)†	5.4 ± 0.2	–0.3 ± 0.1 (–0.4 to –0.2)†	5.5 ± 0.1	–0.2 ± 0.1 (–0.3 to –0.1)†	5.6 ± 0.2	–0.3 ± 0.1 (–0.4 to –0.2)†	0.314	—
LDL cholesterol (mmol/l)	3.6 ± 0.1	–0.1 ± 0.1 (–0.3 to 0.3)	3.4 ± 0.2	–0.2 ± 0.1 (–0.5 to 0.1)	3.6 ± 0.2	–0.1 ± 0.1 (–0.2 to 0.1)	3.3 ± 0.2	–0.1 ± 0.1 (–0.3 to –0.1)*	3.4 ± 0.1	–0.2 ± 0.1 (–0.3 to –0.1)*	3.6 ± 0.2	–0.2 ± 0.1 (–0.3 to –0.1)†	0.376	—
HDL cholesterol (mmol/l)	1.0 ± 0.1	0.1 ± 0.1 (–0.1 to 0.1)	1.0 ± 0.1	0.1 ± 0.1 (–0.1 to 0.1)	1.0 ± 0.1	0.1 ± 0.1 (–0.1 to 0.2)	0.1 ± 0.1	0.1 ± 0.1 (0.1 to 0.2)†	0.1 ± 0.1	0.3 ± 0.1 (0.2 to 0.4)*	1.0 ± 0.1	0.2 ± 0.1 (0.1 to 0.2)†	0.000	ABC vs. EF
Triglycerides (mmol/l)	2.3 ± 0.1	0.1 ± 0.1 (–0.1 to 0.2)	2.2 ± 0.1	0.1 ± 0.1 (–0.1 to 0.2)	2.4 ± 0.1	–0.5 ± 0.1 (–0.7 to –0.2)†	2.4 ± 0.1	–0.6 ± 0.1 (–0.8 to –0.5)	2.3 ± 0.1	–0.6 ± 0.1 (–0.8 to –0.5)†	2.2 ± 0.1	–0.8 ± 0.1 (–0.9 to –0.6)†	0.000	AB vs. CDEF
10-year CHD risk (%)	24.4 ± 1.9	0.1 ± 0.3 (–0.6 to 0.7)	21.3 ± 1.8	–0.3 ± 0.5 (–1.2 to 0.6)	22.5 ± 1.6	–2.6 ± 0.6 (–3.9 to –1.3)†	22.9 ± 1.7	–3.7 ± 0.7 (–5.2 to –2.2)†	24.6 ± 1.7	–4.8 ± 1.0 (–6.8 to –2.8)†	21.1 ± 1.5	–4.3 ± 1.0 (–6.3 to –2.4)*	0.000	A vs. CDEF

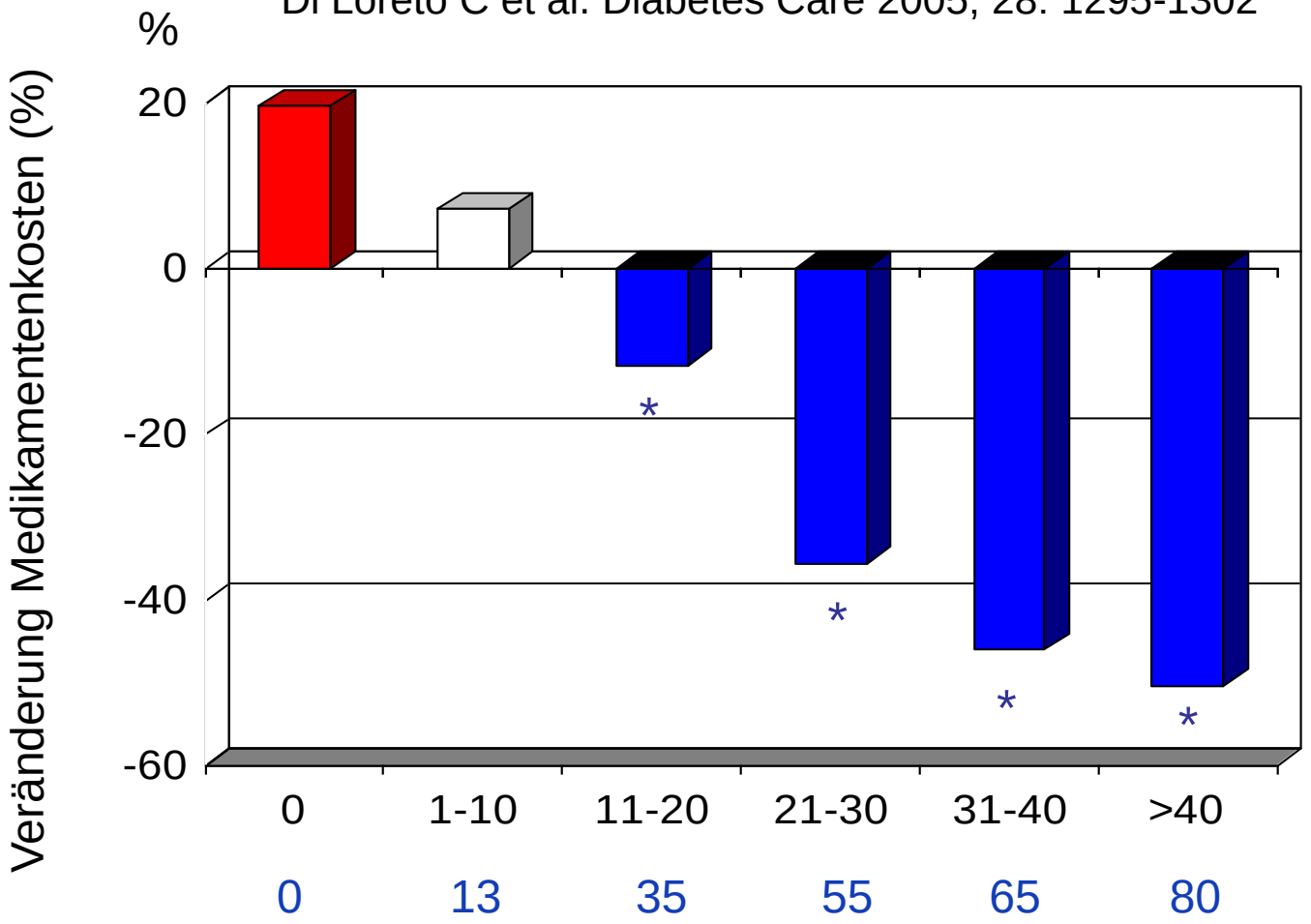
Spazierengehen (min)	0	13	35	55	65	80
KG, kg	+ 0.8	+ 0.6	+ 0.1	- 2.2	- 3.0	- 3.2
Bauch, cm	+ 1.0	+ 1.0	- 0.9	- 3.8	- 5.5	- 7.1
HBA1c, %	+ 0.03	- 0.06	- 0.44	- 0.88	- 1.11	- 1.19
RRsys, mmHg	- 1.8	- 1.5	- 6.4	- 5.5	- 6.6	- 9.1
RRdia, mmHg	- 4.6	- 2.4	- 2.9	- 4.8	- 5.3	- 7.1
Ges.-Chol., mg/dl	- 3.8	- 3,8	- 11,6	- 11,6	- 7,2	- 11,6
LDL-Chol., mg/dl	- 3,8	- 7.7	- 3.8	- 3,8	- 7,7	- 7.7
HDL-Chol., mg/dl	+ 3,8	+ 3,8	+ 3,8	+ 3,8	+ 10.4	+ 7,7
TG, mg/dl	+ 8,8	+ 8,8	- 43,8	- 52,5	- 52,5	- 70
10-J-KHK-Risiko %	+ 0.1	- 0.3	- 2.6	- 3.7	- 4.8	- 4.3

p<0.05 p<0.01

Di Loreto C et al. Diabetes Care 2005; 28: 1295-1302

Einsparung von Medikamenten-Kosten je nach Trainingsumfang

Di Loreto C et al. Diabetes Care 2005; 28: 1295-1302



* = p<0.05

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Fitness und Mortalität bei Diabetikern

Wei M et al., Ann Int Med 2000; 132: 605-611

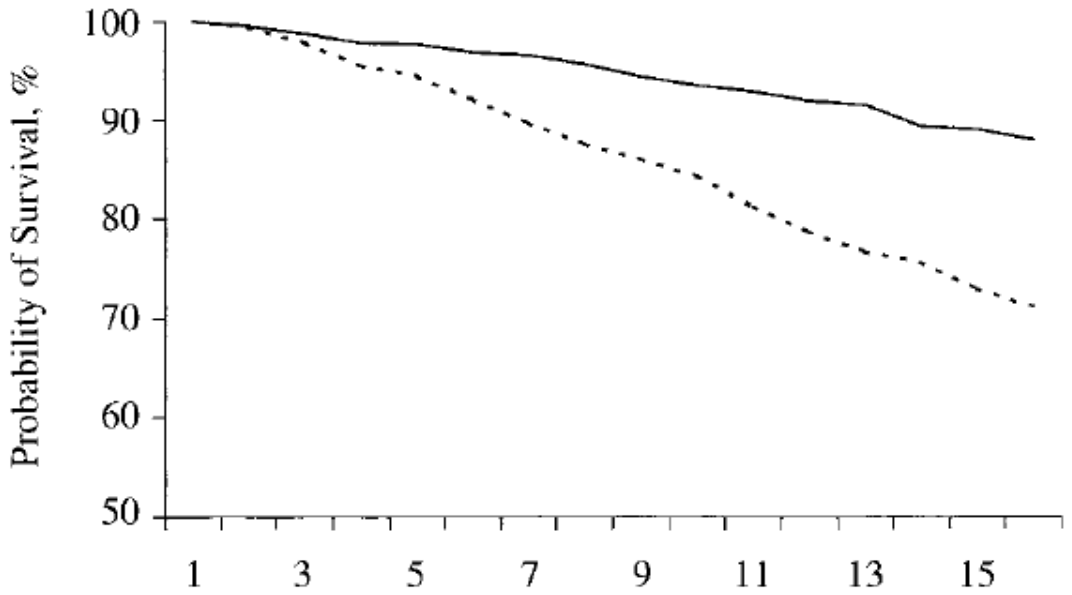

Figure. Survival curves for all-cause mortality by cardiorespiratory fitness category. Data are from 1263 men with 180 all-cause deaths during 14 777 man-years of observation. The solid line represents fit participants and the dashed line represents unfit participants.

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Gewichtsreduktion mit/ohne Krafttraining bei Typ 2-Diabetikern

Dunstan, DW et al., Diabetes Care 2002; 25: 1729-1736

- Studientyp: prospektive Interventionsstudie (Ernährung und Krafttraining)
- Studienteilnehmer:
  - 29 Typ 2-Diabetiker (16 Männer, 13 Frauen)
  - sportlich nicht aktiv, BMI ~32, HbA1c 7,0% - 10,0%, keine Insulintherapie
  - Vergleich Gewichtsreduktion mit / ohne Krafttraining
- Studiendesign:
  - Ernährungsumstellung mit dem Ziel Gewichtsreduktion (-1kg pro Monat)
  - Vergleich systematisches Krafttraining vs. "Placebo-Aktivität"
- Endpunkte: Kraftzuwachs, Stoffwechseleffekte

Gewichtsreduktion mit/ohne Krafttraining bei Typ 2-Diabetikern: Interventionen

Dunstan, DW et al., Diabetes Care 2002; 25: 1729-1736

- Für alle: Ernährungsplan („healthy eating plan“)
  - Ziel - 1 kg pro Monat: < 30% Fett, < 10% ges. FS
- Gruppe 1: Ernährungsberatung + Krafttraining
  - an 3 Tagen pro Woche je 45 min
  - hoch-intensives Training (Hypertrophietraining)

    1. und 2. Woche 50-60% 1-RM (Kraftausdauer),

    ab 3. Woche 75-85% 1 RM (Hypertrophietraining)
- Gruppe 2: Ernährungsberatung + „Bewegung“
  - Radfahren ohne Belastung + Stretching

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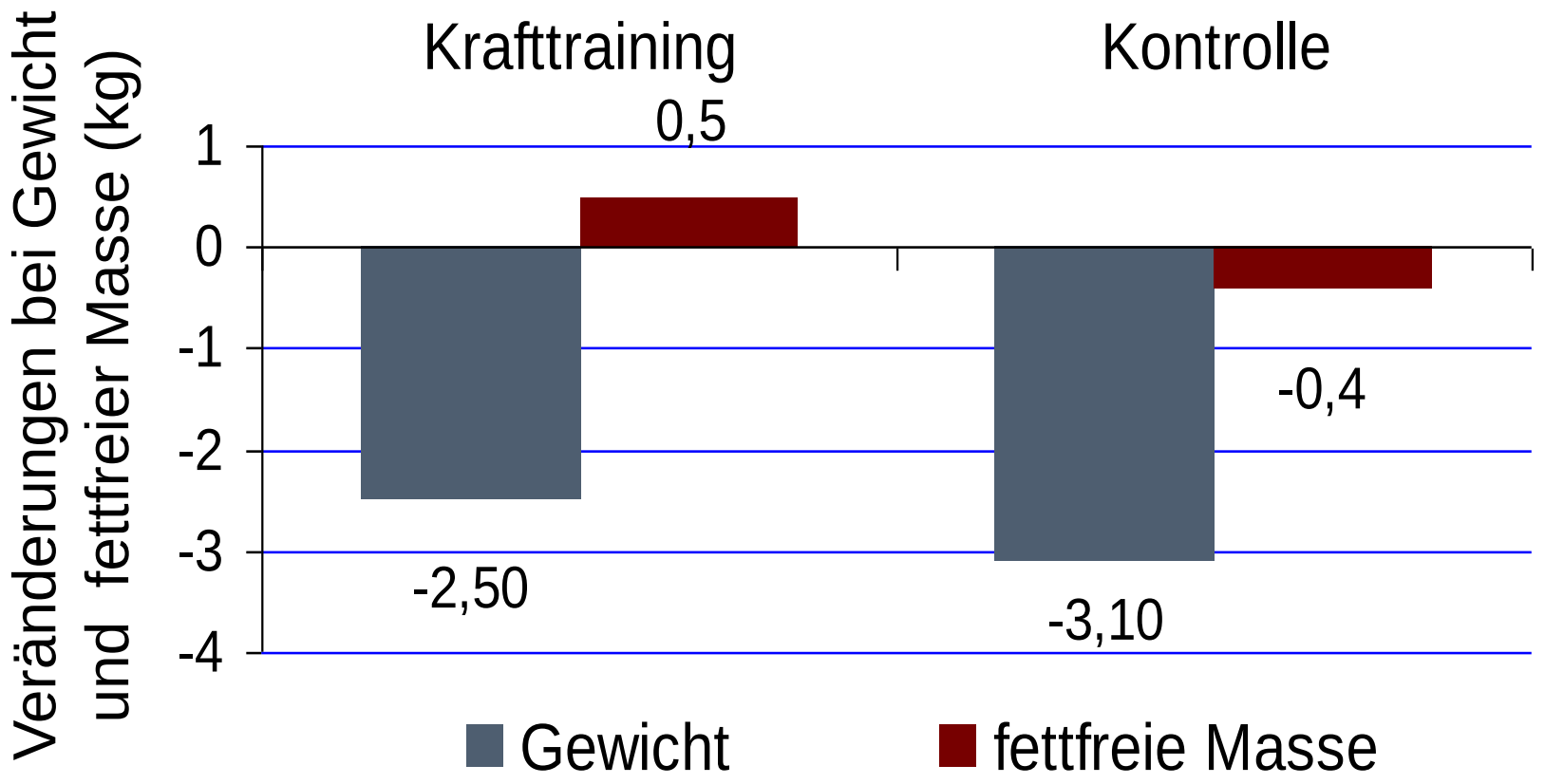
Gewichtsreduktion mit/ohne Krafttraining bei Typ 2-Diabetikern

Dunstan, DW et al., Diabetes Care 2002; 25: 1729-1736



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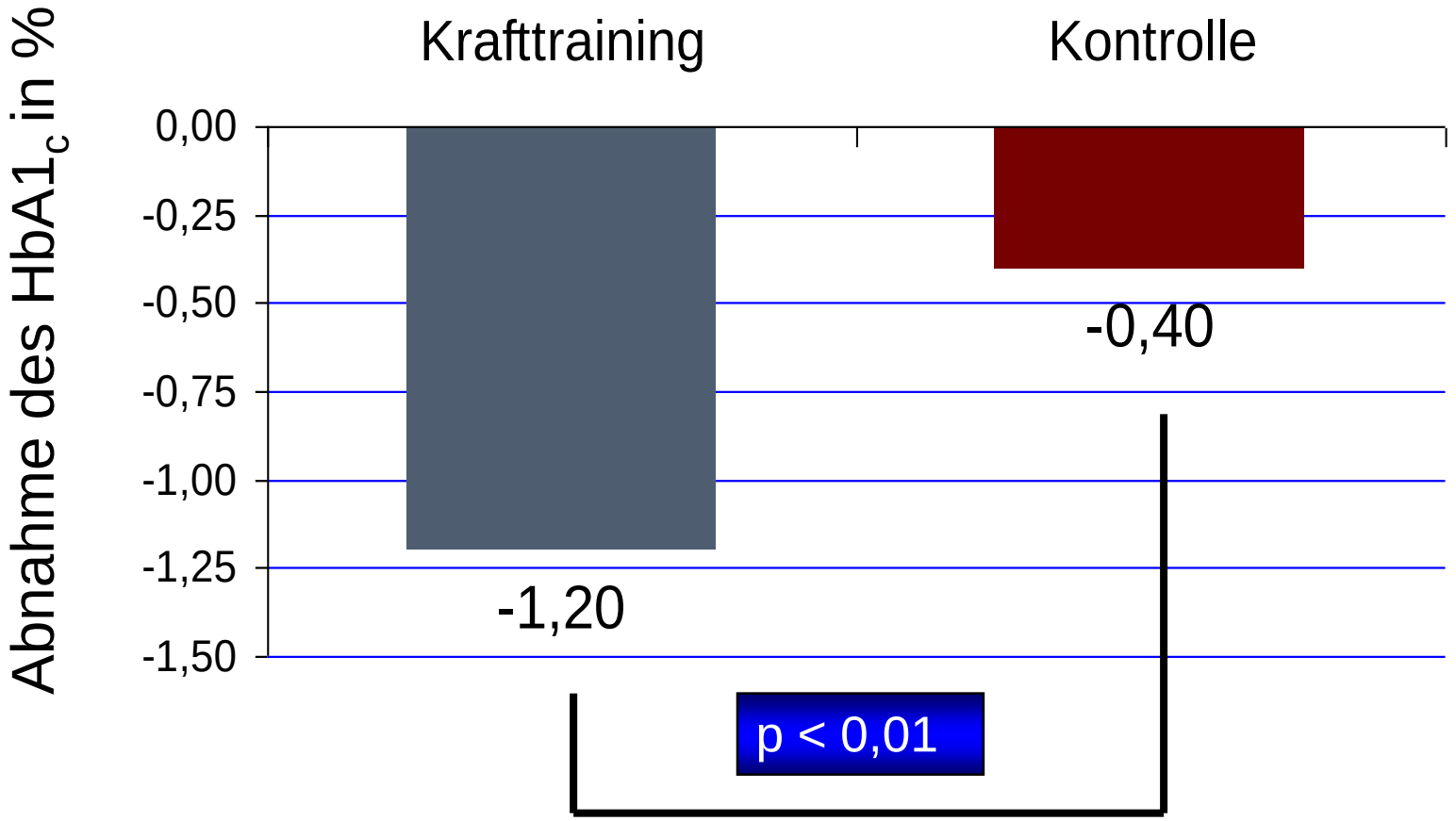
Gewichtsreduktion mit/ohne Krafttraining bei Typ 2-Diabetikern

Dunstan, DW et al., Diabetes Care 2002; 25: 1729-1736



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Ausdauertraining, Krafttraining oder beides in der Therapie des Typ 2-Diabetes

Sigal RJ, Ann Int Med 2007; 147: 357-369

- Studientyp: randomisierte, kontrollierte Interventionsstudie
- Studienteilnehmer:
  - 251 Typ 2-Diabetiker (39-70 Jahre), Diabetesdauer > 6 Monate
  - sportlich nicht aktiv, HbA1c 6,6% - 9,9%, keine Insulintherapie
  - unauffällige Ergometrie; erfolgreiche Teilnahme an 4 Wochen "run-in"
- Studiendesign:
  - Randomisierung auf 4 Gruppen:
    Ausdauertraining, Krafttraining, Ausdauer- und Krafttraining bzw. inaktiv
- Endpunkte:
  - primär: HbA1c nach 26 Wochen
  - sekundär: Körperzusammensetzung, Lipide, Blutdruck

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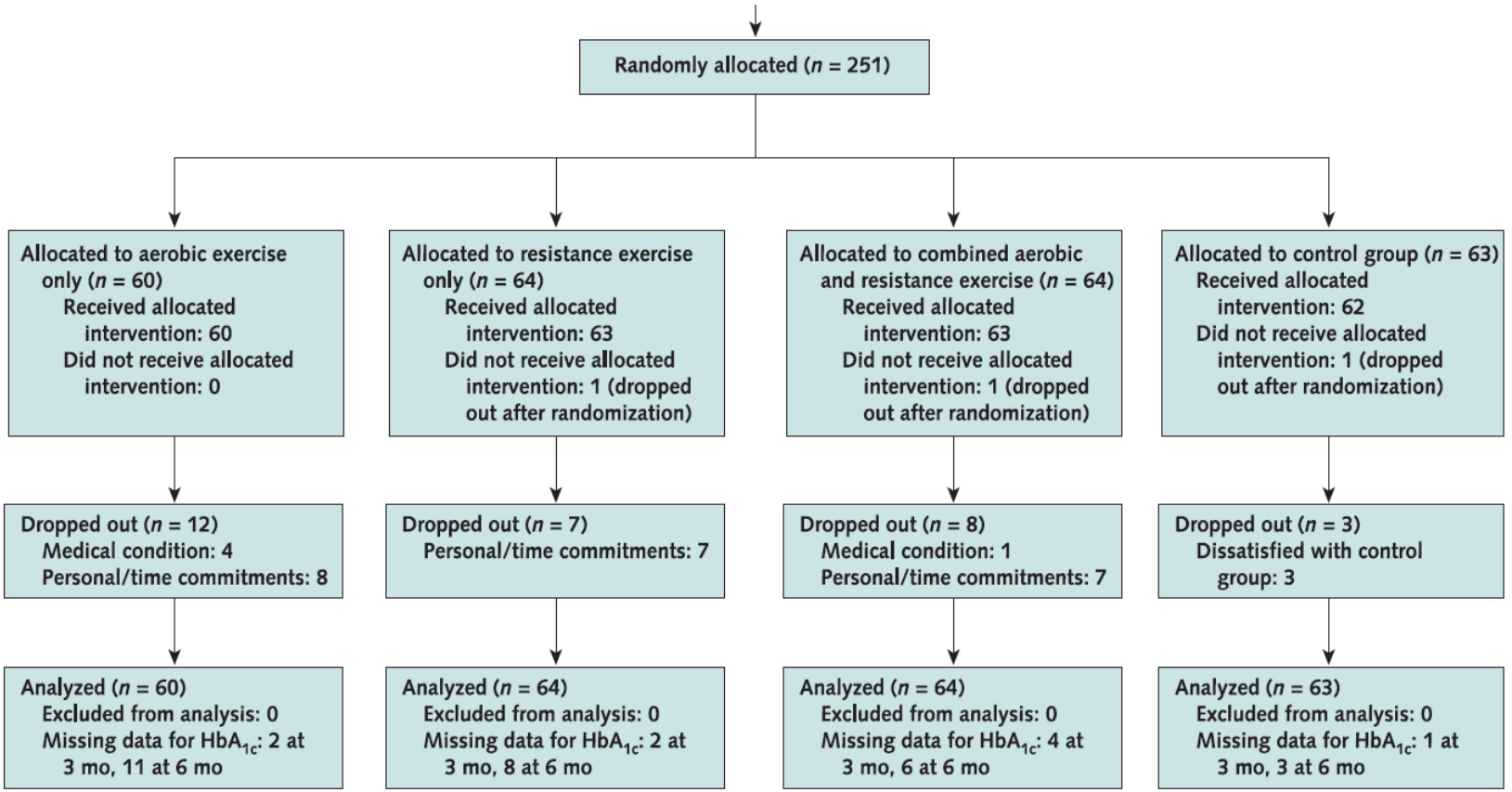
Ausdauertraining, Krafttraining oder beides in der Therapie des Typ 2-Diabetes

Sigal RJ, Ann Int Med 2007; 147: 357-369

- Trainingspläne: Training grundsätzlich an drei Tagen pro Woche
- Ausdauer:
  Beginn mit 15-20 min bei 65% HFmax, Steigerung auf 45 min bei 75% HFmax
- Kraft:
  7 Übungen, kontinuierliche Steigerung, 7-9 Wiederholungen, je 2-3 Sätze
- Ausdauer + Kraft:
  höherer Zeitaufwand, da beide volle Trainingseinheiten nacheinander
- Kontrollgrupe:
  Rückkehr zu früherer Aktivität vor "run-in"
- Ernährung: nach Leitlinien der Canadian Diabetes Association

Ausdauertraining, Krafttraining oder beides in der Therapie des Typ 2-Diabetes

Sigal RJ, Ann Int Med 2007; 147: 357-369



HbA_{1c} = hemoglobin A_{1c}.

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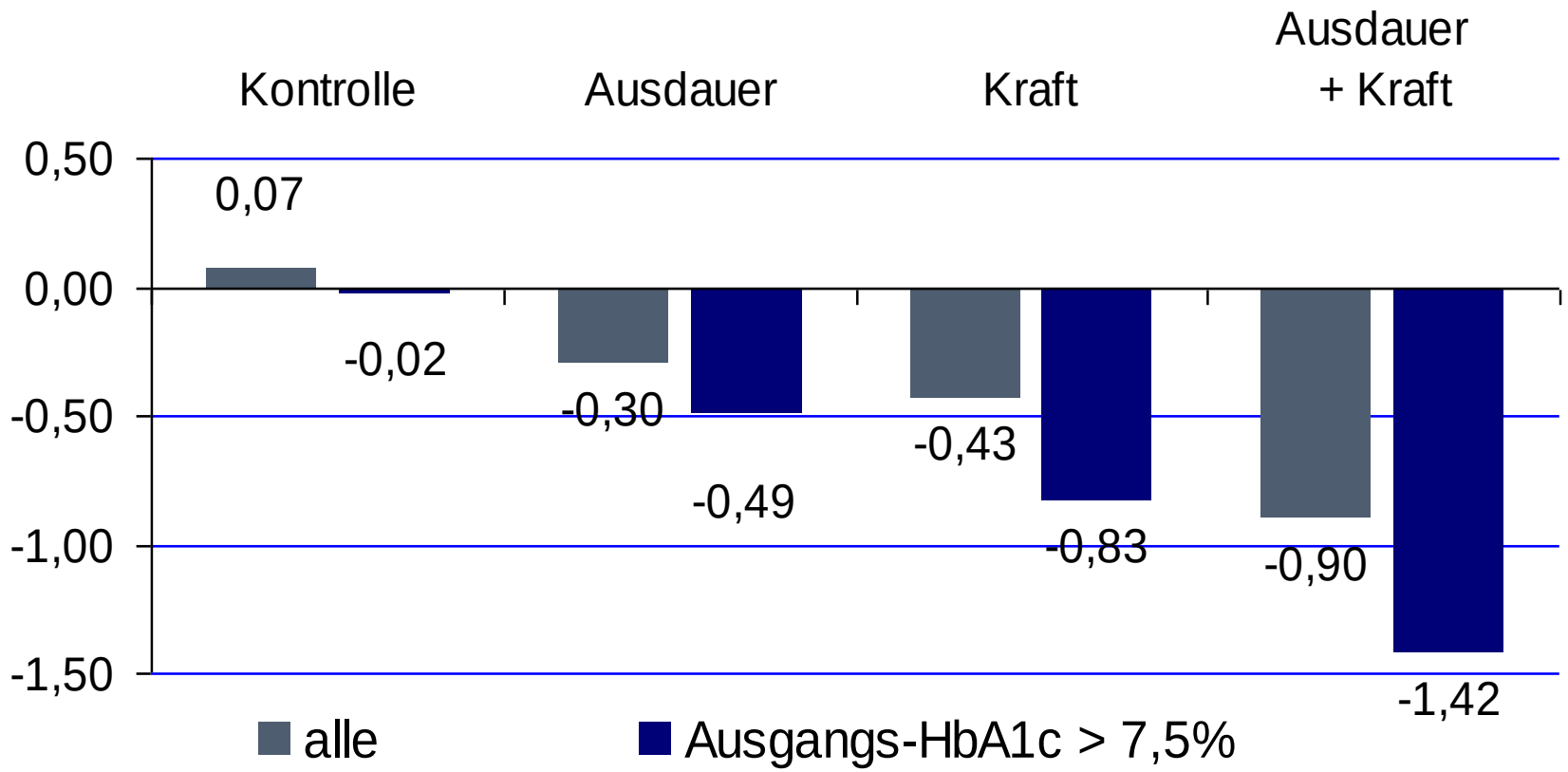
Ausdauertraining, Krafttraining oder beides in der Therapie des Typ 2-Diabetes

Sigal RJ, Ann Int Med 2007; 147: 357-369



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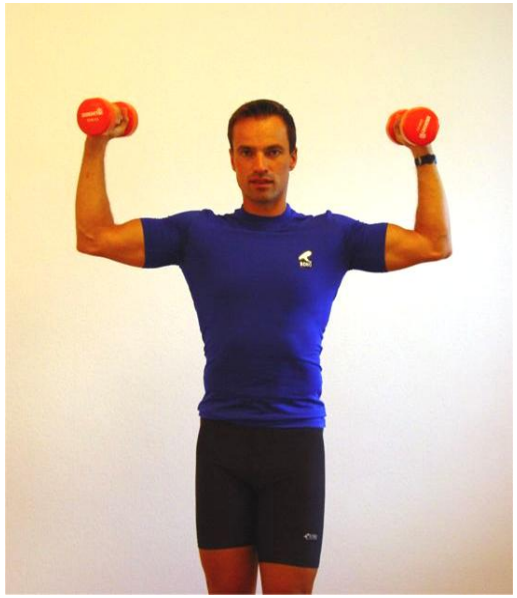

- **Position**: Halten Sie die Knie immer leicht gebeugt und den Rücken gerade.
- **Bewegung**: Bewegen Sie die Hände aus leicht gebeugter Armhaltung zu den Schultern und betont langsam wieder zurück.
- **W** 15 / **S** 2-3 / **P** 30 sec

- **Position**: Nehmen Sie eine leichte Schrittstellung ein. Halten Sie die Knie immer leicht gebeugt und den Rücken immer gerade.
- **Bewegung**: Bewegen Sie das Tube aus einer leicht gebeugten Armhaltung seitlich nach oben und betont langsam wieder zurück.
- **W** 10 / **S** 2-3 / **P** 30 sec
  im Wechsel mit Bizepsübung

Trainingsempfehlungen zum Krafttraining

- Programm mit Übungen für alle Muskelgruppen, Lernen unter Supervision!
- zu Beginn Kraftausdauertraining = ca. 50% 1RM, 25-30 Wdh.
  - Vorsicht: Knochen, Sehnen und Bänder passen sich langsamer an die Belastungen an als die Muskulatur.
- nach 6-8 Woche: Hypertrophietraining = ca.70-80% 1RM, 8-15 Wdh.
  - Vorsicht: Pressatmung mit Blutdruckspitzen vermeiden
- 2x Krafttraining pro Woche ist ausreichend. 3x bringt kaum mehr Zuwachs.

Anweisungen zum Krafttraining an die Patienten

- Führen Sie die gesamte Bewegung immer von der Ausgangs- bis zur Endposition durch.
- Atmen Sie ruhig, fließend und gleichmäßig im Bewegungsrhythmus:
  - In der überwindenden Phase ausatmen.
  - In der nachgebenden Phase einatmen.
- Das Tempo der Bewegungsausführung ist grundsätzlich sehr langsam.
- Auch die letzten Wiederholungen sollten technisch einwandfrei ausgeführt werden können.

Trainingsempfehlungen bei Typ 2-Diabetes (American Diabetes Association)

Sigal RJ et al., Diab Care 2006; 29: 1633-1638

Reviews/Commentaries/ADA Statements
CONSENSUS STATEMENT

Physical Activity/Exercise and Type 2 Diabetes

A consensus statement from the American Diabetes Association

RONALD J. SIGAL, MD, MPH[1,2,3]
GLEN P. KENNY, PHD[2,3]
DAVID H. WASSERMAN, PHD[4]
CARMEN CASTANEDA-SCEPPA, MD, PHD[5]
RUSSELL D. WHITE, MD[6]

For decades, exercise has been considered a cornerstone of diabetes management, along with diet and medication. However, high-quality evidence on the importance of exercise and fitness in diabetes was lacking until recent years. The present document summarizes the most clinically relevant recent advances related to people with type 2 diabetes and the recommendations that follow from these. Our recently published technical review on physical activity/exercise and type 2 diabetes (1) includes greater detail on individual studies, on prevention of diabetes, and on the physiology of exercise.

The present statement focuses on type 2 diabetes. Issues primarily germane to type 1 diabetes will be covered in a subsequent technical review and ADA Statement. The levels of evidence used are defined by the ADA in ref. 2.

PHYSICAL ACTIVITY AND PREVENTION OF TYPE 2 DIABETES — Two randomized trials each found that lifestyle interventions including ~150 min/week of physical activity and diet-induced weight loss of 5–7% reduced the risk of progression from impaired glucose tolerance (IGT) to type 2 diabetes by 58% (3,4). A cluster-randomized trial found that diet alone, exercise alone, and combined diet and exercise were equally effective in reducting the progression from IGT to diabetes (5). Therefore, there is firm and consistent evidence that programs of increased physical activity and modest weight loss reduce the incidence of type 2 diabetes in individuals with IGT.

EFFECTS OF STRUCTURED EXERCISE INTERVENTIONS ON GLYCEMIC CONTROL AND BODY WEIGHT IN TYPE 2 DIABETES — Boulé et al. (6) undertook a systematic review and meta-analysis on the effects of structured exercise interventions in clinical trials of ≥8 weeks duration on HbA_{1c} (A1C) and body mass in people with type 2 diabetes. Postintervention A1C was significantly lower in exercise than control groups (7.65 vs. 8.31%, weighted mean difference −0.66%; $P < 0.001$). In contrast, postintervention body weight did not differ between the exercise and control groups. Meta-regression confirmed that the beneficial effect of exercise on A1C was independent of any effect on body weight. Therefore, structured exercise programs had a statistically and clinically significant beneficial effect on glycemic control, and this effect was not primarily mediated by weight loss. A subsequent meta-analysis by the same authors (7) showed that exercise intensity predicted postintervention weighted mean difference in A1C ($r = -0.91, P = 0.002$) to a larger extent than exercise volume ($r = -0.46, P = 0.26$). These results provide support for encouraging type 2 diabetic individuals who are already exercising at moderate intensity to consider increasing the intensity of their exercise in order to obtain additional benefits in both aerobic fitness and glycemic control.

PHYSICAL ACTIVITY, AEROBIC FITNESS, AND RISK OF CARDIOVASCULAR AND OVERALL MORTALITY — Large cohort studies have found that higher levels of habitual aerobic fitness and/or physical activity are associated with significantly lower subsequent cardiovascular and overall mortality (8–10), to a much greater extent than could be explained by glucose lowering alone. For example, Church et al. (8) found that men in the lowest, second, and third quartiles of cardiorespiratory fitness had 4.5-, 2.8-, and 1.6-fold greater risk for overall mortality than men in the highest quartile of cardiorespiratory fitness, even after adjustment for age, examination year, baseline cardiovascular disease (CVD), hypercholesterolemia, hypertriglyceridemia, BMI, hypertension, parental CVD, smoking, and baseline fasting glucose levels. Essentially all of the association between higher BMI and higher mortality was explained by confounding with cardiorespiratory fitness; there was no difference in mortality among normal-weight, overweight, and obese men after adjustment for cardiorespiratory fitness.

In the same cohort, it was shown that among moderately fit subjects (21st–60th percentile for age) whose only exercise was walking, the mean time spent per week on exercise was 130 min for men and 148 min for women (11). These times are consistent with recommendations from the U.S. Surgeon General (12) and other respected bodies (13–15) stating that 150 min/week of moderate-intensity exercise should be accumulated. Moderately fit subjects whose only exercise was jogging or running reported a mean of 90 min/week for men and 92 min/week for women. These times are consistent with

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Abbreviations: CAD, coronary artery disease; CVD, cardiovascular disease; ECG, electrocardiogram; IGT, impaired glucose tolerance.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc06-9910

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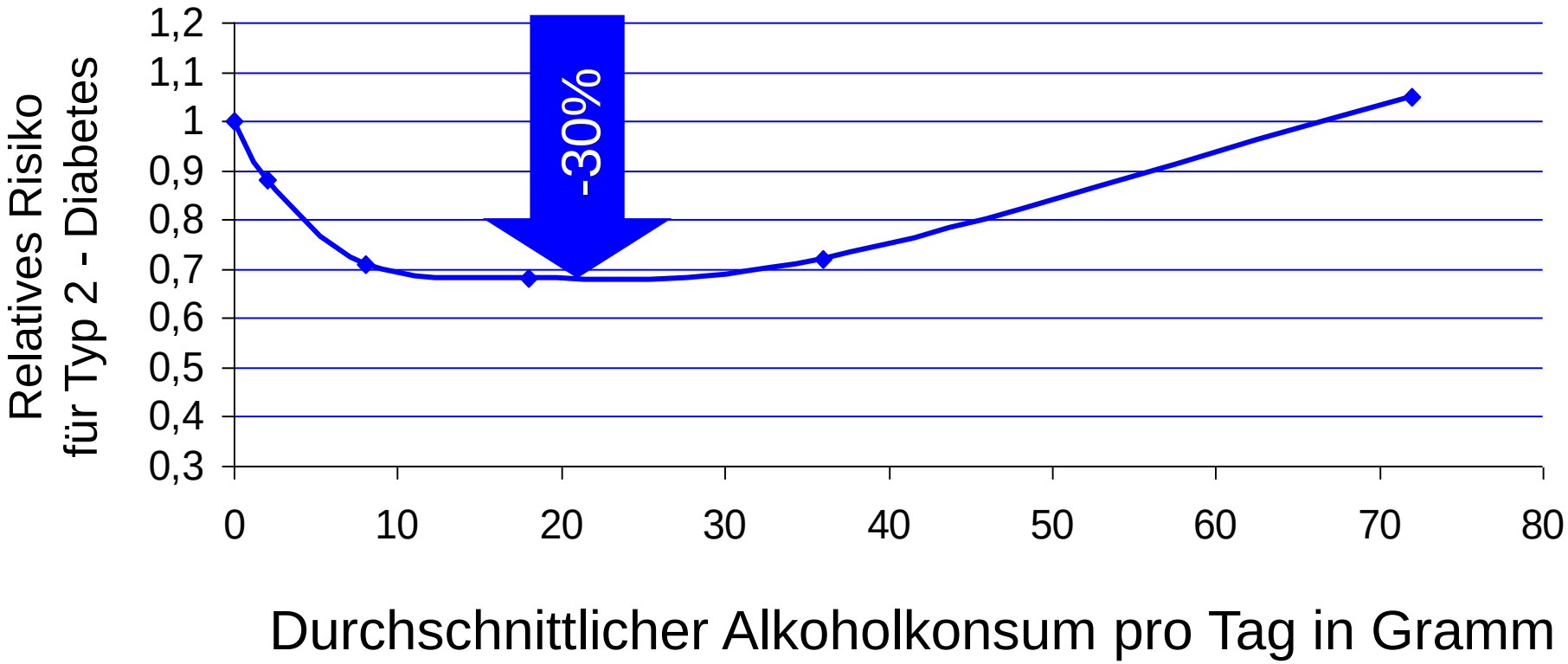
Meta-Analyse 2005:
Alkoholkonsum und Risiko für Typ 2-Diabetes

Koppes LLJ et al., Diabetes Care 2005; 28: 719-725



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Das ideale „Diabetes-Preventicum“

- senkt die Insulinresistenz
- verzögert die Diabetesmanifestation
- verbessert das Herz-Kreislauf-Risikoprofil
- ist nebenwirkungsarm
- ist langfristig betrachtet kostengünstig

Das ideale „Diabetes-Preventicum“

1. Ausdauertraining: ≥ 5x30 min / Woche (GA-I-Bereich)
2. 2x / Woche Krafttraining zum Muskelaufbau (Kraftausdauer)
3. LOGI-Methode: Reduktion der glykämischen Last
4. 1 Glas Wein pro Tag (ohne Kontraindikationen!)

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Insulinresistenz, Metabolisches Syndrom und die Prävention des Typ 2-Diabetes

1. Epidemiologie: Metabolisches Syndrom, Typ 2 – Diabetes und KHK
2. Pathophysiologie der Insulinresistenz: Risikofaktor für KHK
3. Screening auf erhöhtes Diabetes-Risiko: praxistaugliche Methoden
4. Einfluss von Lebensstil-Faktoren: (Ernährung) und körperliche Aktivität
5. Medikamente in Prävention und Therapie

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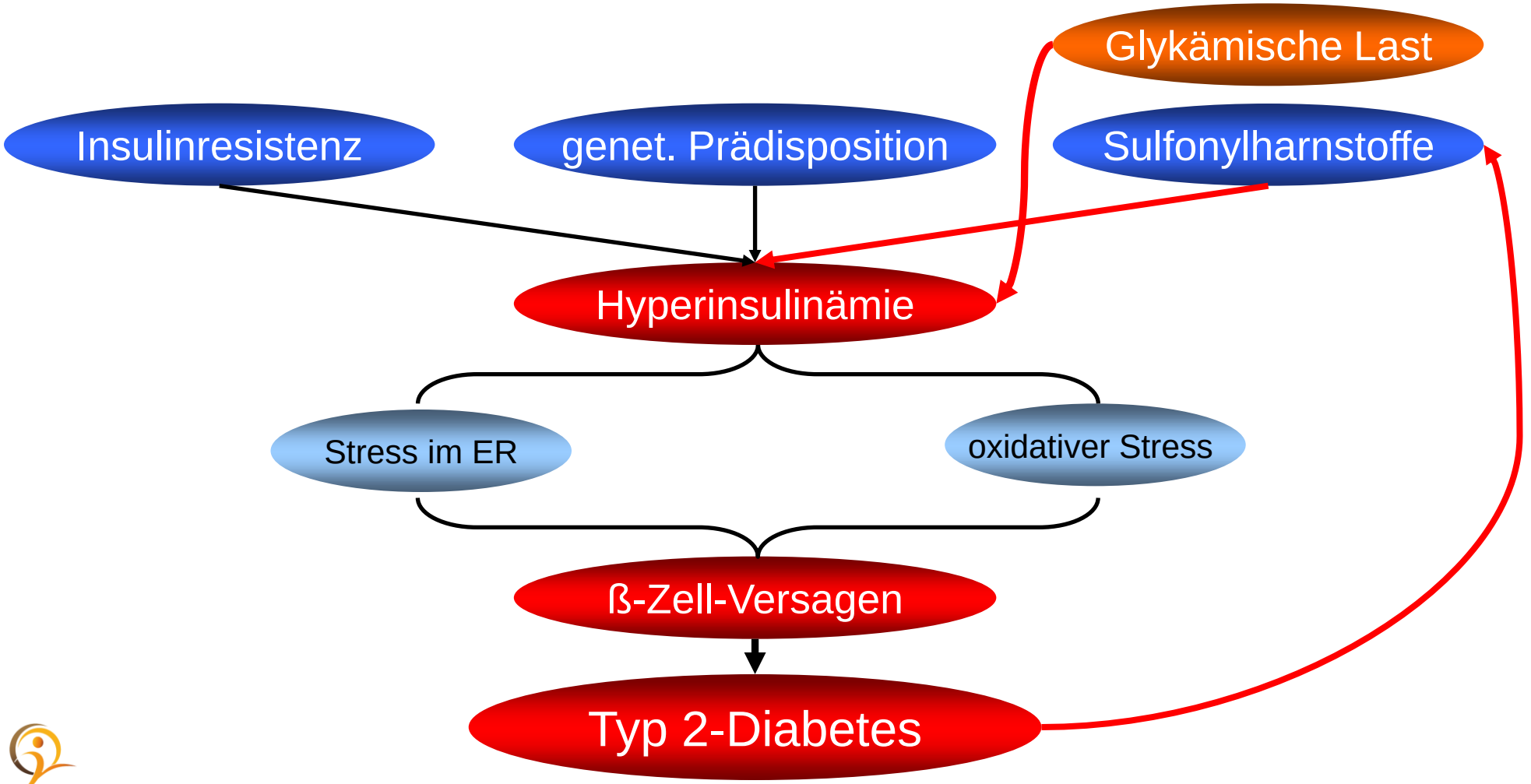
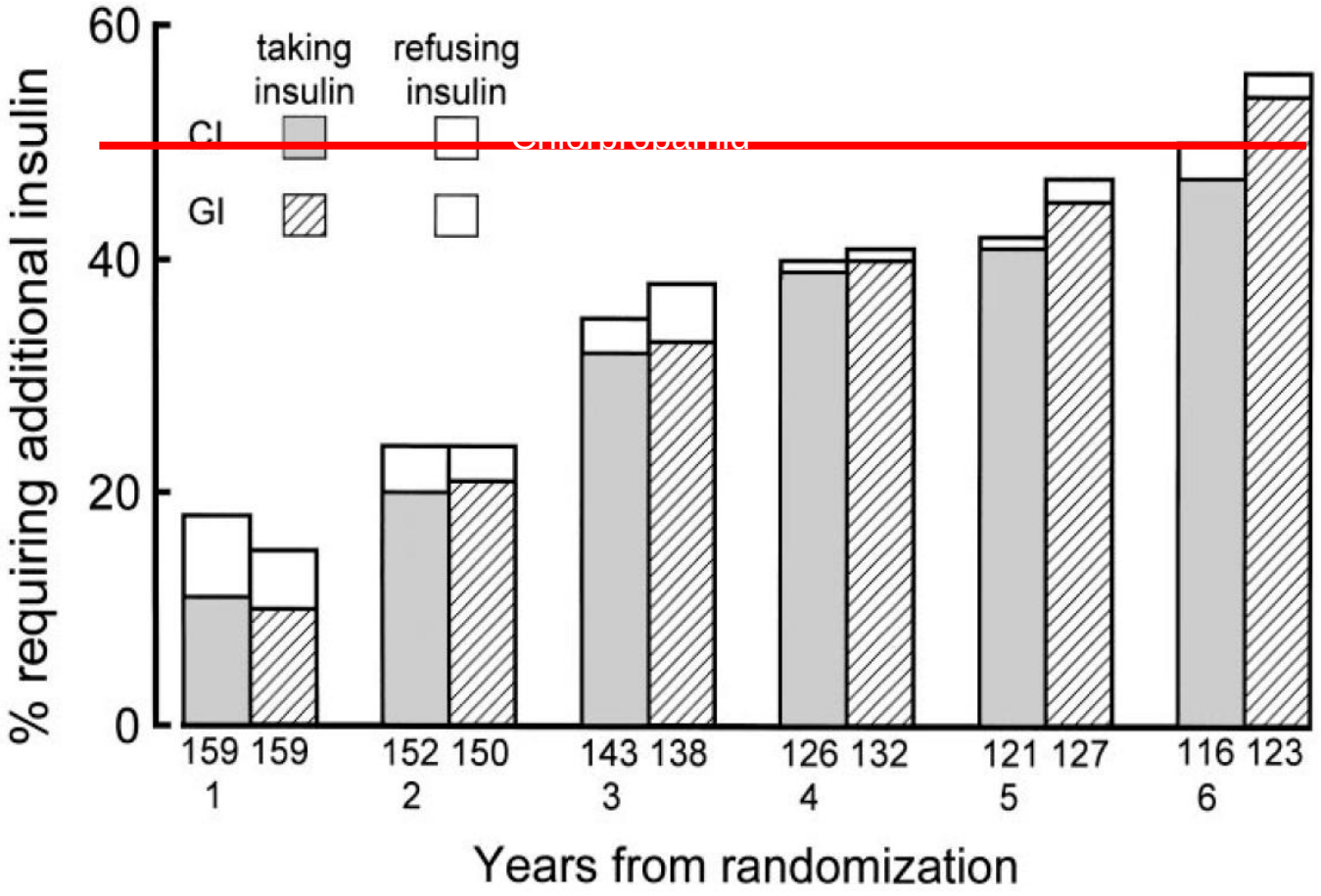
ß-Zell-Stimulation beschleunigt ß-Zell-Versagen

Aston-Mourney K, Diabetologia 2008; 52: 540-545



Zeitverlauf bis zum Sekundärversagen (UKPDS 57)

Wright A et al., Diabetes Care 2002; 25: 330-336



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DREAM Trial Investigators, Lancet 2006; Published online September 15, 2006
DOI:10.1016/S0140-6736(06)69420-8

Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial

*The DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators**

Summary

Background Rosiglitazone is a thiazolidinedione that reduces insulin resistance and might preserve insulin secretion. The aim of this study was to assess prospectively the drug's ability to prevent type 2 diabetes in individuals at high risk of developing the condition.

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DREAM Trial Investigators, Lancet 2006; Published online September 15, 2006
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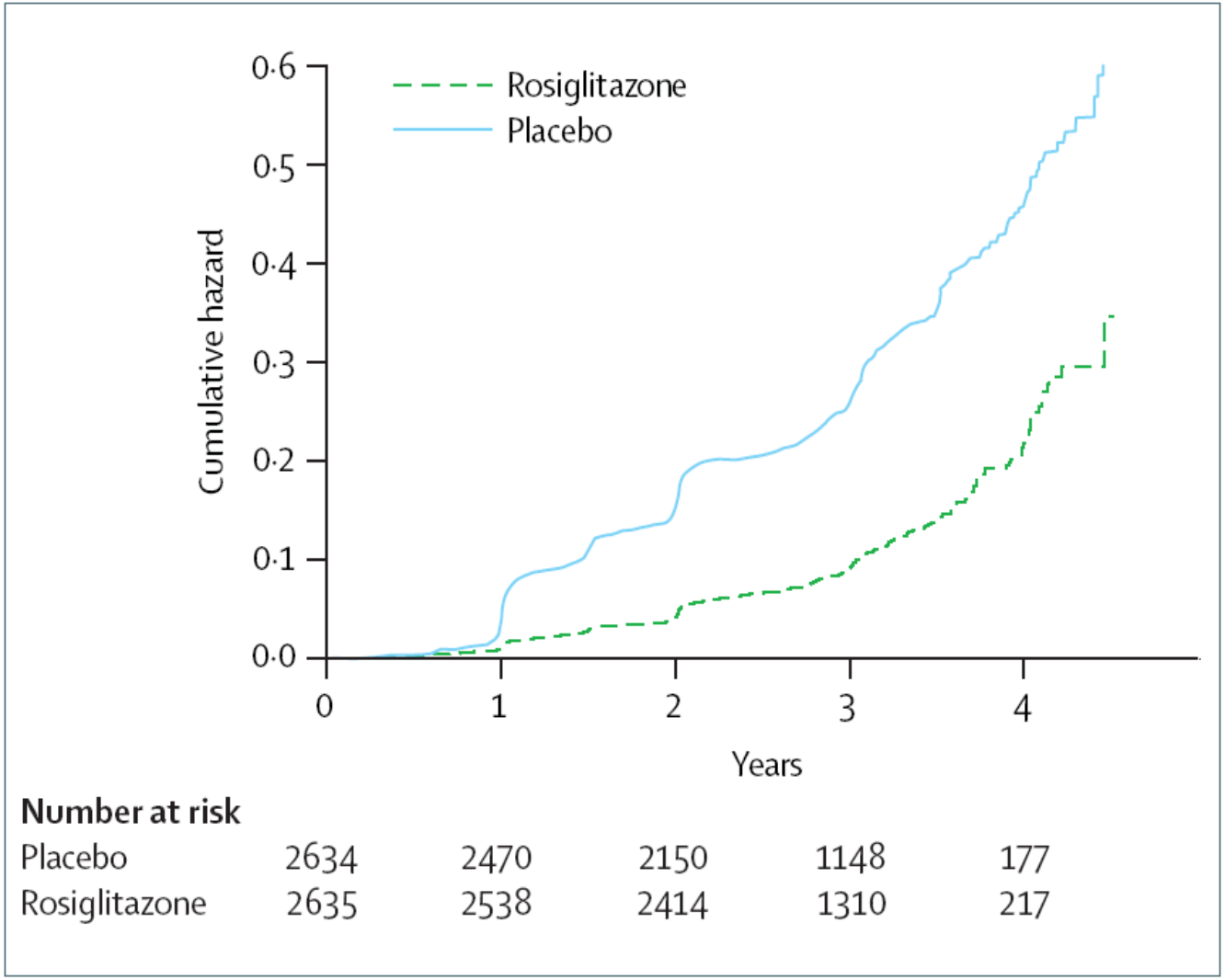

Figure 2: **Time to occurrence of primary outcome**

DREAM Trial Investigators, Lancet 2006; Published online September 15, 2006
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	Rosiglitazone group (n=2635)	Placebo group (n=2634)	HR (95% CI)	p
Composite primary outcome*	306 (11·6%)	686 (26·0%)	0·40 (0·35–0·46)	<0·0001
Diabetes	280 (10·6%)	658 (25·0%)	0·38 (0·33–0·44)	<0·0001
Diagnosed by FPG/OGTT	231 (8·8%)	555 (21·1%)	0·38 (0·33–0·44)	<0·0001
Physician diagnosed	49 (1·9%)	103 (3·9%)	0·47 (0·33–0·66)	<0·0001
Death	30 (1·1%)	33 (1·3%)	0·91 (0·55–1·49)	0·7
Regression (FPG <6·1 mmol/L)†	1330 (50·5%)	798 (30·3%)	1·71 (1·57–1·87)	<0·0001
Regression (FPG <5·6 mmol/L)†	1016 (38·6%)	540 (20·5%)	1·83 (1·65–2·04)	<0·0001

...

Data are number (%). *Rows are not mutually exclusive for components of the composite—if a participant had more than one component of the composite then they are counted in the relevant row. †Regression implies achieving a normal fasting glucose concentration (as defined in both rows) and 2-h plasma glucose level. ‡Defined as acute treatment with at least two of the following criteria: typical signs and symptoms, typical radiological evidence, use of diuretics, vasodilators, or inotropes. FPG=fasting plasma glucose. OGTT=oral glucose tolerance test.

Table 2: **Primary and other outcomes**

Montori VM et al., BMJ 2007; 334;882-884

Waking up from the DREAM of preventing diabetes with drugs

A drug to prevent diabetes would be attractive. But despite promotion of recent research evidence, **Victor Montori**, **William Isley**, and **Gordon Guyatt** argue that we are not there yet

"We can tell patients at 25% risk of requiring a diabetes drug that we are going to give them a 100% chance of receiving that drug for three years in order to reduce their risk of requiring it in the future to 10%."

Preventing diabetes

Several randomised trials have shown that modest weight loss and physical activity can greatly reduce the risk of diabetes.[5-7] The Diabetes Prevention Program documented a 58% relative risk reduction (confidence interval 48% to 66%) in high risk individuals[5]; other trials have shown similar results.[6 7]

Nevertheless, the possibility of preventing diabetes

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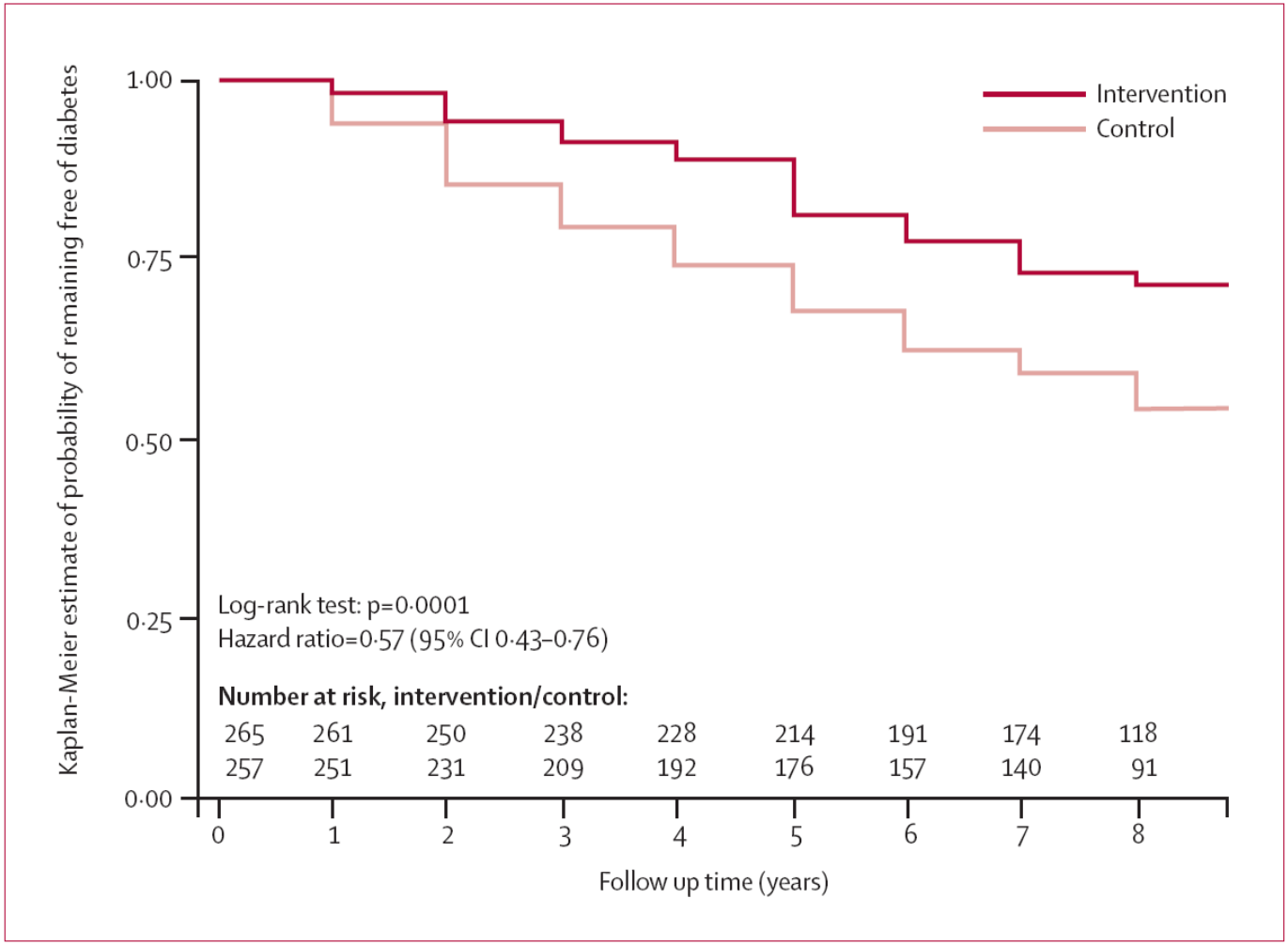
troglitazone was 0.25 (P<0.001), but the effect disappeared in the year after drug discontinuation[12]

Angiotensin converting enzyme inhibitors, angiotensin receptor blockers

- Systematic reviews of trials in hypertension, heart failure, and coronary disease that assessed diabetes as a secondary or post hoc outcome found large preventive effects[13]
- DREAM trial failed to confirm the effect[14]

Langzeit-Ergebnisse in der Finnischen Diabetes-Präventionsstudie

Lindström, J et al., Lancet 2006; 368: 1673-1679



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Langzeit-Ergebnisse in der China Da Qing Diabetes-Präventionsstudie

Li, G et al., Lancet 2008; 371: 1783-1789

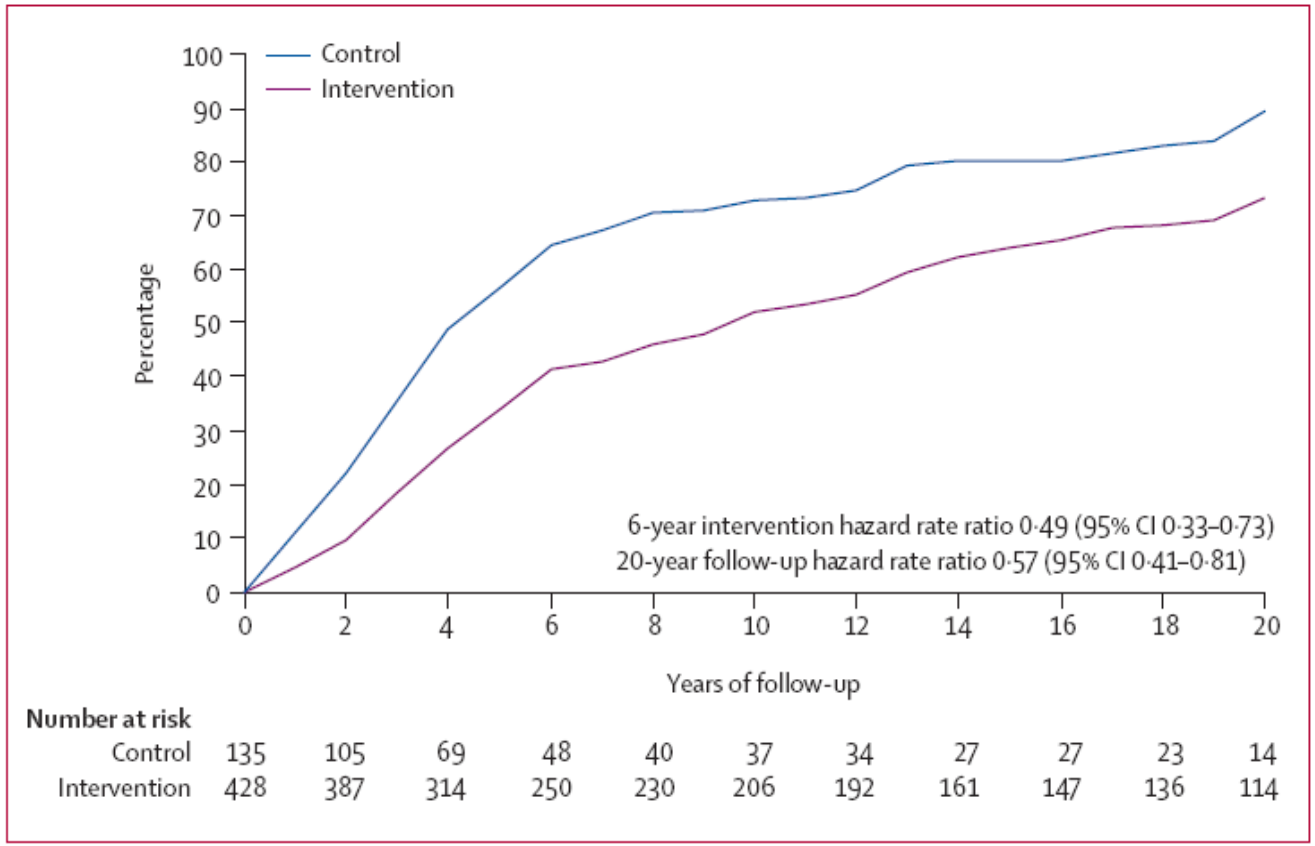

Figure 2: Cumulative incidence of diabetes mellitus during follow-up in China Da Qing Diabetes Prevention Outcome Study

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Das ideale „Diabetes-Preventicum“

1. Ausdauertraining: ≥ 5x30 min / Woche (GA-I-Bereich)
2. 2x / Woche Krafttraining zum Muskelaufbau (Kraftausdauer)
3. LOGI-Methode: Reduktion der glykämischen Last
4. 1 Glas Wein pro Tag (ohne Kontraindikationen!)

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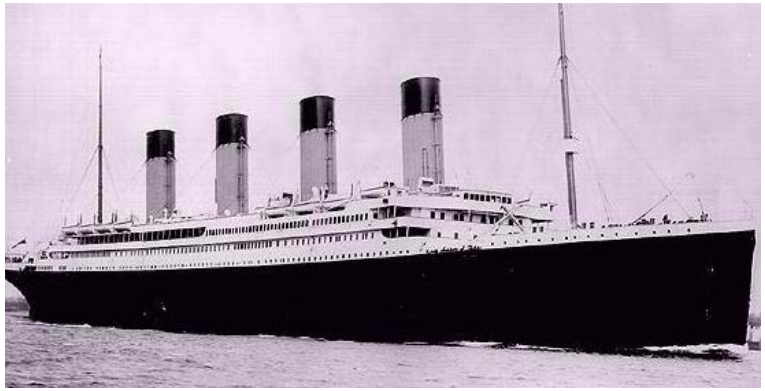
Take-Home-Message



„Kurswechsel auf der Titanic“

Die Prävention des Typ-2-Diabetes mit Sport und LOGI vermeidet Pillen *und* Komplikationen.

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