Decline in physical function in people with diabetes

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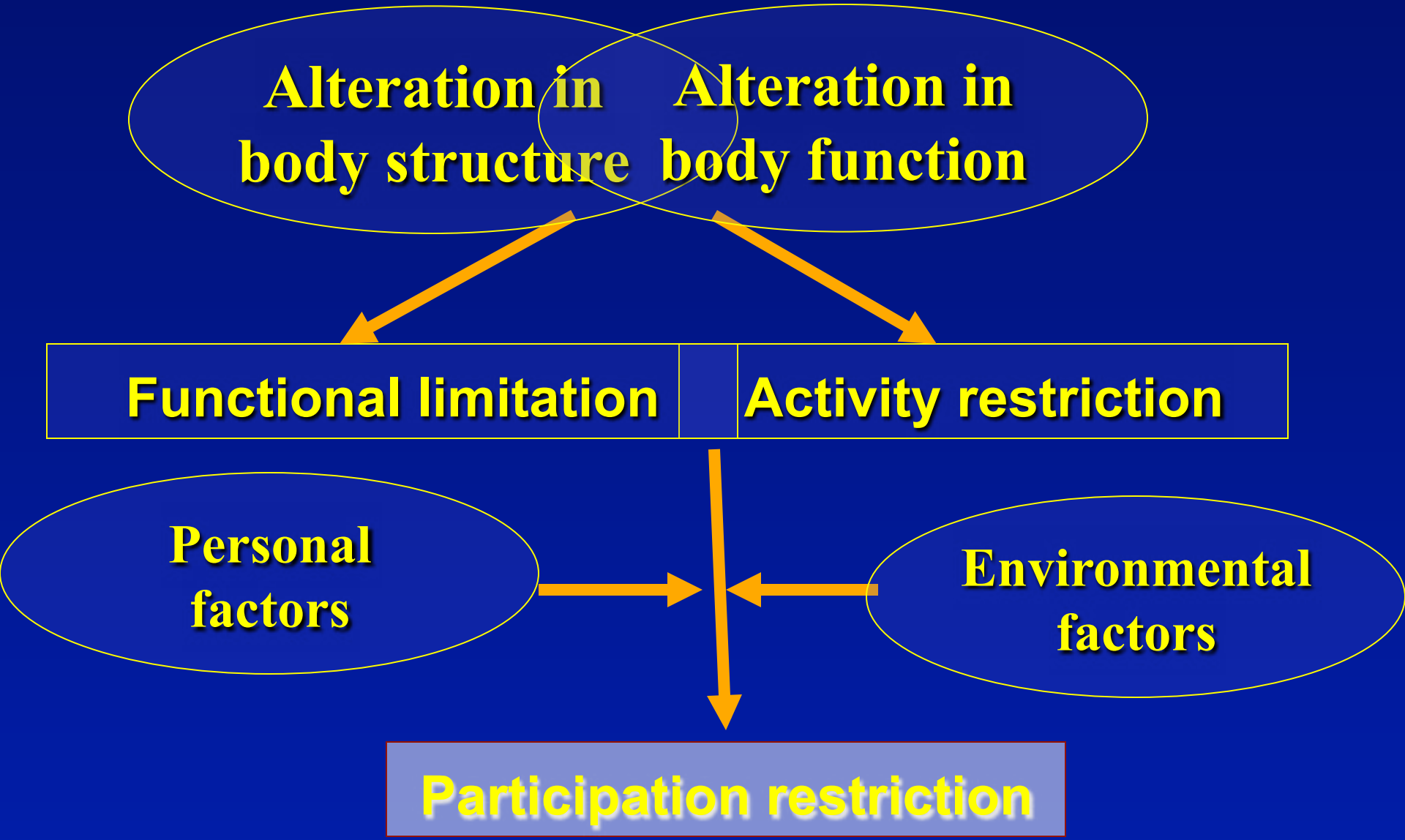
cnrs

Successful aging

- To avoid severe diseases and impairments
- To have high level of physical and cognitive functioning
- To remain engaged in social life and production

Rowe & Kahn Sciences 1987

Disability WHO 2001



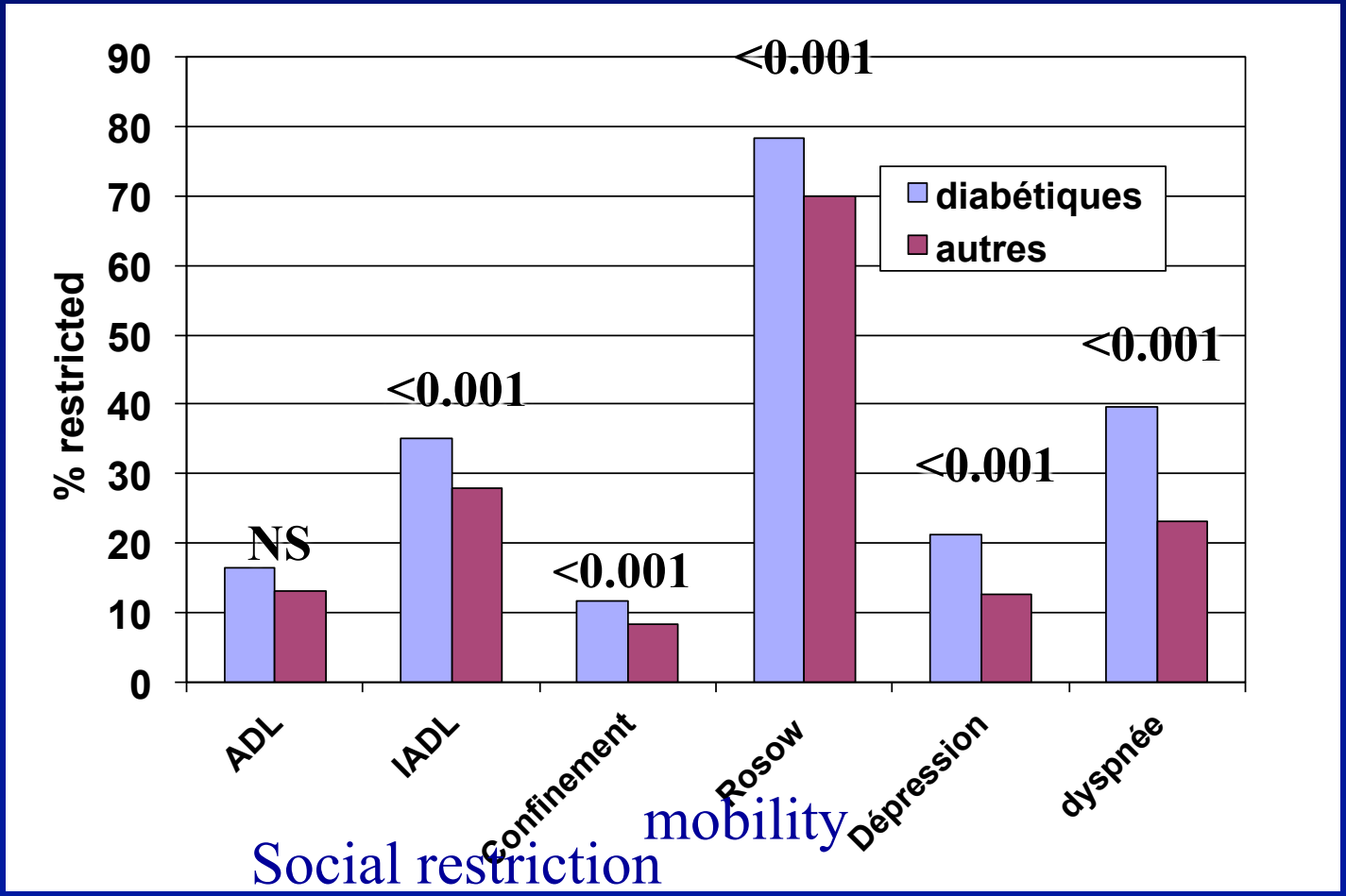
Activity restrictions and functional limitations

- Mobility restriction
  - restriction for mobility for heavy tasks (doing heavy housework, walking half a mile, climbing stairs)
  - Nagi score ability of performing five activities of upper or lower extremity function (heavy tasks or subtle tasks)
- IADL (instrumental activities of daily living)
  - abilities for telephoning, shopping, transferring using transportation, managing medications and finances
  - strongly associated with cognitive impairment

Activity restrictions and functional limitations

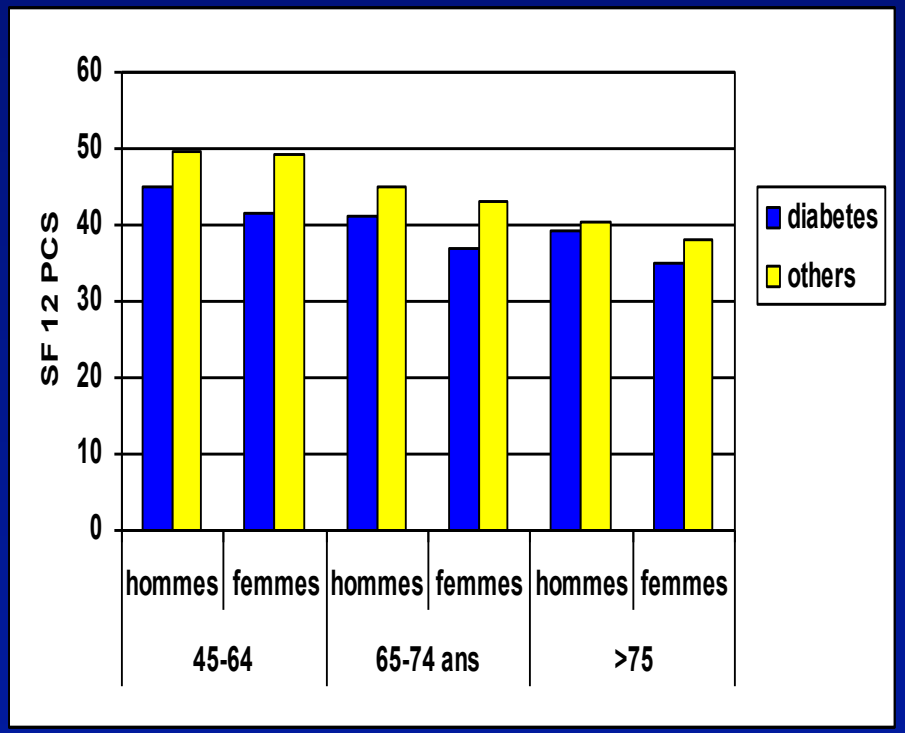
- ADL (activities of daily living)
  - Katz index: 5 items for activity restriction (bathing, dressing, inside locomotion, toiletting and eating) and one for functional limitation (incontinence)
  - Barthel index: 6 items for activity restriction, two for functional limitation (incontinence)
  - Functional independence measure (FIM) ADL + 1 measure for social participation

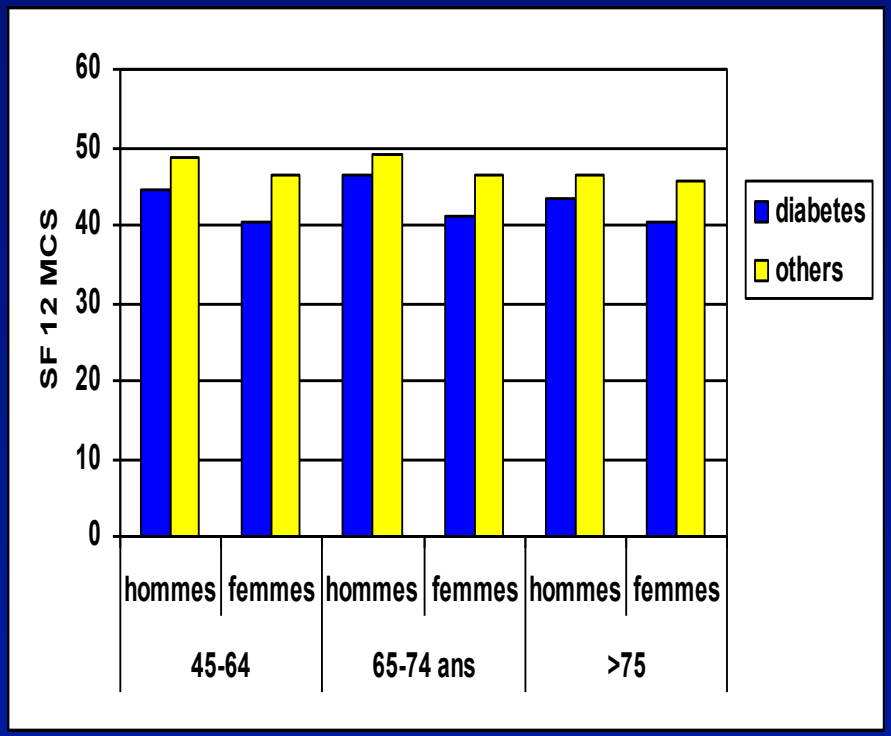
Diabetes in older : quality of life alteration



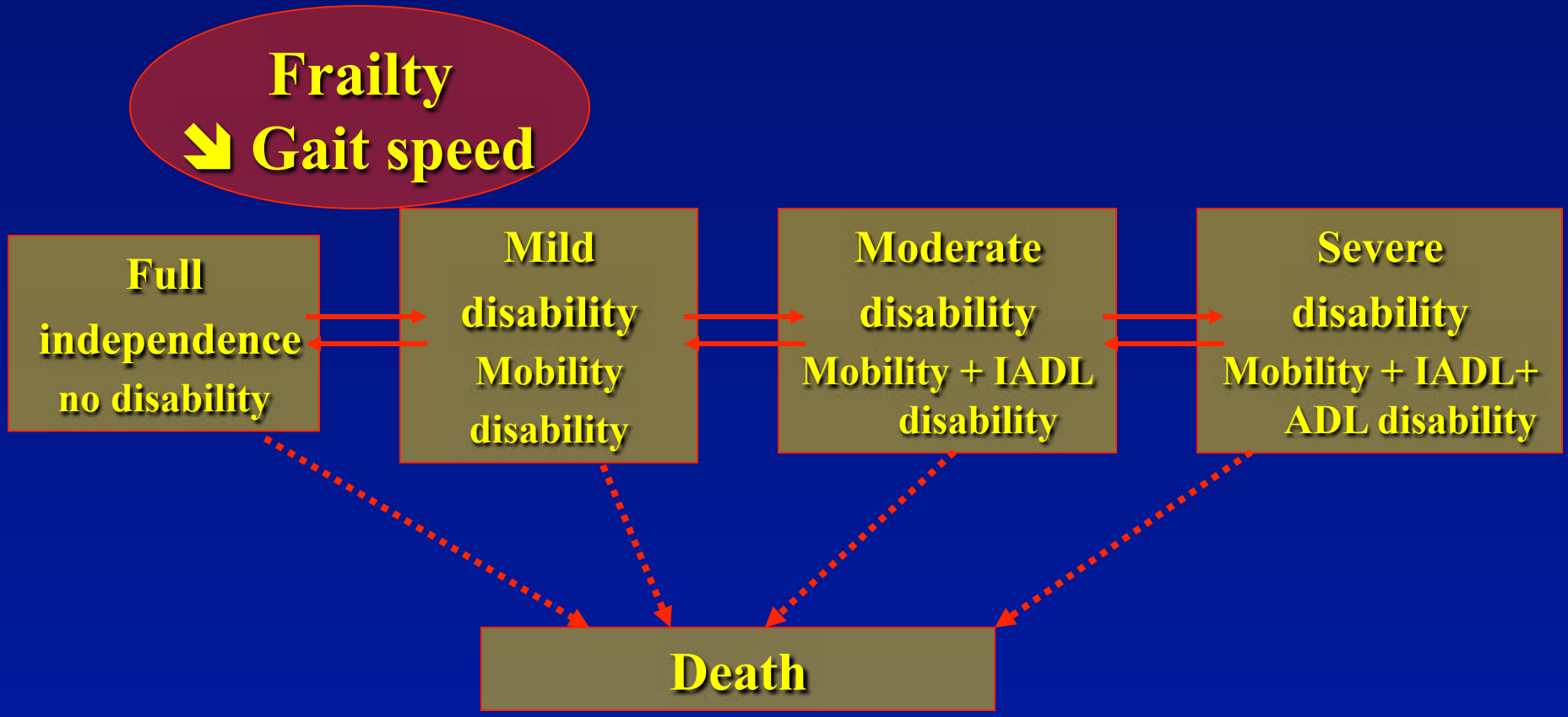
Bourdel-Marchasson, J Am Geriatr Soc 1997, 45: 295

MOS SF-12, French Population (INSEE)





The disablement process



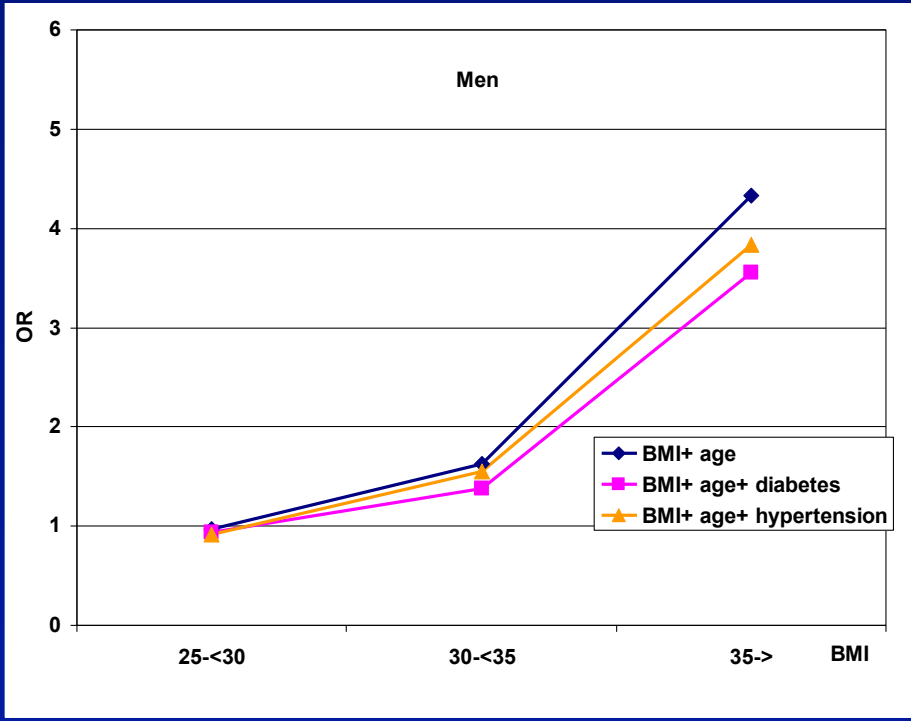
Diabetes in the disablement process

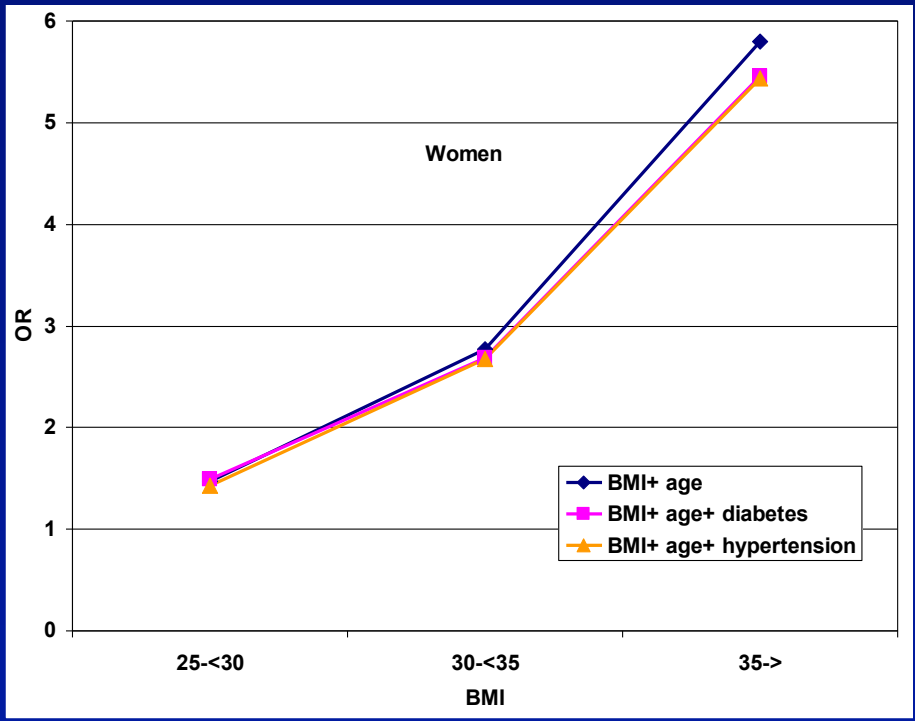
- Most of the longitudinal studies have shown an effect Independent of complications and associated conditions
  - Women‘s Health and Aging study
  - British Medical Research Council Cognitive and Ageing study
  - PROSPER
  - H-EPESE
  - AHEAD survey
  - PAQUID
  - Italian Longitudinal Study on Aging
- Other mechanisms?

Obesity

- **Obesity increases risk for disability particularly in women**

Stenholm S Aging Clin Exp Res 2007 : 277



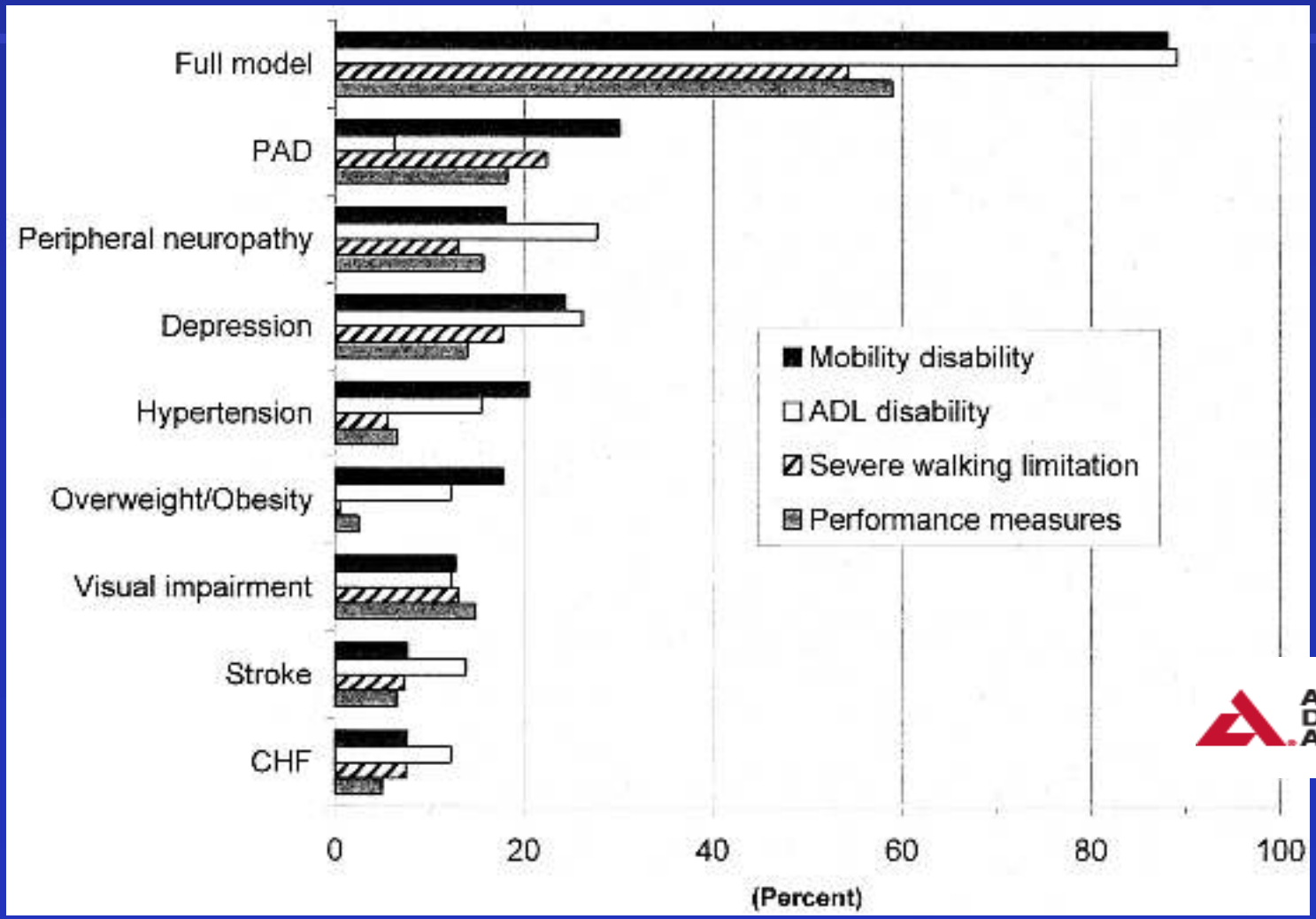


Mobility limitations in older disabled women and diabetes

- 1,002 women>65 in the highest tertile of disability from the Women's health and Aging Study (16% with diabetes)
- Mobility, ADL, severe walking impairment, SPPB
- Potential confounders for increased risk of disability
  - Overweight and obesity
  - Hip and knee osteoarthritis, hip fracture
  - Cognitive impairment
  - Severe depression
  - Chronic obstructive pulmonary disease
  - Cancer

Volpato S Diabetes Care, 2002: 678

Percent reduction in the association between diabetes and different physical function outcomes after adjustment for all potential mediators of the association (full model) and for individual covariates.



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Volpato S Diabetes Care, 2002: 678

Transitions in the disablement process

- **Transitions in disability : progression or recovery,**
  PAQUID study : 10-year follow-up, 6 visits
  - **Transition Intensity Ratio (TIR) from each state of disability to other**
  - **Independent Study factors associated with progression or recovery**
    - **80 years or + vs 65 – 79**
    - **Female gender**
    - **Stroke**
    - **Diabetes**
    - **Cardiovascular disease**
    - **Visual impairment**
    - **Cognitive impairment**
    - **Dyspnoea**



The disablement process, PAQUID

80 years or + vs 65 – 79	+
Female gender	+
Stroke	+
Cardiovascular disease	+
Visual impairment	+
Cognitive impairment	+

80 years or + vs 65 – 79	+
Stroke	+
Diabetes	+
Cardiovascular disease	+
Visual impairment	+
Cognitive impairment	+

80 years or + vs 65 – 79	+
Stroke	+
Cardiovascular disease	+
Visual impairment	+
Cognitive impairment	+

Full independence
no disability

Mild disability
mobility disability

Moderate disability
Mobility + IADL disability

Severe disability
Mobility + IADL+ ADL disability

80 years or + vs 65 – 79	-
Female gender	-
Diabetes	-
Visual impairment	-
Cognitive impairment	-
Dyspnoea	-

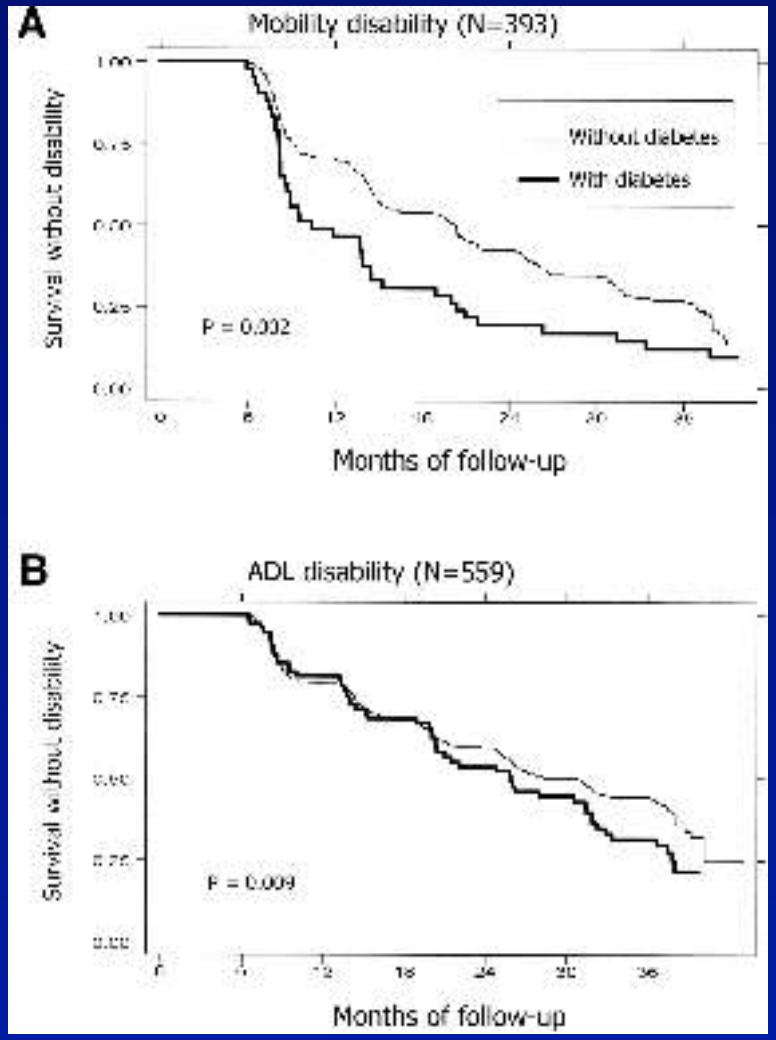
80 years or + vs 65 – 79	-
Female gender	-
Visual impairment	-
Cognitive impairment	-
Dyspnoea	-

80 years or + vs 65 – 79	-
Female gender	-
Visual impairment	-
Cognitive impairment	-
Dyspnoea	-



Peres K Disab Rehab 2005

Age-adjusted Kaplan-Meier survival curves exploring the association between diabetes and risk of developing mobility disability (A) and ADL disability (B).



Volpato S et al. Dia Care 2003;26:70-75

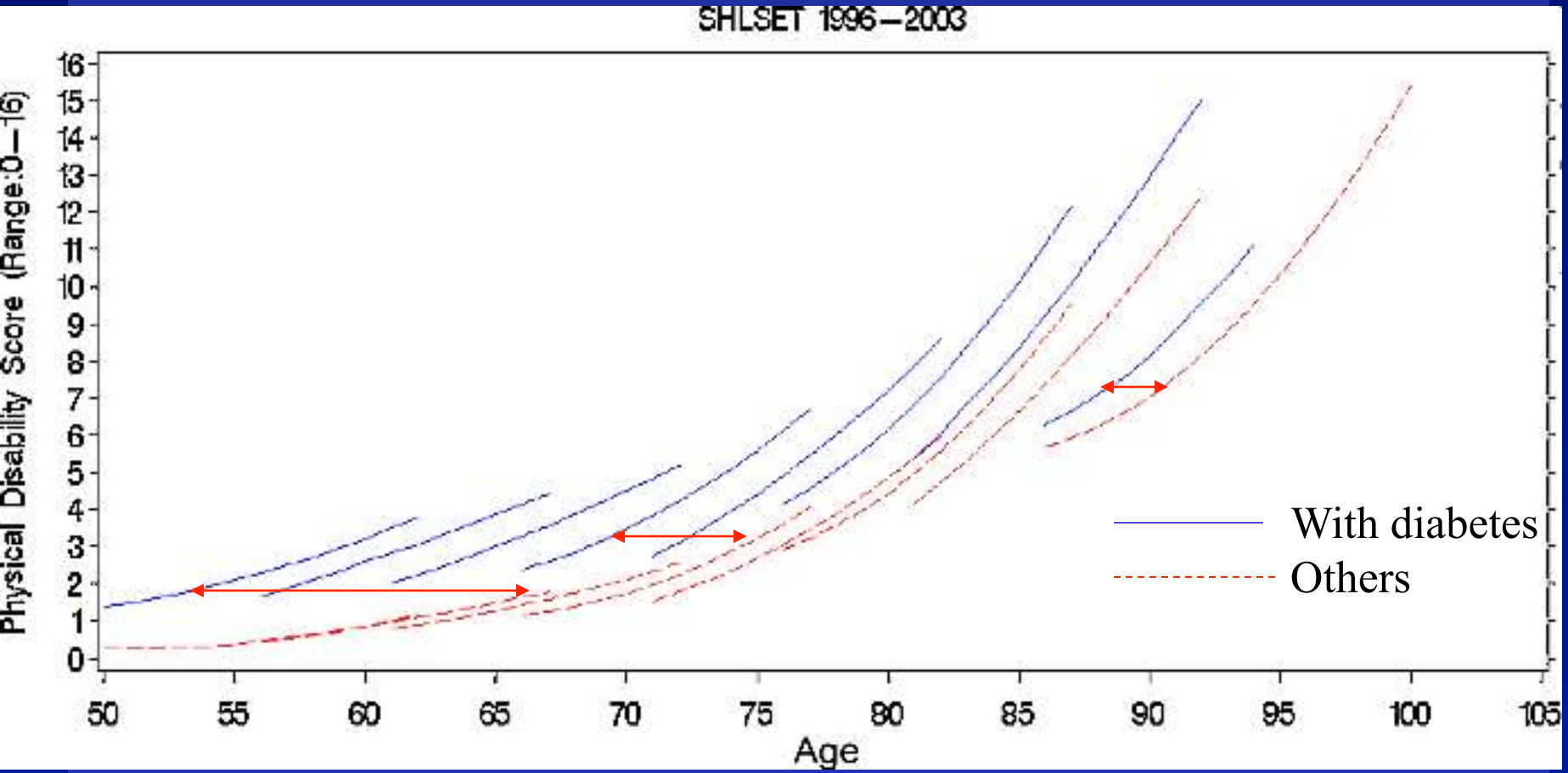
Copyright © 2011 American Diabetes Association, Inc.

Physical disability trajectories and diabetes

- Survey of Health and Living Status of the Elderly in Taiwan (1996-2003), 4412 subjects >60y
- Self-reported diabetes (11.4%)
- Sum of ADL, IADL and Nagi physical activities limitations scale = disability score

Chiu CJ, Diabetes Research and Clinical practice 2011: 413

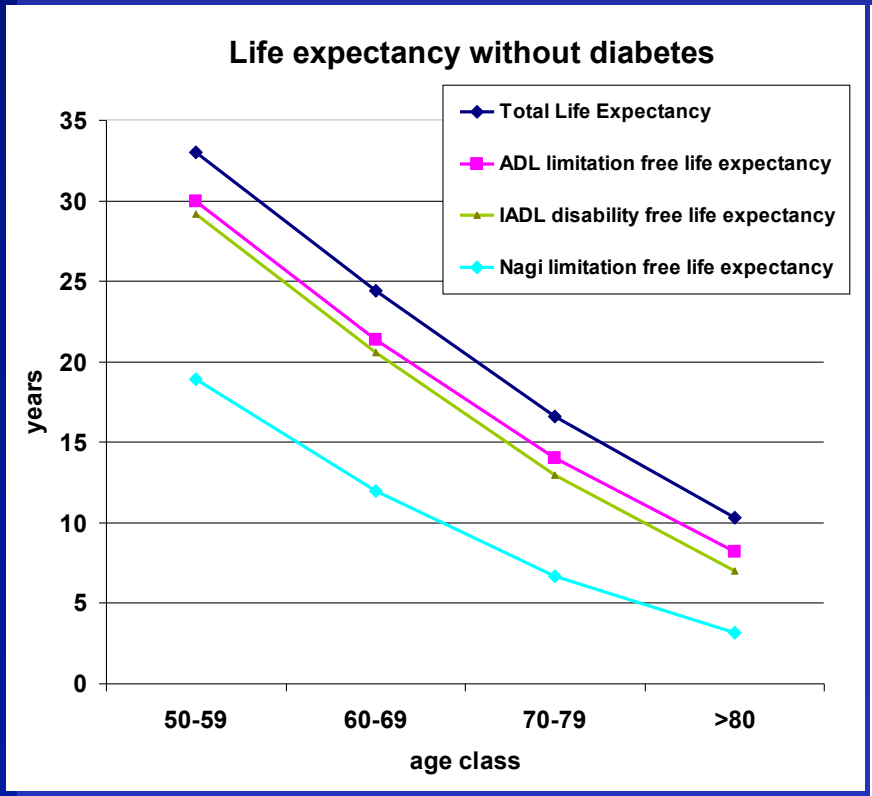
Physical disability trajectories and diabetes

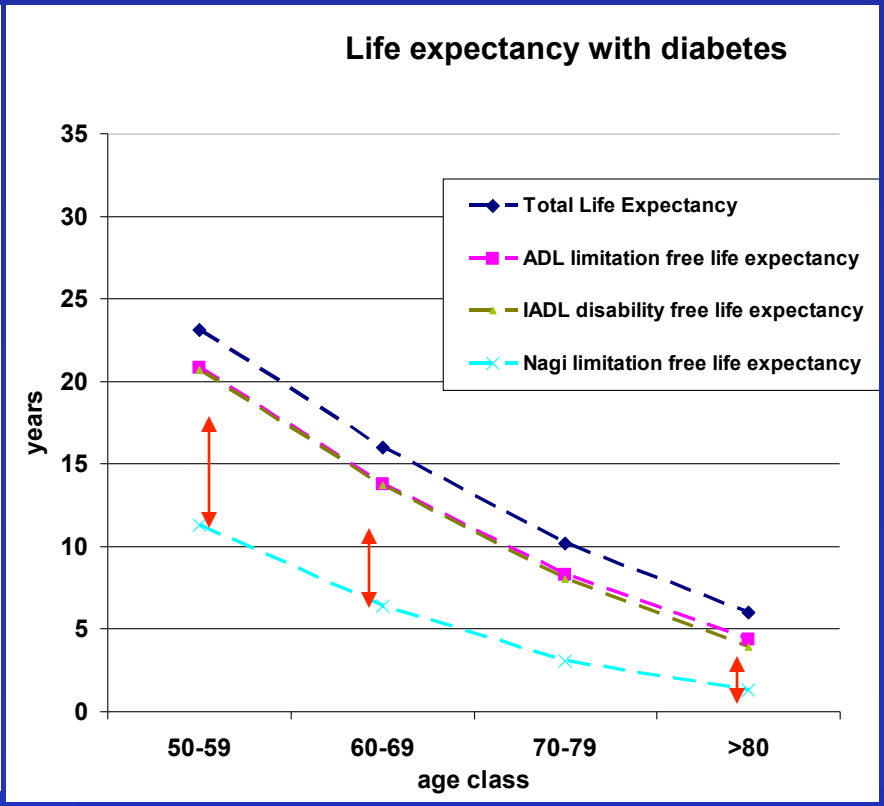


Chiu CJ, Diabetes Research and Clinical practice 2011: 413

Disability free life expectancy and diabetes

- Cohort of people in Mexico (Mexican Health and Aging Study) 12,000 subjects 2001-2003





Andrade FC, J Gerontol 2010: 381

Transversal risk factors for frailty

- Cohort of 4000 subjects (1/2women, >65y) able to walk independently
- Measures
  - Physical performance assessment (composite)
  - Cognitive assessment
  - Body composition assessment: DEXA, appendicular skeletal muscle mass (ASM)
  - Metabolic Conditions (diabetes, 14.7%)
- 6 year mortality

Lee JSW, JNHA 2011:857

Transversal risk factors for frailty

- **Independent risk factors**
  - **Lower ASM**
  - **Higher age**
  - **Diabetes**
  - **Hypertension (not in women)**
  - **Heart disease**
  - **Stroke history**
  - **High Waist/Hip ratio**
- **Increased frailty associated with higher mortality**

Lee JSW, JNHA 2011:857

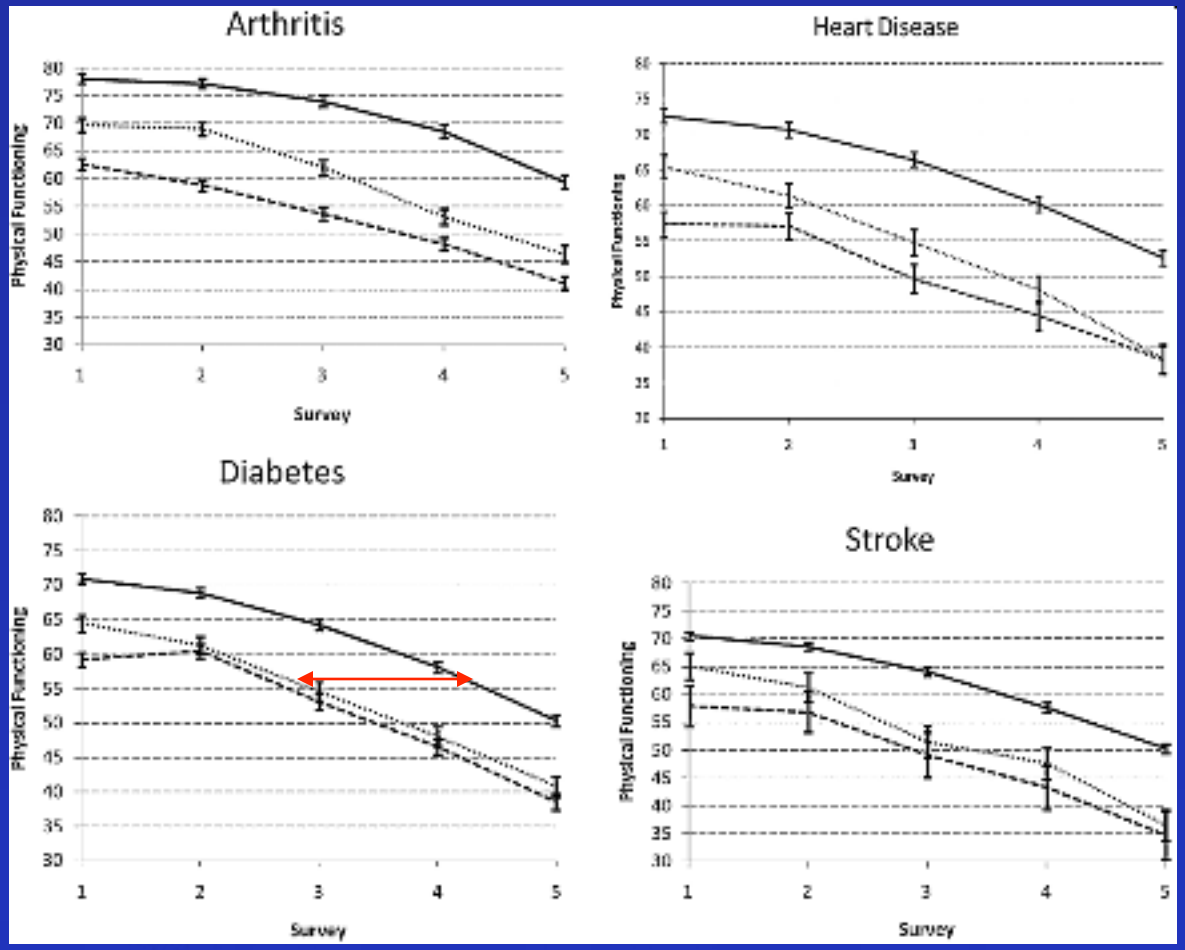
Diabetes in older Australian Women

- Surveys 1996-2008,
  - The older cohort (born) 1921-1926, from 12,432 women to 5,526 in 2008, 28.4% mortality
- Changes in physical functioning score (SF36) among survivors in 2008
  - General decrease (only 3% improved)
  - Determinant of poor scores and higher decline:
    - Older age
    - Overweight or obesity
    - Few physical activity
    - Smokers or ex-smokers
    - Diabetes
    - Arthritis
    - Heart disease
    - Stroke
    - Bronchitis/asthma
    - Falls

Byles JE, Australian Journal of Ageing 2011: 6

Physical functioning (SF36) in older Australian Women

- **Surveys 1996-2008**

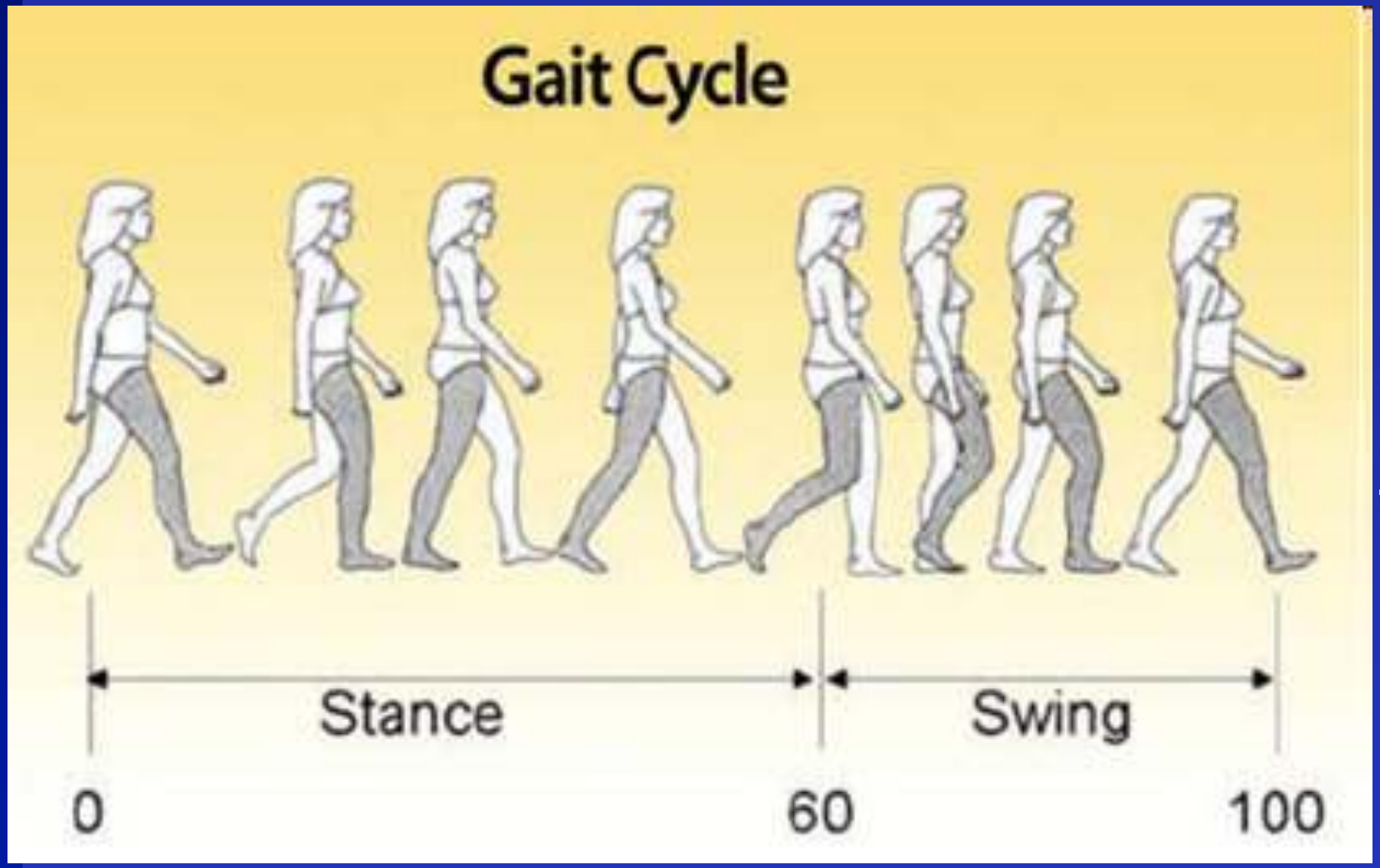


-------- existing cases; ····· new cases; ——— never

Byles JE, Australian Journal of Ageing 2011: 6

Determinants of gait speed

- For each limb 2 phases



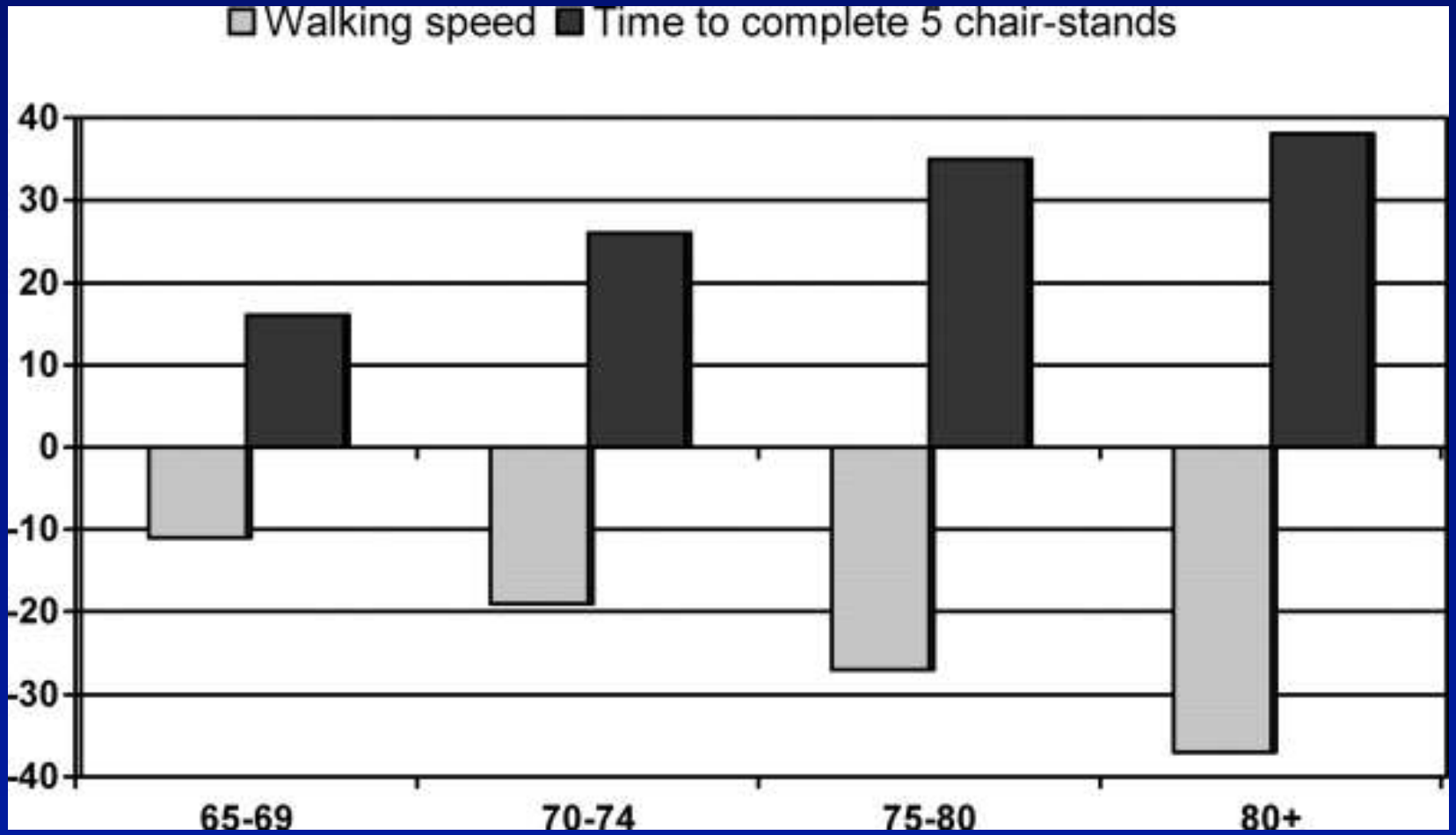
– Stance phase
– • heel contact
forefoot contact
• midstance
• propulsion
• heel off
• toe off
– Swing phase
– • early swing
• late swing
• double and single support

Gait characteristics and diabetes

Characteristic	Individuals Without Diabetes (n=439)	Individuals With Diabetes (n=119)	P
Demographics			
Age, y	79.5 (4.0)	79.1 (4.3)	.32
Gait characteristics			
Gait speed, m/s	1.02 (0.23)	0.95 (0.25)	.01
Step length, m	0.57 (0.10)	0.53 (0.11)	<.001
Step width, m	0.21 (0.05)	0.24 (0.05)	<.001
Stance time, s	0.74 (0.12)	0.77 (0.13)	.04
Double-support time, s	0.17 (0.05)	0.18 (0.05)	.01

Brach JS, Physical Therapy 2008: 1365

Change in lower extremity performance in older women during 10 years of follow-up by age.



Forrest K Y Z et al. J Gerontol A Biol Sci Med Sci 2006;61:1194-1200

the Journals of gerontology Series a

Frailty in older women

- 5178 women 65-91y
- 10 year changes determinants
  - Walking speed ↘
    - Age
    - Higher weight and lower height
    - Height loss
    - Higher systolic blood pressure
    - Lifetime smoking
    - Diabetes
    - Arthritis
    - Slow baseline walking speed
    - History of estrogen use
    - History of thyroid hormones use

Forrest KYZ, J Gerontol Med Sciences 2006: 1194

Frailty in older women

- 5178 women 65-91y
- 10 year changes determinants
  - 5 chair-rise time ↗
    - Age
    - Higher weight and lower height
    - Height loss
    - Lifetime smoking
    - Diabetes
    - Arthritis
    - Slow baseline walking speed
    - History of thyroid hormones use
    - History of thiazide diuretics use

Forrest KYZ, J Gerontol Med Sciences 2006: 1194

Determinants of gait speed

- Multiple models including diabetes diagnosis and characteristics of cohort subjects
- Diabetes remains and independent factor of gait speed
- Other gait speed determinants
  - Health status (heart diseases, stroke, polypharmacy)
  - Cognition
  - Mood
  - Visual impairment
  - Lower-extremity perfusion
  - Lower extremity sensory status
  - Lower extremity strength
  - Physical activity
  - BMI
- Diabetes diagnosis was the only factor associated with step width

Brach JS, Physical Therapy 2008: 1365

Walking speed and cognition

Transversal association

- **Benton Visual Retention Test**
- **Isaacs Set Test**
- **TMT A and TMT B**

Longitudinal (decrease in walking speed during 7 years of follow-up)

- **Isaacs Set Test**
- **TMT A**

Soumaré, J Gerontol 2009, 64: 1058

Alterations in cognitive function in metabolic syndrome and diabetes

Cognitive functions explored in this paper	Examples of tests	Metabolic syndrome with different component associated	Diabetes
Global Cognitive Functioning	MMSE	Cross-sectional studies: Impairment [9 Studies] Unchanged [1 study]; Longitudinal studies: Predictive factor [1] Not a predictive factor [1]	Cross-sectional studies: Impairment [2] Unchanged [2] Longitudinal studies: Impairment [1] Unchanged [1]

Bourdel-Marchasson, Diabetes Metab 2010, 36: 173

Alterations in cognitive function in metabolic syndrome and diabetes

Cognitive functions explored in this paper	Examples of tests	Metabolic syndrome with different component associated	Diabetes
Memory			
Declarative			Cross-sectional study: Impairment [1]
Semantic			Cross-sectional study: Impairment [1]
Verbal	Paragraph or word list recall		Longitudinal study: Impairment [1]
Short Term Memory	Immediate recall		No change according to glycaemic index of ingested food [1]

Bourdel-Marchasson, Diabetes Metab 2010, 36: 173

Alterations in cognitive function in metabolic syndrome and diabetes

Cognitive functions explored in this paper	Examples of tests	Metabolic syndrome with different component associated	Diabetes
Executive Functions and Attention	Digit Symbol Test TMT-B	Cross-sectional study: Impairment [1]	Cross-sectional studies: Impairment [2] Longitudinal studies: Impairment [4]
Processing Speed	Digit Symbol Test	Cross-sectional study: Impairment [1]	Cross-sectional studies: Impairment [2] Longitudinal studies: Impairment [2]
	Verbal Fluency		Longitudinal study: Impairment [1]

Bourdel-Marchasson, Diabetes Metab 2010, 36: 173

Cognitive decline

- Survey of Health and Living Status of the Elderly in Taiwan (1993-2003), 1,626 subjects >60y free form cognitive impairment
- Self-reported diabetes (11.4%)
- Nine-item Short Portable Mental Status Questionnaire (0-9, 0 = no cognitive impairment)
- Independent predictors of 10-y cognitive impairment

– Older age	OR 2.60 (1.79-3.78)	p<0.001
– Female gender	OR 2.94 (2.08-4.00)	p<0.001
– Lower educational level	OR 3.33 (1.05-10)	p=0.040
– IADL disability	OR 2.06 (1.38-3.09)	p=0.029
– History of diabetes	OR 1.70 (1.06-2.74)	p=0.029
– History of stroke	OR 2.36 (1.06-5.26)	p=0.036

Yen CH, Archives of Gerontology and Geriatrics 2010: S53-S57

EVA study, baseline

Table 2—*Baseline results on cognitive tests, adjusted for age, sex, and education, according to glycemic status*

	Normal FBG	IFG	Diabetes	*P*
MMSE	29.0 (28.9–29.1)	29.2 (29.0–29.4)	29.0 (28.7–29.3)	0.20
TMTB*	2.05 (2.00–2.11)	1.96 (1.80–2.12)	2.22 (2.00–2.44)	0.17
AVLT	44.0 (43.3–44.6)	44.1 (42.3–45.9)	44.6 (42.1–47.1)	0.87
TRF	21.4 (21.2–21.5)	21.4 (21.0–21.9)	21.0 (20.4–21.6)	0.53
DSS	45.3 (44.7–46.0)	46.9 (45.0–48.7)	42.7 (40.2–45.3)	0.037
FTT	123.6 (122.3–124.8)	124.4 (121.0–127.9)	123.7 (118.9–128.5)	0.90
BVRT	11.7 (11.6–11.8)	11.8 (11.4–12.1)	11.4 (10.9–11.9)	0.41
RPM	15.5 (15.3–15.6)	15.2 (14.7–15.7)	15.8 (15.2–16.5)	0.31
PASAT	15.4 (15.1–15.8)	15.0 (13.9–16.0)	14.7 (13.3–16.2)	0.50

Data are means (95% CI). *Only test where poorer performance is indicated by higher score.

Fontbonne, Diabetes Care 2001, 24: 366

EVA study: 4–year follow-up

Table 3—*The 4-year results on cognitive tests, adjusted for age, sex, and education, according to glycemic status*

	Normal FBG	IFG	Diabetes	*P*
MMSE	27.9 (27.8–28.1)	27.9 (27.6–28.2)	27.7 (27.3–28.2)	0.67
TMTB*	1.71 (1.66–1.76)	1.64 (1.50–1.78)	1.94 (1.75–2.13)	0.033
AVLT	54.1 (53.5–54.7)	53.7 (52.1–55.4)	50.8 (48.5–53.0)	0.020
TRF	21.1 (20.9–21.2)	21.3 (20.8–21.7)	20.2 (19.6–20.8)	0.016
DSS	49.3 (48.6–50.1)	51.0 (49.0–53.1)	44.8 (42.0–47.5)	0.002
FTT	140.9 (139.6–142.2)	141.3 (137.6–144.9)	135.6 (130.6–140.6)	0.12
BVRT	11.6 (11.4–11.7)	11.6 (11.2–11.9)	11.0 (10.5–11.5)	0.11
RPM	14.1 (13.9–14.3)	14.6 (14.1–15.0)	13.9 (13.3–14.6)	0.16
PASAT	17.1 (16.8–17.3)	17.7 (16.9–18.4)	16.4 (15.4–17.4)	0.12

Data are means (95% CI). *Only test where poorer performance is indicated by higher score.

Fontbonne, Diabetes Care 2001, 24: 366

Diabetes and dementia

	RR*	95% CI	p
Dementia			
- Diabetes without treatment	1.3	0.6 - 2.8	0.51
- Diabetes with treatment	2.3	1.5 - 3.5	0.0003
Alzheimer probable/possible			
- Diabetes without treatment	1.5	0.6 - 3.8	0.36
- Diabetes with treatment	1.8	0.96 - 3.4	0.066
Alzheimer probable			
- Diabetes without treatment	1.01	0.2 - 4.2	0.99
- Diabetes with treatment	1.5	0.6 - 3.9	0.39
Vascular dementia			
- Diabetes without treatment	0.98	0.13 - 7.4	0.98
- Diabetes with treatment	3.0	1.3 - 7.2	0.014

Blood glucose control : HbA1C

- **Sub-population 3C of 1700 subjects**
  - **170 with diabetes and dosage of baseline HbA1c**
    HbA1c : 7.3% (SD : 1.2)
  - **40 cases of dementia during 4 years**

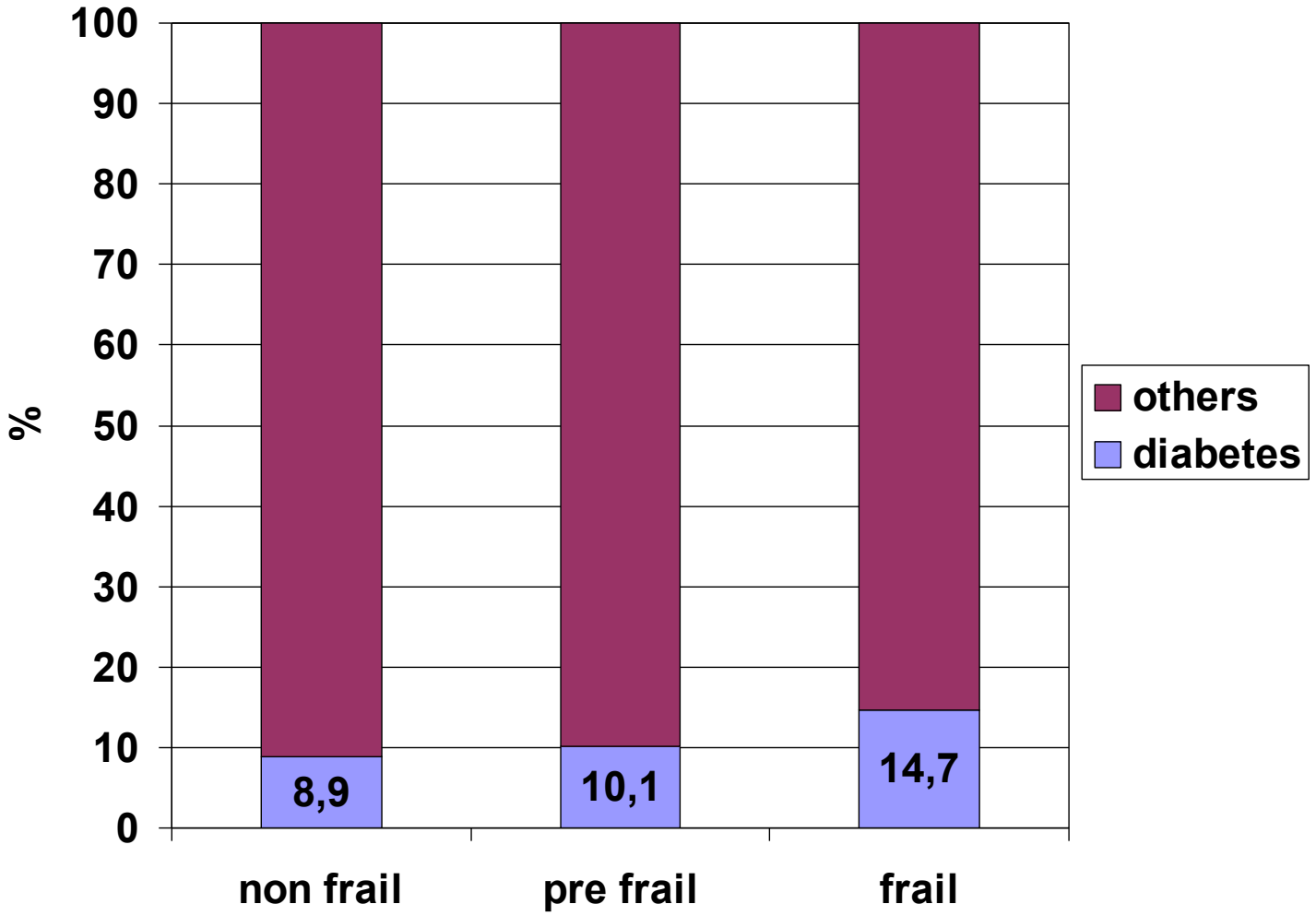


	RR	95% CI	p
HbA1c (%) Adjusted on socio-demographic characteristics	1.55	1.1-2.2	0.01
HbA1c (%) Adjusted on socio-demographic characteristics + ApoE4 + vascular co-morbidity and risk factors	1.50	0.87-2.6	0. 14

Univariate analysis of stroke risk

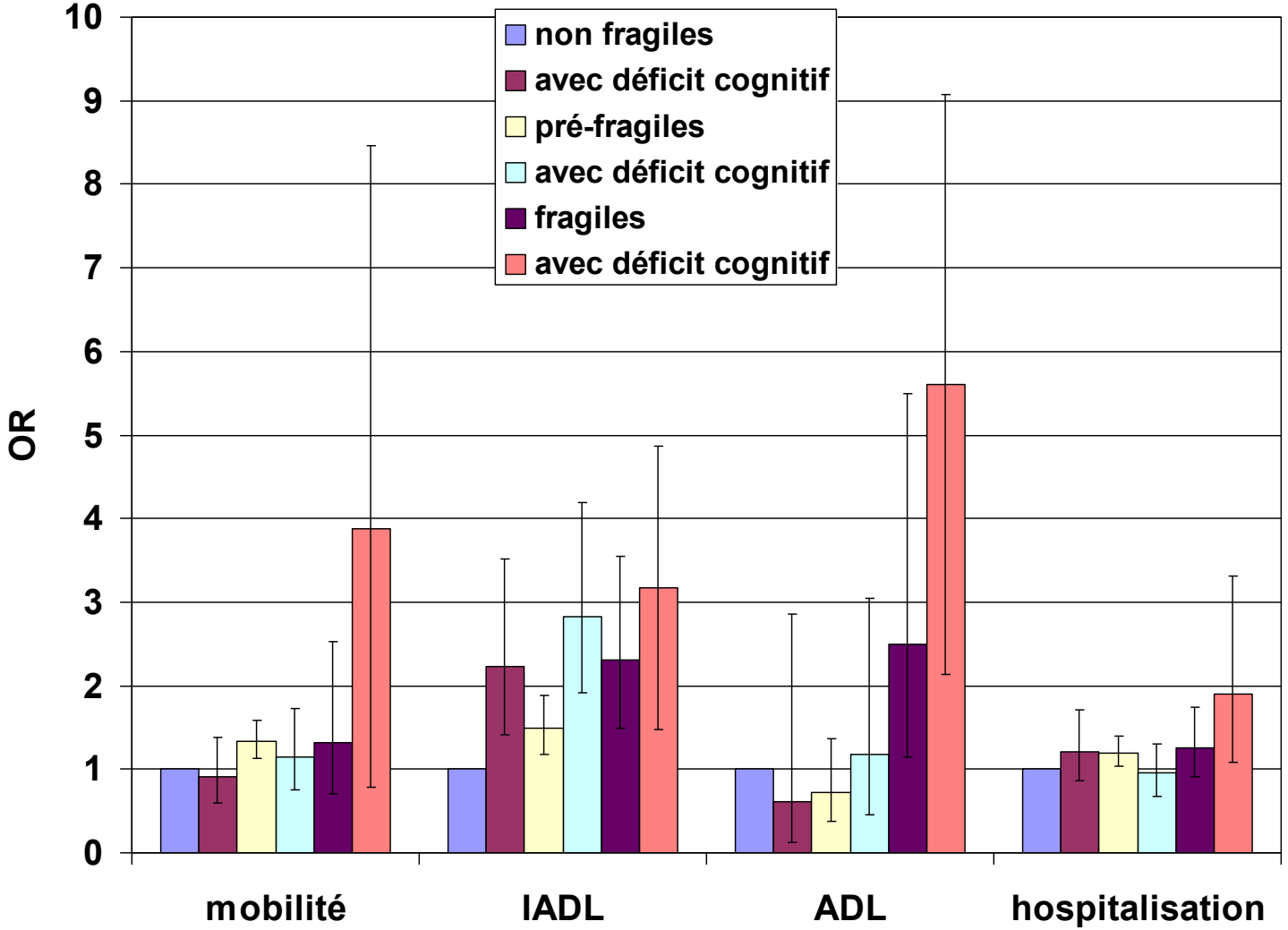
Variables	RR	IC95 %	
Age (for 1 year)	1.1	[1.08-1.13]	*<0.0001*
Female	0.65	[0.47-0.91]	*0.01*
Impaired Fasting Glucose	1.05	[0.43-2.58]	*0.29*
Diabetes	1.48	[0.90-2.40]	
BMI < 21	0.59	[0.27-1.30]	*0.003*
27 ≤ BMI < 30	1.83	[1.24-2.72]	
BMI ≥ 30	1.53	[0.95-2.47]	
Ex-smokers	1.35	[0.95-1.91]	*0.23*
Smokers	1.00	[0.48-2.23]	
Hypertension	1.57	[1.09-2.26]	*0.02*
Atrial fibrillation	2.98	[1.39-6.39]	*0.005*
↗ Cholesterol	1.28	[0.90-1.83]	*0.17*

Diabetes and frailty



Avila-Funes, J Gerontol 2008, 64:1089

4-year disability incidence in frail subjects according to cognitive status



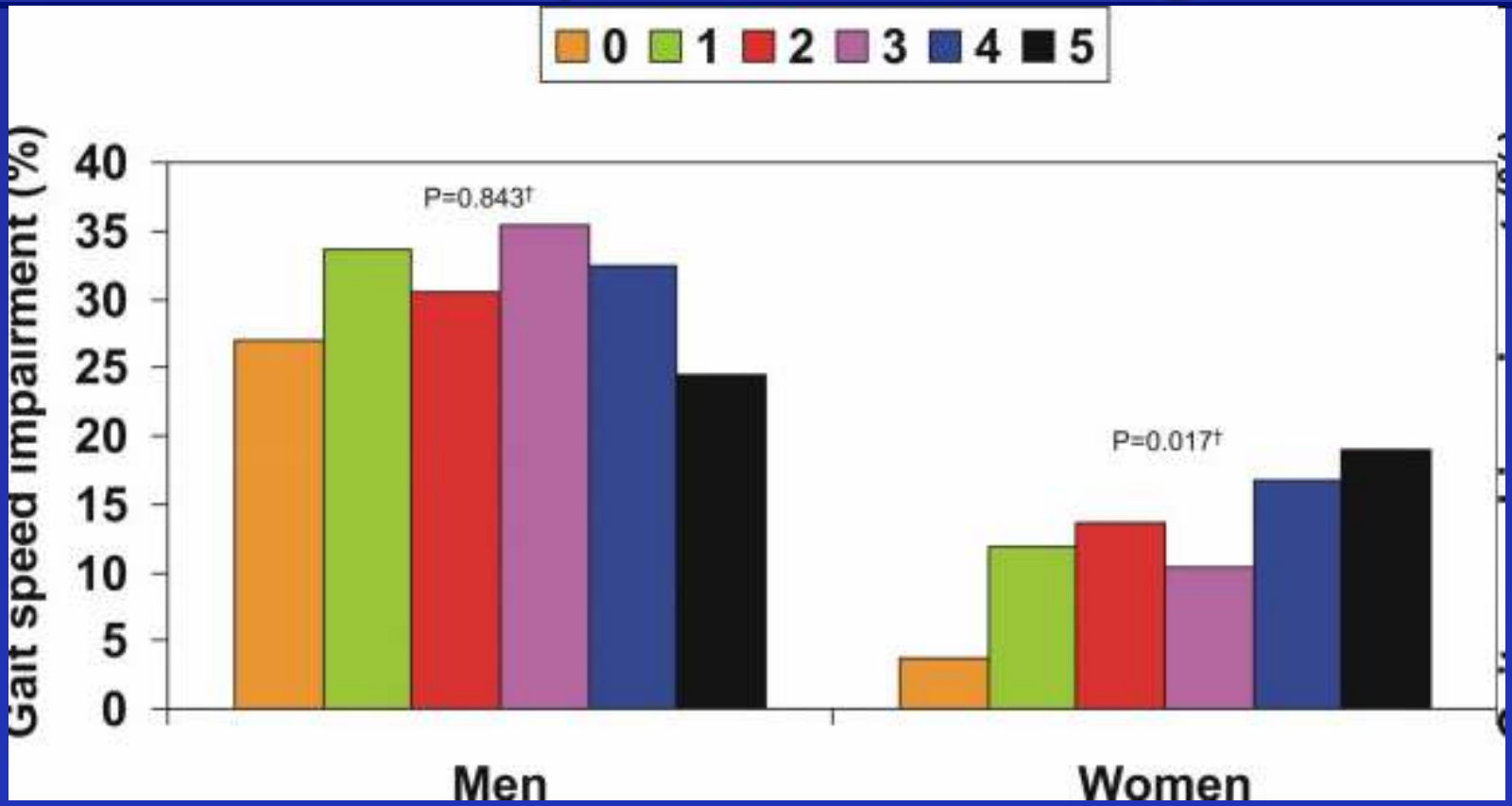
Avila-Funes, J Am Geriatr Soc 2009, 57:453

Falls and diabetes

- Health Aging and Body composition study
  - 446 participants with diabetes
  - 70-79y old, mean duration of diabetes 4.9y
- Independent predictors of falls during the first year
  - Neuropathy
  - Reduced renal function (↗ Cystatin C)
  - Poorer visual function
  - Low HbA1c in insulin users

Schwartz AV Diabetes Care 2008: 391

Metabolic syndrome and gait ?



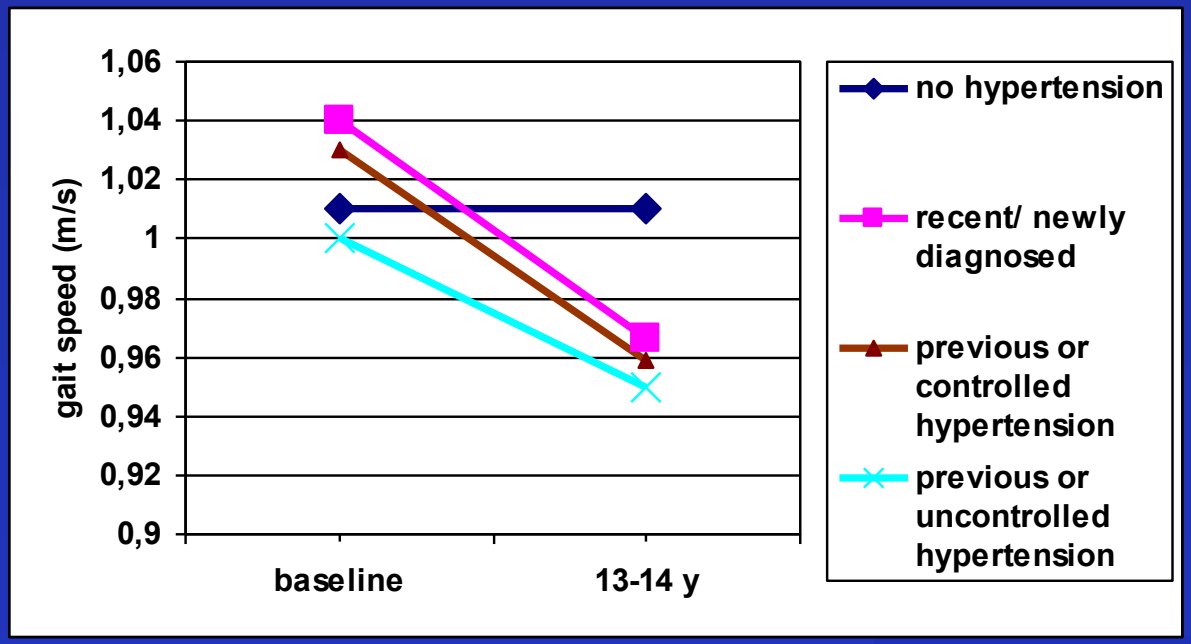
Age-adjusted prevalence of gait speed impairment according to number of metabolic syndrome components, NHANES 1999–2002. NHANES, Age-adjusted to the 2000 U.S. standard population.

†Denotes test for trend (*P*-value).

Schwartz AV Diabetes Care 2008: 391

Relationships Hypertension / gait

- Cardiovascular Health Study, 2733 subjects >65y, not disabled at baseline
- Change in gait speed during 13-14 years
- Faster decline in ALL subjects with hypertension irrespective of treatment, or BP control



Rosano C, J Am Geriatr Soc 2011: 390

Hyperglycemia hypothesis

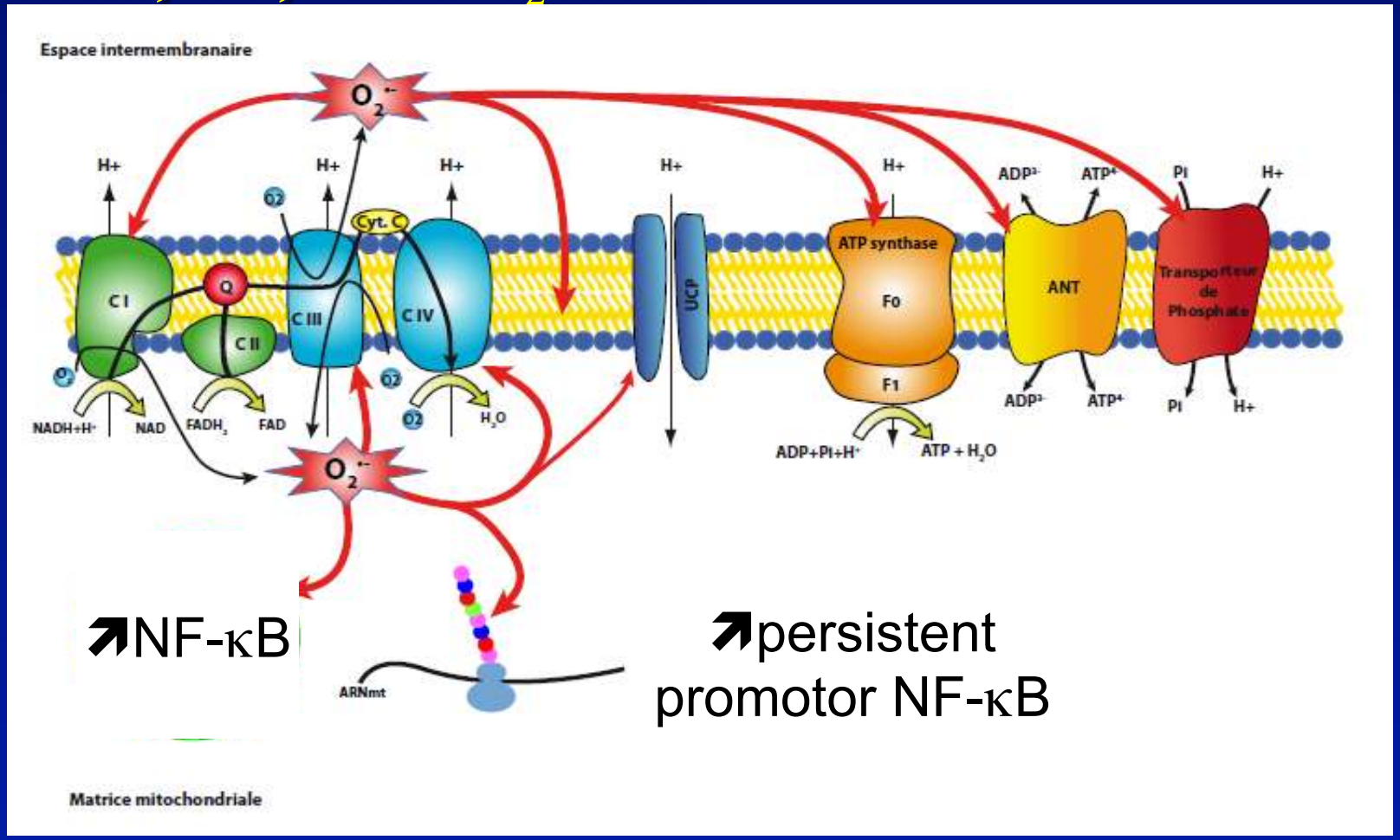
- Association hyperglycemia and cognitive decline
  - Yaffe, J Nut Health Aging 2006
- Glycemia fluctuations // cognitive decline
  - Few relation with HbA1c ou fasting blood glucose
    - Rizzo, Diabetes Care 2010
- Activation in endothelial cell
  - Polyols pathway
  - RAGE
  - C Protein kinase
  - hexosamines pathway

→ ↗ VEGF
↗ ROS
↗ NFκB → complications

  - Brownlee, Nature 2001

Hyperglycemia memory ?

↗NADH, H^+, $FADH_2$ Pics

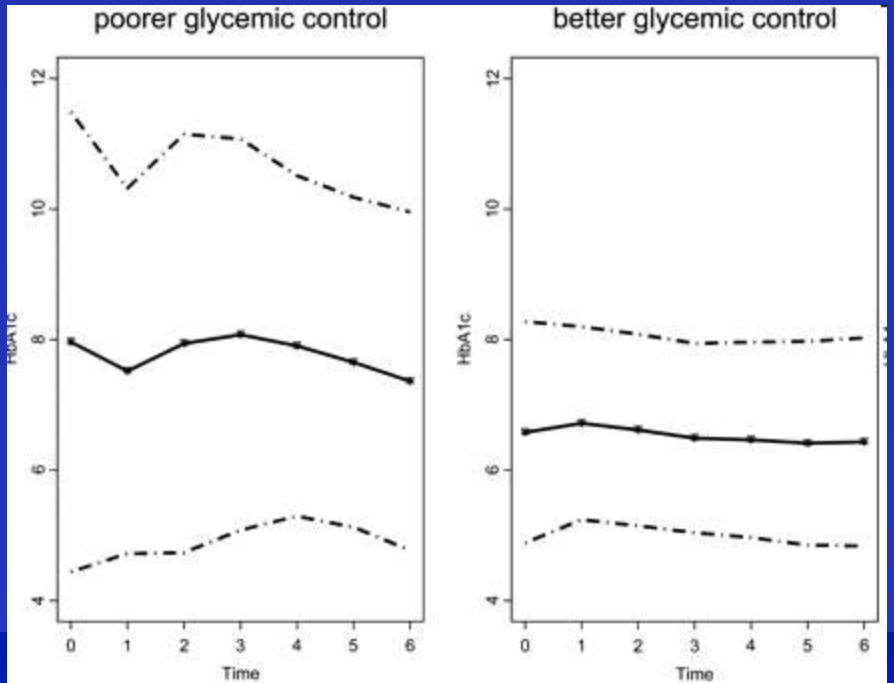


→ Perennisation

El-Osta, J Exp Med 2008

Relationships Blood glucose / physical functioning

- San Antonio Longitudinal Study of Ageing (7y follow-up), 1,626 subjects >65y
- 119 subjects with diabetes
- HbA1c measured at 6 month interval
  - Profile of better glucose control or poorer glucose control
- SPPB measured 3 times



Wang CP Diabetes Care 2011:268

Relationships Blood glucose / physical functioning

- **San Antonio Longitudinal Study of Ageing (7y follow-up), 1,626 subjects >65y**

Table 2—*Covariate-adjusted correlation among SPPB scores by latent glycemic control class*

	Better glycemic control (44.7%)			Poorer glycemic control (55.3%)		
	Estimate	SE	Z value	Estimate	SE	Z value
Total SPPB						
Follow-up 1→follow-up 2	0.86	0.2	5.54**	0.68	0.1	5.09**
Follow-up 1→follow-up 3	0.62	0.2	3.74*	0.42	0.2	2.32*
Walking time						
Follow-up 1→follow-up 2	0.94	0.2	4.85**	0.50	0.2	2.84**
Follow-up 1→follow-up 3	0.87	0.2	4.43**	0.50	0.2	2.75**
Balance						
Follow-up 1→follow-up 2	0.52	0.2	3.23**	0.37	0.1	2.54*
Follow-up 1→follow-up 3	0.28	0.2	1.34	0.17	0.2	1.01
Chair stands						
Follow-up 1→follow-up 2	0.64	0.1	6.84**	0.45	0.2	2.85**
Follow-up 1→follow-up 3	0.39	0.2	2.02*	0.49	0.1	4.3**

*For effects with $0.01 \leq P$ values < 0.05. **For effects with P values < 0.01.

Wang CP Diabetes Care 2011:268

Peripheral arterial disease
Impaired balance ?

Population-based study (1323) with PAD defined by self reporting (possible, 32) or hospitalization for PAD (confirmed, 45), diabetes in 413

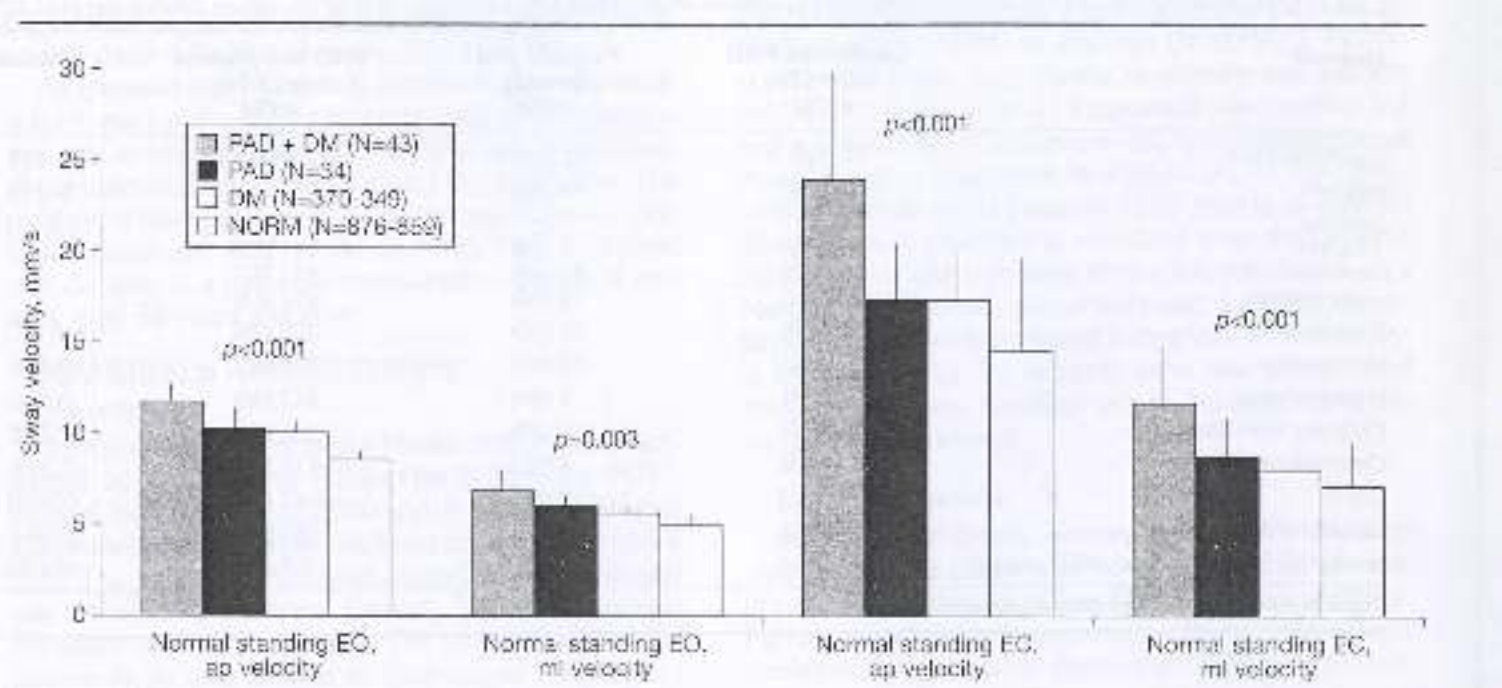


Fig. 1 - Balance behavior according to presence of PAD and diabetes (Mean±SE), adjusted for age, sex, smoking, COPD, congestive heart failure, and number of risk factors.

Peripheral arterial disease

- **PAD associated with diabetes**
- **Both conditions impaired balance**

Table 3 - *Odds of not being able to perform tandem-standing test among those with PAD or diabetes, compared with subjects without these diseases. Logistic regression model.*

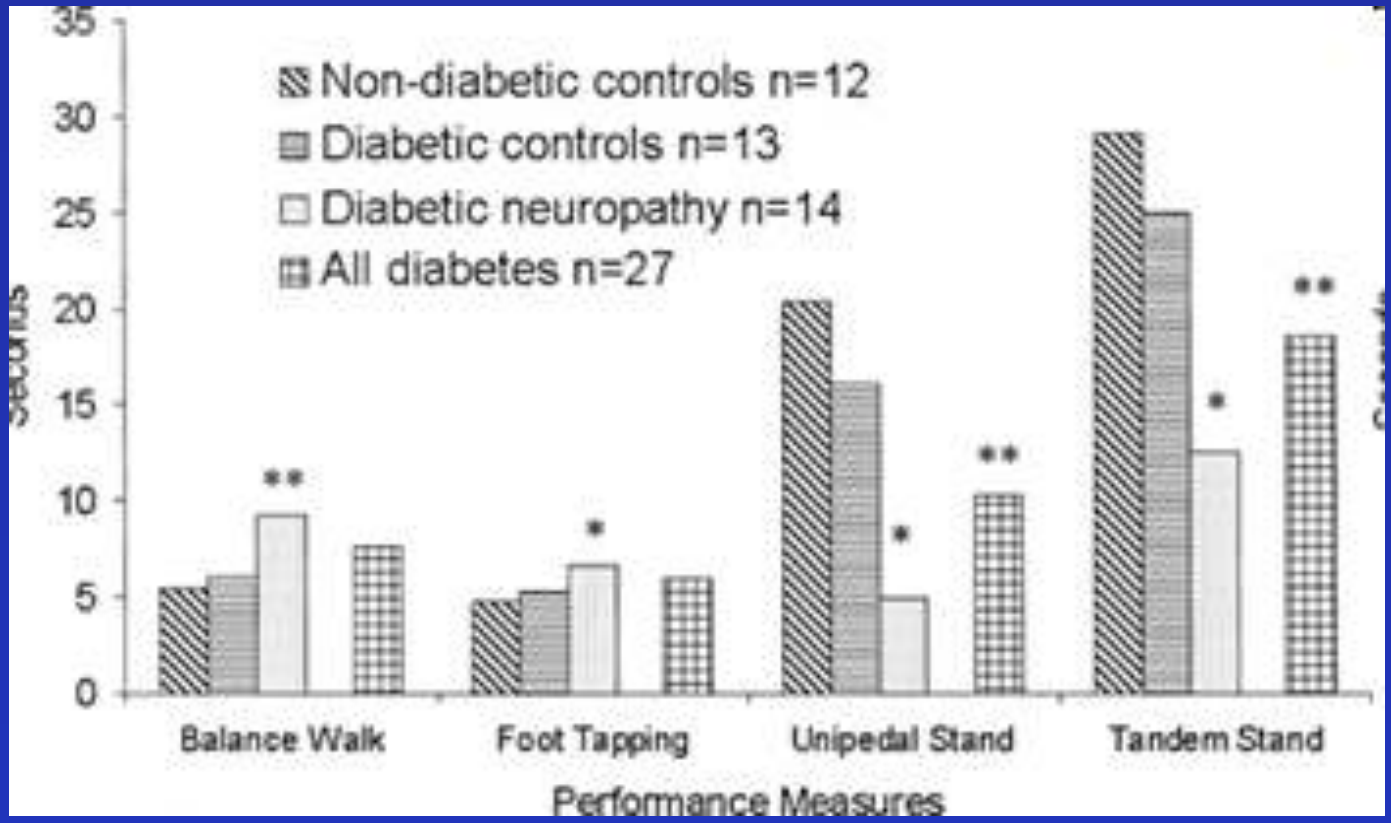
Measure	OR	95% CI
	Unadjusted analyses	
Confirmed PAD	2.64	1.04-6.85
Possible PAD	1.12	0.50-2.53
DM	1.59	1.25-2.03
PAD*+ diabetes	1.67	0.57-4.88
	Partially adjusted analyses**	
Confirmed PAD	2.76	1.05-7.21
Possible PAD	1.06	0.46-2.45
DM	1.59	1.24-2.05
PAD*+ diabetes	1.92	0.65-5.70
	Fully adjusted analyses#	
Confirmed PAD	3.20	1.09-9.37
Possible PAD	1.17	0.47-2.95
DM	1.44	1.07-1.93
PAD*+ diabetes	2.28	0.69-7.53

*Confirmed + possible cases; **Adjusted for sex, smoking, COPD, and congestive heart failure. #Adjusted for age, sex, hypertension, hyperlipidemia, coronary heart disease, cerebrovascular disease, COPD, and congestive heart failure.

Suominen V Aging Clin Exp Res 2008 : 540

Neuropathy and consequences on gait

- 39 subjects 70-79y, case-control study



Resnick HE, Muscle & Nerve 2002: 43

Joint limitations

- **Association diabetes, obesity, osteoarthritis**
  - **Shown for shoulders (Italian Longitudinal Study of Aging)**
    - **Siviero P, Aging Clin Exp Res. 2009: 458**
- **Effect of obesity on prevalence of knee osteoarthris combined with clustering of cardio metabolic risk**

Table 3. At MBHMS visit 11, the ORs (95% CIs) of having knee OA (K/L score ≥2) according to the presence or absence of cardiometabolic clustering within each obesity category*

	With knee OA, no. (%)	OR (95% CI)†
Nonobese (BMI <30 kg/m^2)		
Without clustering (n = 212)	10 (4.7)	Reference group
With clustering (n = 85)	5 (5.9)	1.28 (0.43–3.87)
Obese (BMI ≥30 kg/m^2)		
Without clustering (n = 47)	6 (12.8)	3.00 (1.03–8.71)‡
With clustering (n = 138)	32 (23.2)	6.20 (2.93–13.07)§

Sowers M, Arthritis Rheum. 2009 Oct: 1328

Joint limitations

- Effect of non-enzymatic glycation of collagen
  - Capsule
  - Ligaments
  - Tendons
  - ↗ Stiffness

Limitation of mobility in comparison to age and sex matched subjects with no diabetes (74y old)

  - Shoulder
  - Ankle

- No difference for Knee and Elbow flexion

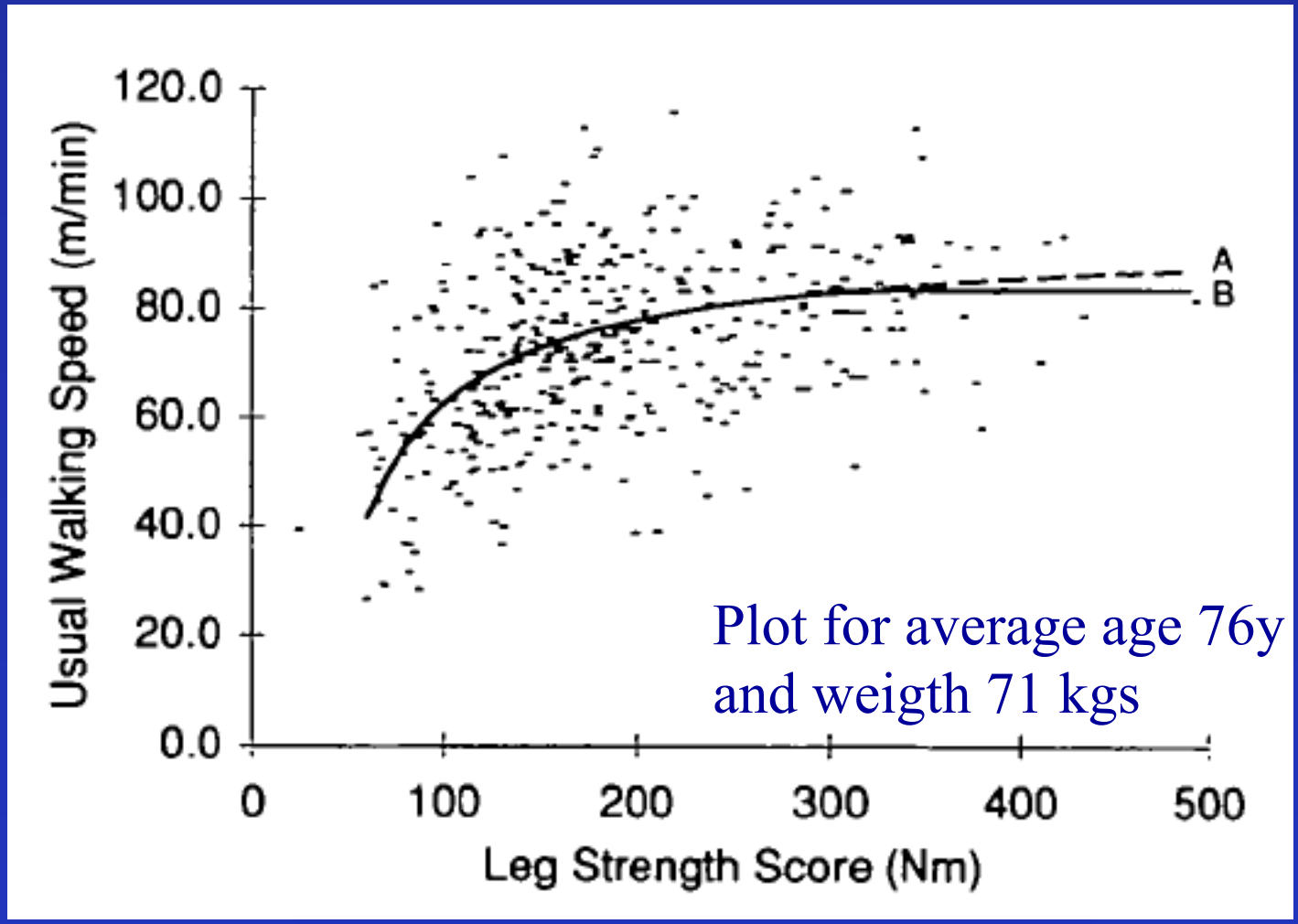
Abate M, Archives of Gerontolgy and Geriatric 2011:

Diabetes and muscle strength

Muscle alterations in diabetes:

- feeling of weakness (Women health and Aging study)
- Greater decrease in handgrip strength in men (Honolulu Heart Program) Rantanen J Appl Physiol 1998
  - independent effect from:
    - arthritis
    - COPD
    - Coronary heart disease
    - Stroke
      - » Bourdel-Marchasson Diabetes Metab 2007 33: s66

Gait speed and muscle strength



» **Buchner, Age and Ageing 1996, 25: 386**

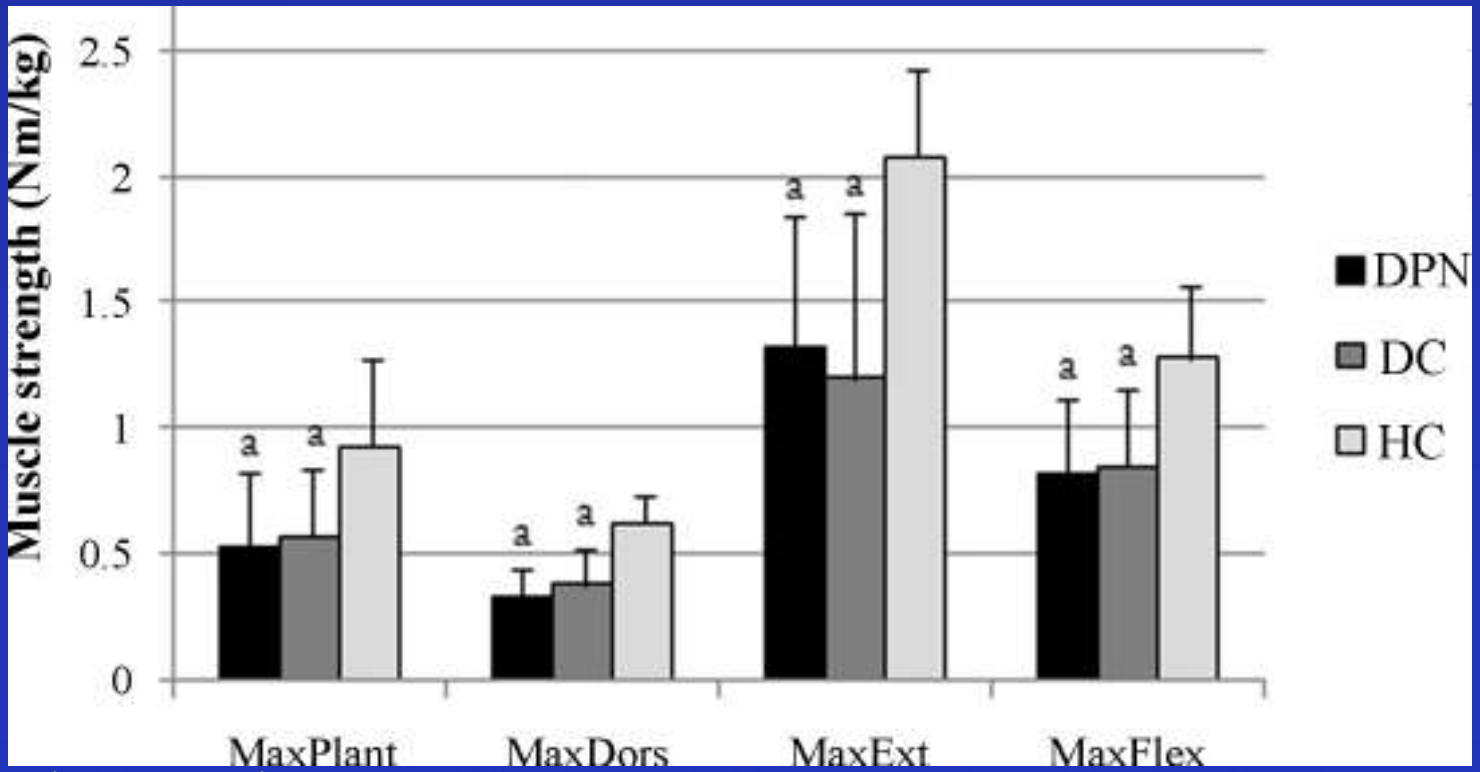
PAD, Neuropathy, strength, obesity and walking activity in people with diabetes

- Cohort of 100 people > 40y (mean 64.5y) with diabetes and without mobility limitations or severe associated diseases
- Independent determinants of physical capacity and activity limitation
  - Peripheral arterial disease versus none
    - 6-minute walking distance
  - Peripheral neuropathy versus none
    - Number of steps / day
  - Low hand grip strength (<20th percentile)
    - 6-minute walking distance
    - Number of steps / day
    - Timed up and go test time
    - Stair climbing
  - BMI
    - 6-minute walking distance
    - Number of steps / day
    - Timed up and go test time
    - Stair climbing

Van Sloten, Diabetes Research and Clinical Practice 2011: 32

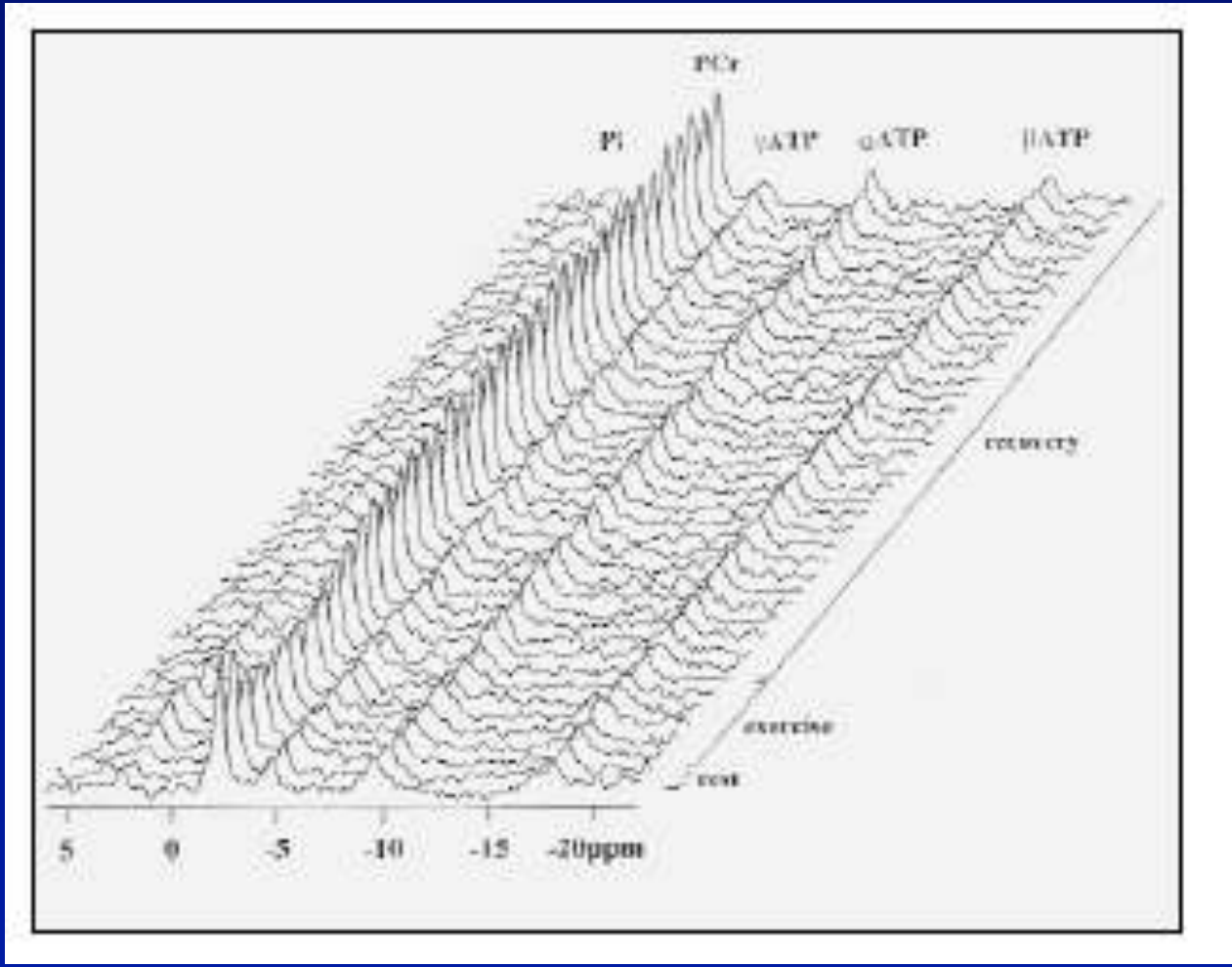
Neuropathy, strength in people with diabetes

- Subjects with diabetes: DPN (*n* = 98) with neuropathy, DC (*n* = 39) without neuropathy, similar HbA1c (7.3%)
- Healthy subjects (HC) (*n* = 19)
- Man age 63y



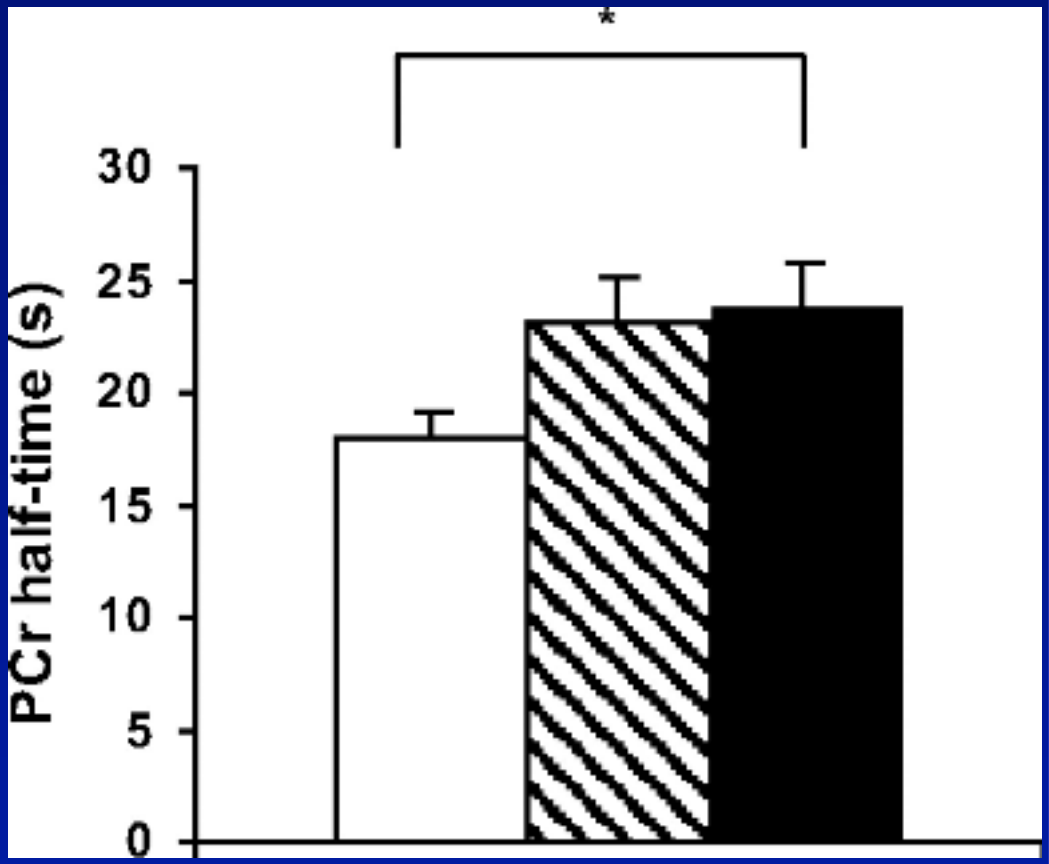
Isokinetic lower limb muscle strength Ijzerman, Diabetes Res Clin Pract 2012: 345

^{31}P NMR spectroscopy in older people



Bourdel-Marchasson JNHA 2007, 11:215

Muscle bioenergetics and diabetes



- 31P NMR spectroscopy
  - ½ time recovery of Pcr after a 60% o maximal capacity exercise
- □, control
- ▨FDR
- ▪type 2 diabetic patients. *P < 0.05 compared with diabetic patients

Phielix, Diabetes 2008:2943

Muscle metabolism in diabetes

- **Insulin resistance**
  - **decreased muscle glycogen synthesis**
    - **➔Decrease muscle quality :**
      - **less effective anaerobic glycolysis**
      - **less effective oxidative phosphorylation**
  - **impaired synthesis of mitochondrial proteins**
    - **➔Decreased oxidative capacities**
- **Effect of diet**
  - **Increased dietary lipids**
    - **➔insulin resistance**

Muscle metabolism in diabetes

- Sedentary life style

  ✚

- Diet rich in lipids

  – "Inflammageing"

  – Continuous stimulation of cytokines (IL-6)

  ↘ Muscle mass

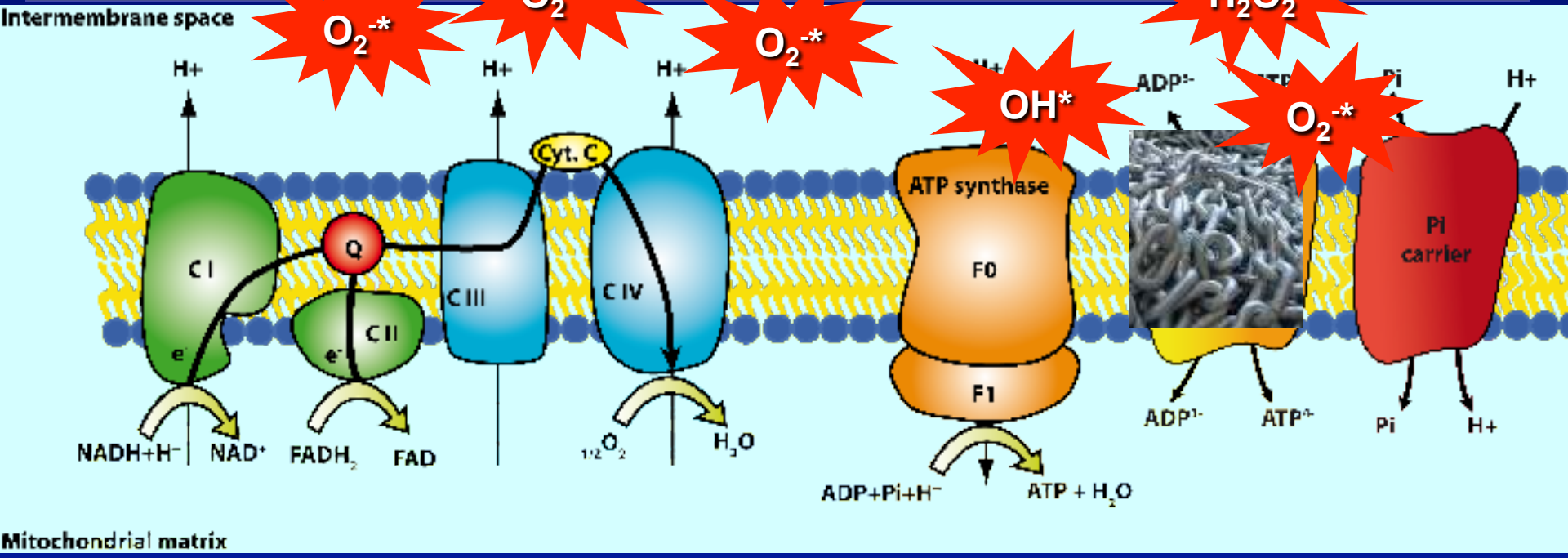
- Effect of sedentary life style
  - Decreased mitochondrial muscle density
  - Decreased muscle perfusion

  ↘ Oxidative capacities

Muscle metabolism in diabetes

- Increase in oxidative stress in muscle cells due to glucose overload and blood glucose fluctuations ?
- Effects close to ageing ?

Increase in oxidative stress due to glucose overload and fluctuations ?
Effects close to ageing ?



Hypothesis : Carbonylation of ATP/ADP translocator due to oxidative stress

For ageing Gouspillou Biochim Biophys Acta. 2010 Feb;1797(2):143

Decrease muscle quality other hypothesis

- **Effect of non-enzymatic glycation of contractile proteins**
  - **Single fiber**
  - **Incubation of myosin + glucose**

  ➔ Glycation of myosin

  ➔ Decrease mobility of myosin

Ramamurthy B, Faseb J 2001: 2415

Interventions

Muscle bioenergetics and diabetes

- Patients with diabetes (14) and controls (15) matched for age (59y) and BMI (30)
- Exercise training program: combined resistance and endurance 12 weeks
- In both groups:
  - Increase in mitochondria density
  - Increase in intrinsic mitochondria respiration

Phielix, Diabetologia 2010: 1714

Home-based walking intervention

- 145 patients with diabetes and PAD. Mean age 66.5y
- Randomized intervention of engagement in routine walking
  - *1*) a one-on-one interaction with the research coordinator at baseline
  - *2*) walking training and weekly group walking classes with an instructor
  - *3*) biweekly telephone calls for 6 months.
- Endpoints
  - Walking distance
  - Walking speed
  - Quality of life
  - Self-efficacy

Collins TC Diabetes Care 2011: 2174

Home-based walking intervention

Comparison of intervention and control groups and change from baseline to 6 months			
	Control	Intervention	P value
Treadmill walk, maximum pain distance meters	39.2 (19.6)	24.5 (19.6)	0.598
Treadmill walk, onset of pain distance meters	52.3 (23.6)	66.7 (21.0)	0.651
Exercise behavior score	35.0 (13.3)	55.3 (17.1)	0.349
Walking distance	1.4 (3.3)	5.6 (3.5)	0.383
Walking speed	−1.9 (2.8)	5.7 (2.2)	0.034
Stair climbing	2.9 (2.8)	6.0 (3.5)	0.487
Physical functioning	−0.5 (1.9)	4.5 (1.9)	0.063
Role-physical	−7.4 (5.6)	4.0 (4.6)	0.120
Bodily pain	2.2 (4.2)	5.5 (3.7)	0.568
General health	0.9 (1.6)	1.6 (2.0)	0.769
Vitality	1.2 (2.2)	1.1 (2.2)	0.985
Social functioning	−4.2 (2.6)	−2.9 (2.5)	0.717
Role-emotional	−7.8 (4.3)	2.9 (4.2)	0.080
Mental health	−2.4 (1.5)	3.2 (1.5)	0.010
Geriatric depression scale	0.0 (0.2)	−0.3 (0.2)	0.380

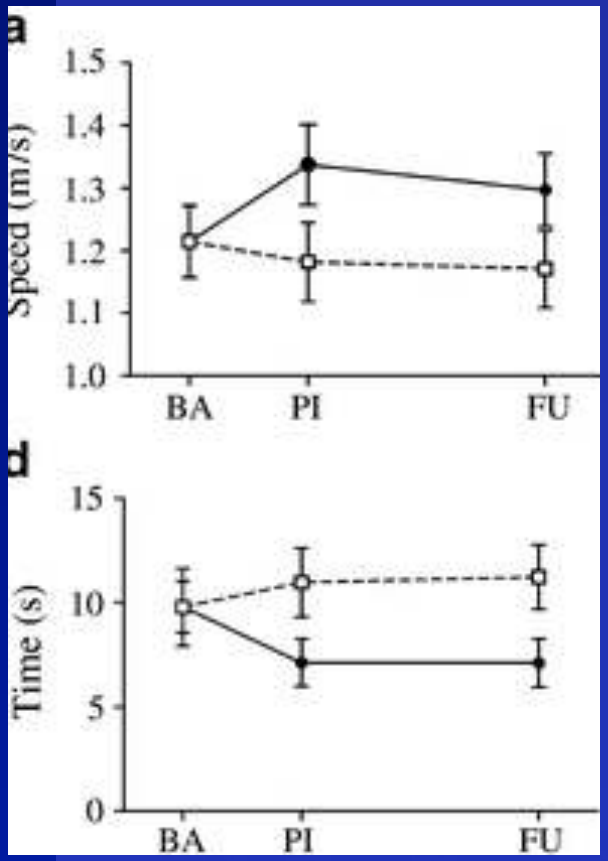
Collins TC Diabetes Care 2011: 2174

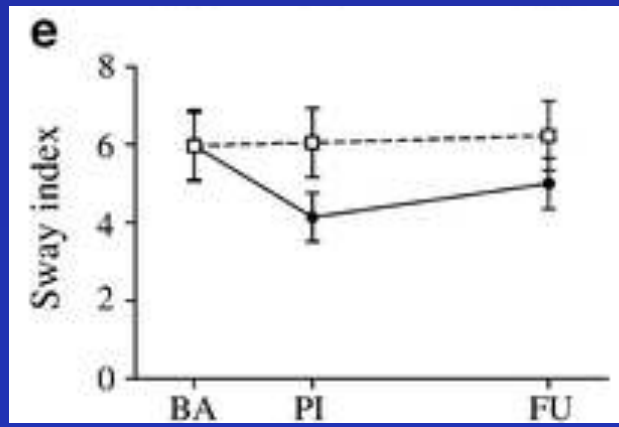
Physical intervention in patients with neuropathy

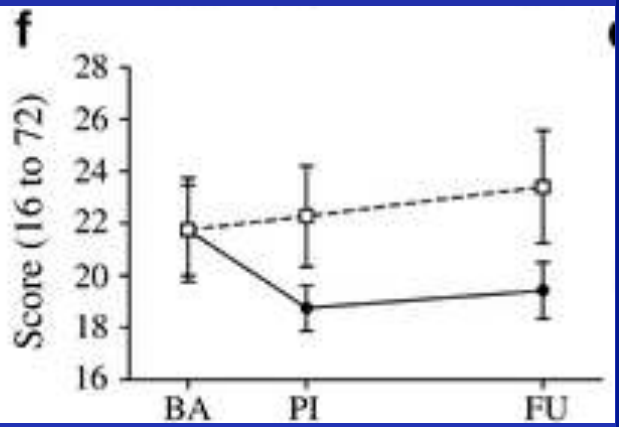
- 71 patients with diabetes and neuropathy (vibration perception threshold of 4 or < with tuning folk
- Mean age: 65y old
- Intervention
  - Twice a week sessions, 60 min, 12 weeks
  - Warm up 5min
  - Training 40 min
    - Balance tasks
    - Strength and endurance exercise
    - Increasing intensity if possible
  - Interactive games 10 min
  - Short session with suggestion for home exercise

Allet l Diabetologia 2010: 458

Physical intervention in patients with neuropathy







Control

Intervention

Fear of falls

BA: baseline; PI: post intervention; FU: 6 month follow-up

Allet l Diabetologia 2010: 458