Diabetes mellitus–
how frequent, how serious, how manageable

Hans-Peter Hammes
Heidelberg University
Universitätsmedizin Mannheim, Germany

Barometer meeting
Berlin, Germany

THE INTERNATIONAL DIABETES FEDERATION

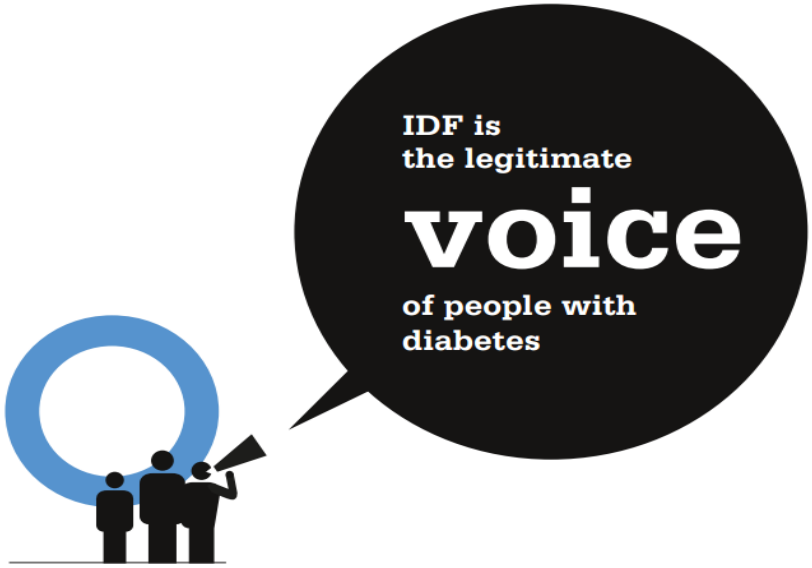
230 member associations

representing 2 million members

in 170 countries

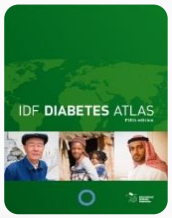
World Health Organization

The NCD Alliance
Putting non-communicable diseases on the global agenda



IDF's 7 Roles

Evidence



Translational Research

BRIDGES
Bringing Research in Diabetes to Global Environments and Systems

Best Practice Projects

DIABETES CONVERSATIONS

D-NET

3C study
Coverage · Cost · Care
Type 1 Diabetes in China

Global Guidelines

Humanitarian Programmes

LIFE FOR A CHILD
an International Diabetes Federation Programme

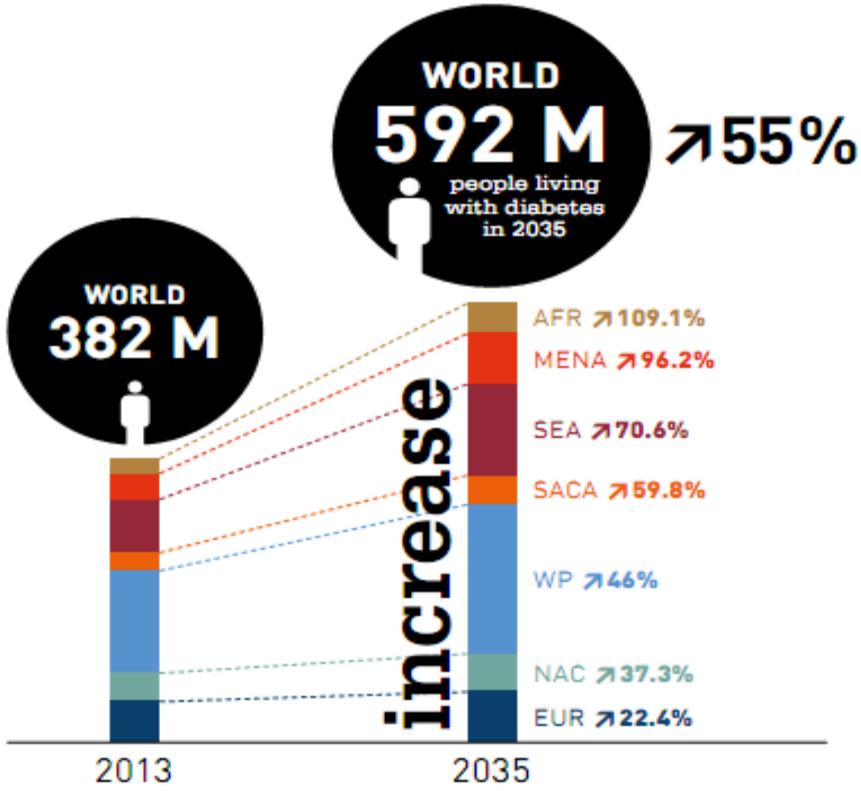
Convening

IDF 2013
melbourne
world diabetes congress
2 - 6 December 2013

Advocacy + Campaigning

world diabetes day
14 Nov

Diabetes is a **huge and growing problem**, and the costs to society are **high and escalating**



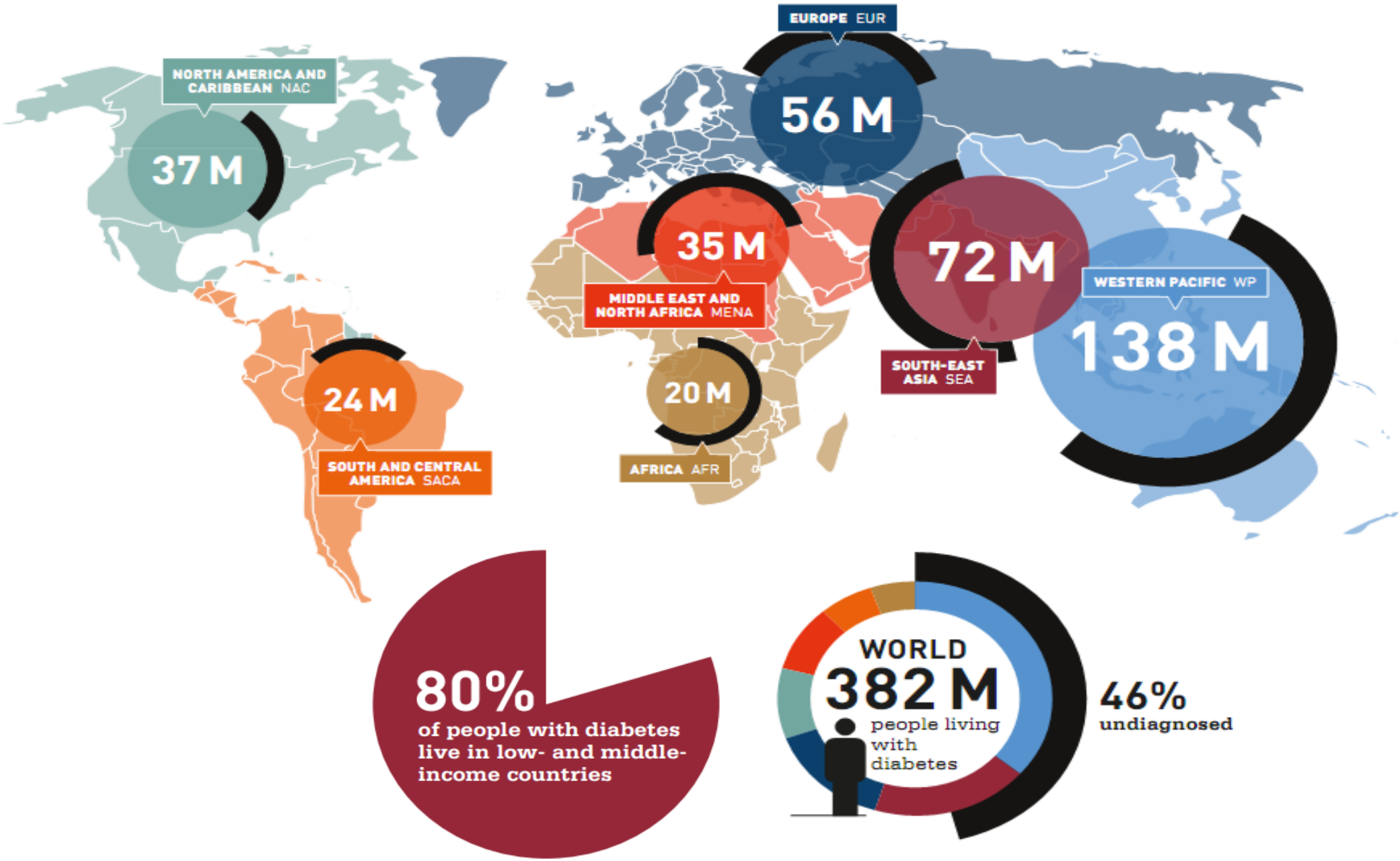
382 million people have diabetes

By **2035**, this number will rise to **592 million**

Urbanisation…..

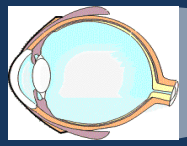
Coca-Cola

Number of people with diabetes by IDF Region, 2013



Diabetic Complications

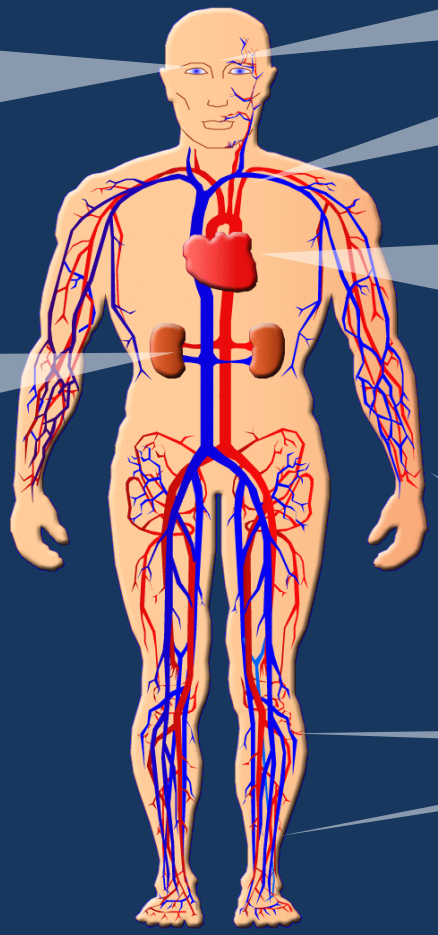
Leading cause of blindness in working age adults



Diabetic Retinopathy

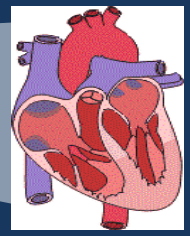
Diabetic Nephropathy

Leading cause of end-stage renal disease

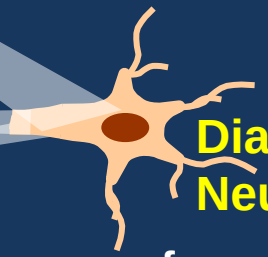


Stroke

2- to 4- fold increase in cardiovascular events and stroke



Cardiovascular Disease



Diabetic Neuropathy

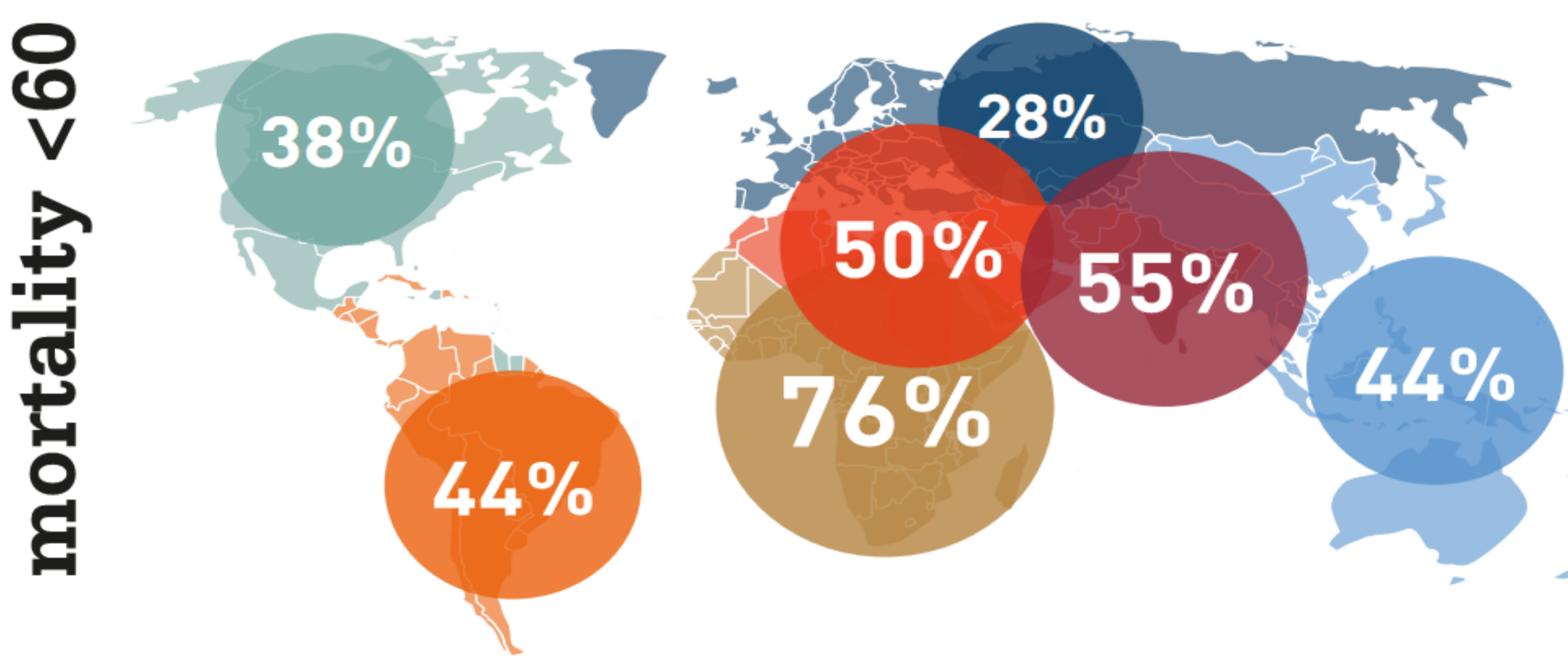
Leading cause of non-traumatic lower extremity amputations

National Diabetes Information Clearinghouse. Diabetes Statistics–Complications of Diabetes. (website) http://www.niddk.nih.gov/health/diabetes/pubs/dmstats/dmstats.htm#comp.

… and the costs to society are **high and escalating**

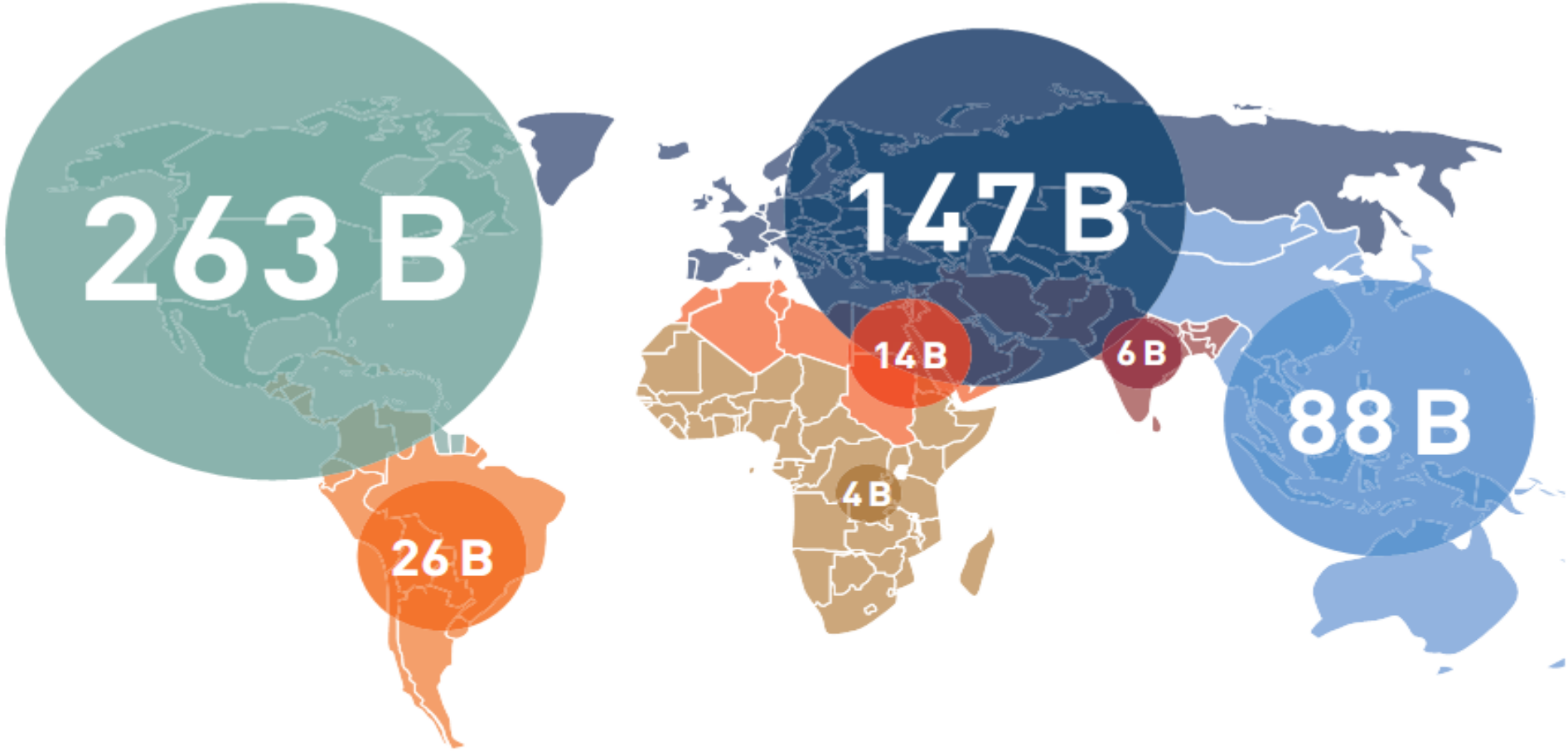
Diabetes kills one person every **six seconds**

5.1 million deaths due to diabetes **in 2013**



Of those who die from diabetes, what proportion do so before the age of 60?

expenditures



Health expenditure (USD) due to diabetes (20-79 years), 2013

RESEARCH ARTICLE

Prevalence and Cardiovascular Associations of Diabetic Retinopathy and Maculopathy: Results from the Gutenberg Health Study

Philipp Raum[1], Julia Lamparter[1], Katharina A. Ponto[1,4], Tunde Peto[2], René Hoehn[1], Andreas Schulz[3], Astrid Schneider[3], Philipp S. Wild[4,5,6], Norbert Pfeiffer[1], Alireza Mirshahi[1,7]*

PLoS One. 2015 Jun 15;10(6):e0127188

15010 Individuals (35-74 Years)

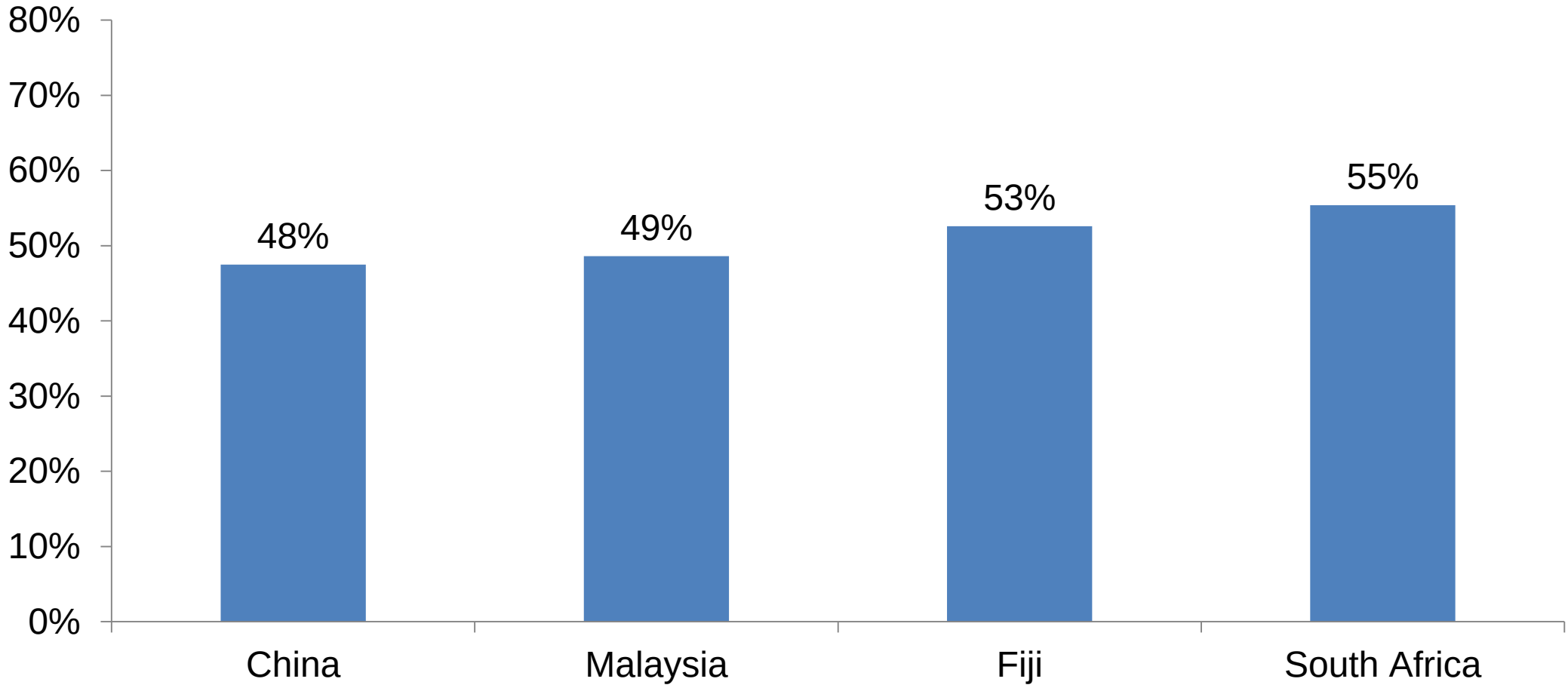
→ **1124 (= 7.5 %) Diabetes mellitus:**

HbA_{1c} 6.8 % (6.4-7.3 %)
79.6 % T2D
13 % unknown
6 % T1D
0.7 % GDM
0.3 % T3D

→ ***27.7 % Diabetes unknown: screening detected!***

→ **22.7 % Any retinopathy → 5 % VTDR**

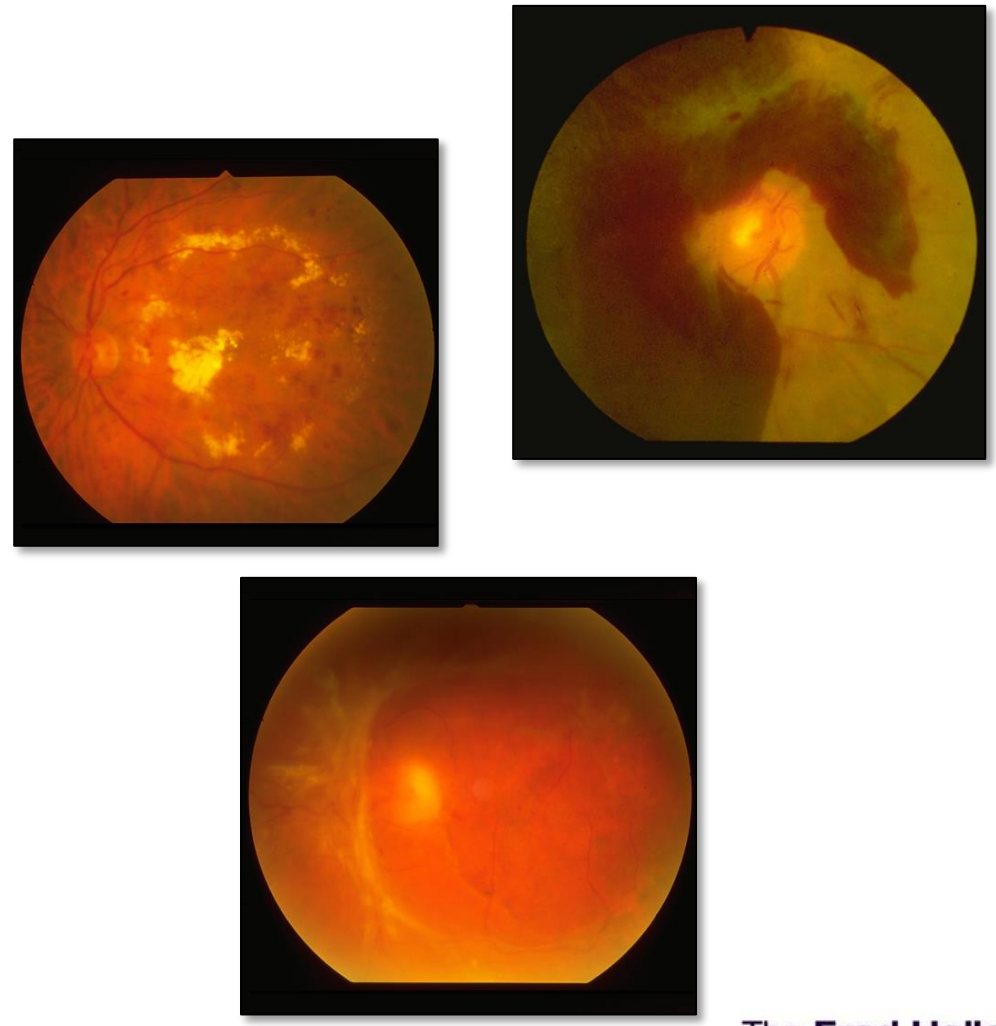
Countries with High Rates of Diabetic Retinopathy in People with Diabetes



Chi et al (2001); Levitt et al (1997); Shriwas et al (1996); Brooks et al (1999)

Sight-threatening diabetic retinopathy at presentation to screening services in Fiji

- **27 %** of patients were graded as having sight threatening retinopathy at presentation
- In **15 %** this was bilateral
- Visual impairment and vision loss was observed in **9.4 %** of diabetic patients
- Comparison with patients entering screening in a UK setting – **6 %** had STR at presentation



Damato E et al., Ophthalmic Epidemiol 2014

The Pacific Eye Institute, Fiji

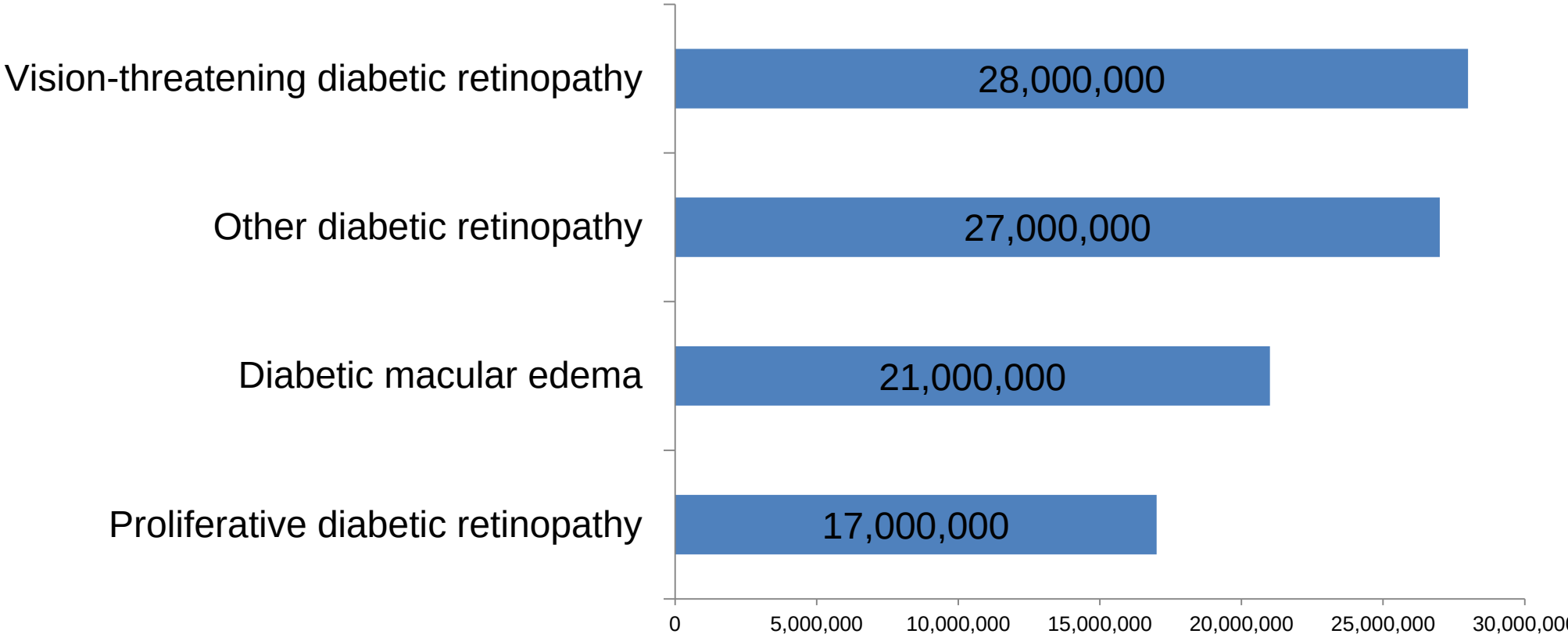
The Fred Hollows Foundation

Global prevalence and major risk factors of diabetic retinopathy

Overall	Studies included	Total N	Cases N	Prevalence *	95 % CI
Any DR	18	12620	4487	35,36	35,17-35,56
PDR	21	13436	957	7,24	7,15-7,33
DME	20	14554	1039	7,48	7,48-7,57
VTDR	18	12710	1481	11,72	11,72-11,83

Yau et al., Diab Care 2012

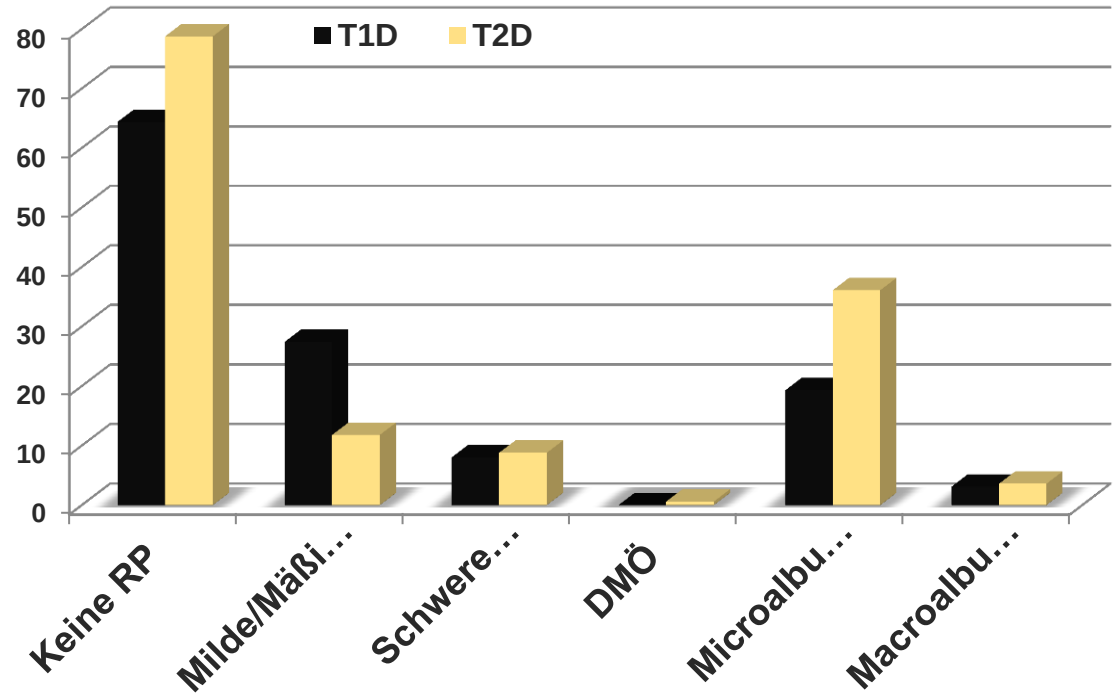
93 Million People have Diabetic Retinopathy



Yau et al. Diabetes Care 35:556–564, 2012

Prevelance of diabetic microvascular complications in T1 and T2 diabetes

	T1D	T2D
n	8784	64784
Age (Y)	31,1±12,1	68,7±10,4
DD (Y)	14,5±10,4	9,2±7,8
HbA1c (%)	8,1±1,9	7,4±1,7
RR (mm Hg)	124/75	135/77
Chol (mg/dl)	192±48	198±49
Trig (mg/dl)	127±100	190±117



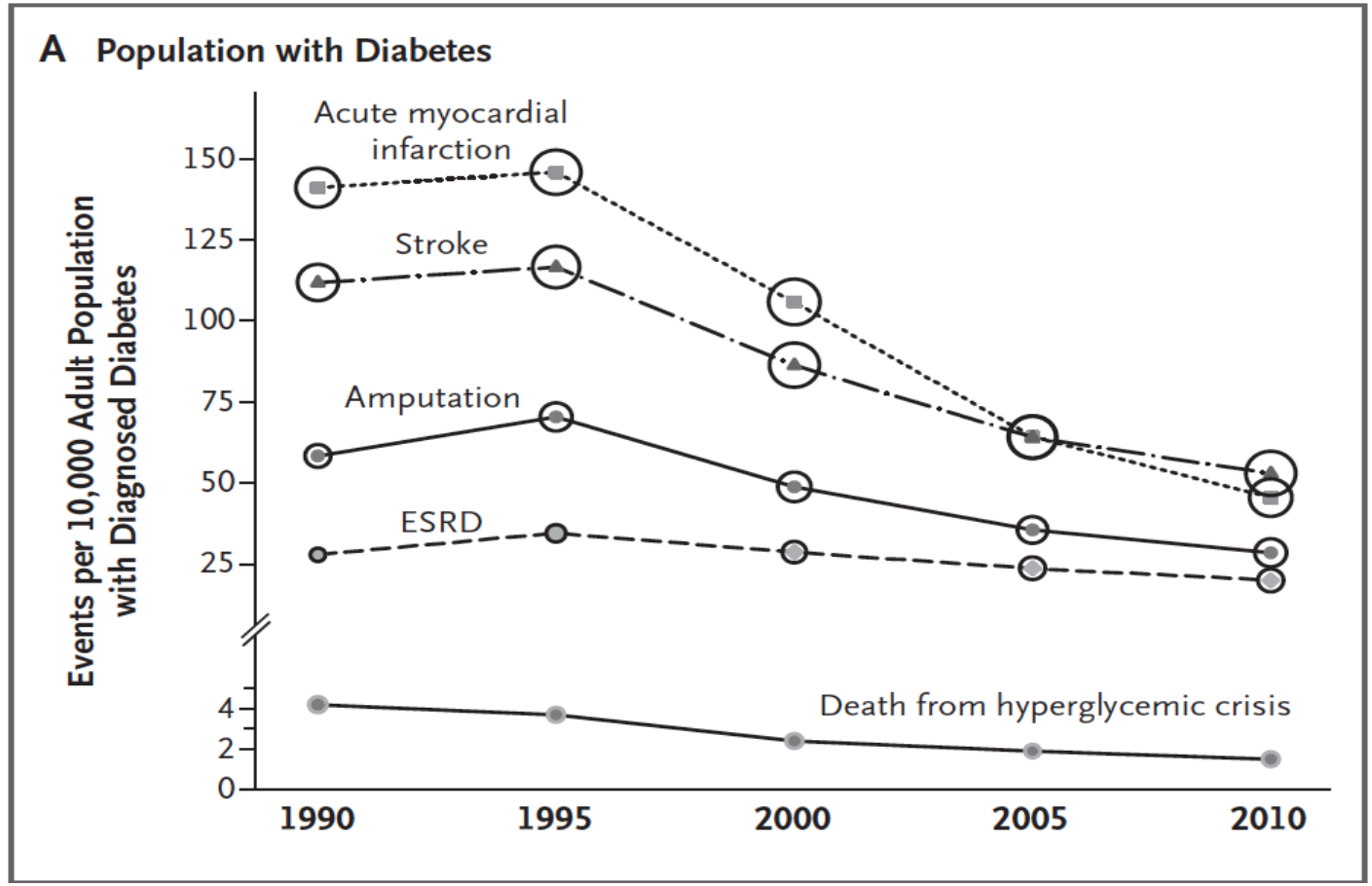
Hammes et al., Diabetologia 2011, PlosOne 2015

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Changes in Diabetes-Related Complications in the United States, 1990–2010

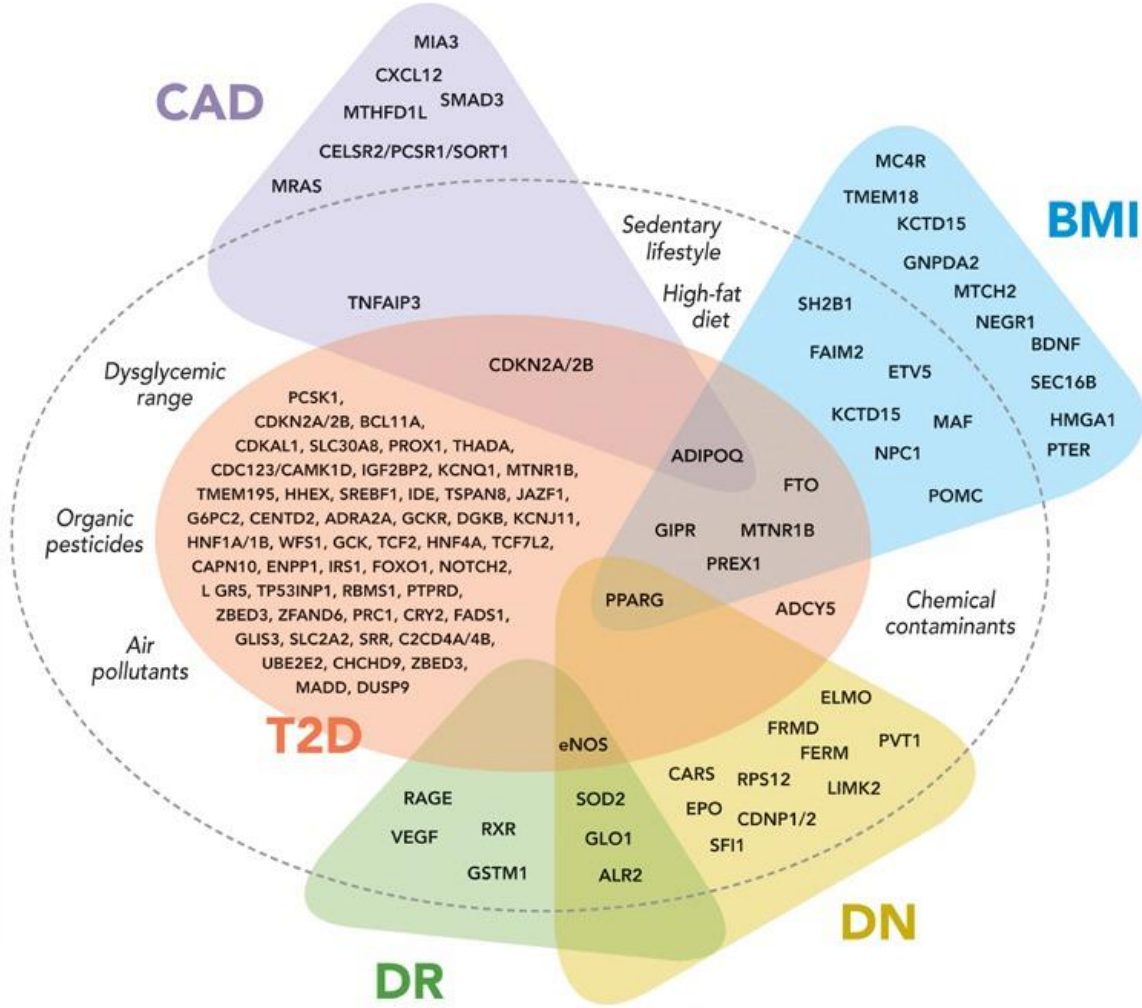
Edward W. Gregg, Ph.D., Yanfeng Li, M.D., Jing Wang, M.D.,



Type 2 diabetes is preventable

Elucidate the reno-retinal syndrome – no fully accepted role of a genetic risk

Hans Häring
Claude Bernard
Medal 2015



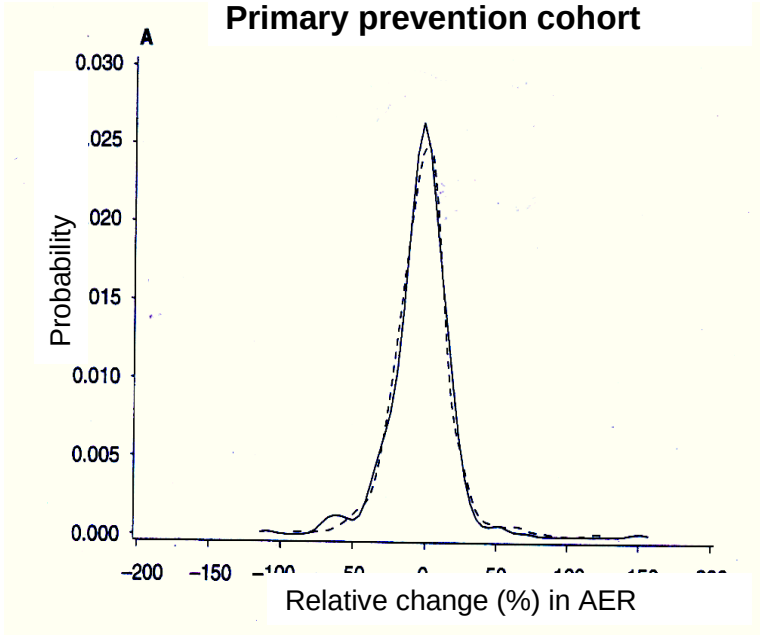
Matthias Blüher
Minkowski Award
2015

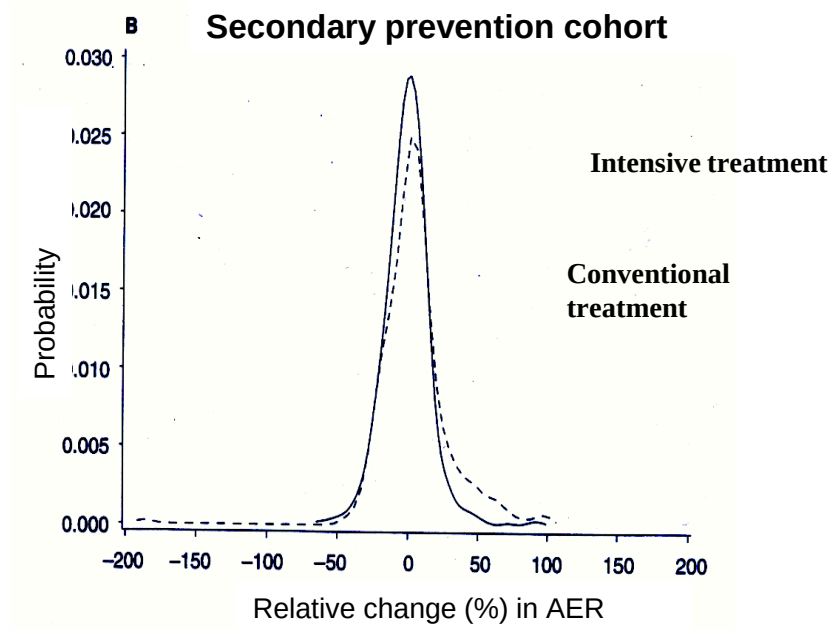
Diabetic retinopathy is preventable

Glycaemia increase	Associated risk increase		
1% increase in HbA_{1c}	21% increase in diabetes-related deaths P<0.0001	14% increase in myocardial infarction P<0.0001	37% increase in microvascular complications P<0.0001

Practice Points

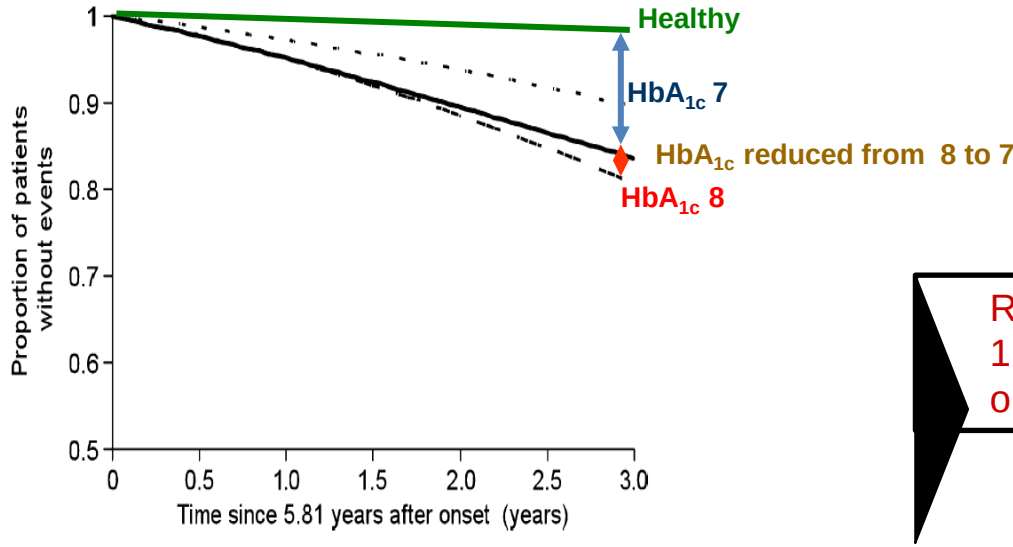
- In Denmark, only 20% of those with undiagnosed diabetes were identified by screening.
- For each person with diabetes identified, another two at high risk of diabetes and six at high risk of cardiovascular disease were identified.
- Screening for diabetes had limited short- and long-term adverse psychological impact on participants.
- Cardiovascular risk factors (weight, blood pressure and cholesterol), including health-related behaviors (smoking), improved substantially following detection of diabetes by screening.
- Small increases in treatment intensity of screen-detected patients were associated with a nonsignificant 17% reduction in risk of a first cardiovascular event.
- Among people with screen-detected diabetes, all-cause mortality over 7 years was twice as high for those with HbA1c <6.0% compared with those with HbA1c ≥6.5% at screening. Those with HbA1c <6.0% were less intensively treated than those with HbA1c ≥6.5%. The latter group had an all-cause mortality that was not significantly different from people with normal glucose tolerance and HbA1c <6.0% at screening, presumably due to more intensive treatment.
- At the population level, invitation of high-risk individuals to screening was not associated with a reduction in all-cause or diabetes-related mortality over 10 years.
- The ADDITION study provides further evidence of the net benefit associated with earlier detection and treatment of Type 2 diabetes. Rather than screening the population for diabetes, primary care teams should focus efforts on earlier detection and treatment of risk factors among those with diabetes, at high risk of diabetes and high risk of cardiovascular disease.





DCCT (*The DCCT Research Group, Kidney Int. 47:1703-1720, 1995)*

Distribution of slopes for urinary albumin excretion, expressed as relative percent change per year



M. Lind et al, Diabetologia 53:1093–1098, 2010

Recent clinical studies have shown that even in type 1 diabetes , HbA_{1c} and the duration of disease can only explain 11% of the late diabetic complications!

Targeting intensive glycaemic control versus targeting conventional glycaemic control for type 2 diabetes (Review)

Analysis 1.59. Comparison 1 Intensive glycaemic control versus conventional glycaemic control, Outcome 59 Retinopathy; stratified according to intervention.

Review: Targeting intensive glycaemic control versus targeting conventional glycaemic control for type 2 diabetes mellitus

Comparison: 1 Intensive glycaemic control versus conventional glycaemic control

Outcome: 59 Retinopathy; stratified according to intervention

Study or subgroup	Intensive control n/N	Conventional control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Exclusively dealing with glycaemic control in usual care setting					
ACCORD 2008	81/1429	126/1427		13.6 %	0.64 [0.49, 0.84]
ADVANCE 2008	88/791	99/811		13.5 %	0.91 [0.70, 1.19]
Kumamoto 2000	13/55	34/55		6.0 %	0.38 [0.23, 0.64]
UGDP 1975	51/204	53/210		10.9 %	0.99 [0.71, 1.38]
UKPDS 1998	363/2729	172/1138		19.1 %	0.88 [0.74, 1.04]
Subtotal (95% CI)	**5817**	**4253**		**86.1 %**	**0.80 [0.67, 0.94]**

Hemmingsen B, et al., Cochrane Database Syst Rev, 2013. 11: p. CD008143

The effects of medical management on the progression of diabetic retinopathy in persons with type 2 diabetes the Action to Control Cardiovascular Risk in Diabetes (ACCORD) eye study

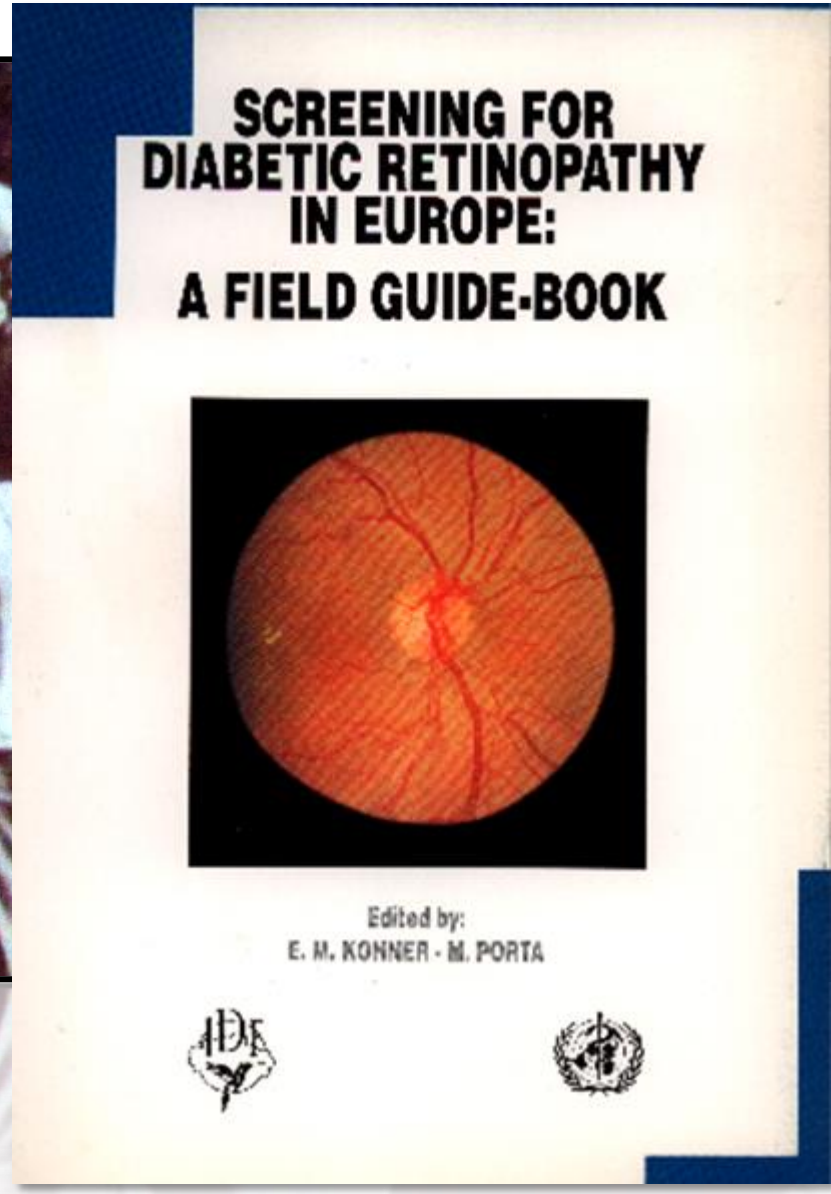
Four year rate of DRP progression in the subgroups

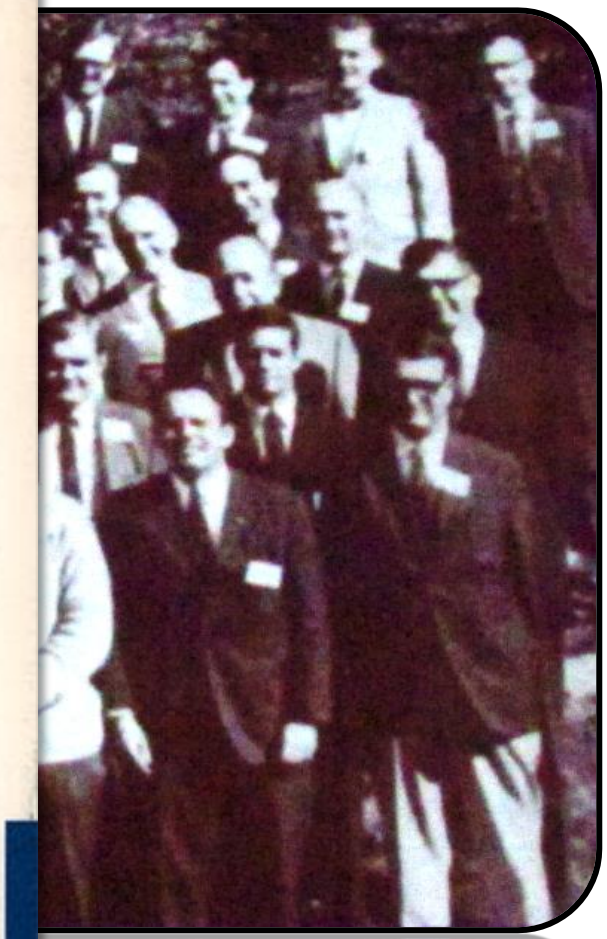
Outcome	Glycemia Trial			Lipid Trial			Blood Pressure Trial		
	Intensive	*Standard*	*OR (95% CI) P*	*Fenofibrate*	*Placebo*	*OR (95% CI) P*	*Intensive*	*Standard*	*OR (95% CI), P*
Original total with progression (≥3 steps, PC, or vitrectomy)	0.073 (104/1429)	0.104 (149/1427)	0.67 (0.51–0.87) P = 0.0025	0.065 (52/806)	0.102 (80/787)	0.60 (0.42–0.86) P = 0.0056	0.104 (67/647)	0.088 (64/616)	1.23 (0.84–1.79) P = 0.29
Revised total with progression (≥3 steps or PC)	0.068 (97/1429)	0.102 (145/1427)	0.64 (0.49–0.84) P = 0.0010	0.061 (49/806)	0.098 (77/787)	0.59 (0.40–0.86) P = 0.0049	0.099 (64/647)	0.084 (52/616)	1.21 (0.82–1.78) P = 0.33
Baseline step* 1 no DR	0.057 (39/683)	0.071 (49/687)	0.78 (0.50–1.21) P = 0.27	0.062 (25/401)	0.059 (22/375)	1.12 (0.61–2.03) P = 0.72	0.067 (21/314)	0.071 (20/280)	1.00 (0.53–1.92) P = 0.99
Baseline steps 2–4: Ma	0.027 (12/439)	0.084 (38/453)	0.30 (0.15–0.59)	0.030 (8/264)	0.101 (26/258)	0.27 (0.12–0.63)	0.046 (8/173)	0.041 (8/197)	1.22 (0.44–3.40)
Baseline steps 2-4: Ma Or mild DR 1 eye, no DR or Ma only in other	0.027 (12/439)	0.084 (38/453)	0.30 (0.15–0.59) P = 0.0002	0.030 (8/264)	0.101 (26/258)	0.27 (0.12–0.63) P = 0.0009	0.046 (8/173)	0.041 (8/197)	1.22 (0.44–3.40) P = 0.71
moderate/moderately severe NPDR									P = 0.20
Baseline steps 10–17: severe NPDR or PDR	0.667 (10/15)	0.583 (14/24)	†	0.667 (4/6)	0.5 (5/10)	†	0.706 (12/17)	0.5 (3/6)	†

Only mild stages benefit!

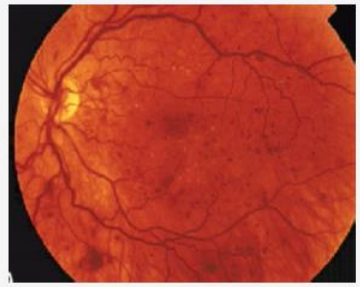
Chew E et al., Ophthalmology, 2014

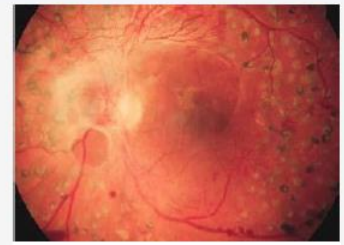
1968 Airlie House Symposium





Diabetic retinopathy severity scale (DRSS)





Mild PDR

High risk PDR

Advanced PDR

Mild NPDR

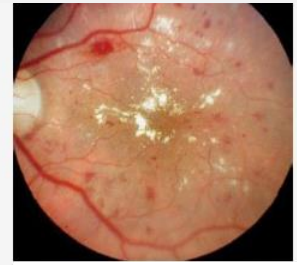
Moderate NPDR

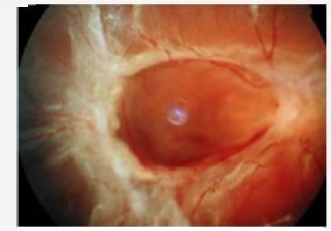
10 20 35 43 47 53 61 65 71 75 81 85

Microaneurysms

Severe-very severe NPDR

Moderate PDR

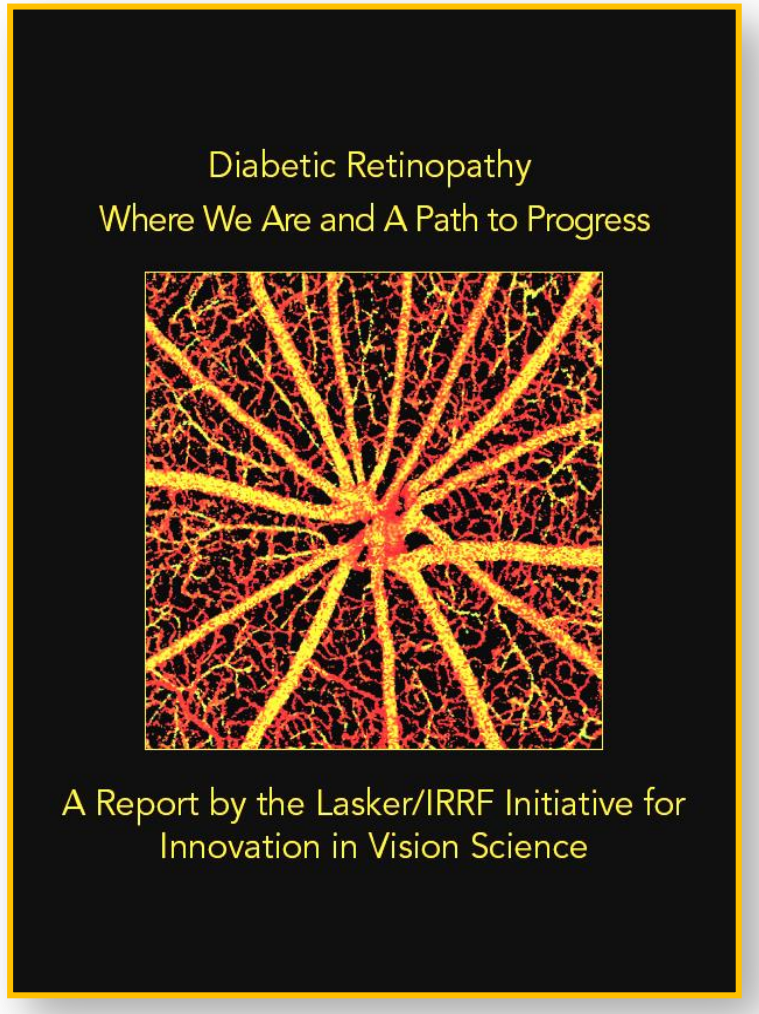




(N)PDR = (non)proliferative diabetic retinopathy

ETDRS, Ophthalmology 1991

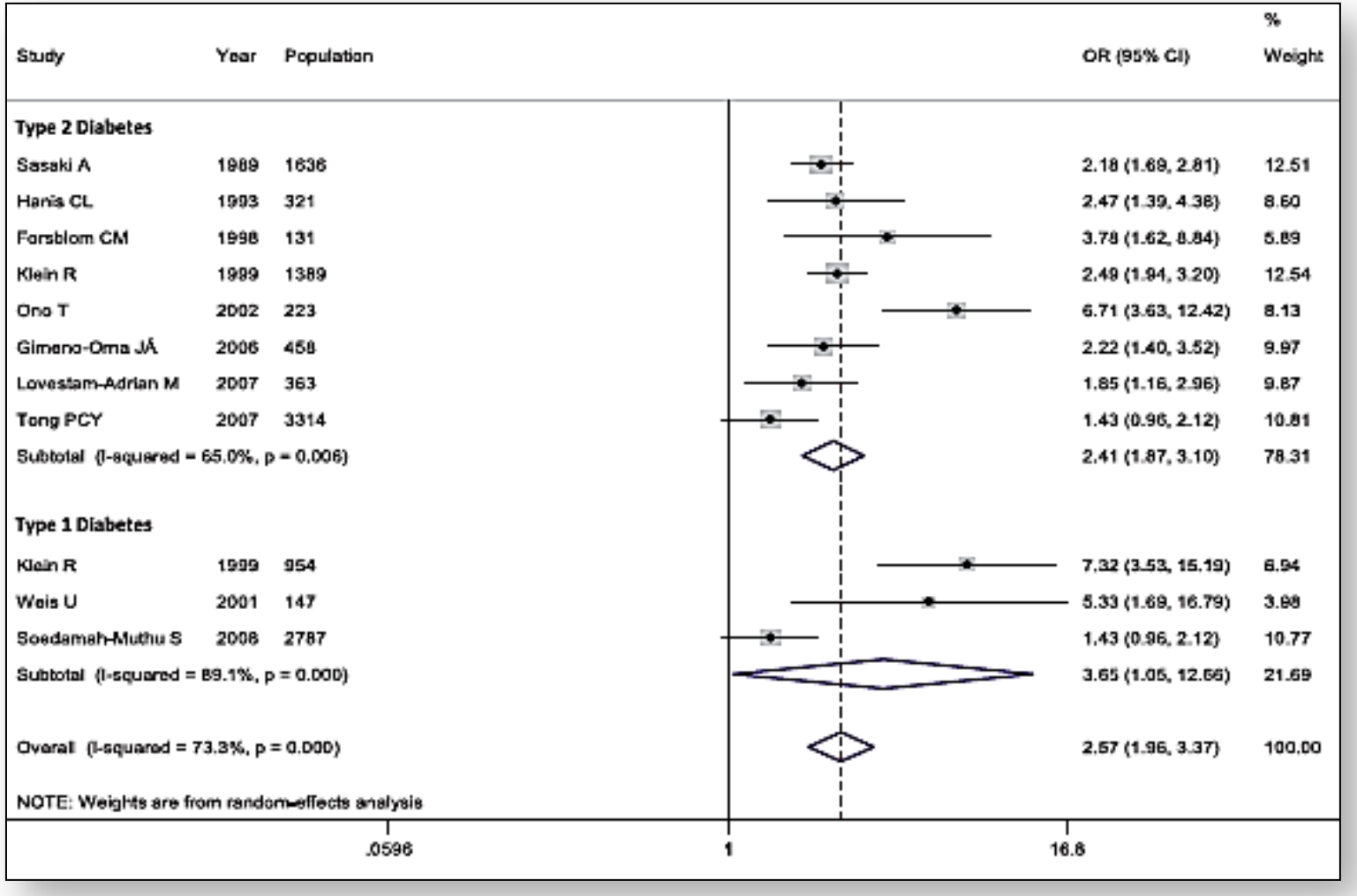
The neurovascular unit in diabetes
Is diabetic retinopathy only a vascular disease?



http://www.laskerfoundation.org/programs/images/irrf_12.pdf

Predict CV-risk from retinal fundus imaging

Diabetic Retinopathy predicts all-cause mortality and cardiovascular events in both type 1 and type 2 diabetes



Kramer et al., Diab Care 2011

ESC Guidelines on diabetes, prediabetes, and cardiovascular diseases developed in collaboration with the EASD

Management of microvascular disease in diabetes		
Recommendations	**Class** [a]	**Level** [b]
Screening for the presence of retinopathy should be considered on annual basis in patients with T2DM.	IIa	B
Multifactorial therapy is recommended when retinopathy is progressing rapidly.	I	B
An HbA_{1c} <7% and a blood pressure <140/85 mmHg are recommended for primary prevention of retinopathy related to DM.	I	A
Lipid lowering should be considered to reduce the progression of retinopathy, the need for laser treatment, and the need for vitrectomy.	IIa	B
It is recommended that proliferative DM retinopathy is treated by pan retinal laser photocoagulation.	I	A
Grid laser photocoagulation should be considered in clinically significant macular oedema.	IIa	B
Intravitreal anti-vascular endothelial growth factor therapy should be considered in patients with vision impairment and clinically significant macular oedema involving the fovea.	IIa	B

Ryden, Grant et al., Eur H J 2013

Future perspectives for ‚medical retina‘

- Elucidate the „reno-retinal syndrome“
- Explain the diabetic „paradox“
- Predict CV-risk from retinal fundus imaging
- Predict visual outcome from novel markers
- Develop multimodal treatment targeting the neurovascular unit

International Diabetes Federation

The Fred Hollows Foundation
www.hollows.org.au

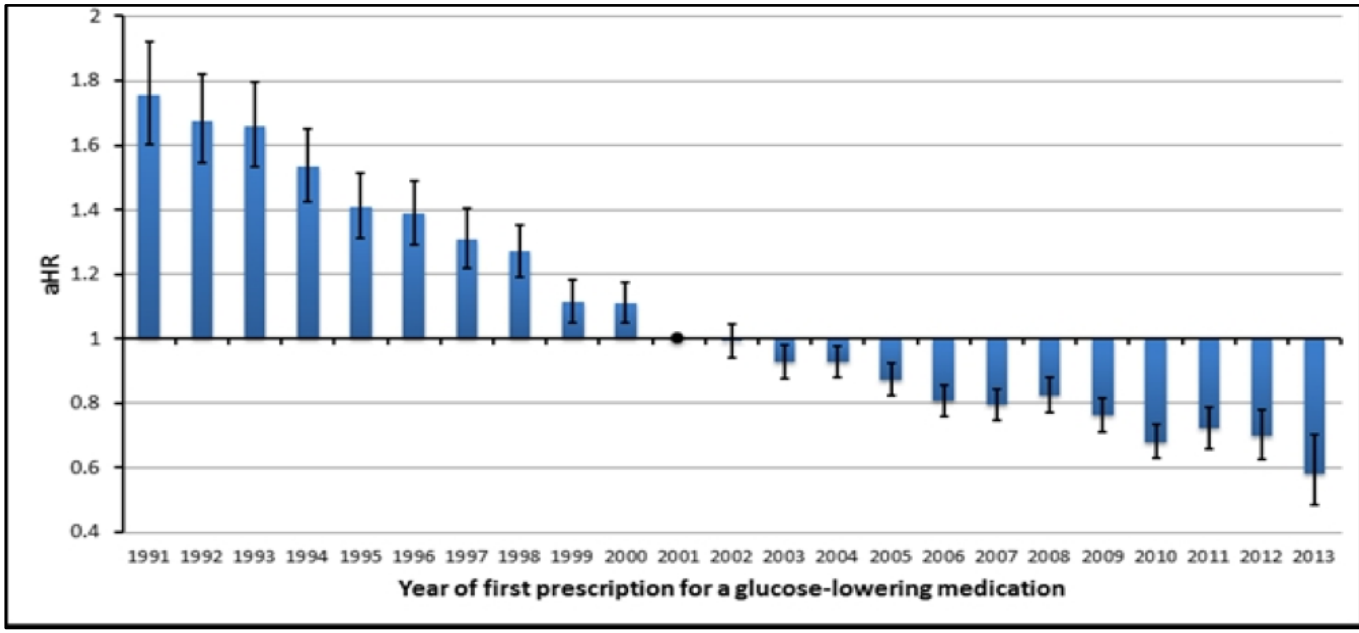
Eye Health Standard

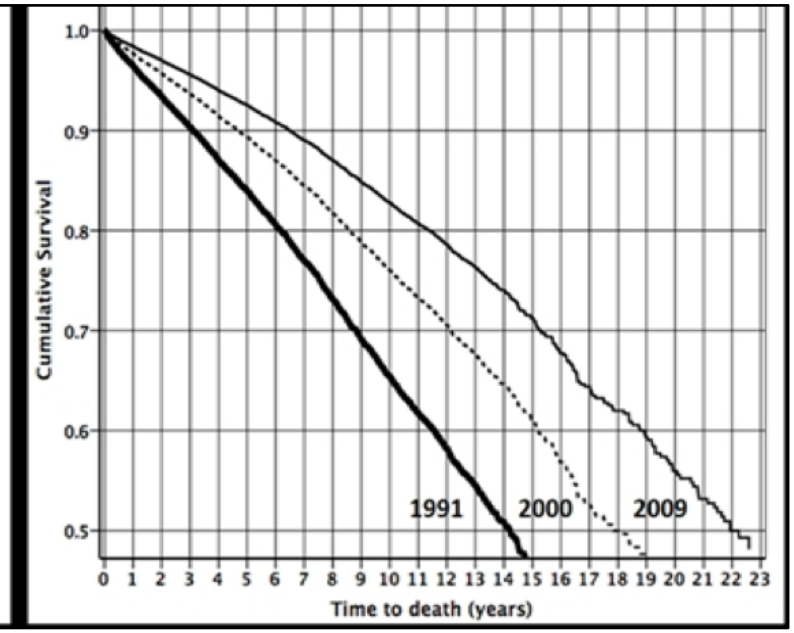
Diabetic Retinopathy Barometer


Act today,
to change tomorrow
Champion a world free of diabetes

Backup slides

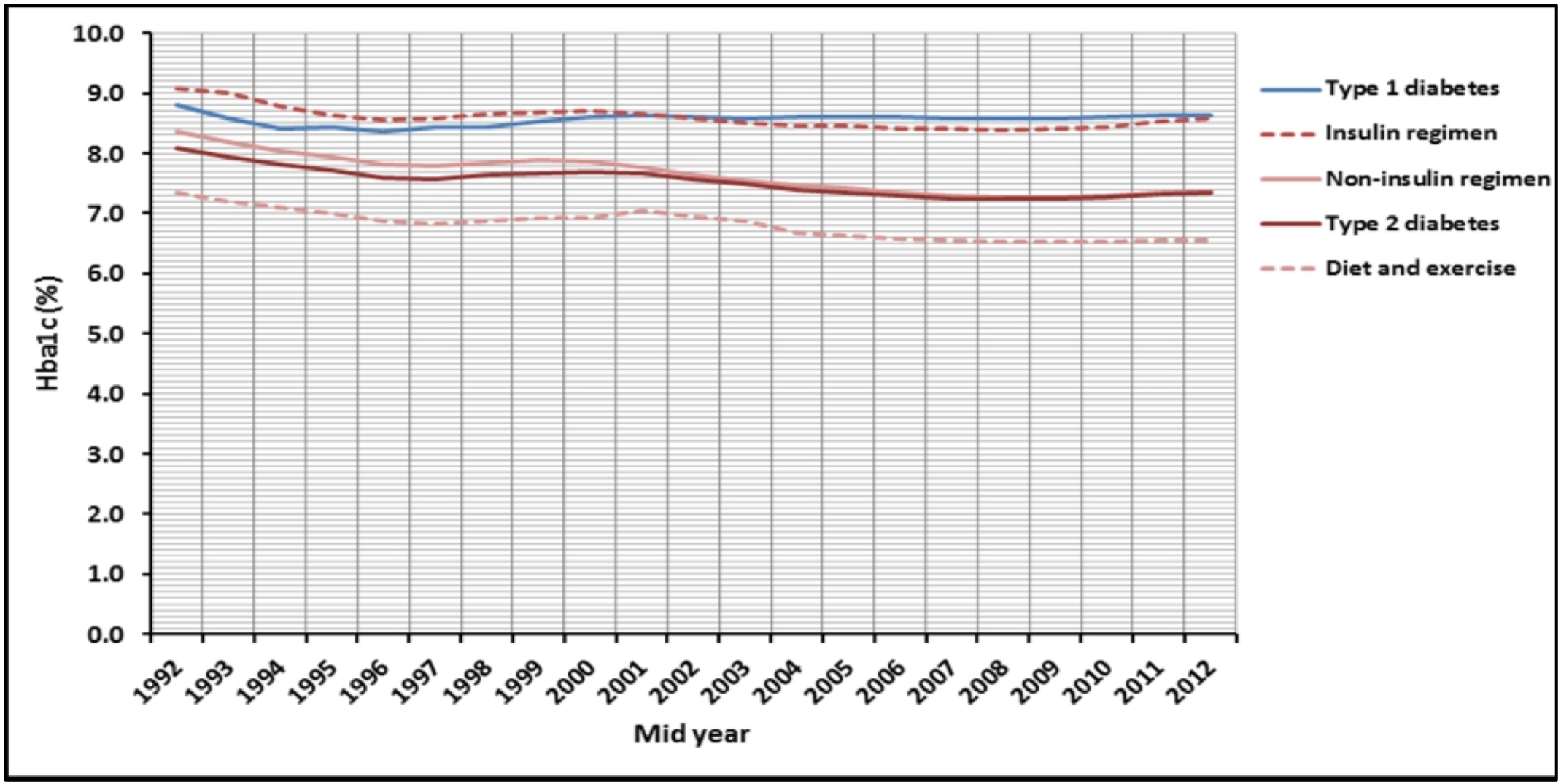
Some good news





Currie CJ et al. unpublished

Some not-so-good news



Currie CJ et al. unpublished

Intensive vs Conventional Treatment in Type 2 Diabetes

	Trials	N. randomized	Non-fatal MI	All-cause mortality	Hypo glycemia
Turnbull FM et al 2009	4	27049	**0.85** (0.70-0.94)	**1.04** (0.90-1.20)	2.48 (1.91-3.21)
Ray KK et al 2009	5	33040	**0.83** (0.75-0.93)	**1.02** (0.87-1.19)	--
Tkac I et al 2009	5	32649	**0.84** (0.75-0.93)	**1.02** (0.89-1.16)	--
Marso SP et al 2010	6	27544	**0.86** (0.77-0.97)	**1.01** (0.86-1.18)	--
Zhang CY et al 2010	7	34144	**0.84** (0.76-0.93)	**NS**	2.30 (1.74-3.03)
Hemmingsen B et al 2011	14	28614	**0.85** (0.6-0.95)	**1.02** (0.92-1.35)	2.39 (1.71-3.34)
Hemmingsen B et al 2011	20	29986	**0.86** (0.78-0.96)	**1.01** (0.9-1.13)	--
Hemmingsen B et al 2013	28	34912	**0.87** (0.77-0.98)	**1.00** (0.92-1.08)	2.18 (1.53-3.11)
Buehler AM et al 2013	20	27654	**0.85** (0.76-0.95)	**1.03** (0.90-1.17)	2.39 (1.79-3.18)

[1]HR; [2]OR; [3]RR; (95% CI)