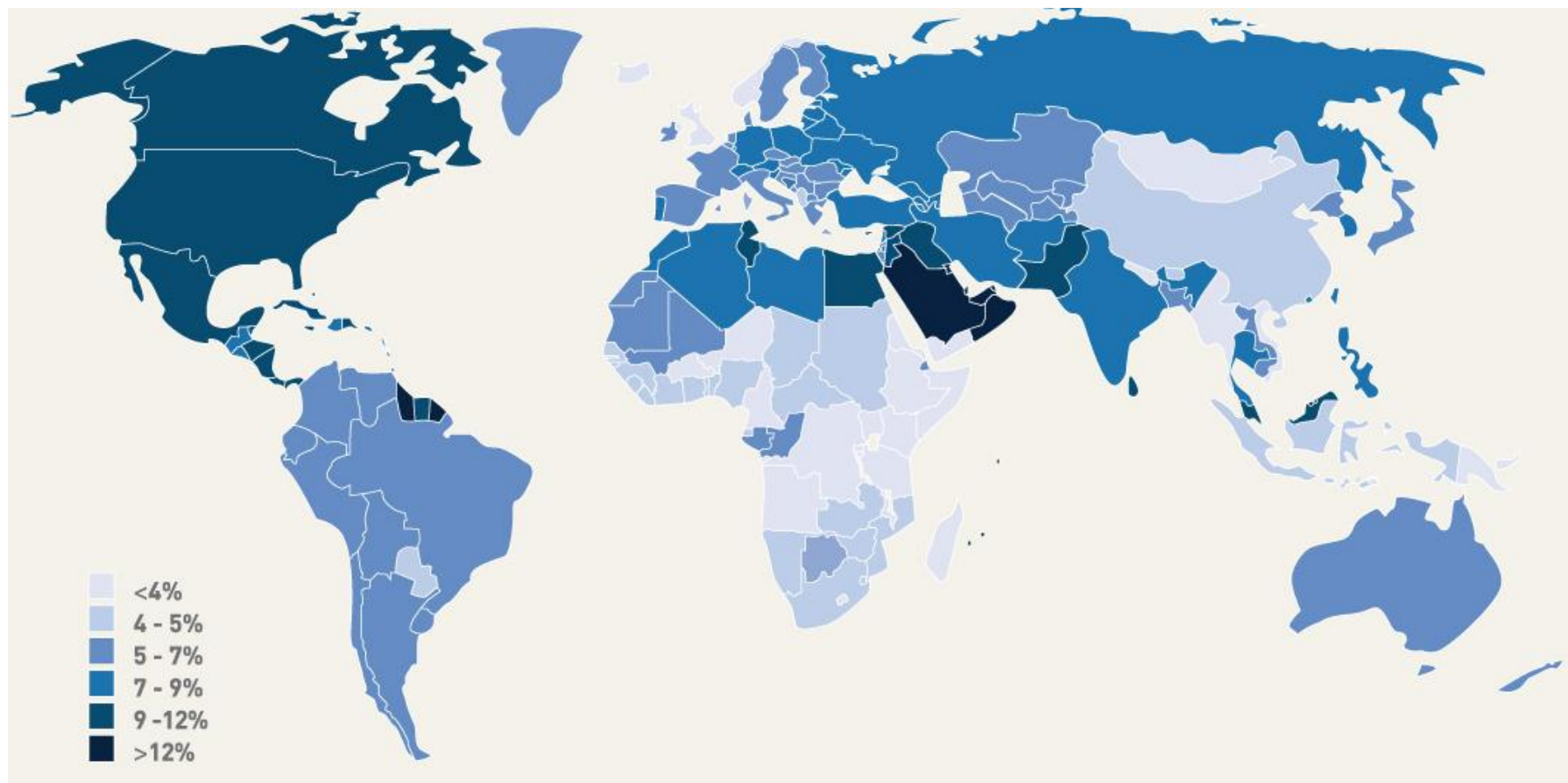# Diabetes:
a risk factor for cancer

Dr. Cesare Berra

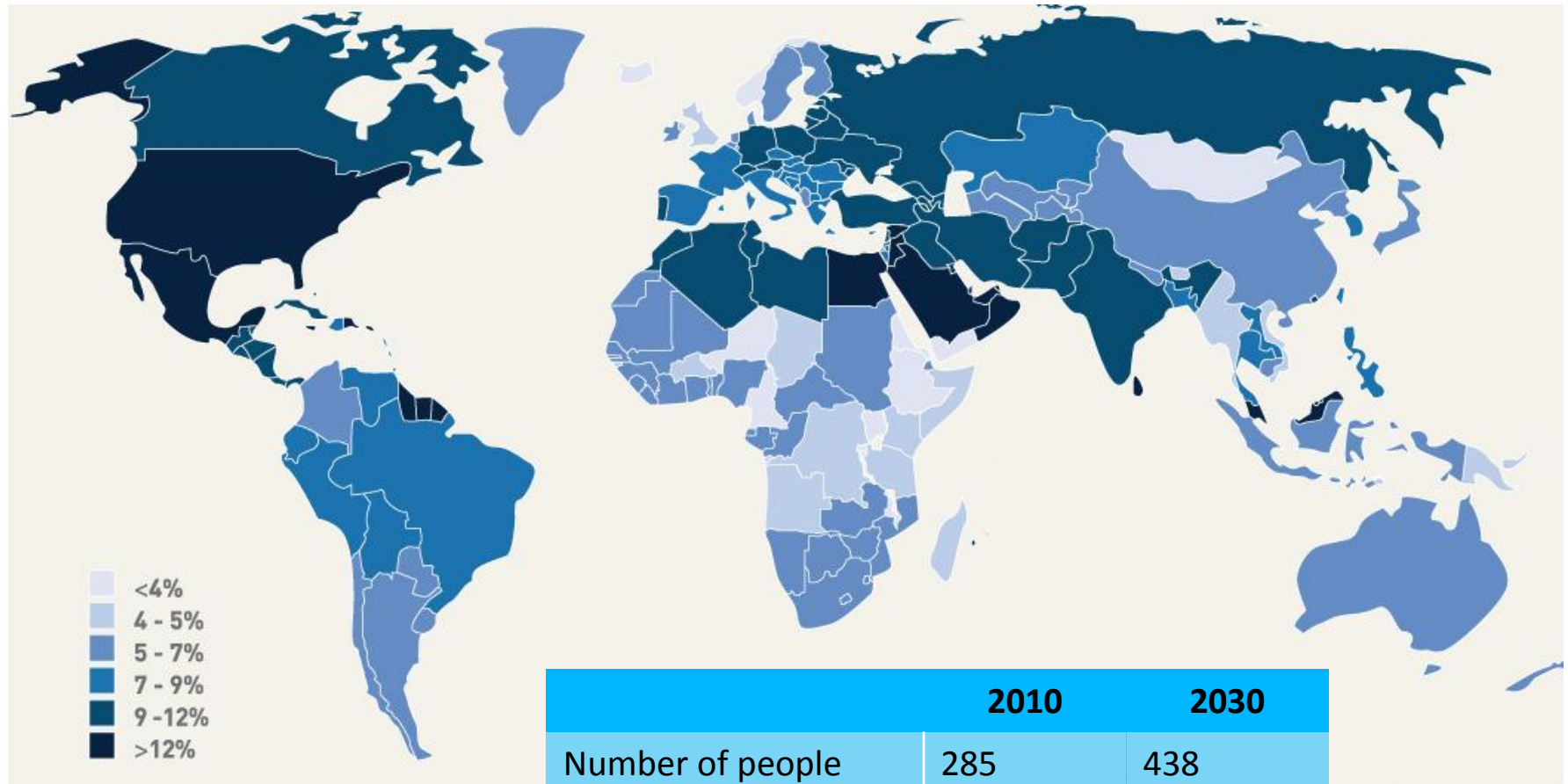# Disclosure information:

No conflict of interests declared

Prevalence diabetes 2010

	<4%
	4 – 5%
	5 – 7%
	7 – 9%
	9 –12%
	>12%

Prevalence diabetes 2030

Legend:
- <4%
- 4 - 5%
- 5 - 7%
- 7 - 9%
- 9 - 12%
- >12%
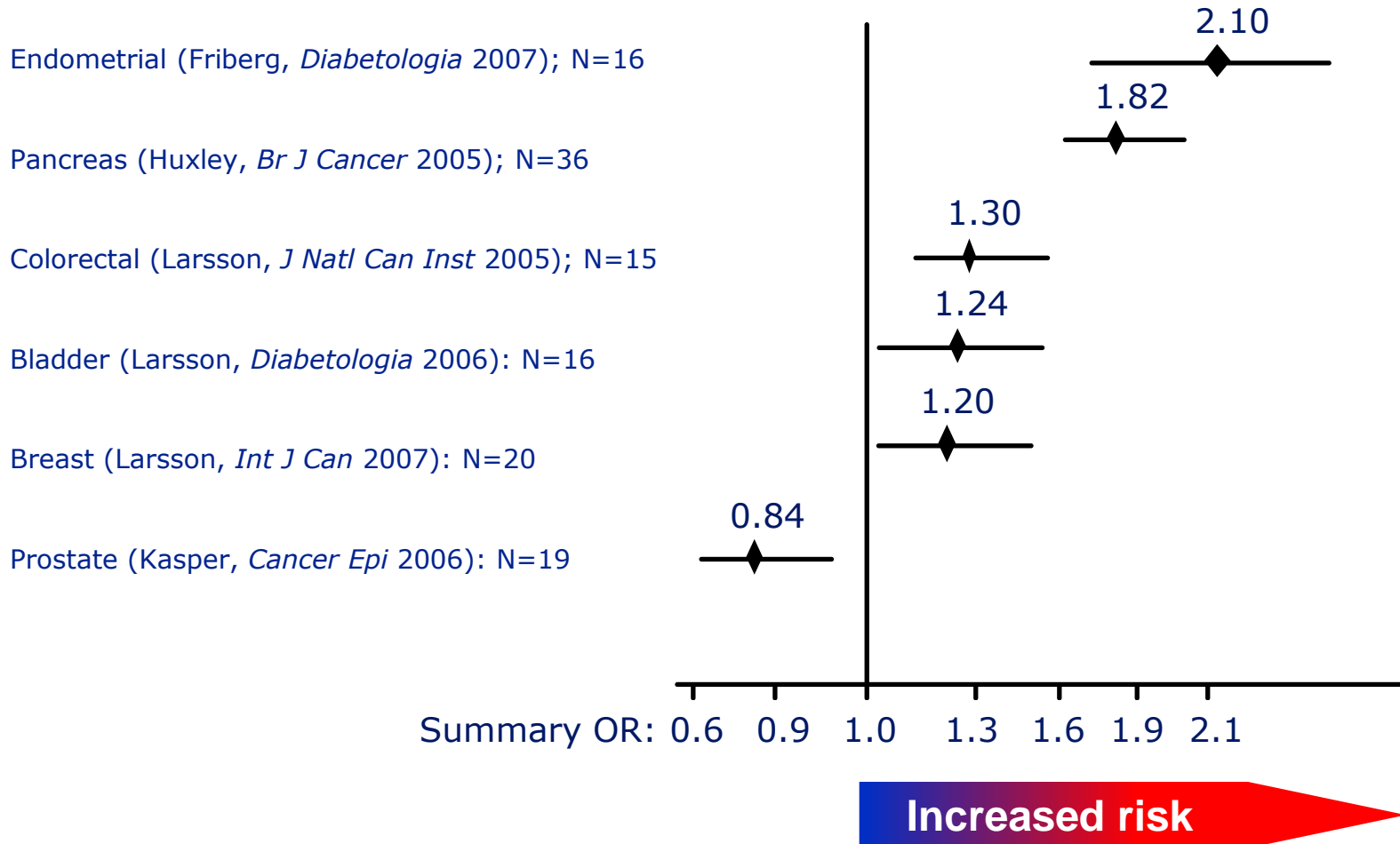
	2010	2030
Number of people with diabetes (age 20-79)	285 millions	438 millions
Prevalence of disease (age 20-79)	6.6 %	7.8 %

IDF diabetes atlas, 4th edition, 2009

Diabetes and cancer incidence: analysis from Tayside, Scotland

	Adjusted RR (95% CI)	Adjusted RR (95% CI) (excluding outcomes in first year)
Any malignant cancer C00-97	0.99 (0.90-1.09)	1.05 (0.93-1.18)
Pancreas C25	**3.06 (1.73-5.39)**	**2.85 (1.27-6.43)**
Liver C22	**2.93 (1.40-6.14)**	**3.50 (1.38-8.91)**
Oesophagus C15	**1.70 (0.98-2.95)**	**1.74 (0.91-3.32)**
Colon C18-19	**1.46 (1.07-2.01)**	**1.56 (1.05-2.32)**
Breast C50	1.05 (0.75-1.47)	1.05 (0.71-1.57)
Prostate C61	**0.77 (0.54-1.09)**	**0.76 (0.50-1.17)**

Codes after cancer type indicate diagnosis code in the ICD-10 diagnosis classification system

RR, relative risk; CI, confidence interval

Diabetes and cancer risk: meta-analyses of 2005–2007 studies

Endometrial (Friberg, *Diabetologia* 2007); N=16 — 2.10

Pancreas (Huxley, *Br J Cancer* 2005); N=36 — 1.82

Colorectal (Larsson, *J Natl Can Inst* 2005); N=15 — 1.30

Bladder (Larsson, *Diabetologia* 2006): N=16 — 1.24

Breast (Larsson, *Int J Can* 2007): N=20 — 1.20

Prostate (Kasper, *Cancer Epi* 2006): N=19 — 0.84

Summary OR: 0.6 0.9 1.0 1.3 1.6 1.9 2.1

Increased risk

OR, odds ratio

Diabetes and cancer mortality

Adapted from Zhou *et al*. *Diabetologia* 2010;53:1867–76
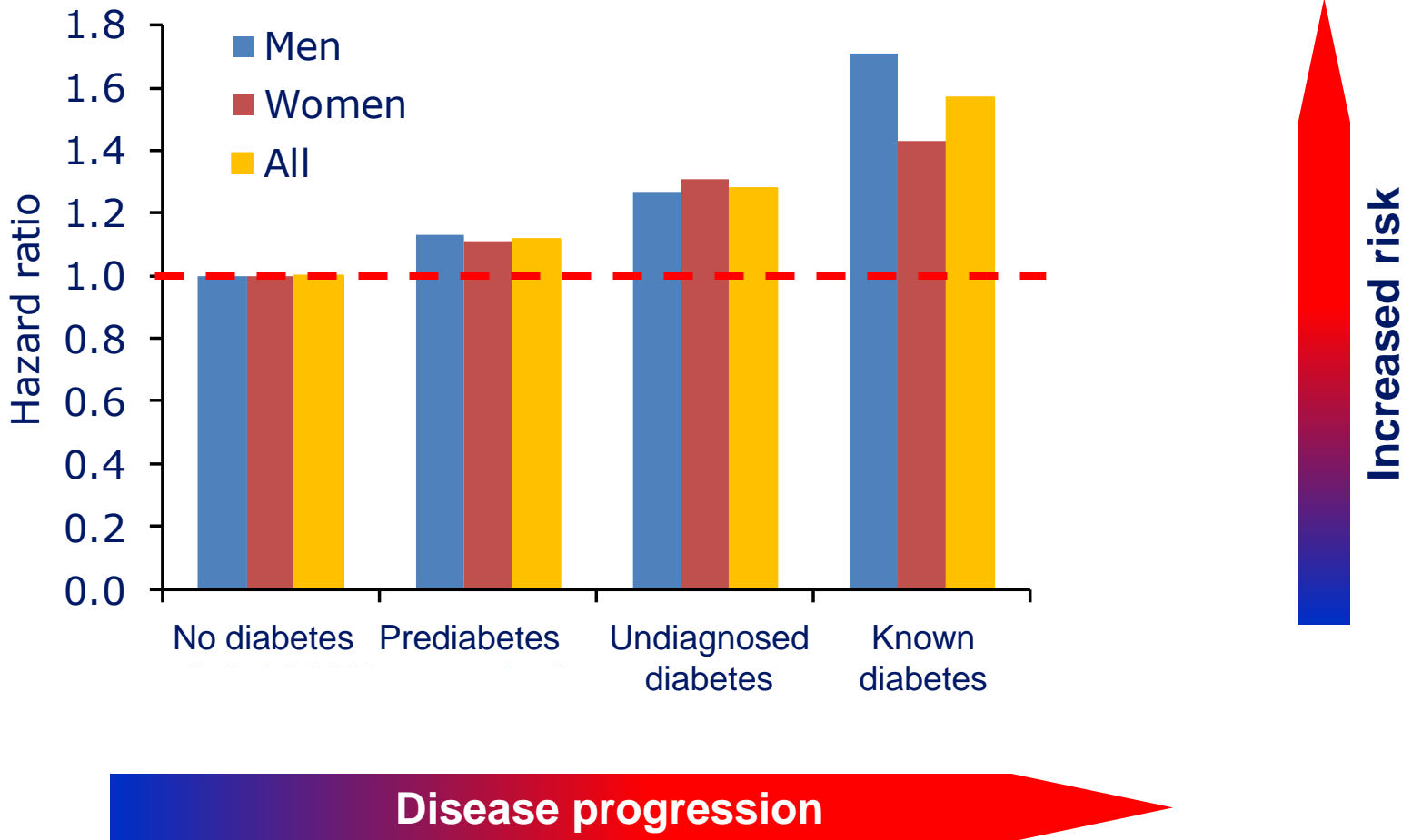
Waist to hip ratio more strongly associated with risk of cancer than BMI

Body size measurement	Category	Pooled effect estimate (95% CI)
BMI	Male (colon cancer)	1.59 (1.35–1.86)
	Female (colon cancer)	1.22 (1.08–1.39)
	Male (rectal cancer)	1.16 (0.93–1.54)
	Female (rectal cancer)	1.23 (0.98–1.54)
Waist circumference	Male (colon cancer)	1.68 (1.36–2.08)
	Female (colon cancer)	1.48 (1.19–1.84)
	Male (rectal cancer)	1.26(0.90–1.77)
	Female (rectal cancer)	1.23 (0.81–1.86)
Waist-to-hip ratio	Male (colon cancer)	1.91 (1.46–2.49)
	Female (colon cancer)	1.49 (1.23–1.81)
	Male (rectal cancer)	1.93 (1.19–3.13)
	Female (rectal cancer)	1.20 (0.81–1.78)

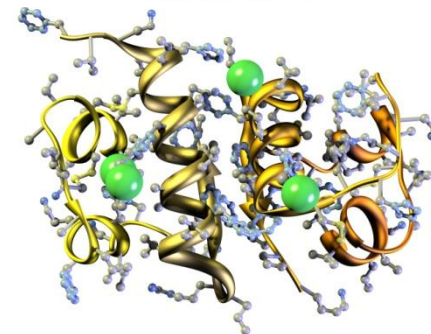# What other factors could be contributing to the increased risk...?

- Three hypotheses:
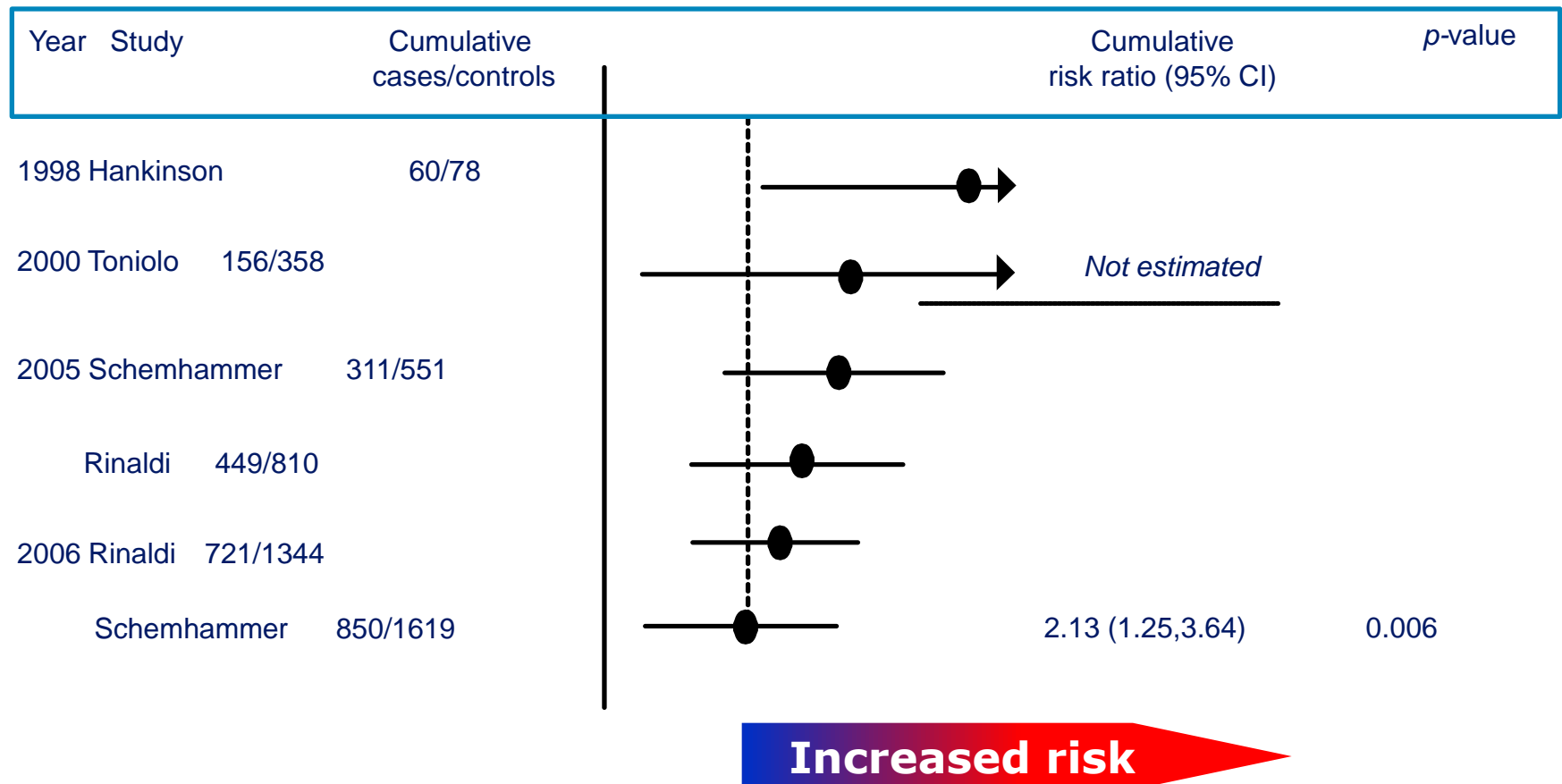
  1. Chronic inflammation
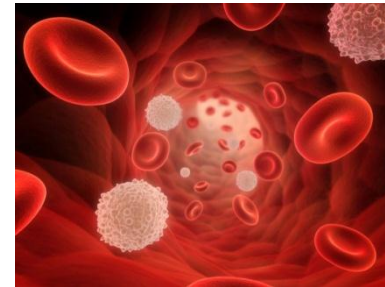
  2. Hyperglycaemia

  3. Insulin/IGF-1

High circulating levels of IGF-1 associated with increased risk of breast cancer

Associations with IGF-1

Breast cancer under age 50 years

Year	Study	Cumulative cases/controls	Cumulative risk ratio (95% CI)	*p*-value
1998	Hankinson	60/78		
2000	Toniolo	156/358	Not estimated	
2005	Schemhammer	311/551		
	Rinaldi	449/810		
2006	Rinaldi	721/1344		
	Schemhammer	850/1619	2.13 (1.25,3.64)	0.006

Increased risk

Renehan *et al. Endocr Relat Cancer* 2006;13:273–8

Insulin receptor and IGF-1 receptor activation associated with poor breast cancer survival

Law *et al. Cancer Res* 2008;68:10238–46

P, phosphorylated; IR, insulin receptor

ARTICLE
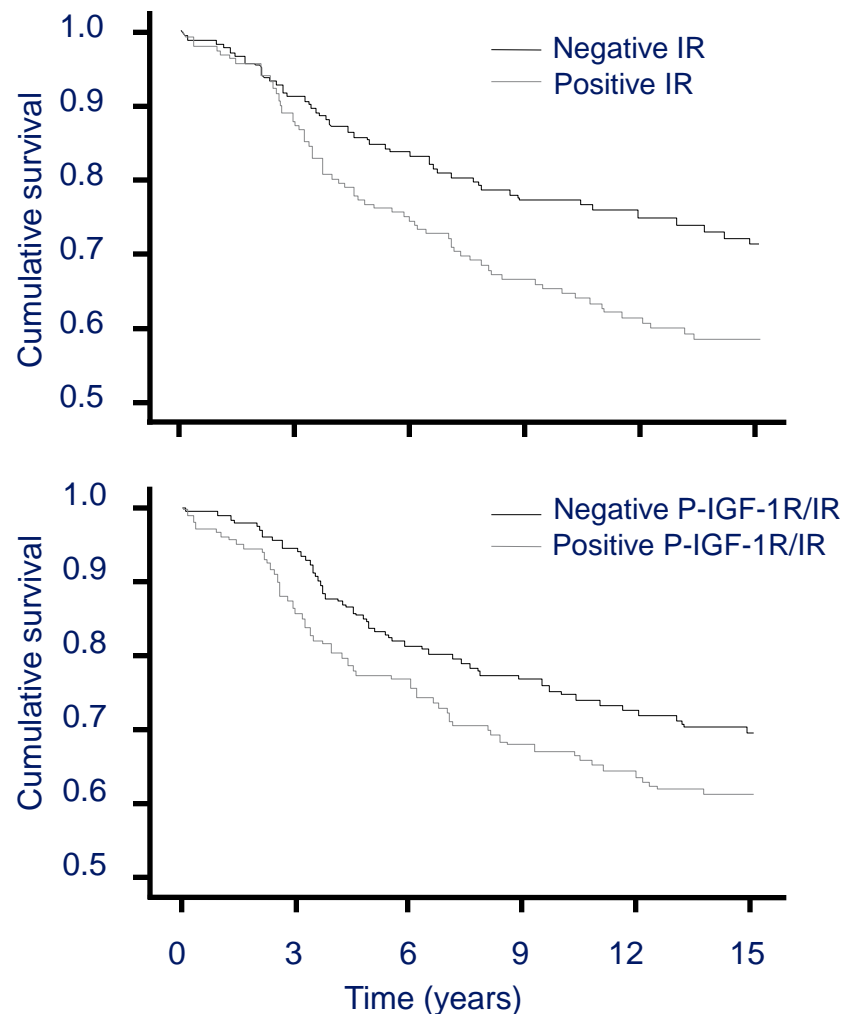
Risk of cancer in patients on insulin glargine and other insulin analogues in comparison with those on human insulin: results from a large population-based follow-up study

R. Ruiter · L. E. Visser · M. P. P. van Herk-Sukel · J. W. W. Coebergh · H. R. Haak ·
P. H. Geelhoed-Duijvestijn · S. M. J. M. Straus · R. M. C. Herings · B. H. Ch. Stricker

Conclusion/interpretation Users of insulin glargine and users of other insulin analogues had a lower risk of cancer in general than those using human insulin. Both associations might be a consequence of residual confounding, lack of adherence or competing risk. However, as in previous studies, we demonstrated an increased risk of breast cancer in users of insulin glargine in comparison with users of human insulin.

Use of thiazolidinediones and the risk of bladder cancer among people with type 2 diabetes: a meta-analysis

Isabelle N. Colmers BScH, Samantha L. Bowker PhD, Sumit R. Majumdar MD, Jeffrey A. Johnson PhD

Interpretation: The limited evidence available supports the hypothesis that thiazolidinediones, particularly pioglitazone, are associated with an increased risk of bladder cancer among adults with type 2 diabetes.

Risk of cancer in patients using glucose-lowering agents: a nationwide cohort study of 3.6 million people

Charlotte Andersson,[1] Allan Vaag,[2] Christian Selmer,[1] Michelle Schmiegelow,[1] Rikke Sørensen,[1] Jesper Lindhardsen,[1] Gunnar H Gislason,[1] Lars Køber,[3] Christian Torp-Pedersen[1,4]

Conclusions: Use of most glucose-lowering agents including sulfonylureas was associated with a comparable increased risk of cancer shortly after initiation of treatment and subsequently a decline to the risk of the background population. This suggests that the relation is not causal.

Target of treatment in T2D

Organizzazioni	HbA$_{1c}$ (%)	FPG (mmol/L)	PPG (mmol/L)
ADA-EASD[1]	<7	—	—
IDF-Europe[2]	<6.5	<6.0 (<110*)	<8.0 (<140*)
AACE[3]	≤6.5	<6.1 (<110*)	<7.8 (<140*)
NICE[4]	<6.5**	—	<8.5 (<153*)
DDG[5]	<6.5	—	—

*mg/dL
**<7.5% for people receiving ≥2 oral glucose-lowering drugs or those requiring insulin

FPG: fasting plasma glucose; PPG: postprandial glucose; ADA: American Diabetes Association; IDF: International Diabetes Federation; AACE: American Association of Clinical Endocrinologists; NICE: National Institute of Clinical Excellence; DDG: Deutschen Diabetes-Gesellschaft (German Diabetes Association)

1. Nathan DM, et al. Diabetologia. 2009;52:17-30.
2. IDF. Global Guidelines 2005.
3. Rodbard HW, et al. Endocr Pract. 2007;13(Suppl. 1):1-68.
4. NICE clinical guideline 87. Quick reference guide. May 2009.
5. Matthaei S, et al. German Diabetes Association guidelines. October 2008.

Personalized Therapy

Skyler J, *et al*. *Diabetes Care* 2009;32:187

| A1c <7.0%	A1c >7.0%
• Short duration of diabetes • Long life expectancy • No significant cardiovascular disease	• History of severe hypoglycemia • Limited life expectancy • Long-standing diabetes • Advanced micro- and macrovascular complications

Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach

Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)
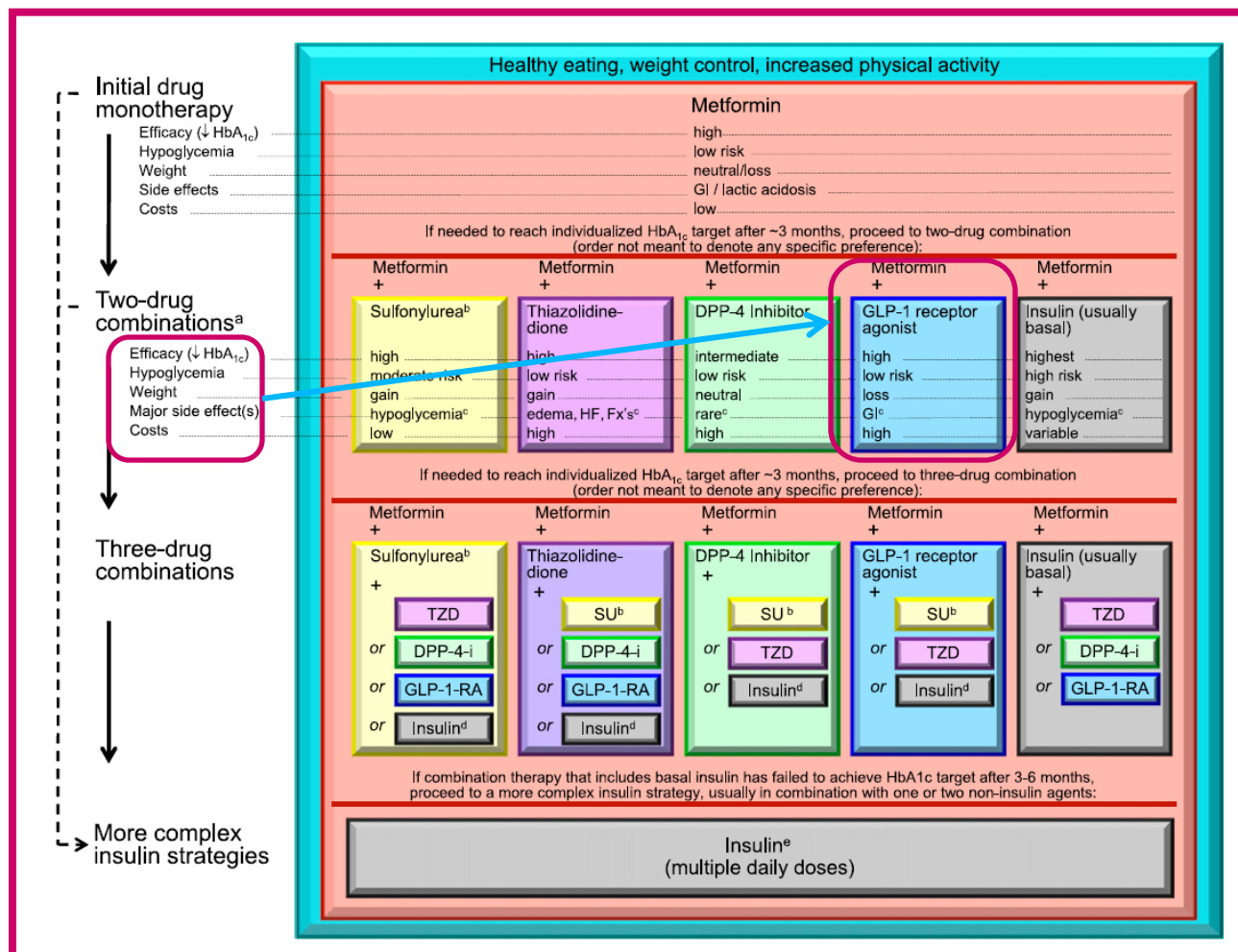
Treating diabetic patients with chemotherapy: single centre experience of toxicity and outcomes
Final publication number 1549PD
Seligmann J et al.

Background

- 1:8 people aged 60-79 in the UK are diabetic
- They have an increased risk of
  - Infection
  - Hospital admission and in-hospital mortality
  - Several solid organ cancers
  - Complications following surgery and adjuvant chemotherapy for solid organ cancers
- Limited data exists about the experience of diabetic patients with palliative chemotherapy

Methods and results

- A retrospective cohort study comparing diabetic patients with age, treatment and disease matched non-diabetic controls during the first 18 weeks of chemotherapy

- Population: 292 patients with advanced colorectal or gynaecological cancer

Outcome	OR	95% CI	p-value
Acute admission	3.32	1.8-5.8	<0.0001
Early stopping of chemotherapy	2.17	1.25-3.85	0.008
Reduced use of 2nd line treatment	0.56	0.34-0.95	0.03

Results and conclusions

Other important results

- Common causes for diabetic patient admissions
    - infection (41%), poor glycaemic control (17%)
- Independent prognostic factors
    - primary site, performance status, age

Conclusions

- Diabetic patients experience more acute complications on chemotherapy possibly limiting further treatment options
- A prospective study would clarify the contributing factors and inform management of diabetic patients with cancer

Comments

How may influence this outcomes the metabolic balance (levels of HbA1c)?

The age and/or the presence of compliations of diabetes could be important?

use of steroids and the percentage of diabetes induced by: an open problem.

Thank you for your attention

Dr. Cesare Berra