Diabetes in Older Adults

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Metabolic Alterations in Aging

Altered Brain Metabolism (AD)

Sarcopenia
Muscle Mass
Strength
Quality

Dyslipidemia CV Disease

Low Bone Mineralization

Type 2 DM Obesity
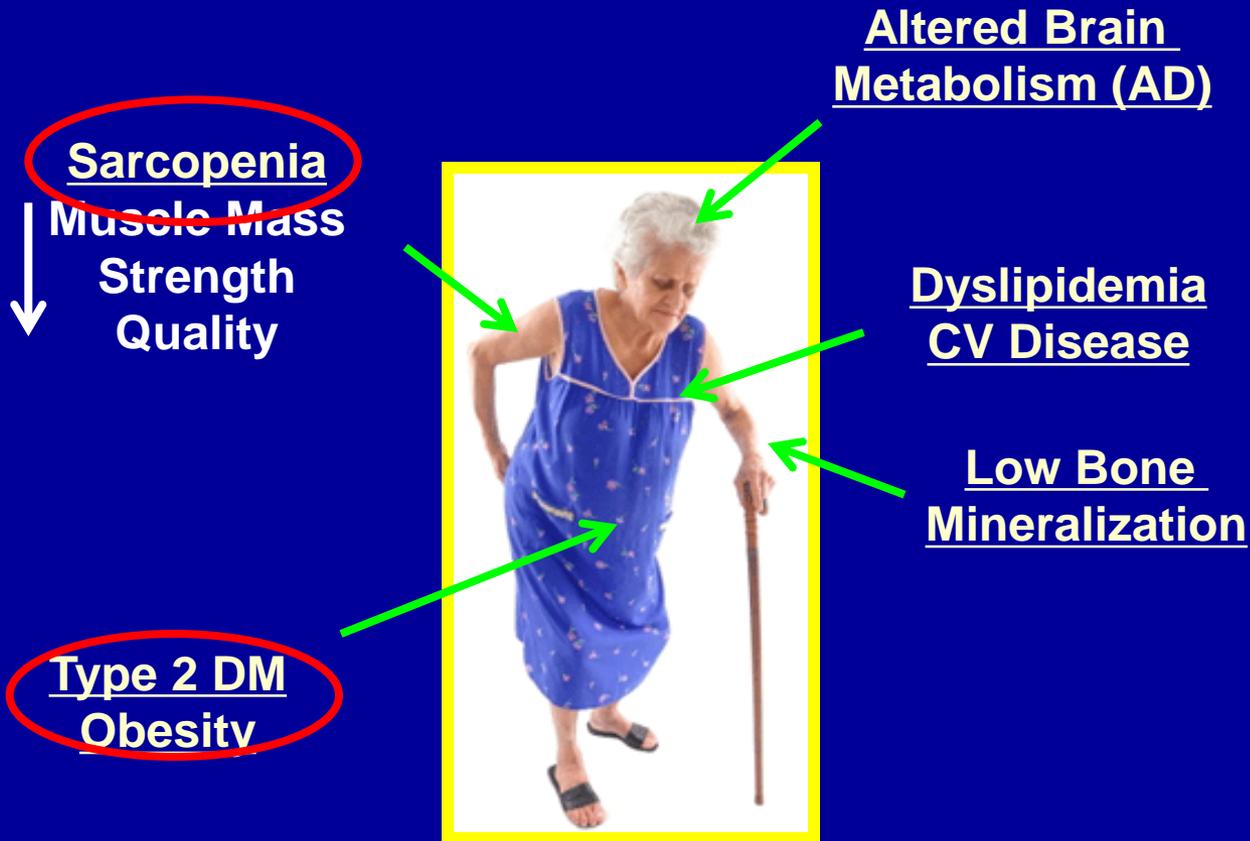
Incidence (per 1,000) of major diabetes complications among adults with diabetes, by age, 2009.

*Jeffrey B. Halter et al. Diabetes 2014;63:2578-2589*
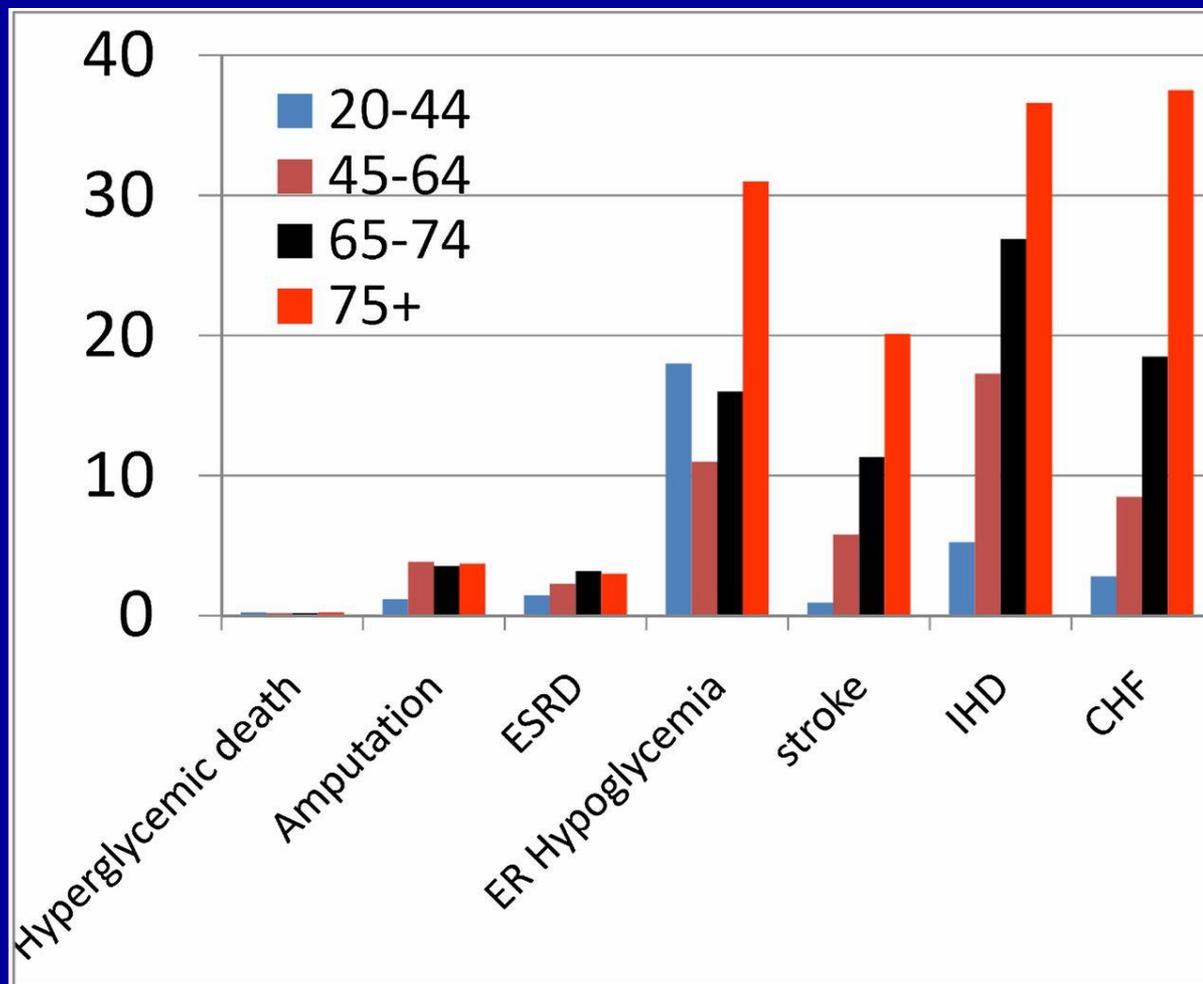
Prevalence of Type 2 Diabetes, Undiagnosed Diabetes, and IGT

Impaired Glucose Tolerance (Prediabetes)

Undiagnosed Type 2 Diabetes

Diagnosed Type 2 Diabetes

Percent of Population

50, 45, 40, 35, 30, 25, 20, 15, 10, 5, 0

Age (years): 20–44, 45–54, 55–64, ≥ 65

Adapted from Harris MI. Consultant 1997;37(Suppl):S9.
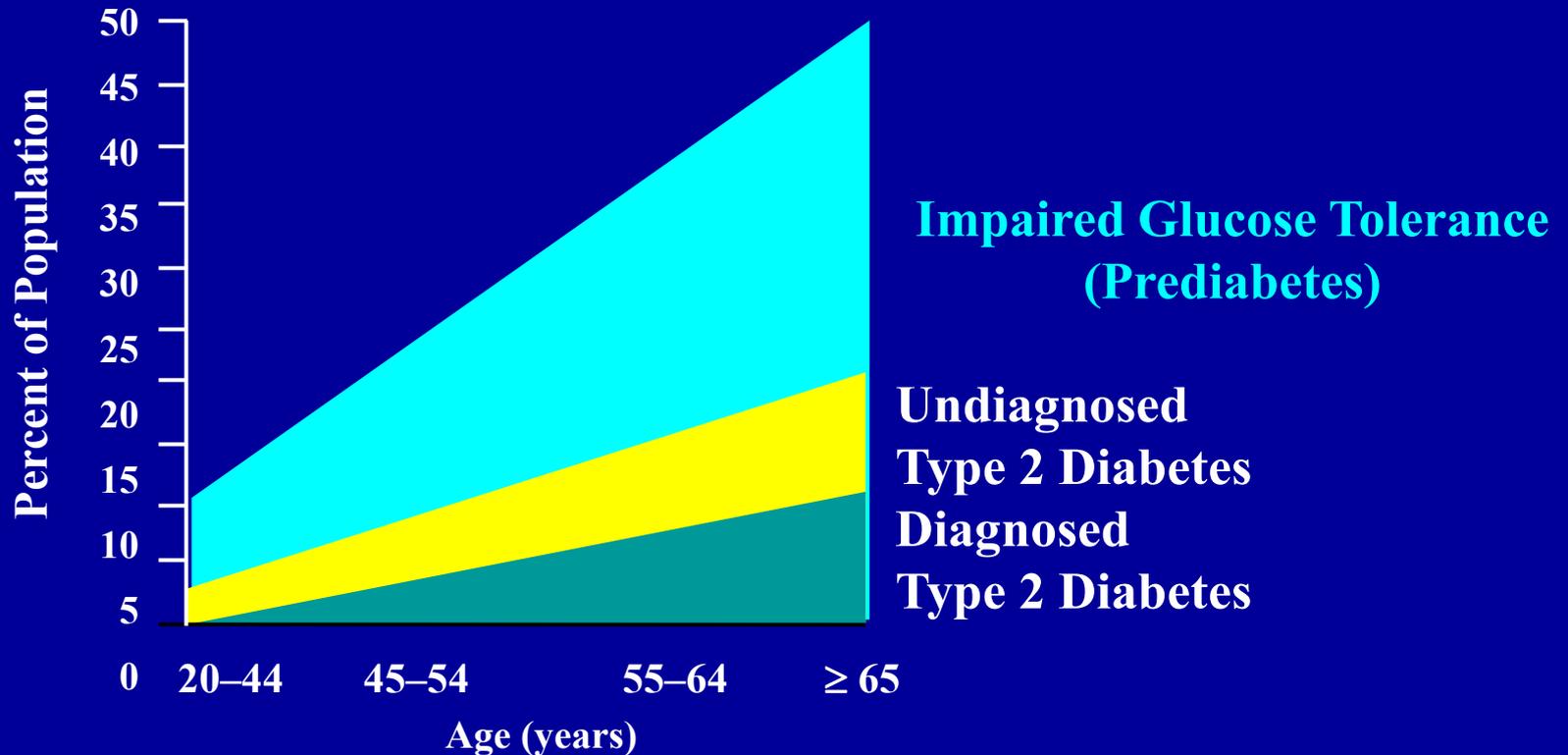
One in every two people age 65 and older have diabetes or pre-diabetes

Why Diabetes Risk Increases With Age?

Type 2 Diabetes in Aging
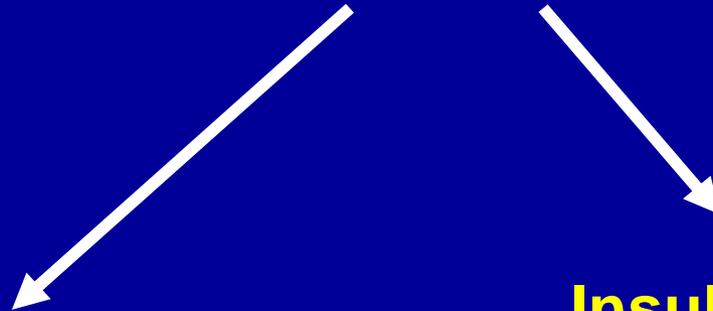
β Cell Failure
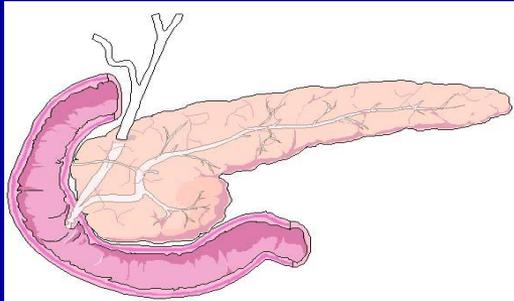
Insulin Resistance
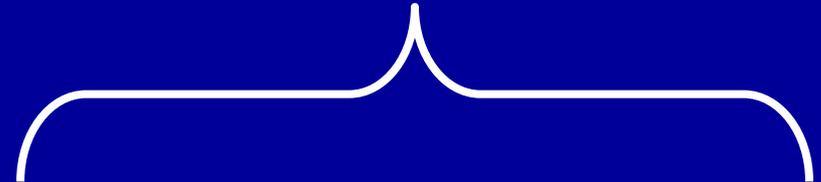
Low Physical Act.

Sarcopenia
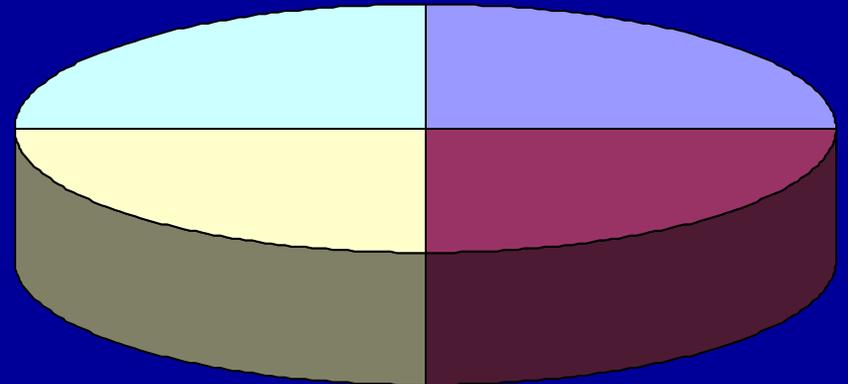
Decreased Insulin Action

Visceral Adiposity

Effect of Age on Insulin Secretion

Metabolic Signaling Pathways in Aging
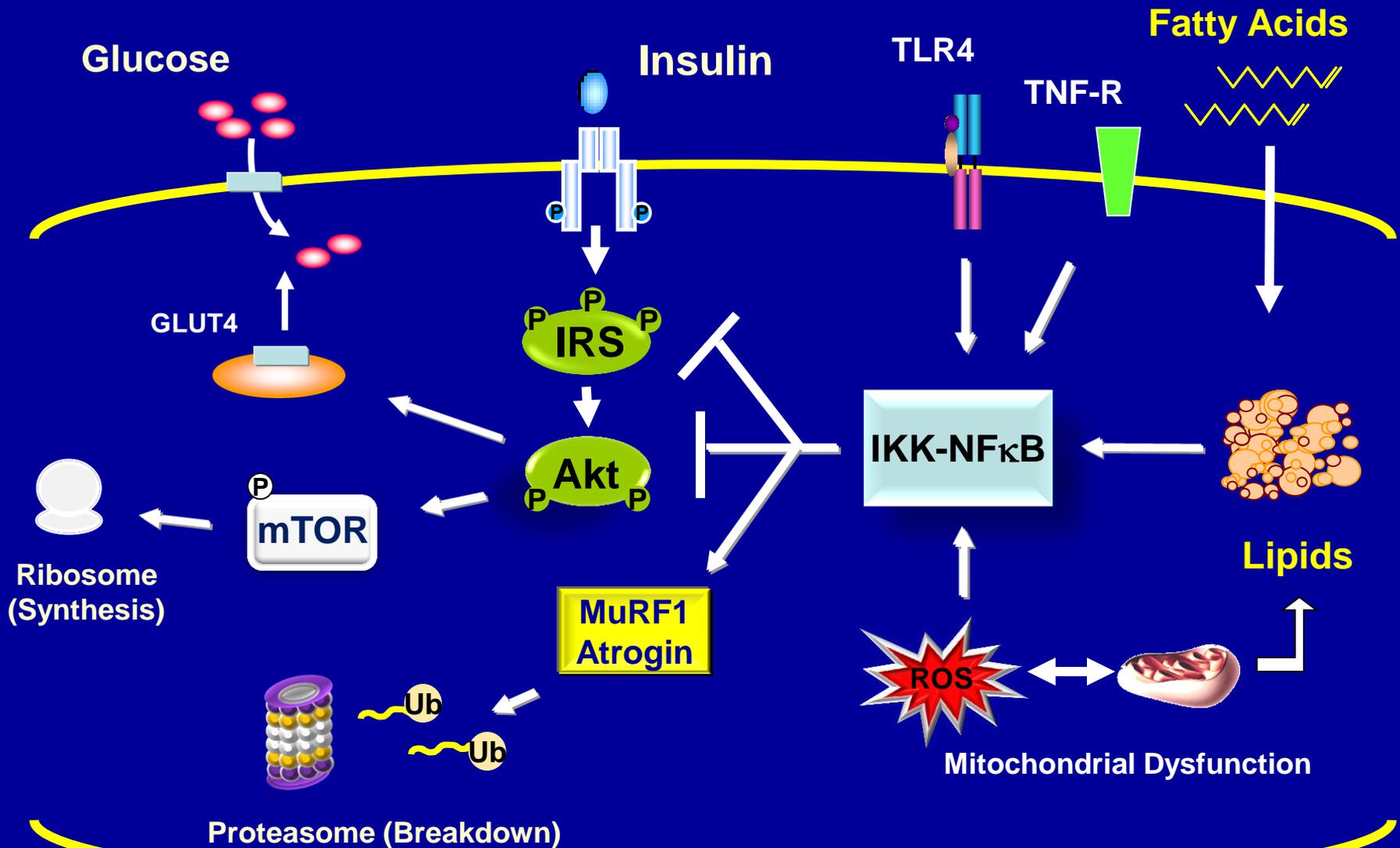
Effect of Age on Insulin Sensitivity

Insulin Sensitivity (M)

Petersen, Science, 2003
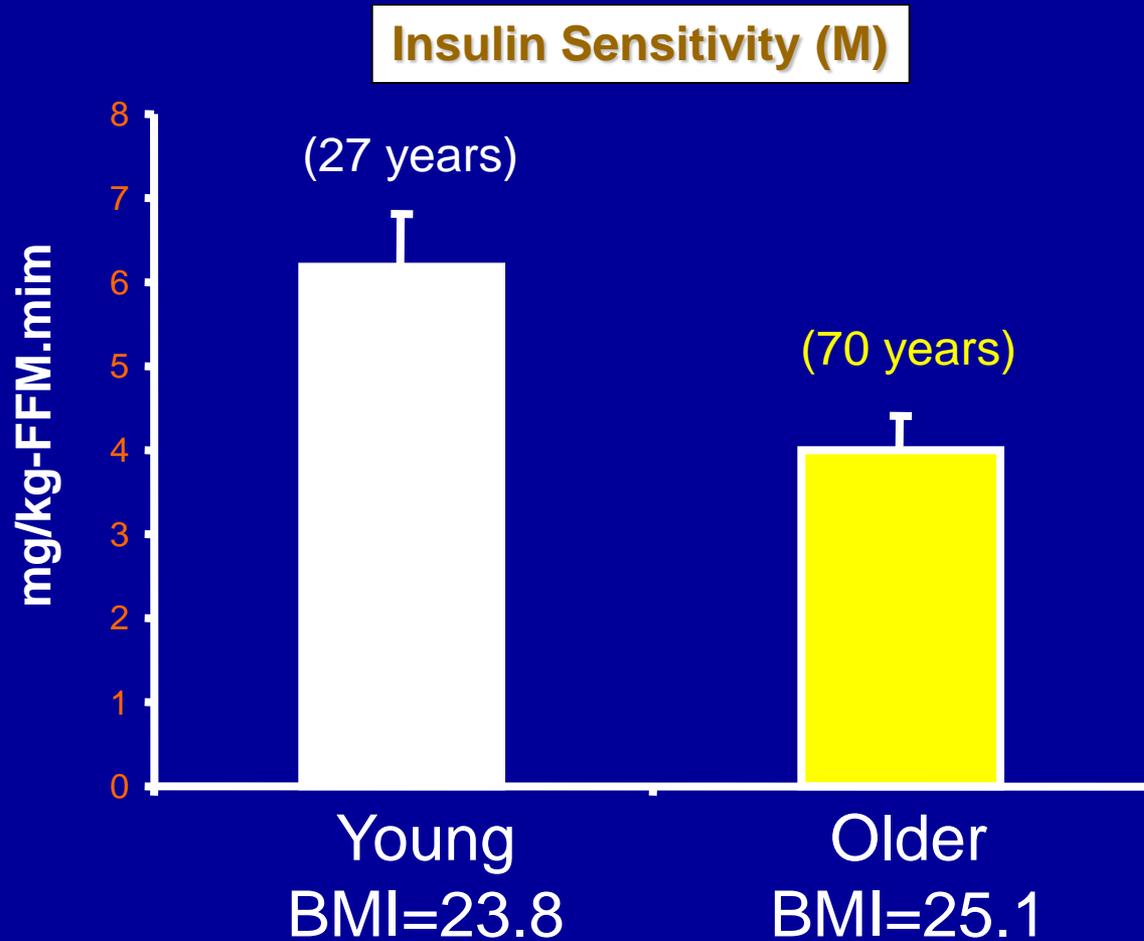
Effect of Age on Lipid Content

Magnetic Resonance Spectroscopy

Muscle
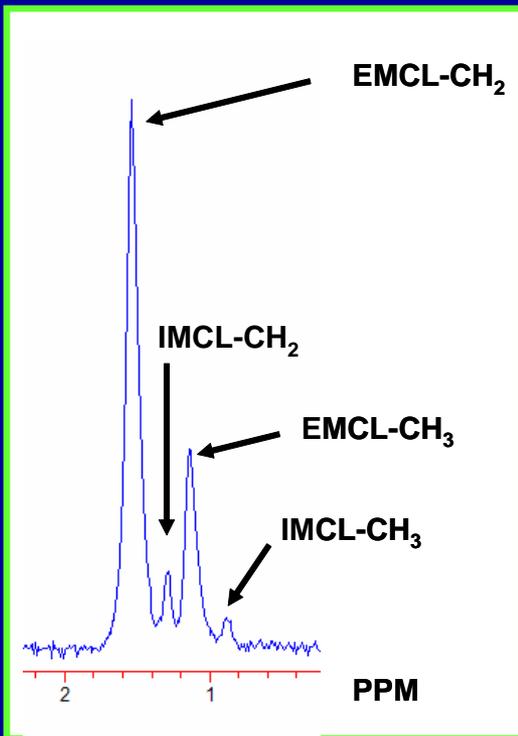
Intramyocellular Lipid Content

Petersen, Science, 2003
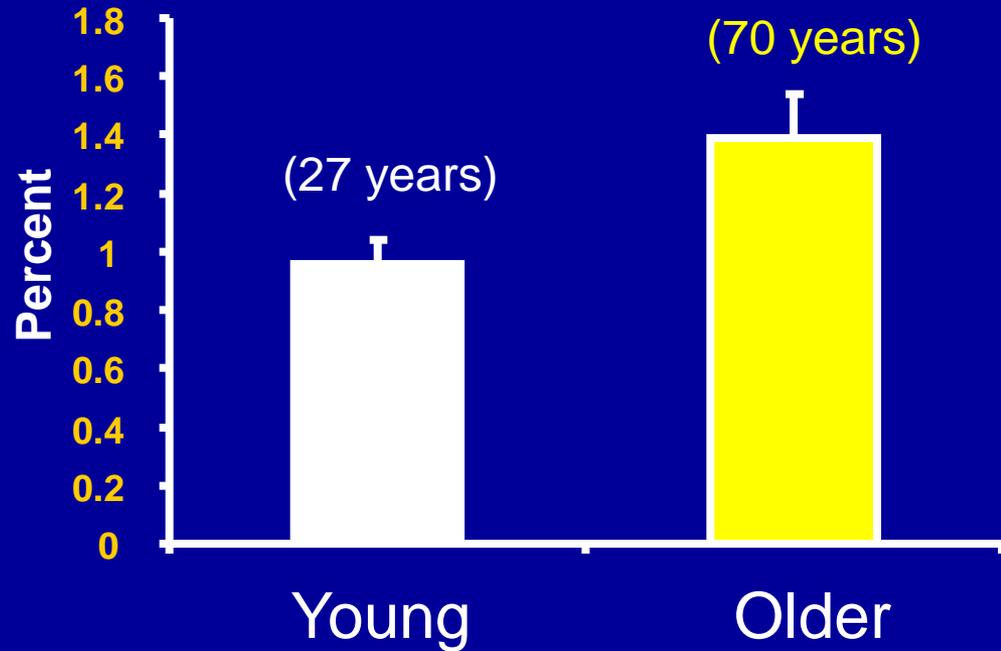
Effect of age on Mitochondrial ATP Production
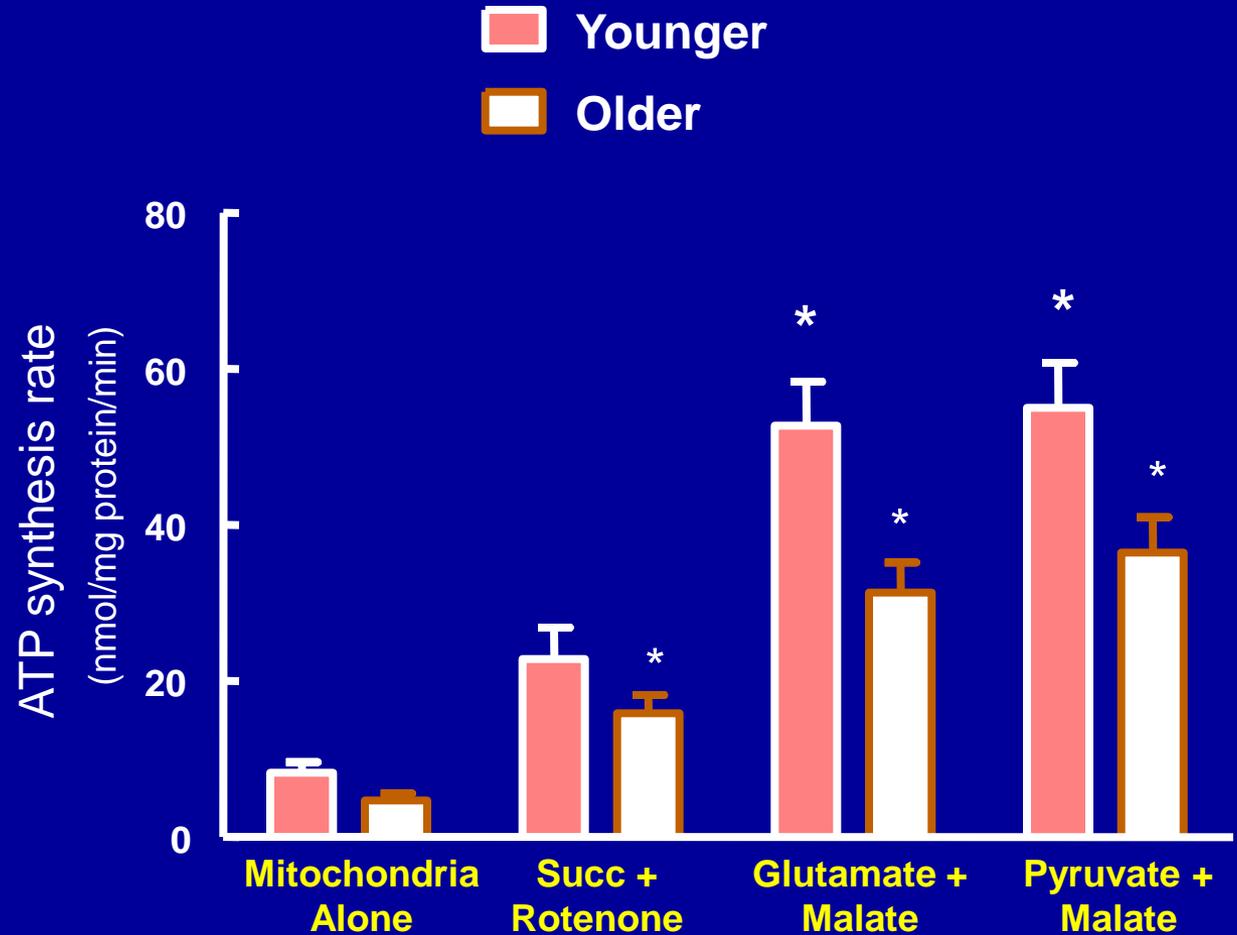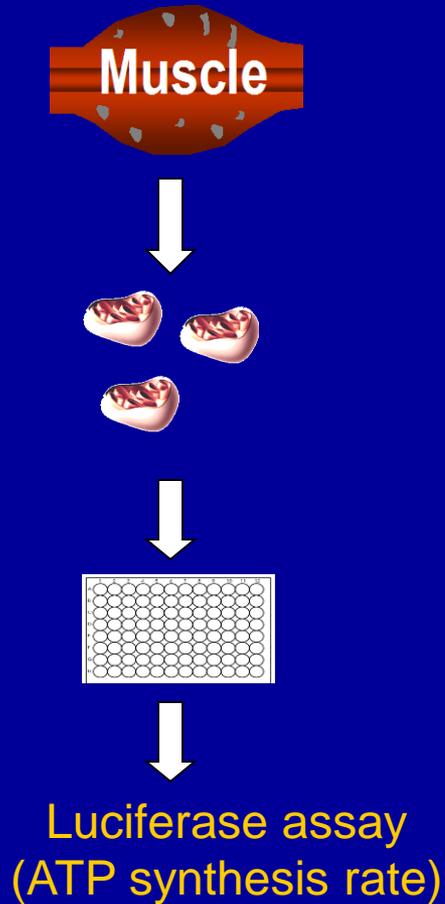
Effect of aerobic exercise on Mitochondrial ATP production in older subjects

S+R: Succinate + Rotenone; G+M: Glutamate + Malate; P+M: Pyruvate + Malate

*, $P<0.05$ vs. older group before exercise.
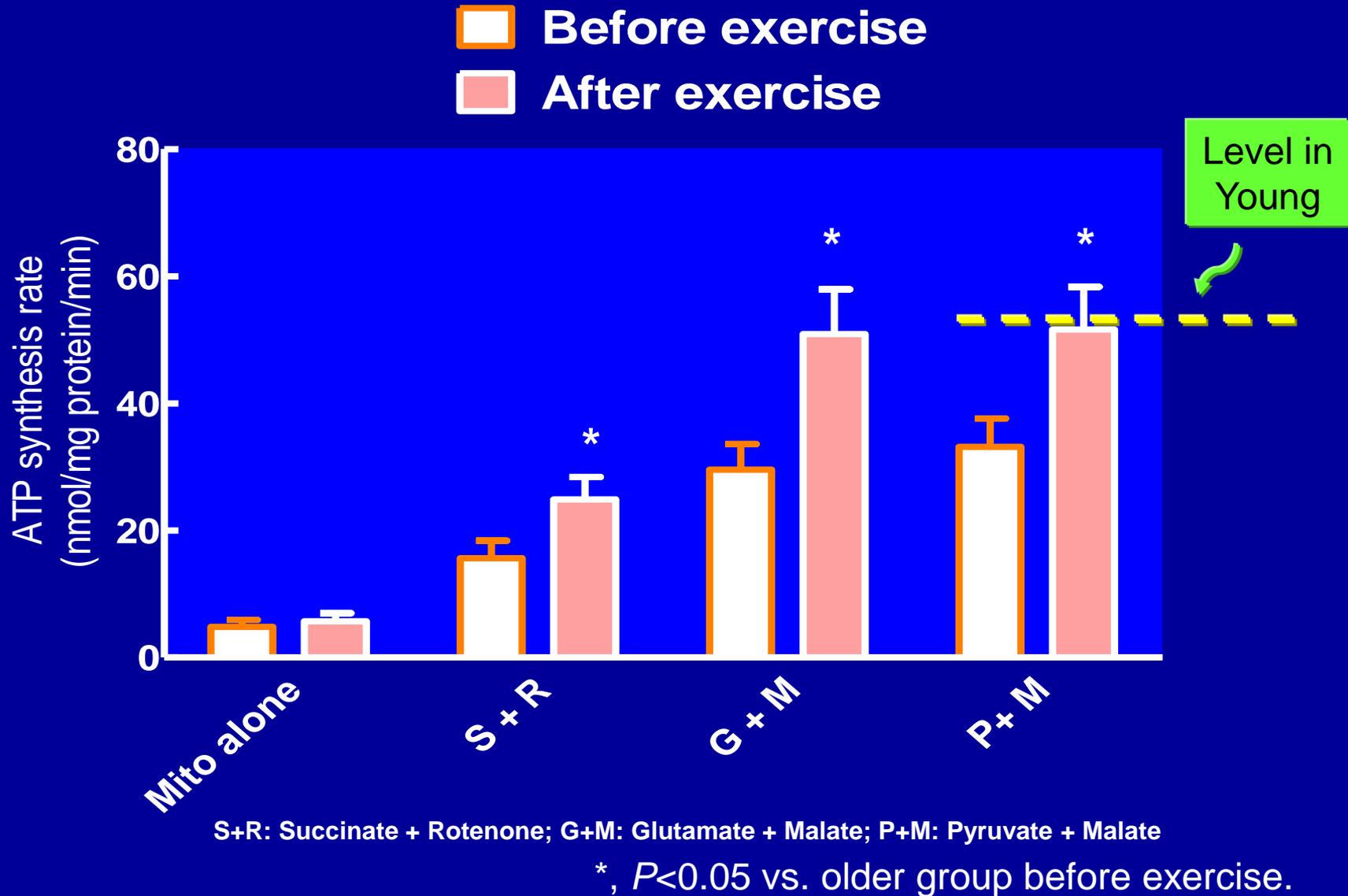
Factors involved in mitochondrial biogenesis

PGC-1

AMPK
α
β
γ

NRF1

NUCLEUS

TFAM

mtDNA

TFAM

mRNA

MITOCHONDRIA

Mitochondrial biogenesis

Modified from Vina et al Adv Drug Del Rev. 2009
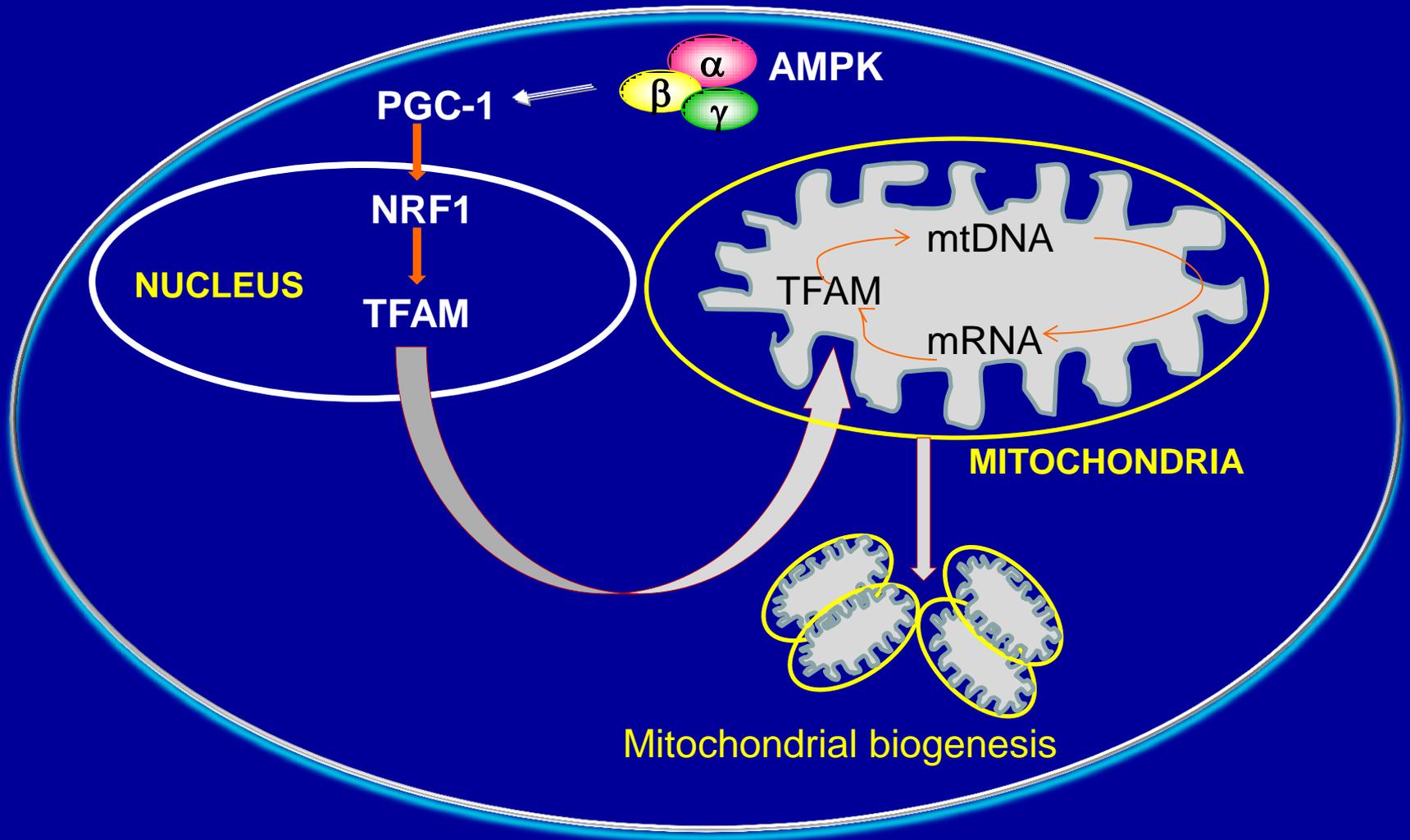
LPS Concentration in Aging

Ghosh et al, J Geron (2014)
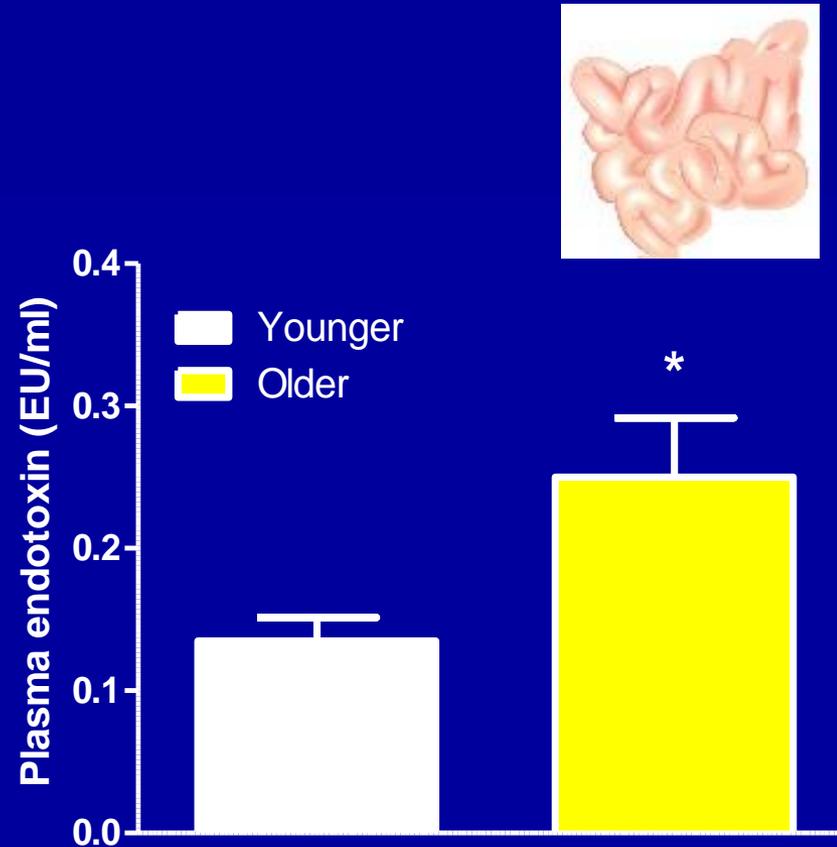
Intestinal Barrier Dysfunction and Aging

Rera, PNAS (2012)
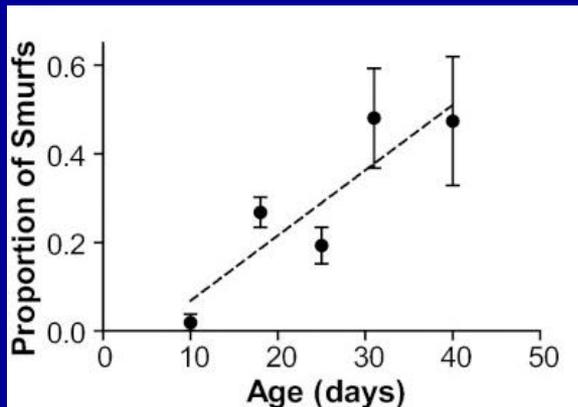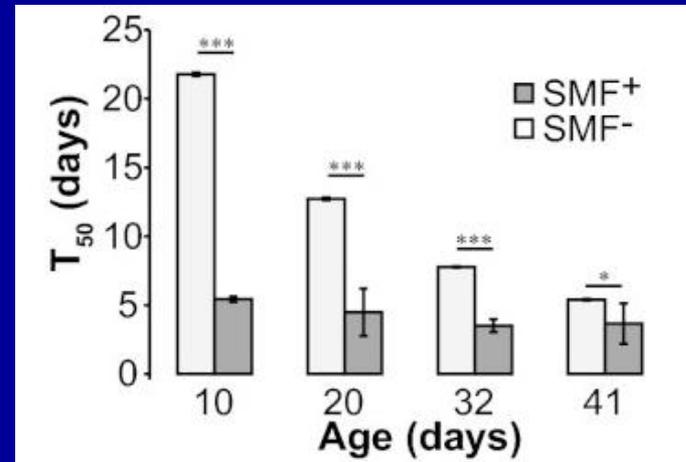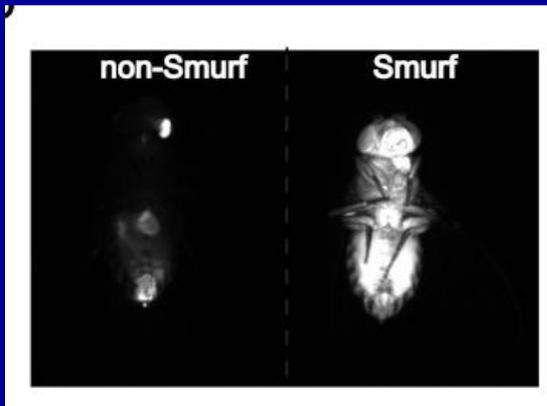
Intestinal Barrier Dysfunction Predicts Death

How should older adults be treated for diabetes?

Recommendations (ADA, AGS)

Goals of Treatment (Tight Control?)

Consider:

1) Functional Status

2) Life expectancy

3) Cognitive Function

4) Clinical Heterogeneity (prone to complications?)

Does every diabetic person develops (mv) complications?

No – approximately 20-40%

How long does it take to develop (mv) diabetic complications?

15 years, on average

How much does the A1c level matter?

It matters – a lot

How long does it take to develop diabetic complications?
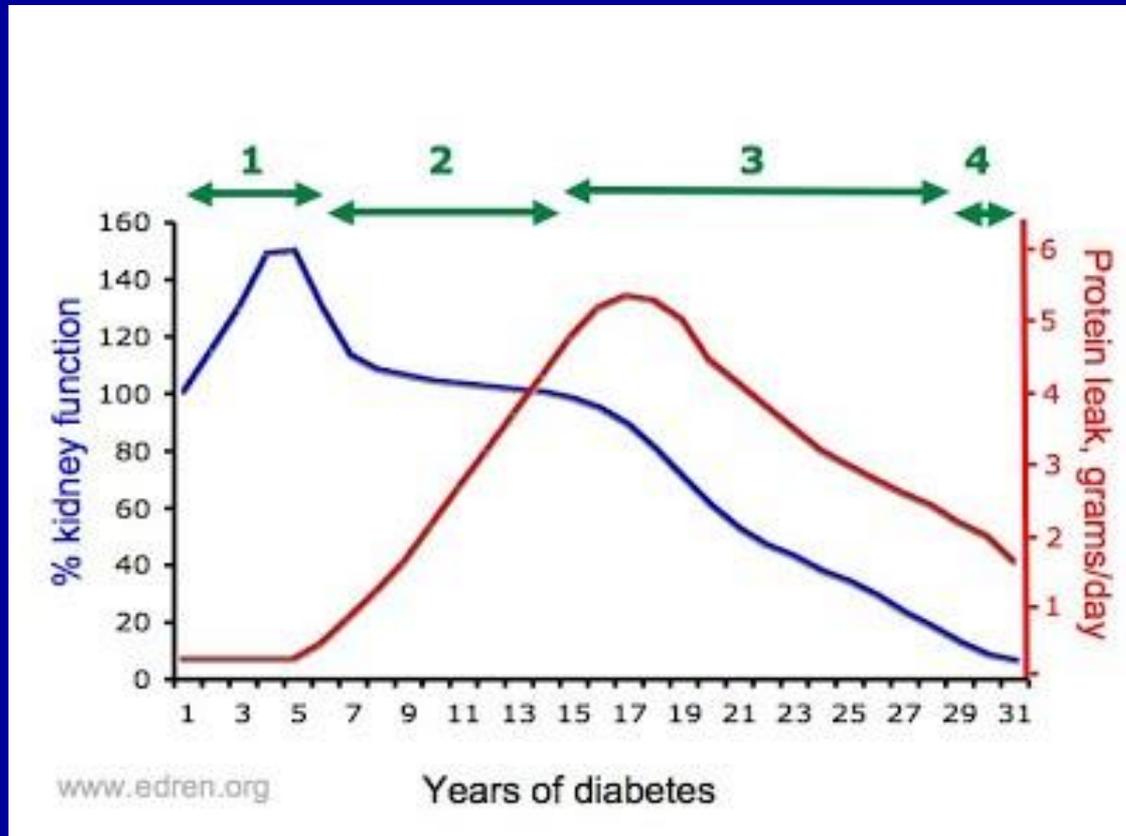
How much does the A1c level matter?

Relationship of HbA$_{1C}$ to Risk of Microvascular Complications

Diabetes Control and Complications Trial (DCCT)
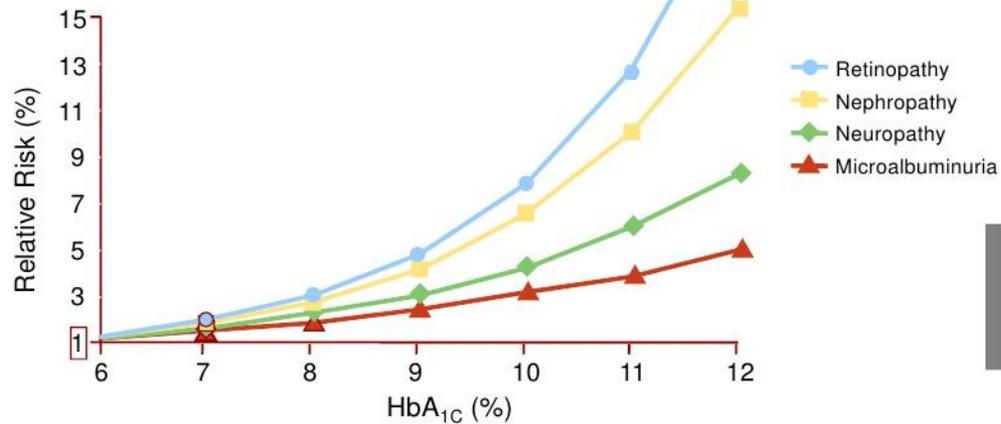
Skyler JS. Endocrinol Metab Clin North Am. 1996;25:243-254.

Kaplan-Meier Survival Curves by Frailty Status

Not Frail

Frail

Time, Days

— Not Frail   — Pre-Frail
— Frail

Espinoza, Hazuda (SALSA)
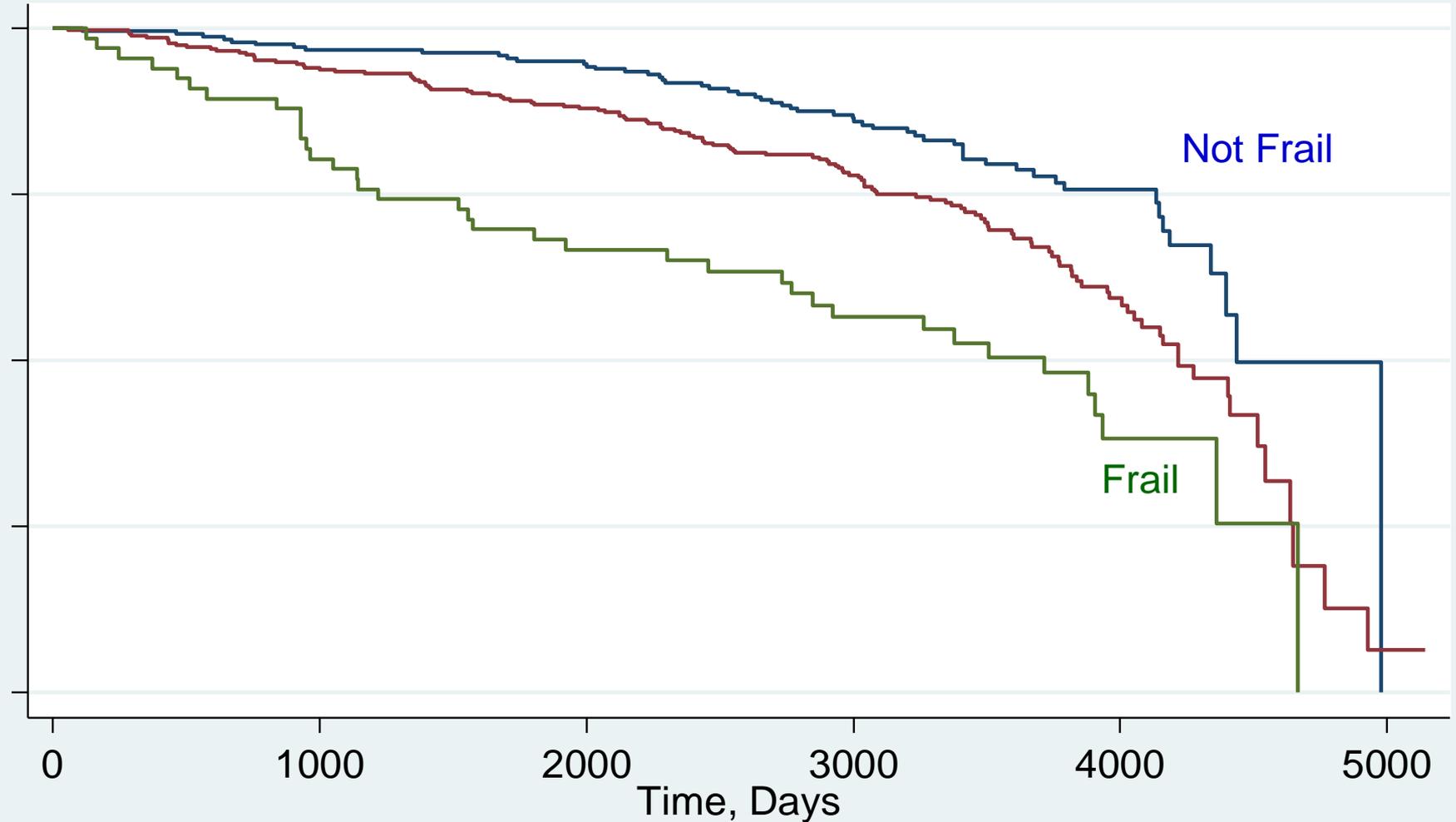
Goals of Treatment (Tight Control?)

Functional, Cognitively Intact, Significant Life Expectancy:

- **Similar Goals as Younger Person**

- **A1c ~ 7%**

Recommendations (ADA, AGS)

Goals of Treatment (Tight Control?)

Decreased Function/Cognition, Short Life Expectancy:

- Glycemic Control can be Relaxed

- Avoid Hyperglycemic Complications!

Antihyperglycemic therapy T2DM (ADA Standards, 2016)

Healthy eating, weight control, increased physical activity, and diabetes education

Mono-therapy

Metformin

Efficacy*	high
Hypo risk	low risk
Weight	neutral / loss
Side effects	GI / lactic acidosis
Costs*	low

If A1C target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

Dual therapy†

	Metformin + Sulfonylurea	Metformin + Thiazolidine-dione	Metformin + DPP-4 inhibitor	Metformin + SGLT2 inhibitor	Metformin + GLP-1 receptor agonist	Metformin + Insulin (basal)
Efficacy*	high	high	Intermediate	Intermediate	high	highest
Hypo risk	moderate risk	low risk	low risk	low risk	low risk	high risk
Weight	gain	gain	neutral	loss	loss	gain
Side effects	hypoglycemia	edema, HF, fxs	rare	GU, dehydration	GI	hypoglycemia
Costs*	low	low	high	high	high	variable

If A1C target not achieved after ~3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

Triple therapy

Metformin + Sulfonylurea +	Metformin + Thiazolidine-dione +	Metformin + DPP-4 inhibitor +	Metformin + SGLT2 inhibitor +	Metformin + GLP-1 receptor agonist +	Metformin + Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or Insulin§	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin§	or Insulin§		or GLP-1-RA
or Insulin§	or Insulin§				

If A1C target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables; (2) on GLP-1-RA, add basal insulin; or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:

Combination injectable therapy‡

Metformin +

Basal insulin + | **Mealtime insulin** or **GLP-1-RA**

Remaining Questions About DM in Older Adults

- Epidemiology of diabetes and complications

- Etiology

- Screening and diagnosis

- Preventative strategies (lifestyle and pharmacological)

- Treatment – goals, target, and interventions

- Clinical trials for prevention and treatment

- DM complications