Type 1 diabetes in older adults: identifying the challenge

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Conflict of interest

I have received speaker honoraria, conference sponsorship, unrestricted educational grants and/or attended meetings (i.e. had free dinner) sponsored by:

- Astra Zeneca, Bayer, Boehringer Ingelheim, Bristol Myer Squib, Colgate Palmolive, Eli Lilly, Glaxo SmithKline, Janssen, Lundbeck, Menarini, Merck, Napp, Novartis, Novo Nordisk, Pfizer, Sanofi Aventis, Servier, Takeda

I currently hold research grants from

- Astra-Zeneca, Bayer, Colgate Palmolive, Novartis, Novo Nordisk & Takeda

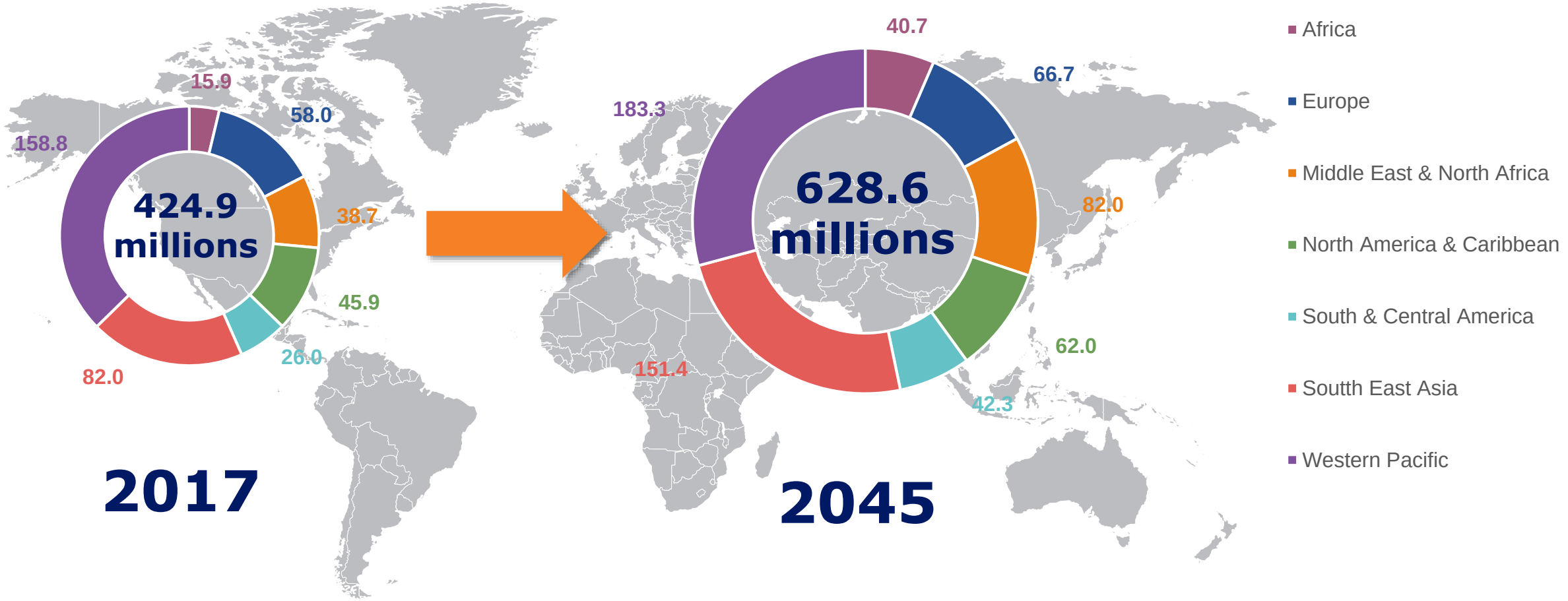
Half of the honoraria I receive are diverted directly to https://www.healthamplifier.org supporting medical services and education in one of the poorest communities in Tanzania

Disclaimer

> *I would never allow a scientist to partake in my government – Give them a new piece of information and they are liable to change their mind*

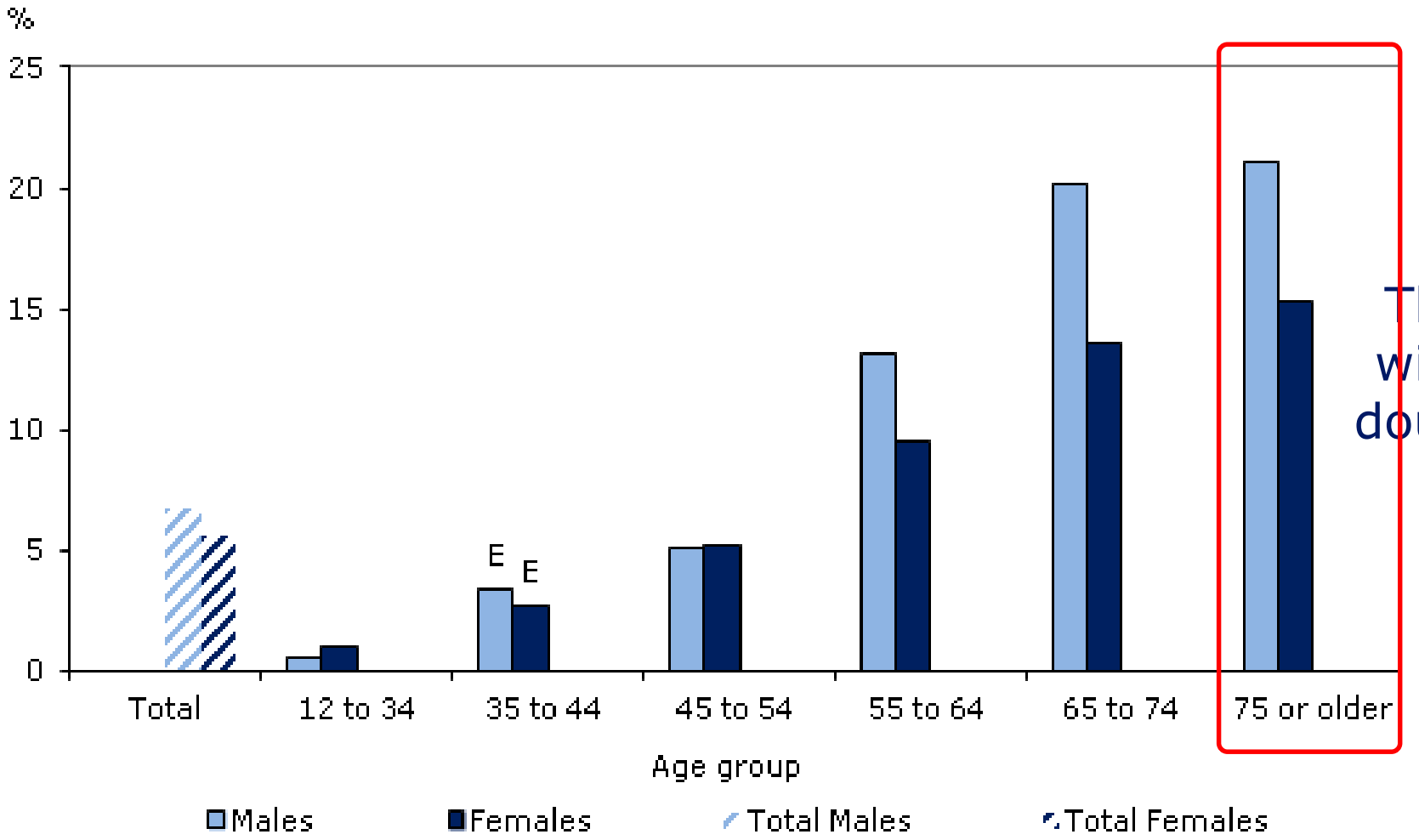
Abraham Lincoln
16th President of the United States

Diabetes is a growing problem



*Numbers expressed in millions
Source: *Diabetes Atlas*, 8th ed. http://www.diabetesatlas.org/resources/2017-atlas.html (accessed 23 Oct 2018)

Age distribution of those with diabetes



x2

The number of older adults with diabetes is expected to double over the next 5 years[2]

1 in **4 people** in residential care have diabetes[2]

1. Canadian Community Health Survey 2011 (accessed at http://www.statcan.gc.ca/pub/82-625-x/2012001/article/11659-eng.htm)
2. Sinclair AJ et al. *Diabetes Care* 2001 Jun;24(6):1066-8

The (mis) perceptions

- T
- T
- U

[1] Thunander M et al. Diabetes Res Clin Pract 82:247–255, 2008

Subdivisions within type

- Adult onset type 1 diabetes more likely to have detectable c-peptide[1]
- As a result they usually have
  - Better clinical outcomes[2]
  - Less hypoglycaemia[2]
- Shorter burden of disease

[1]Merger SR Diabet Med 30:170-178 2013: [2]DCCT Research group, Ann Intern Med 128:517–523, 1998

So what? They're just a bit older…

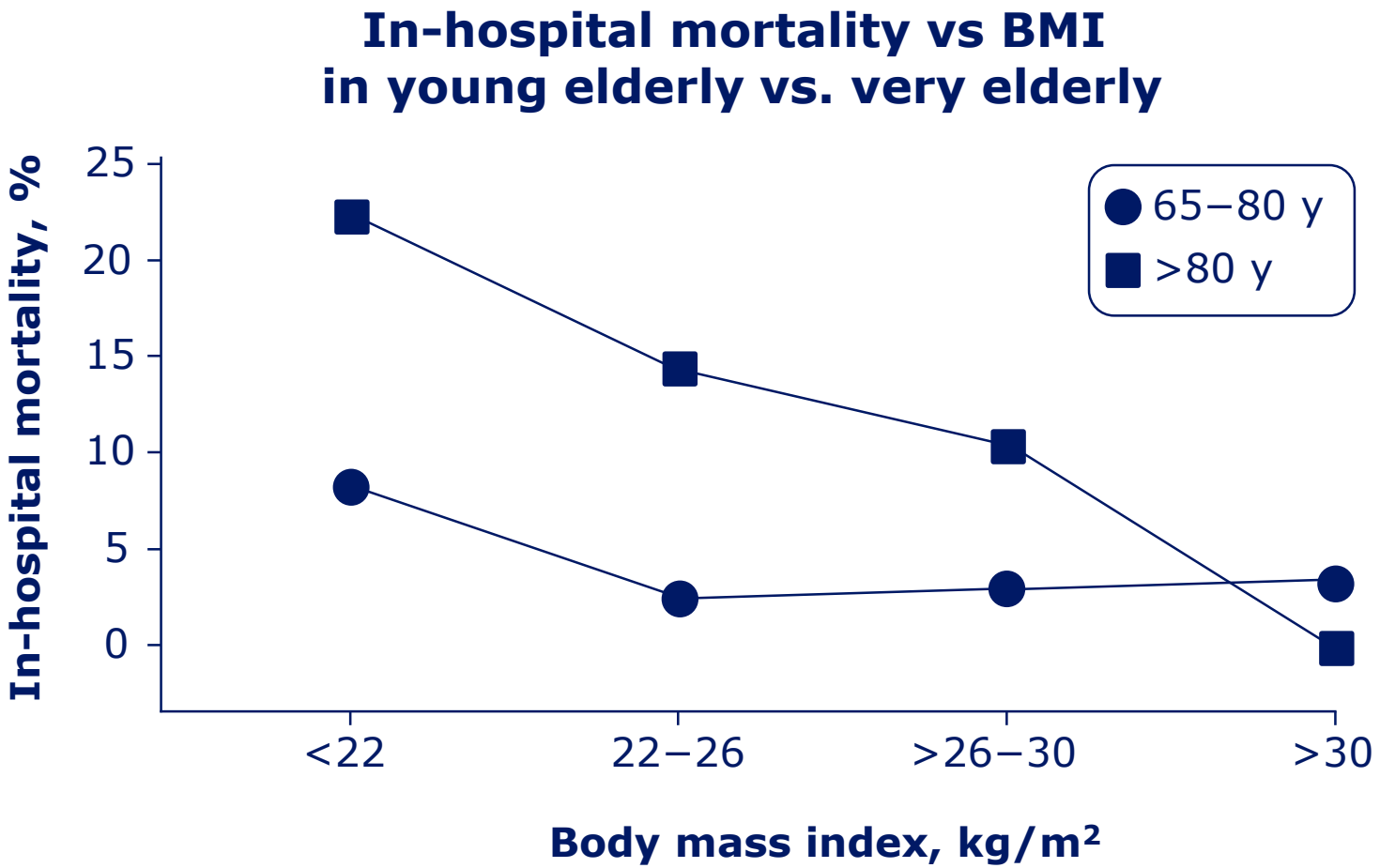
Little person gets bigger

It's just about size!

Fundamental changes in physiology

Kidneys, liver, heart, brain, autonomic nervous system, endocrine system, all start to fail

Mortality and weight in older adults



- In younger patients higher body weight is a poor prognostic indicator
- In older patients the converse is true

In hospital mortality vs. BMI in young elderly vs. very elderly

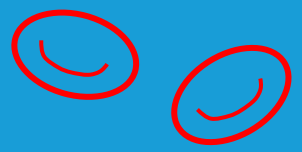
Kamel and Iqbal. *Arch Intern Med.* 2001;161:1459.

HbA_{1c} differs for older adults

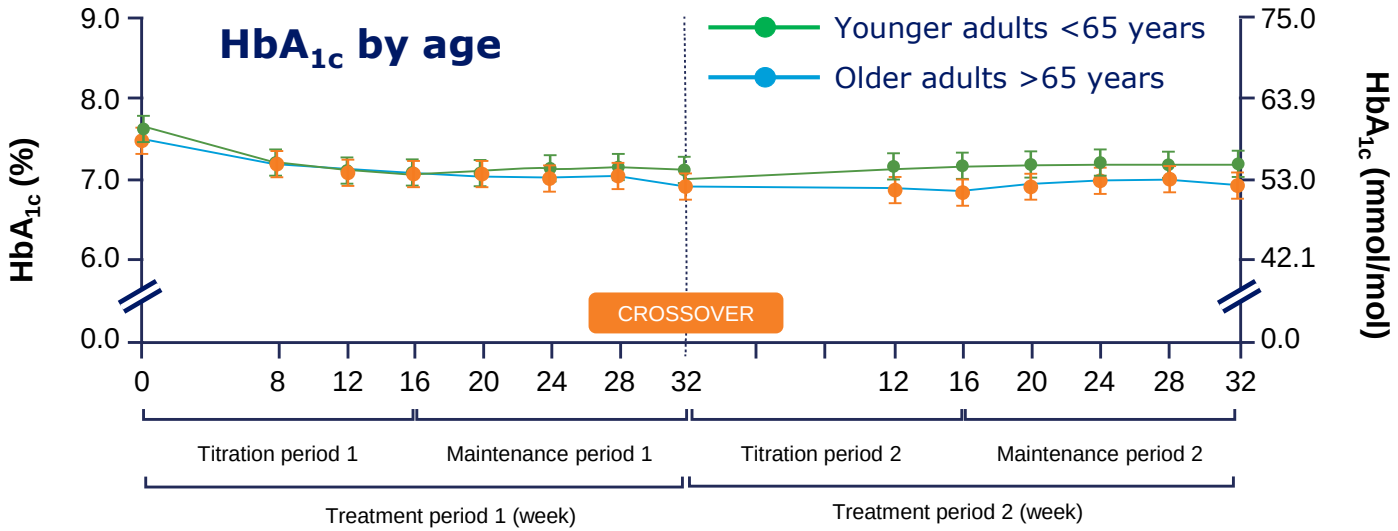
Possible explanation

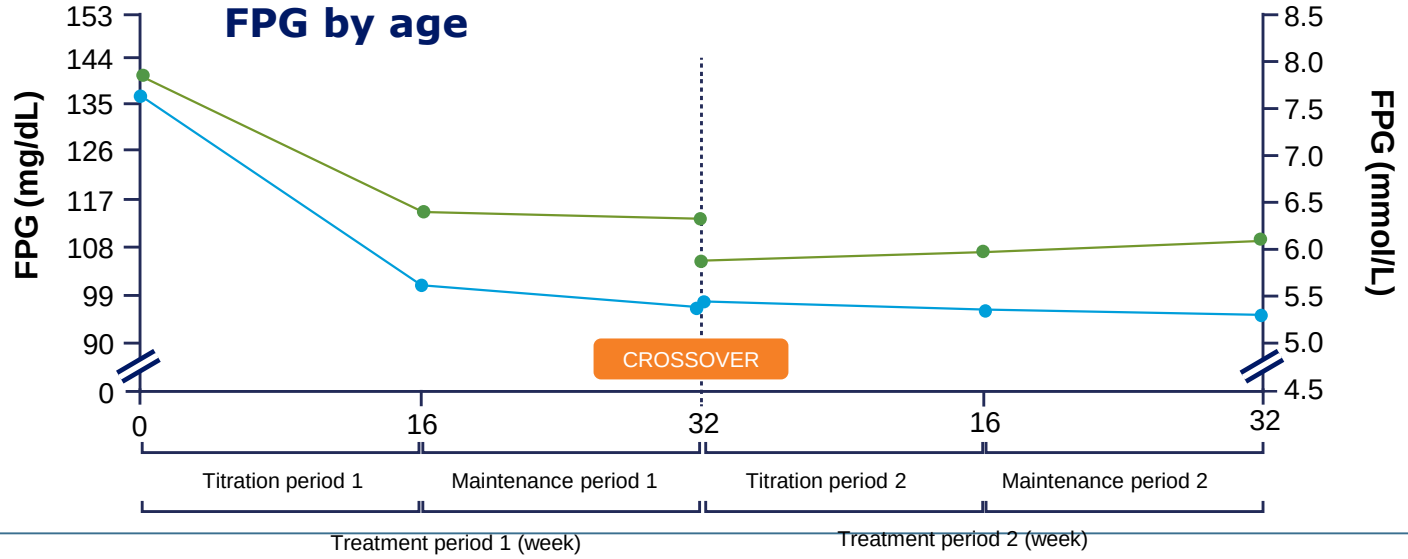
Older vs younger adults

Lower red blood cell (RBC) count[1]



Decreased secretion of EPO due to decline in renal function[1]





EPO, erythropoietin; Hb, haemoglobin; HbA_{1c}, glycated haemoglobin

1. Wu L et al. *PLoS ONE 2017;*12(9): e0184607.; 2. Yau CK et al. *J Am Geriatr Soc* 2012;60(7):1215–21

What is Old…

Chronological vs physiological vs functional age

Office of National Statistics in the UK – 65yrs

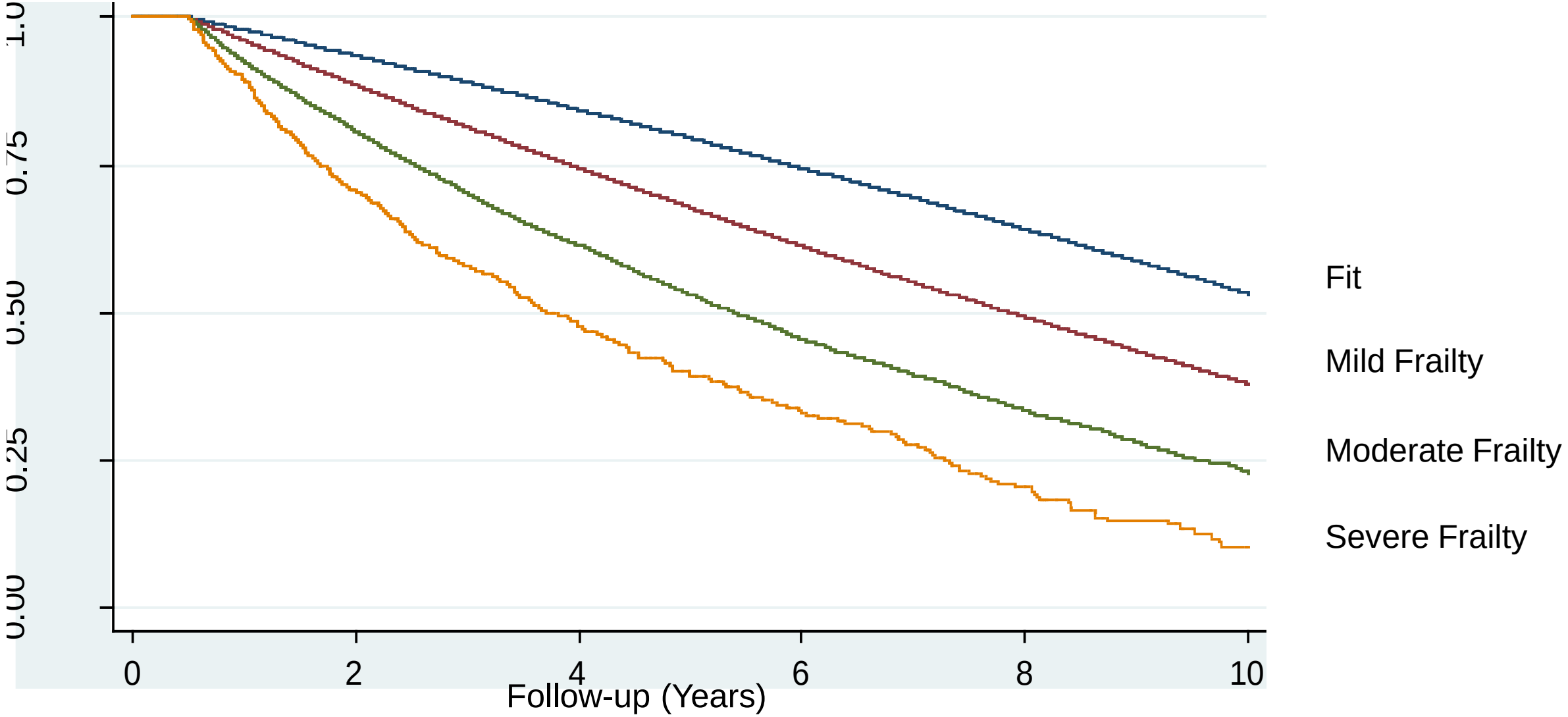
WHO – someone whose age has passed the median life expectancy at birth

- UK – 81.2yrs
- In Africa – 50-55yrs
- Latin America – 60yrs

Age vs. Frailty…

Both of these actors are the same age

Mortality of 75+ year old those who survive 6 months stratified by Frailty status

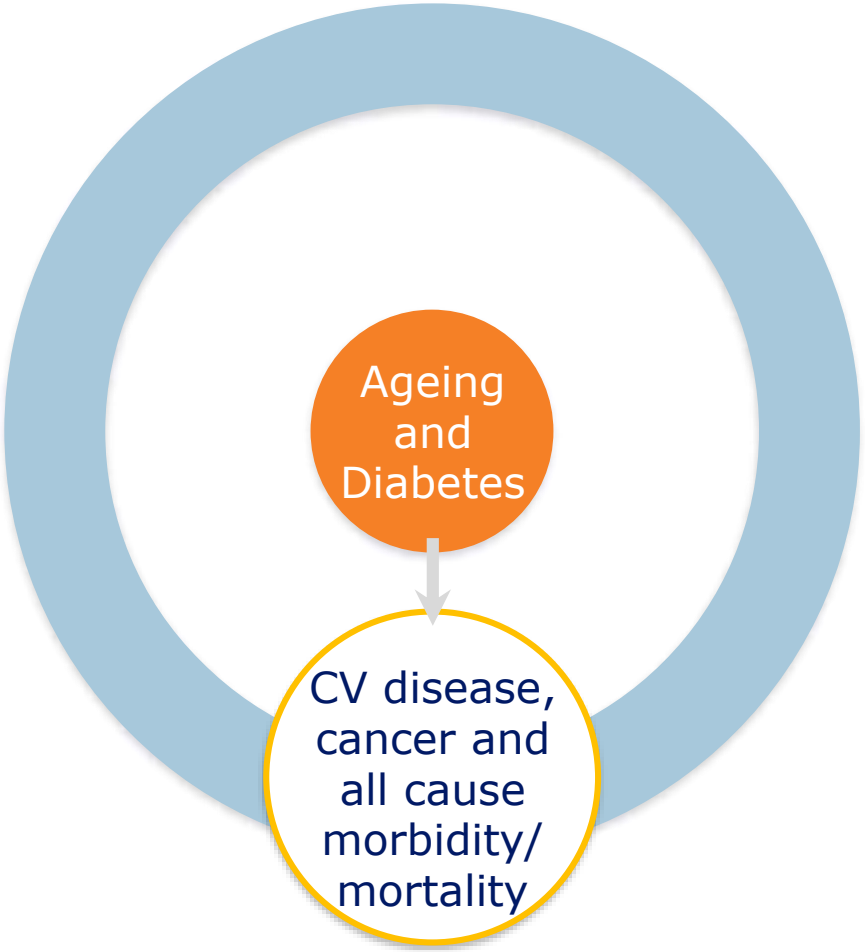


Data on File of Mazoli, J, Strain, WD et al from CPRD database

The frail, elderly patient with diabetes

Older persons with diabetes are at higher risk than those without diabetes of:

- Usual complications of diabetes…



Cukierman T, et al. Diabetologia. 2005;48(12):2460-9

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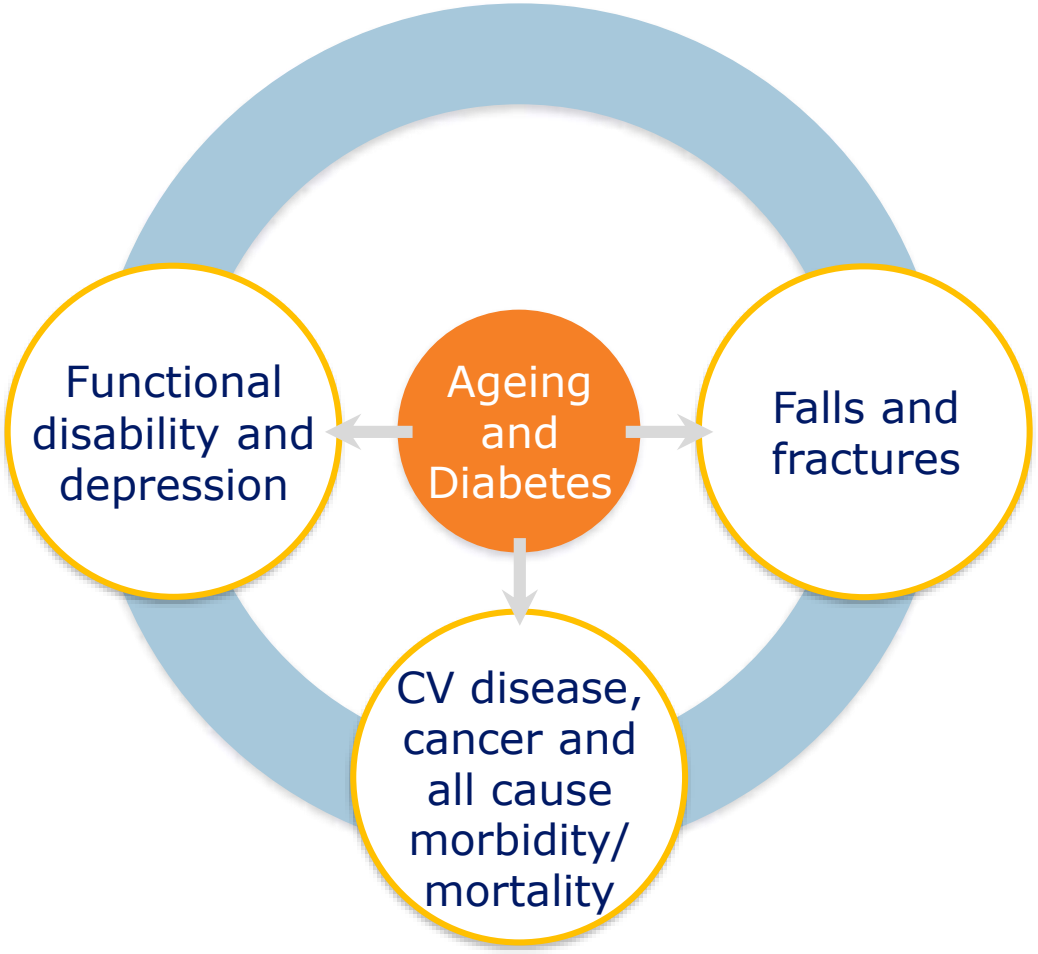
But Also

- Functional disability
- Geriatric syndromes: depression



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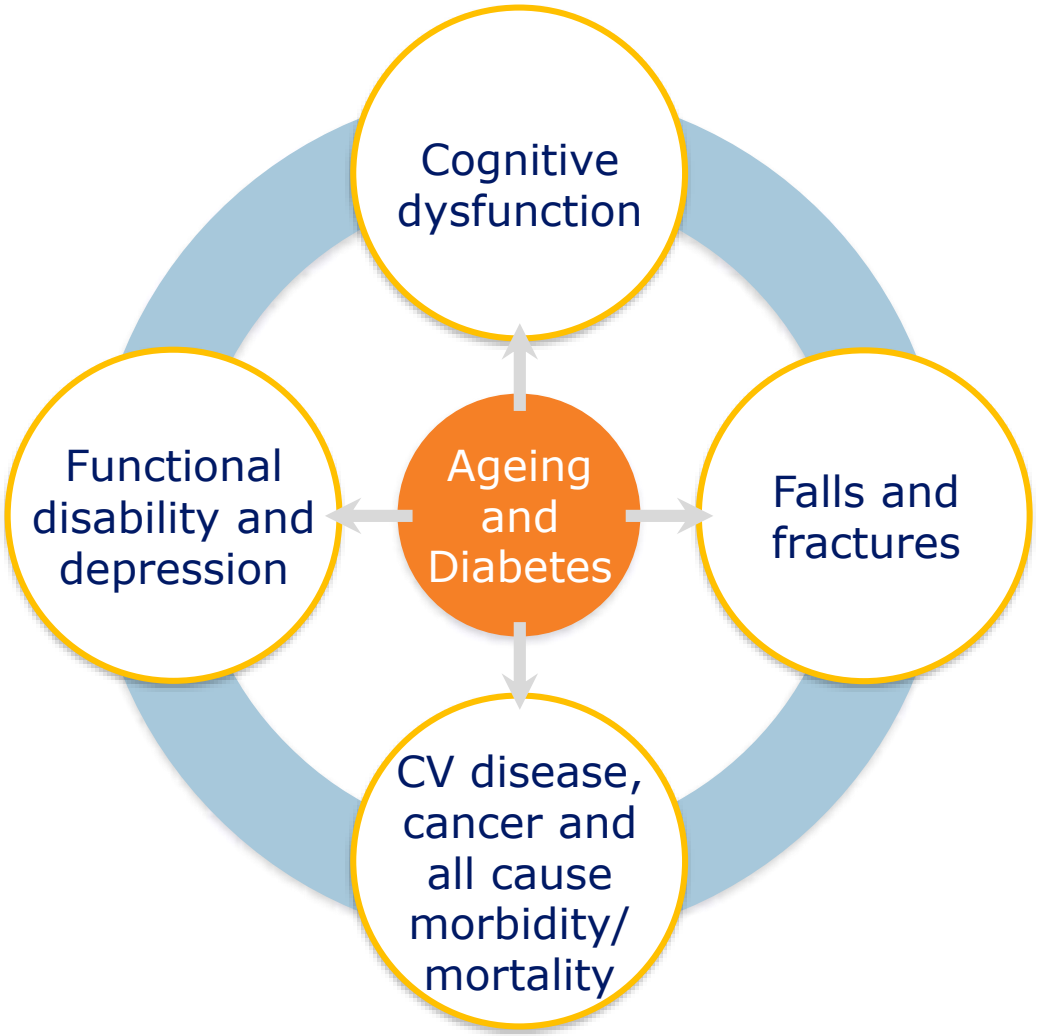

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The frail, elderly patient with diabetes

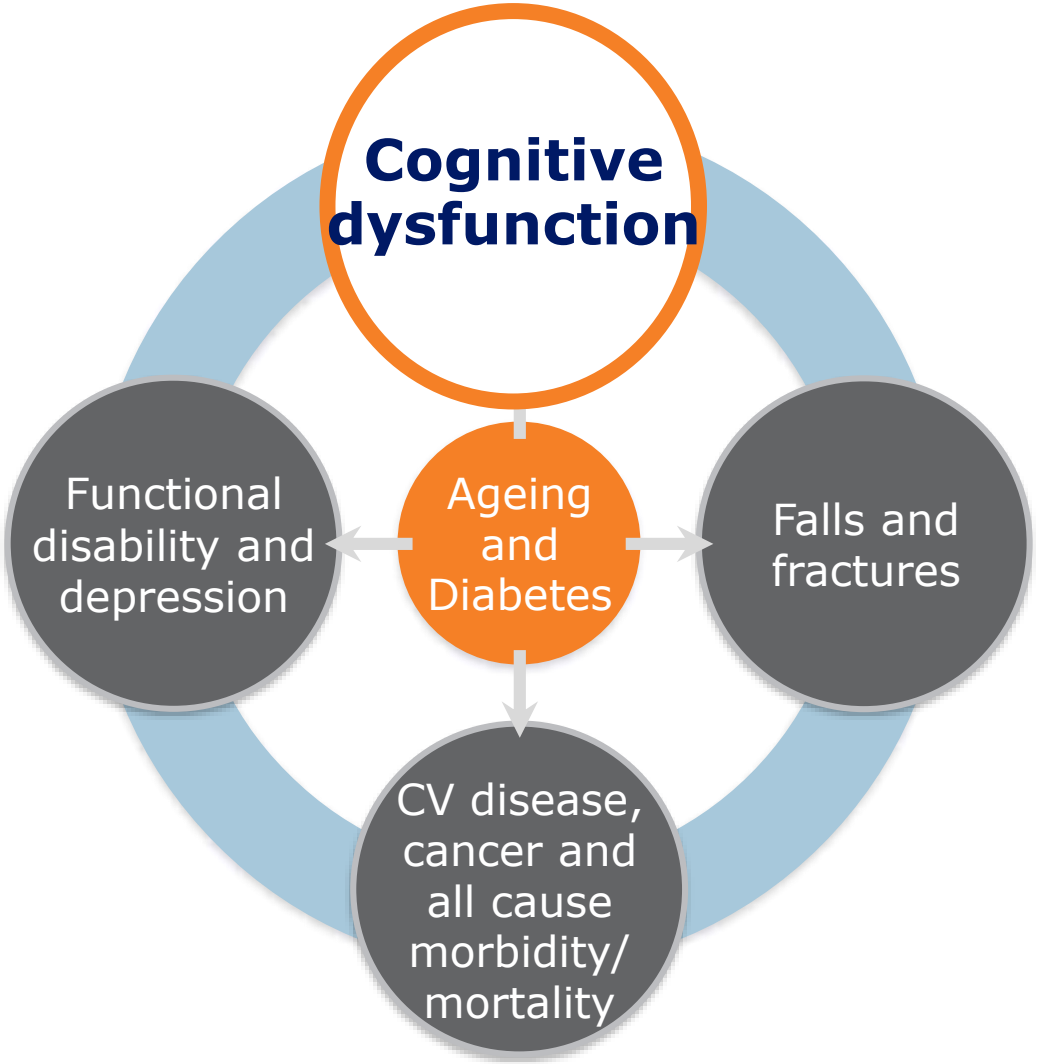
Older persons with diabetes are at higher risk than those without diabetes of:

- Usual complications of diabetes…

But Also

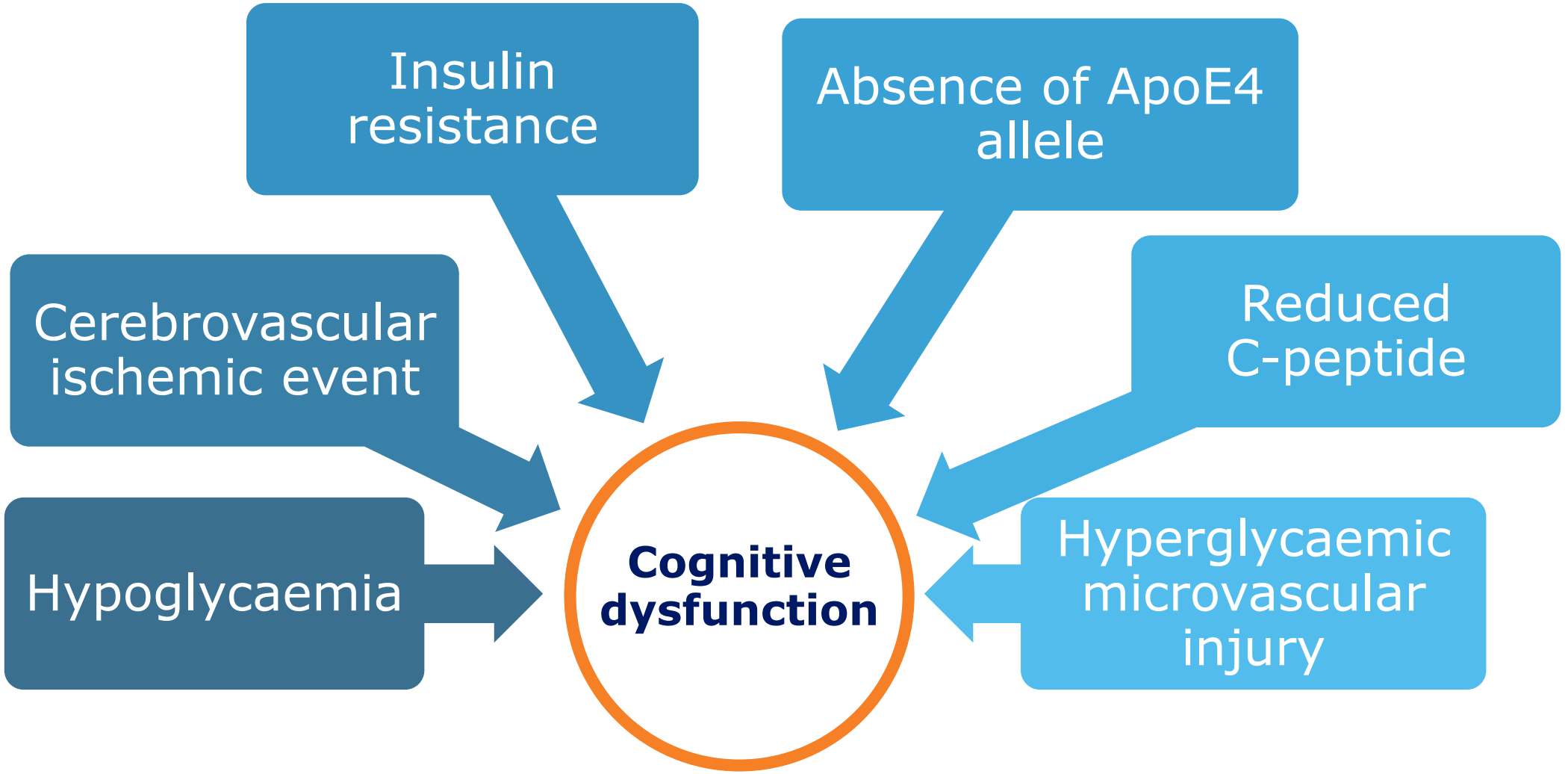
- Functional disability
- Geriatric syndromes: depression
- **Geriatric syndromes: cognitive impairment**

Cognitive dysfunction should be added to the list of the complications of diabetes, along with retinopathy, neuropathy, nephropathy and cardiovascular disease.



Cukierman T, et al. Diabetologia. 2005;48(12):2460-9

Pathophysiology – diabetes and dementia



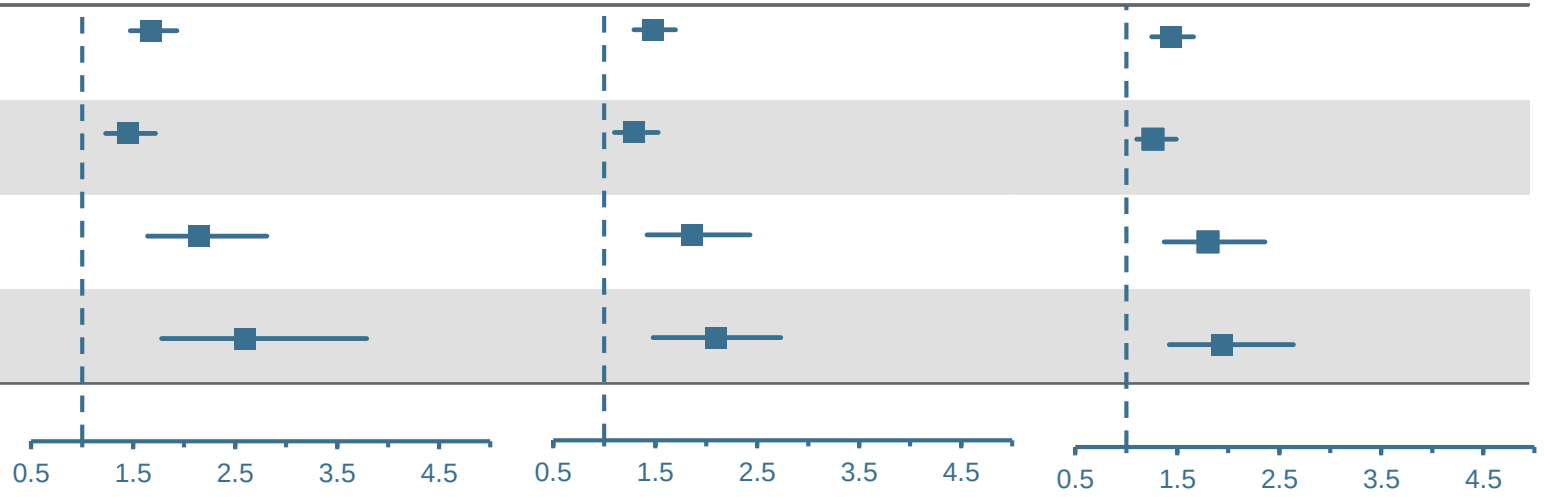
ApoeE4, apolipoprotein E4;
Adapted from Kodl, *et al. Endocrinol Rev* 2008; 29:494 –511

Hypoglycaemia and dementia

A longitudinal cohort study from 1980–2007 of 16,667 patients with a mean age of 65 years and type 2 diabetes who were members of an integrated health care delivery system in northern California

Hypoglycaemia and risk of incident dementia cases[a]

No. of hypoglycaemic episodes[b] (n)	No. of dementia cases	Adjusted for Age (as time scale) BMI, Race/Ethnicity, education, sex, and duration of diabetes	Additionally adjusted for comorbidities[c]	Additionally, adjusted for 7-year HbA_{1c} level, diabetes treatment and years of insulin use
1 or more	250			
1	150			
2	57			
3 of more	43			



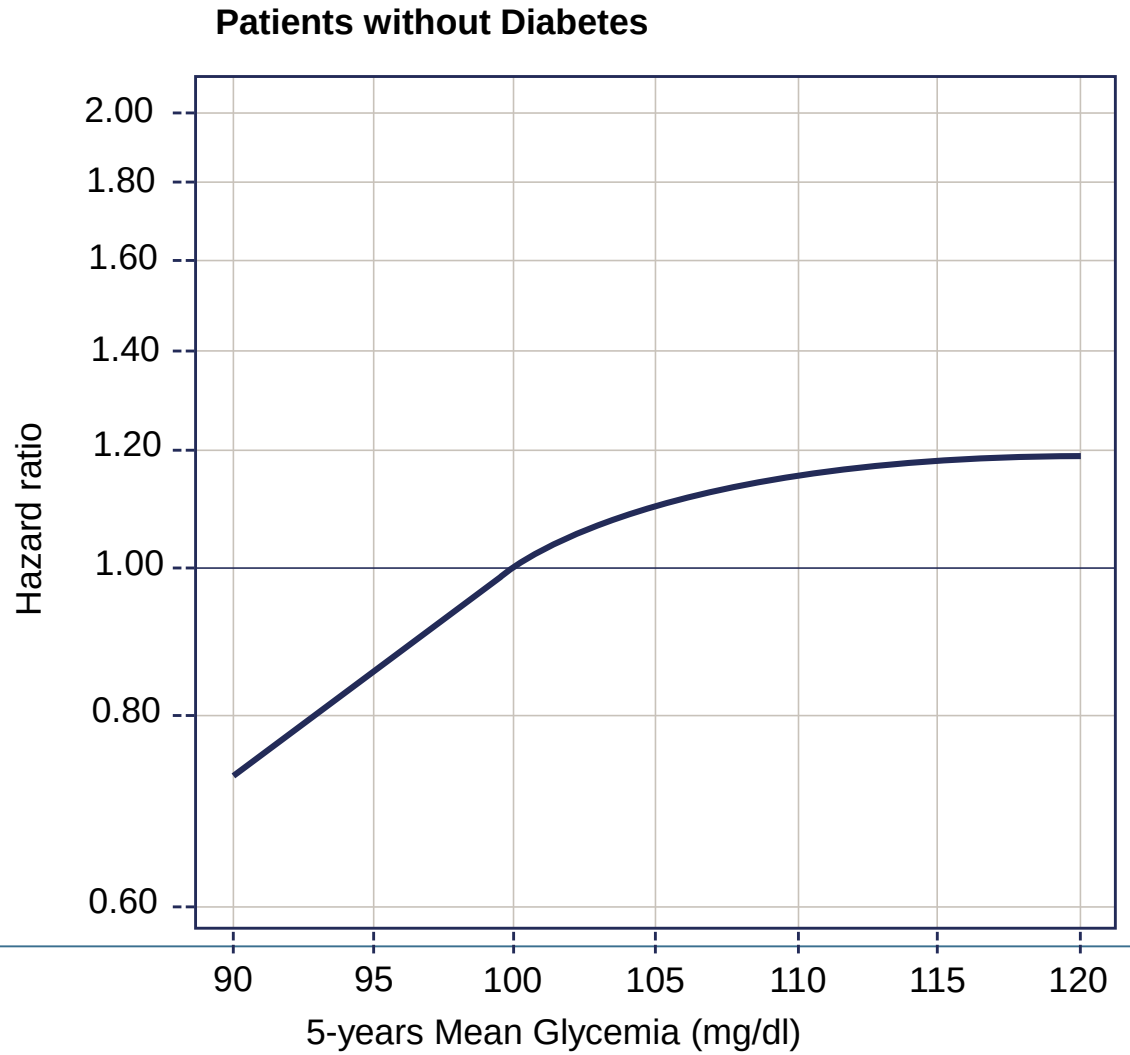
[a] Analyses combined using Cox proportional hazard models; [b]The 1 or more group was compared with 0 and 1, 2 and 3 or more groups were simultaneously compared to 0; [c]Adjustment made using a comorbidity composite scale, BMI=body mass index; CI=confidence interval; HbA_{1c}=haemoglobin A_{1c}

Whitmer *et al. JAMA* 2009; 301:1565–572

Relationship between glucose and risk of dementia

Risk of incident dementia associated with average glucose level over the preceding 5 years among participants **without** diabetes

Average Glucose Level	Hazard Ratio for Dementia (95% CI)
Participants without diabetes	
95 mg/dl	0.86 (0.77-0.97)
100 mg/dl	1.00
105 mg/dl	1.10 (1.03-1.17)
110 mg/dl	1.15 (1.05-1.27)
115 mg/dl	1.18 (1.04-1.33)
p value	0.01

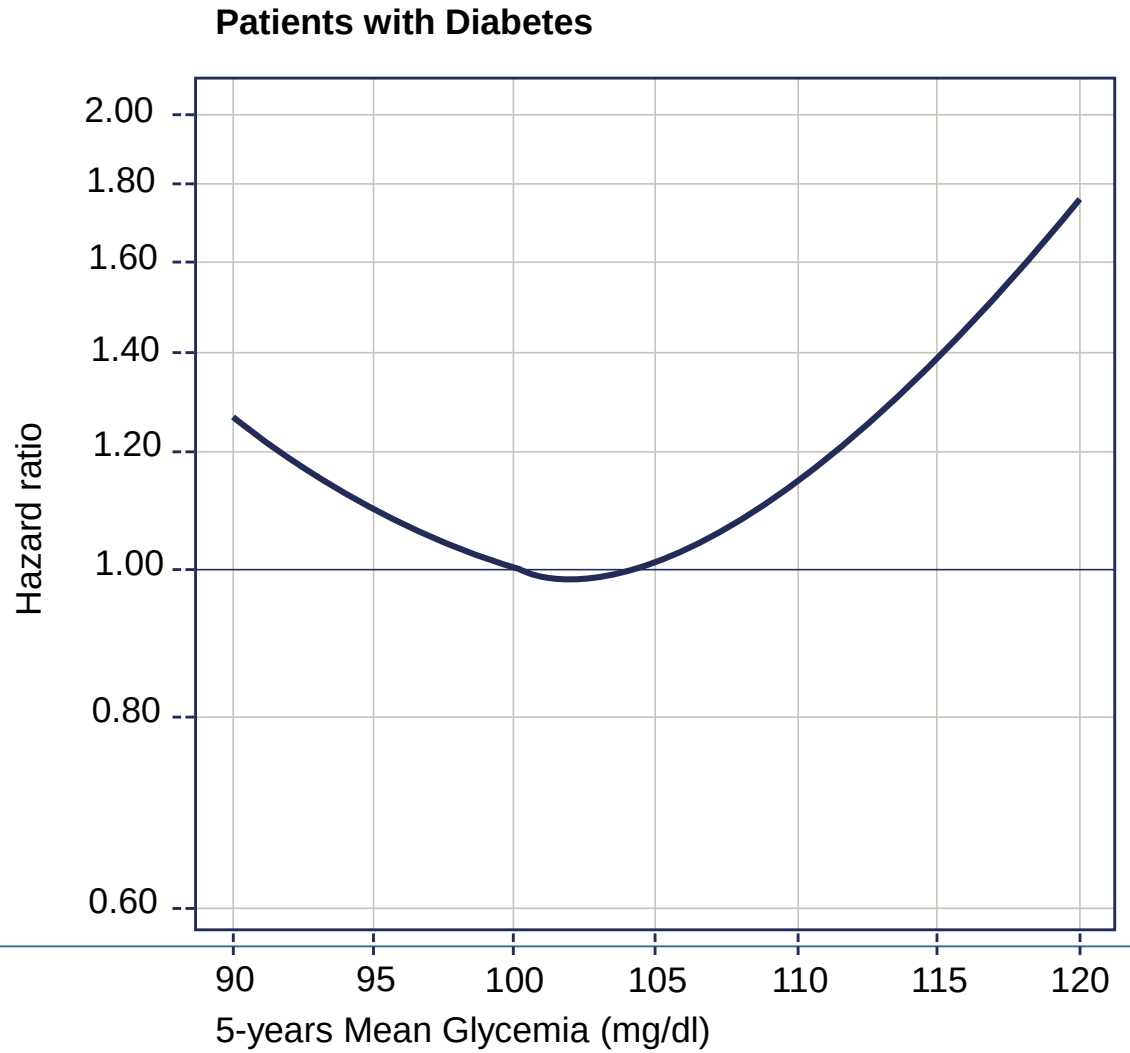


Crane PK et al., N Engl J Med 2013; 369:540-548

Relationship between glucose and risk of dementia

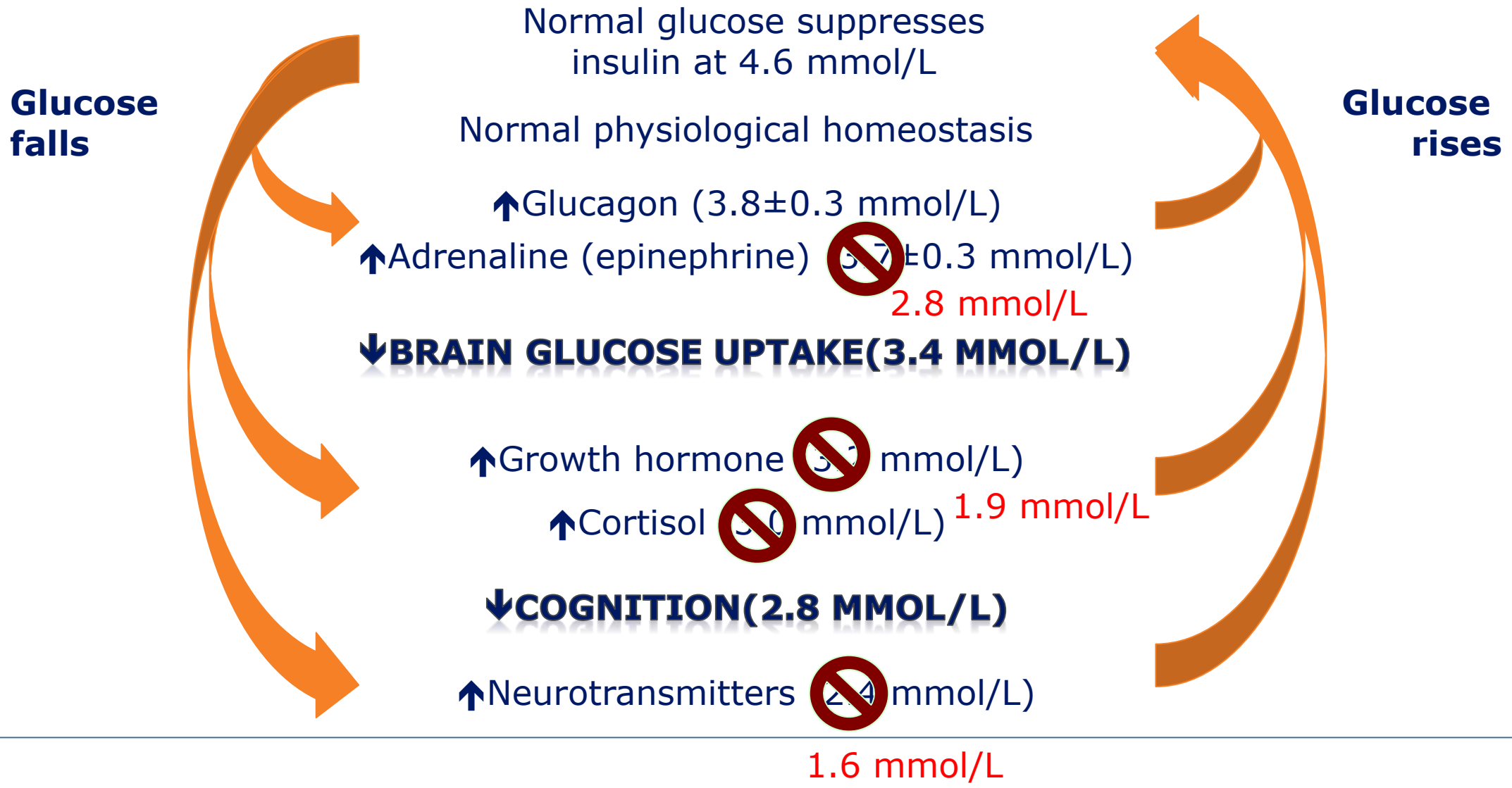
Risk of incident dementia associated with average glucose level over the preceding 5 years among participants **with** diabetes

Average Glucose Level	Hazard Ratio for Dementia (95% CI)
Participants with diabetes	
150 mg/dl	1.10 (0.92-1.30)
160 mg/dl	1.00
170 mg/dl	1.01 (0.92-1.12)
180 mg/dl	1.15 (0.98-1.34)
190 mg/dl	1.40 (1.12-1.76)
p value	0.002



CI, confidence interval
Crane PK et al., N Engl J Med 2013; 369:540-548

The physiology of hypos – older patients



Zammitt NN, Frier BM. Diabetes Care 2005;28:2948–61

Symptoms of hypoglycaemia are non-specific in older people

Autonomic:

Palpitations

Sweating

Anxiety

Neuroglycopenic:

Fatigue

Irritability

Confusion

Dizziness

Drowsiness

Coma

Particularly in older people:

Unsteadiness

Light-headedness

All these are also common in older people without diabetes

Deary IJ et al. *Diabetologia* 1993;36:771–77; Jaap AJ et al. *Diabet Med* 1998;15:398–401

Take Home messages

- Managing elderly patients is complicated by
  - Multiple co-morbidities,
  - Increased risk from the complications of treatment
  - Reduced life expectancy, therefore reduced return
- Treatment should focus on reducing risk of side effects and improving symptoms

Thank you for your attention