



Diabetes y envejecimiento, dos epidemias del siglo XXI: Como abordarlo.

TIME: sept 10, 2013

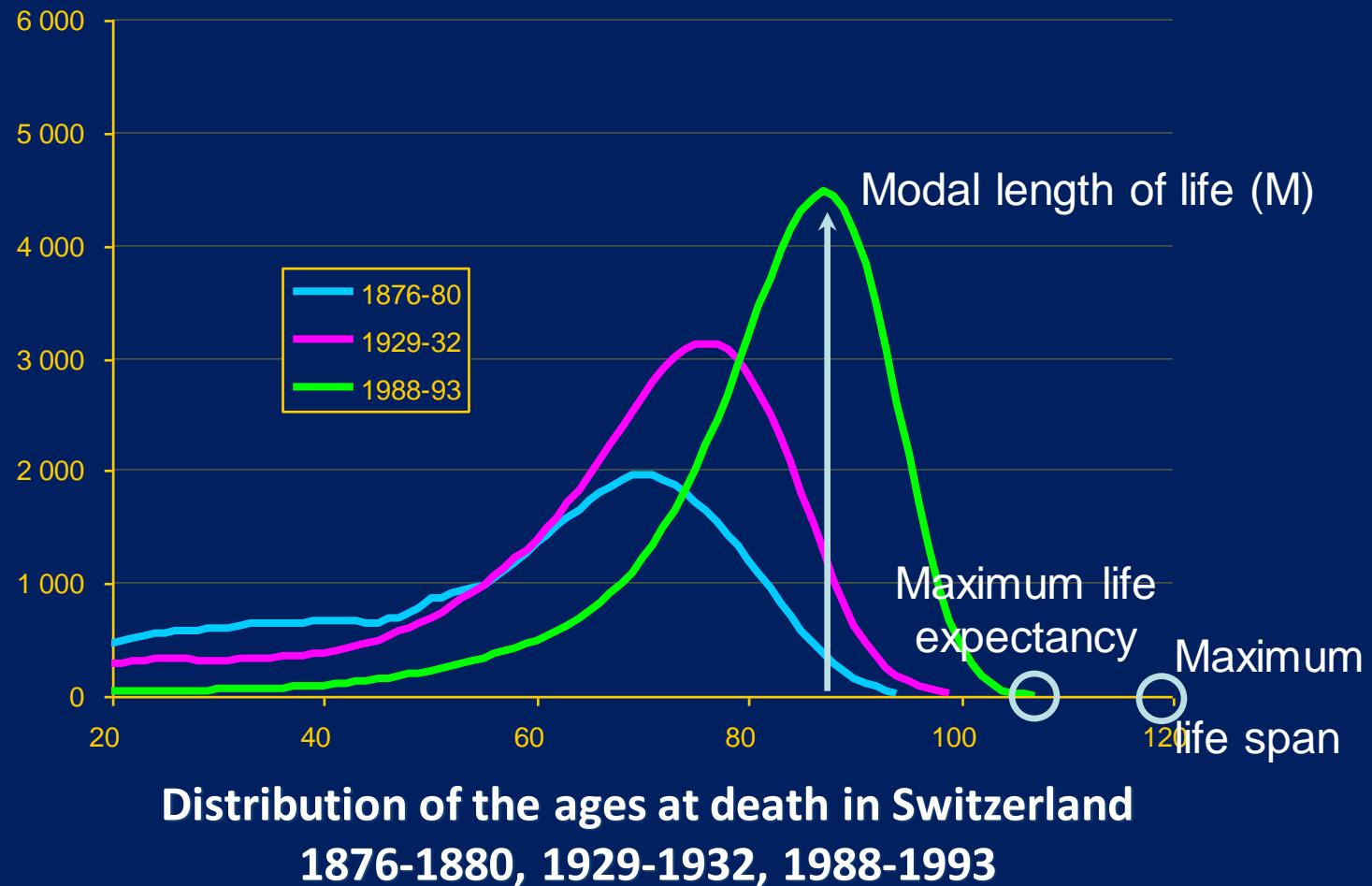


TIME: feb 23, 2015



¿Es este el problema real?

¿Cuánto dura la vida?



LONGEVIDAD VS. FUNCIONALIDAD

Evidence for a limit to human lifespan

Xiao Dong^{1*}, Brandon Milholland^{1*} & Jan Vijg^{1,2}

Nature, October 2016

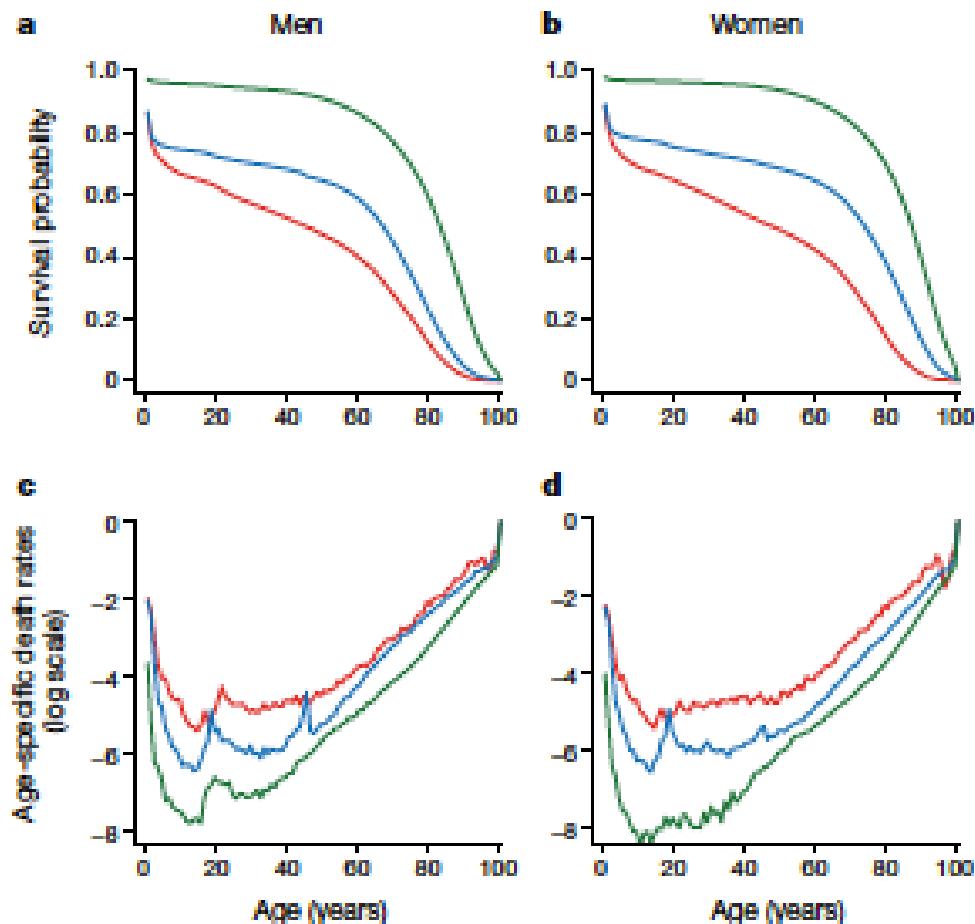
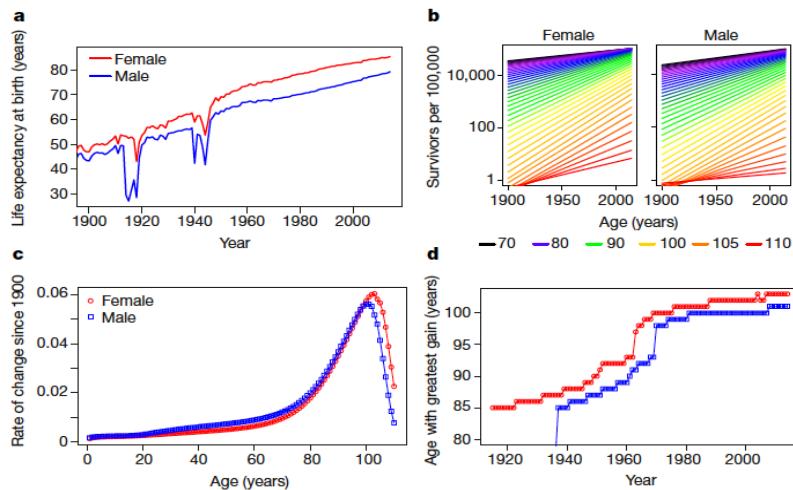
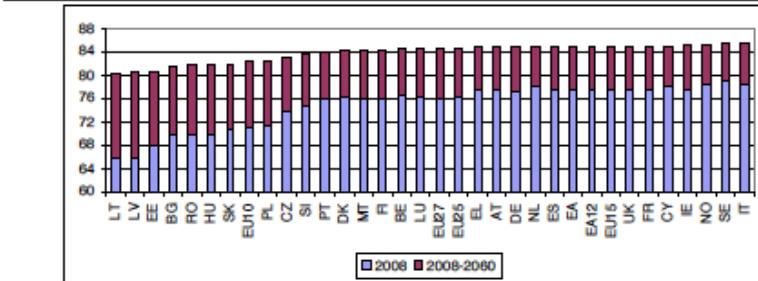


Fig. 1 | Cumulative survival and age-specific death rates in the Netherlands in 1850, 1900 and 1950. a–d, Cumulative survival (a, b) and mortality rates (c, d) in men (a, c) and women (b, d) based on 100,000 individuals per birth cohort (1850 (red), 1900 (blue) and 1950 (green)) from life tables from the Netherlands. c, d, Note that the y axis is a log scale.

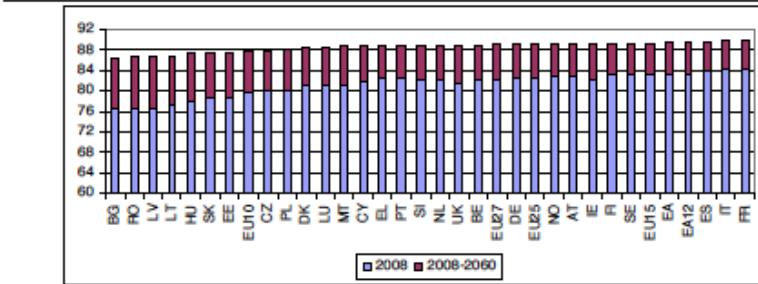
Partridge et al, Nature 2018

Graph 6 - Projection of life expectancy at birth in EUROPOP2008, men (in years)



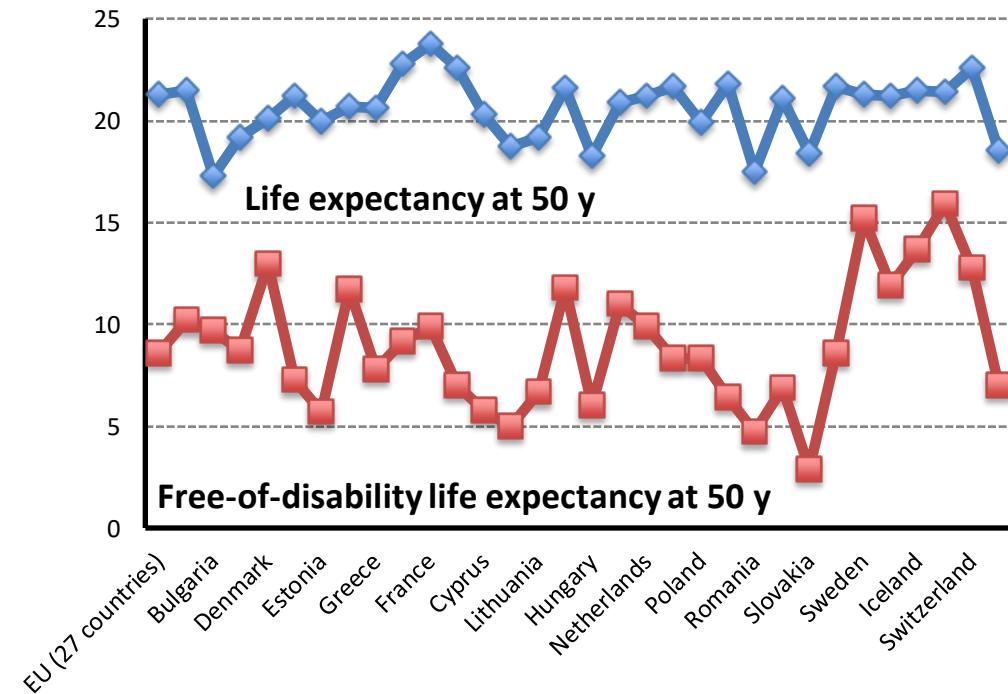
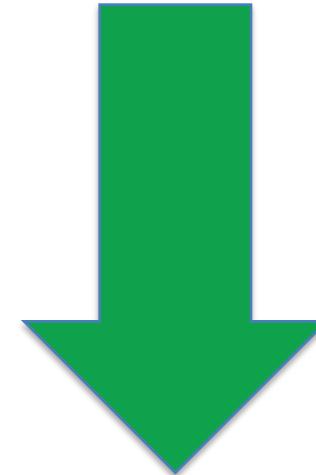
Source: Commission services.

Graph 7 - Projection of life expectancy at birth in EUROPOP2008, women (in years)



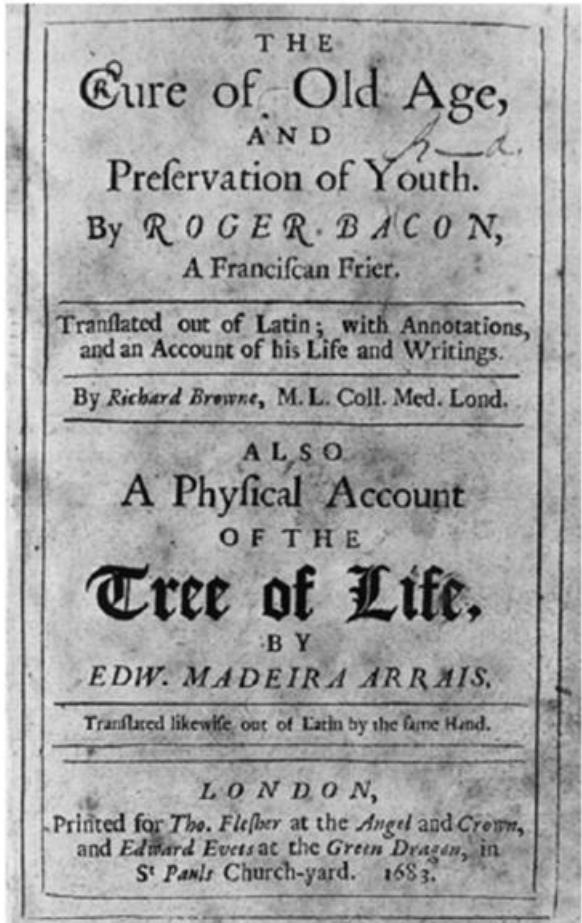
Source: Commission services.

LONGEVIDAD (CANTIDAD DE VIDA)



FUNCION (CALIDAD DE VIDA)

Health span vs lifespan



Dr. Nathan W Shock
(1908-1990)

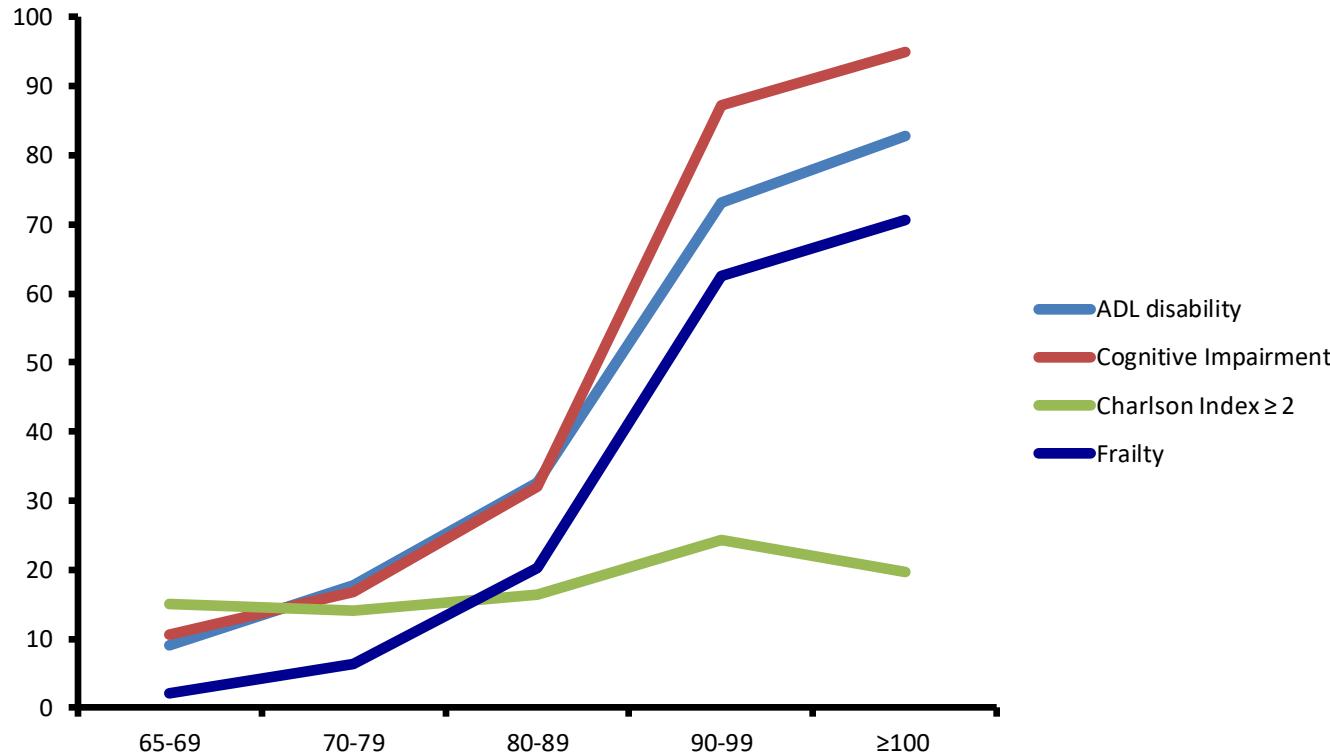
National Institute
■♦★* on Aging

National Institutes of Health

“ The aim of Gerontology is not to prolong the life time, but to minimise disability and dependency in the eldersness”

Figure 2. Roger Bacon, *The Cure of Old Age and Preservation of Youth* (title page), by Roger Bacon; Tho.Flesher and Edward Evets, London (1683); courtesy National Library of Medicine.

Toledo Study for Healthy Aging- Plus



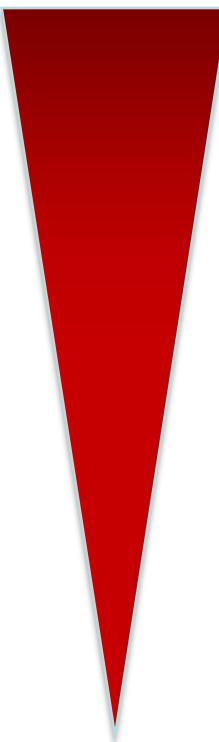
ESTUDIO TOLEDO
ENVEJECIMIENTO SALUDABLE



TOLEDO STUDY FOR
HEALTHY AGING

From disease to function

DISEASE



1. Clinical manifestation
2. Pathophysiology
3. Prognostic value
4. Efficiency marker

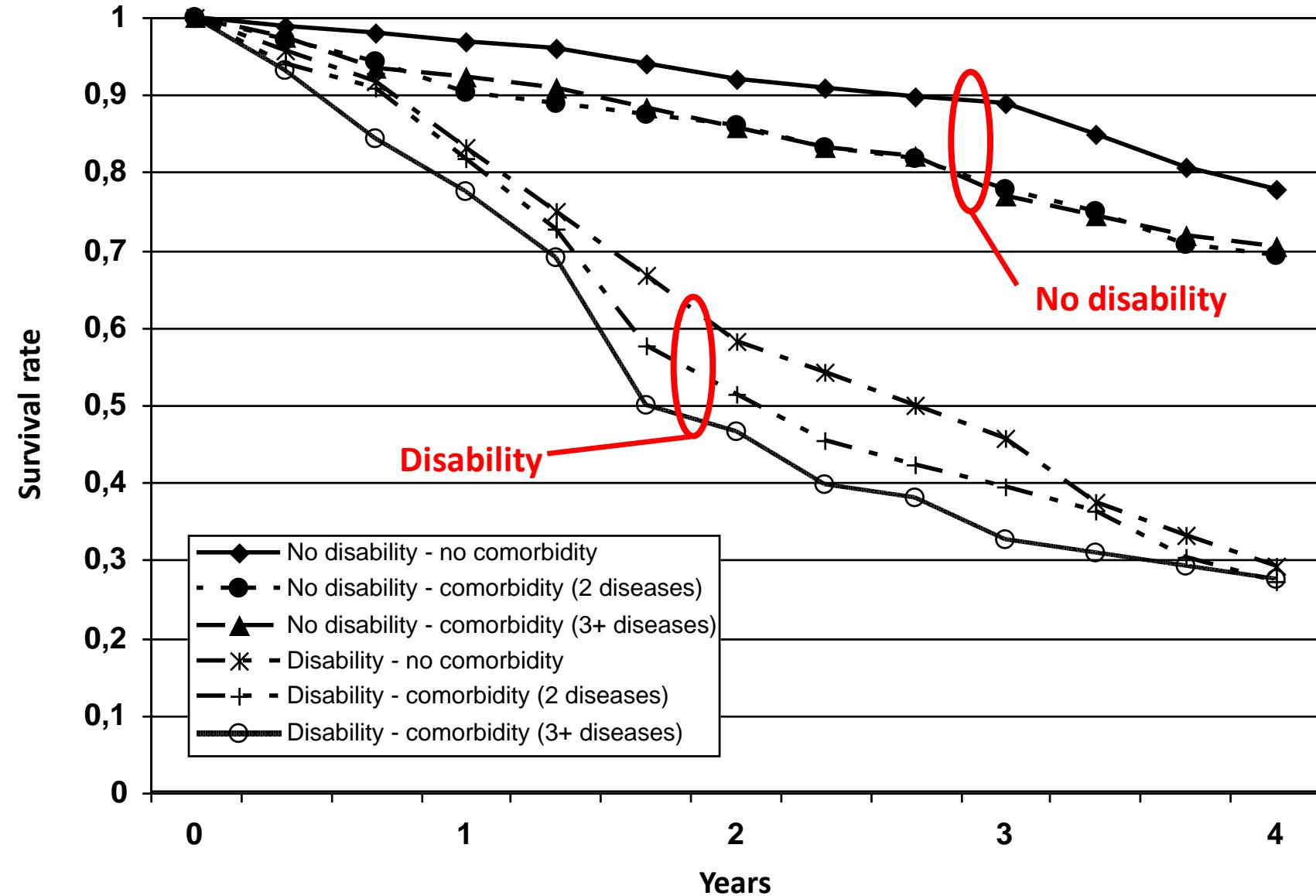
Clinical management
TOTALLY DIFFERENT

FUNCTION



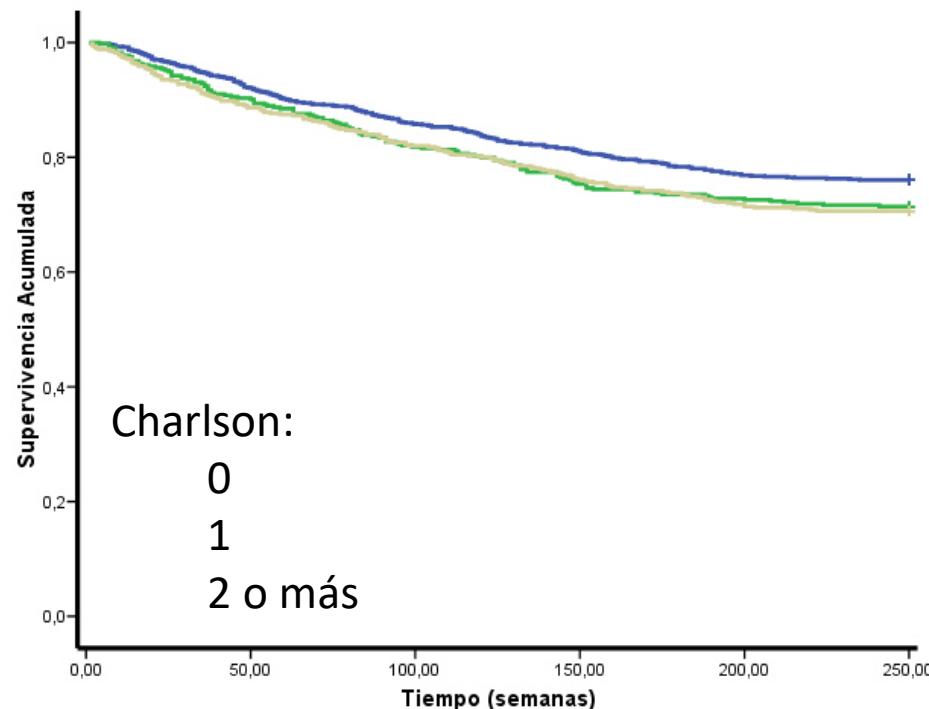
Disability, more than multimorbidity, predicts mortality in advanced age

Landi et al., J Clin Epidemiol 2010



Time until the first hospitalization

Charlson Index



Frailty Trait Scale

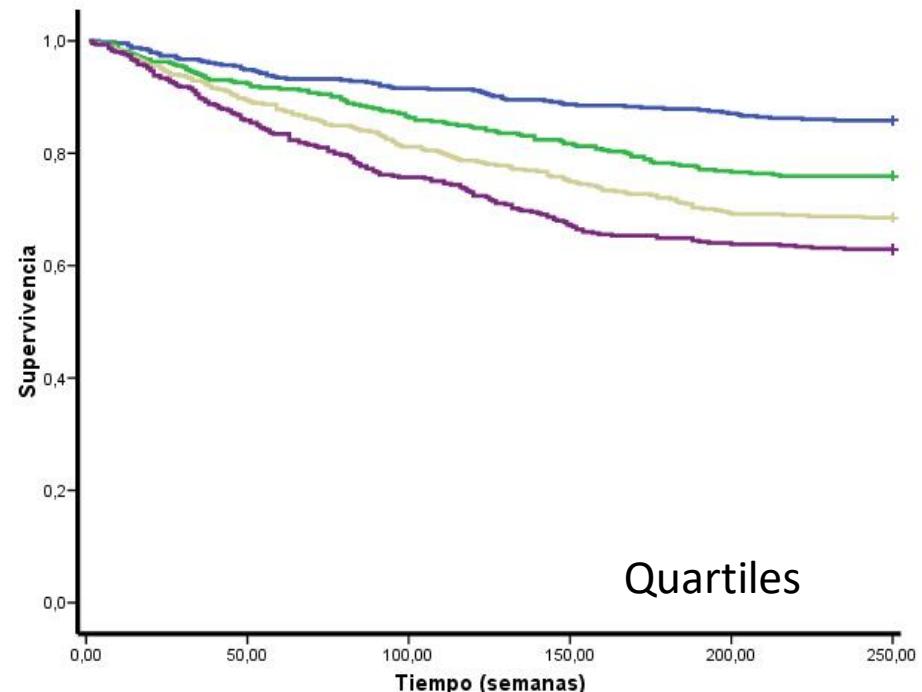
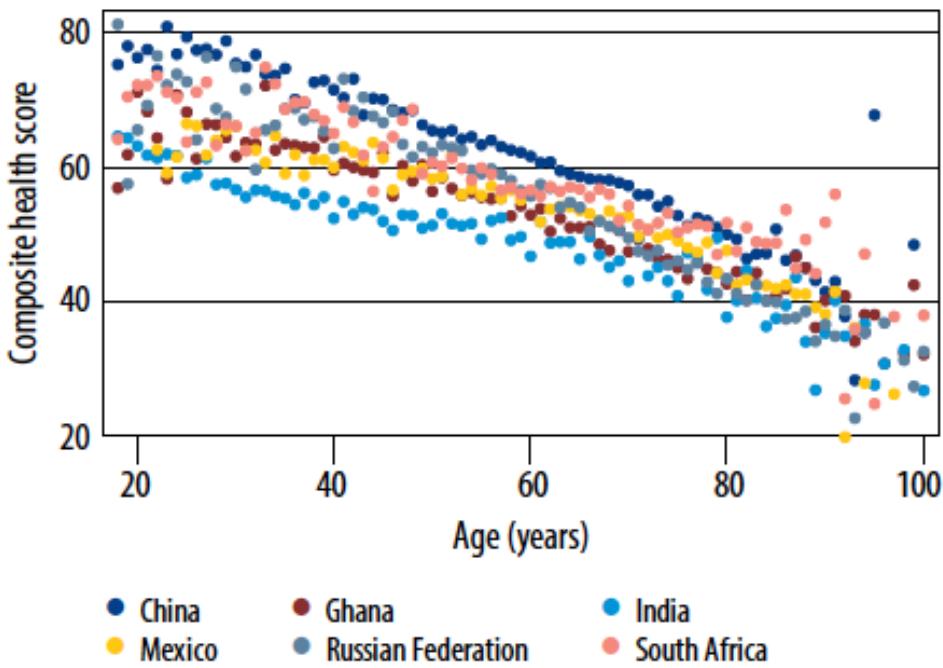
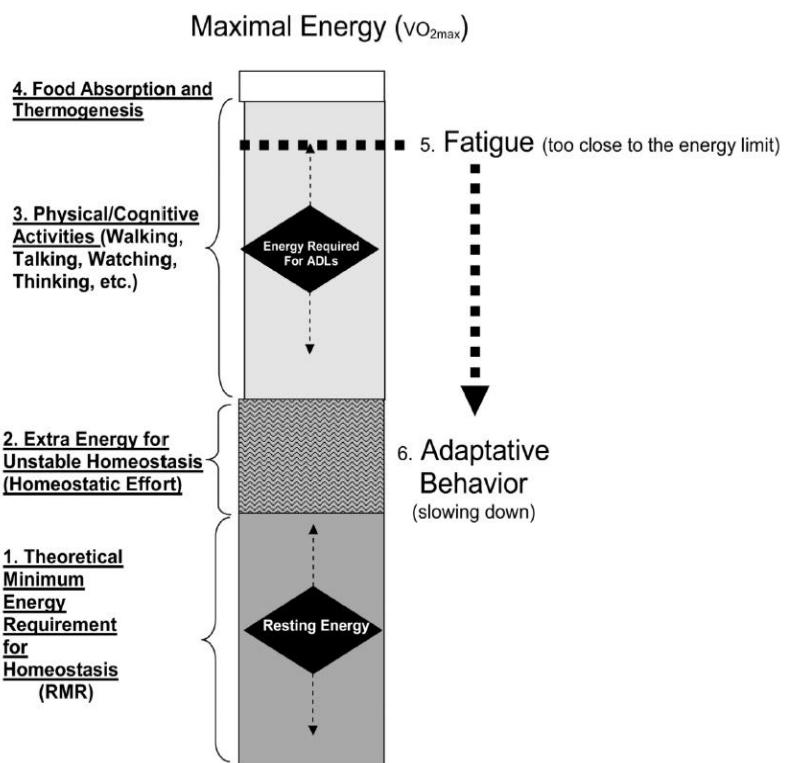


Fig. 3.16. Changes in intrinsic capacity across the life course

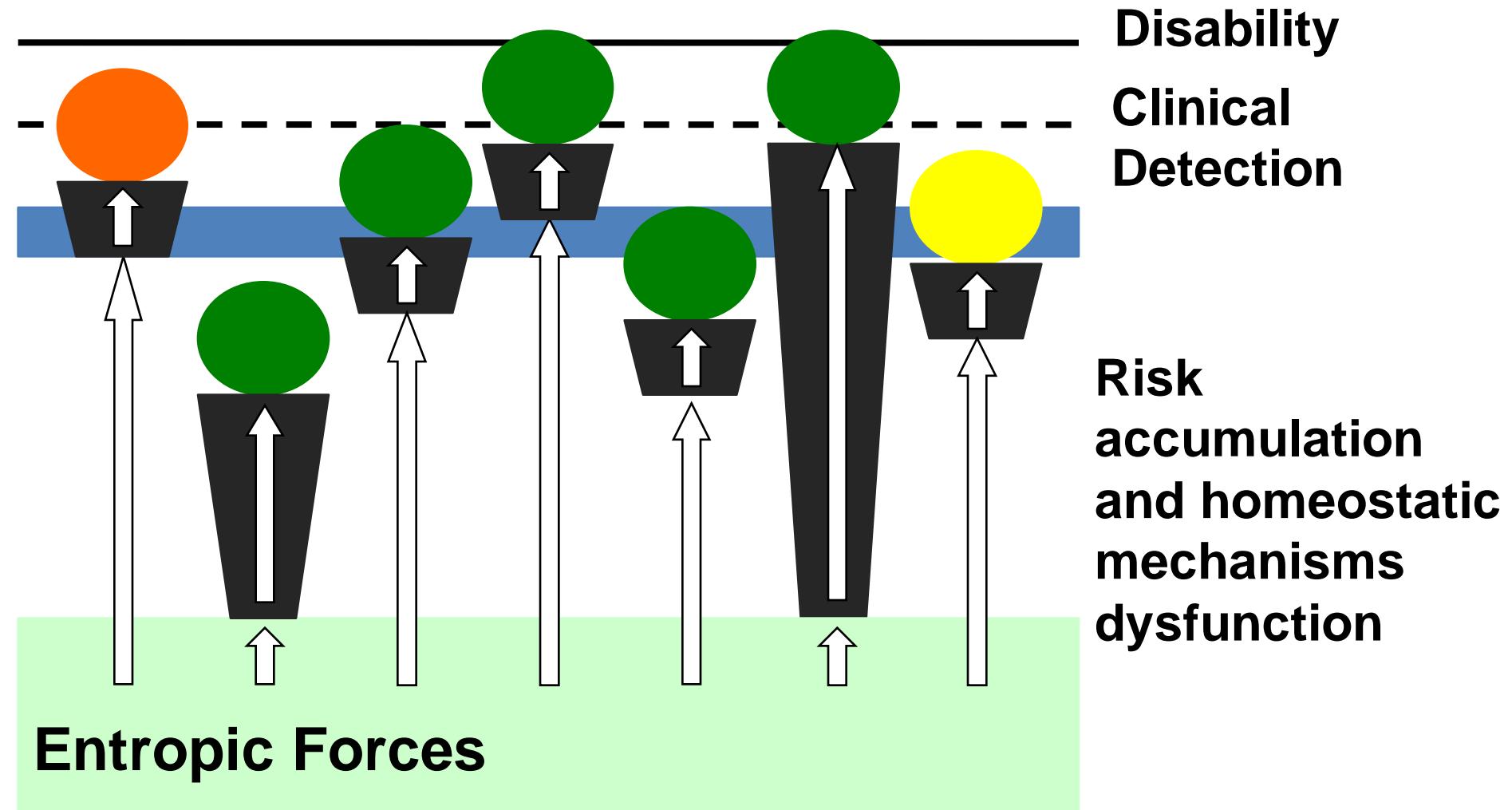


Note: Data on physical and mental capacities were derived from the WHO Study on global AGEing and adult health (SAGE) 2007–2010 (wave 1) (34) and then a vector of capacity was developed. Higher scores indicate higher intrinsic capacity.



The Energetic Pathway to Mobility Loss: An Emerging
New Framework for Longitudinal Studies on Aging
Jennifer A. Schrack, J Am Geriatr Soc . 2010 October ;
58(Suppl 2): S329–S336.

C. Age-related Frailty



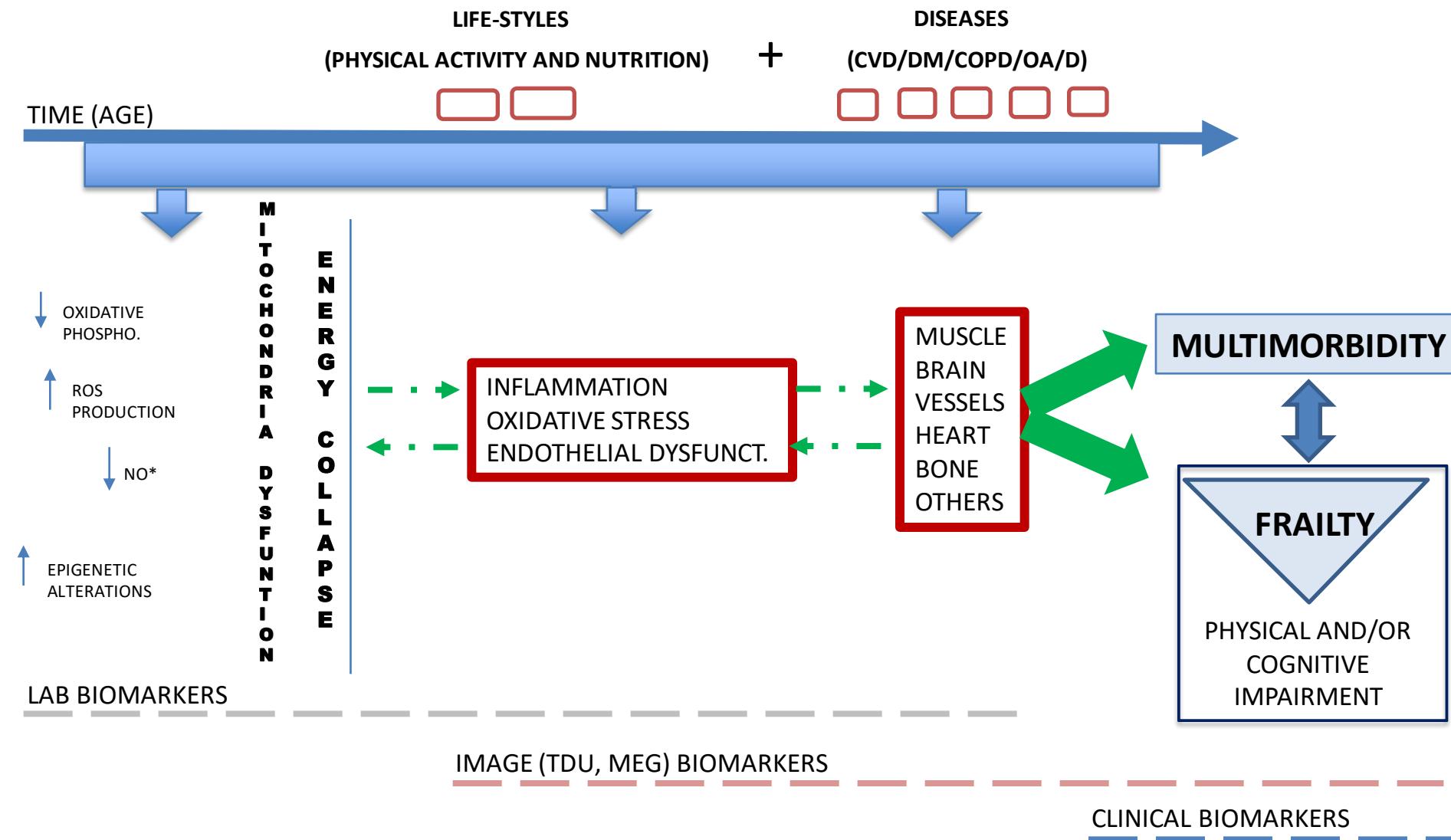
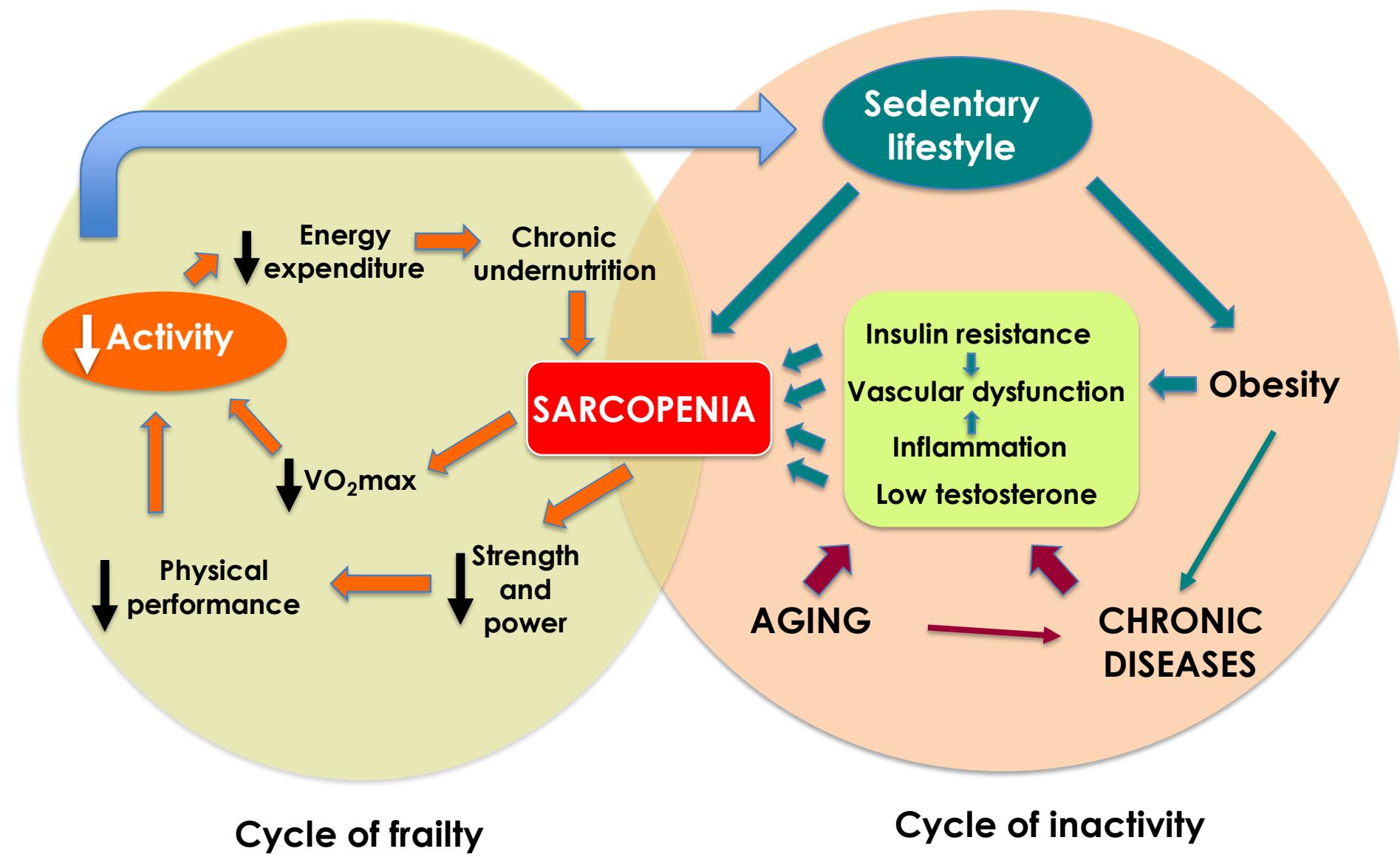
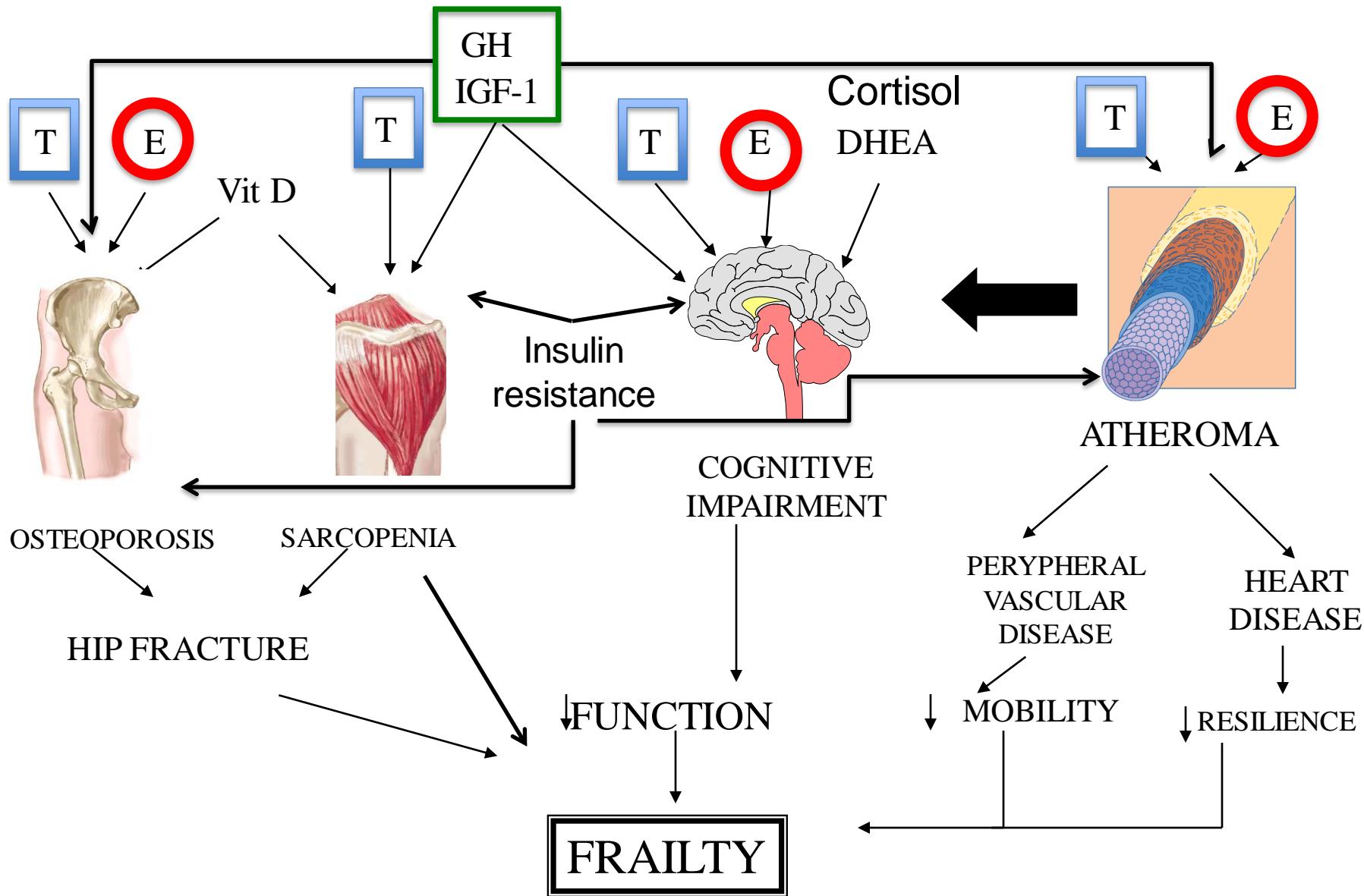


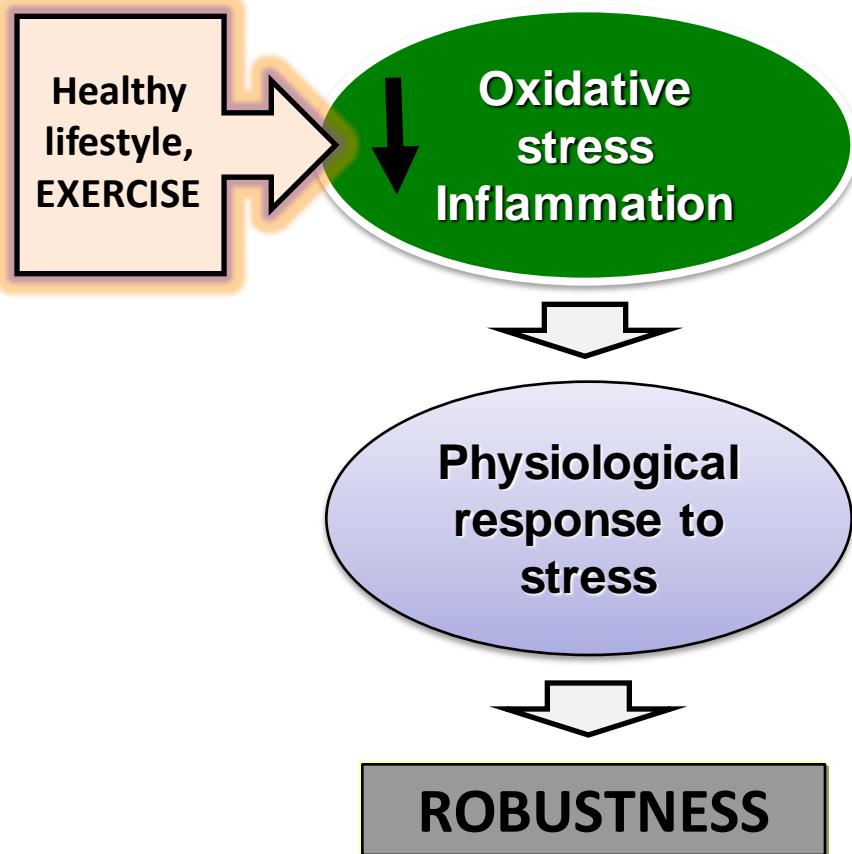
Fig. 2. General scheme of the hypothesis underlying MITOFUN. CVD: Cardiovascular Diseases; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; OA: Osteoarthritis; D: Depression; TDU: Transcranial Doppler Ultrasound; MEG: Magnetoencephalography



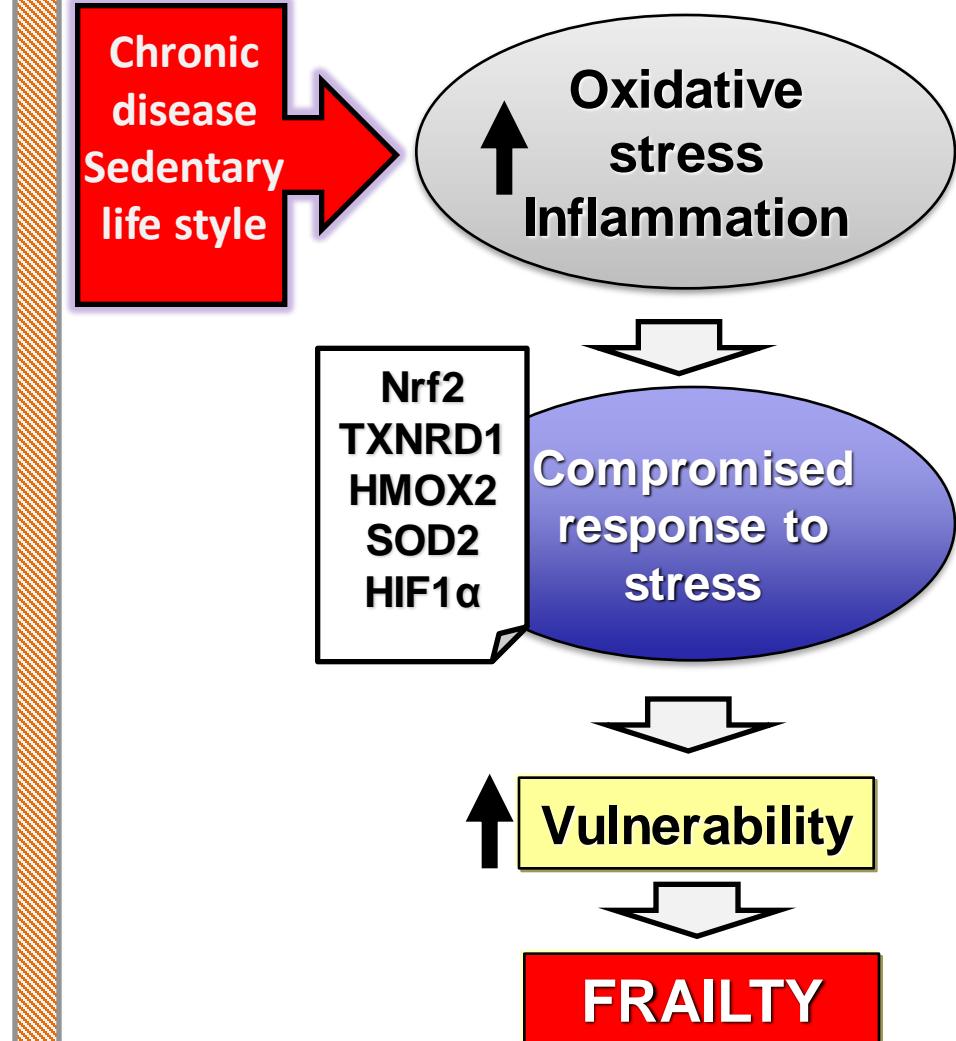
HORMONES, FRAILTY AND TARGET ORGANS



SUCCESSFUL AGING



UNSUCCESSFUL AGING



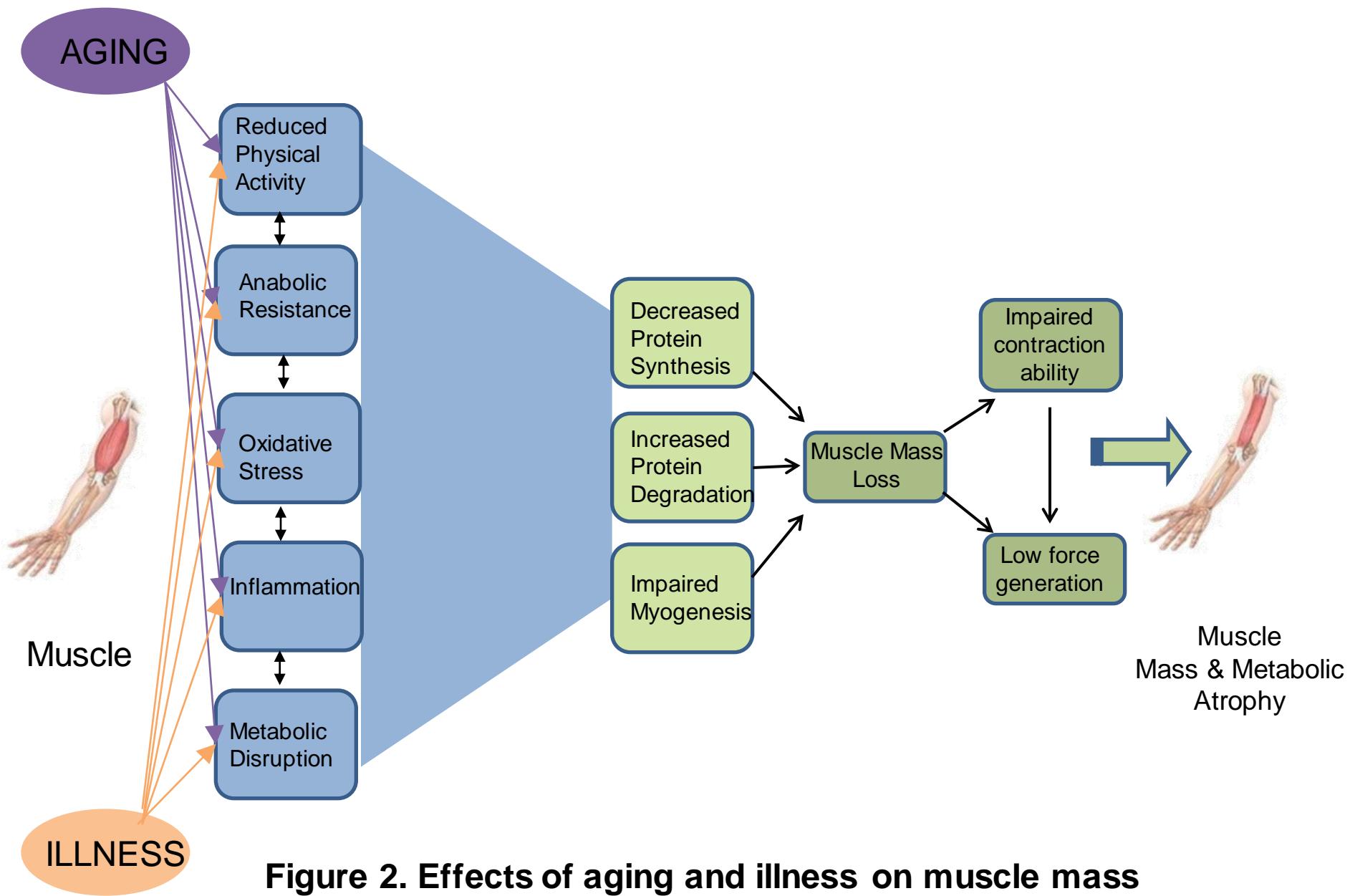
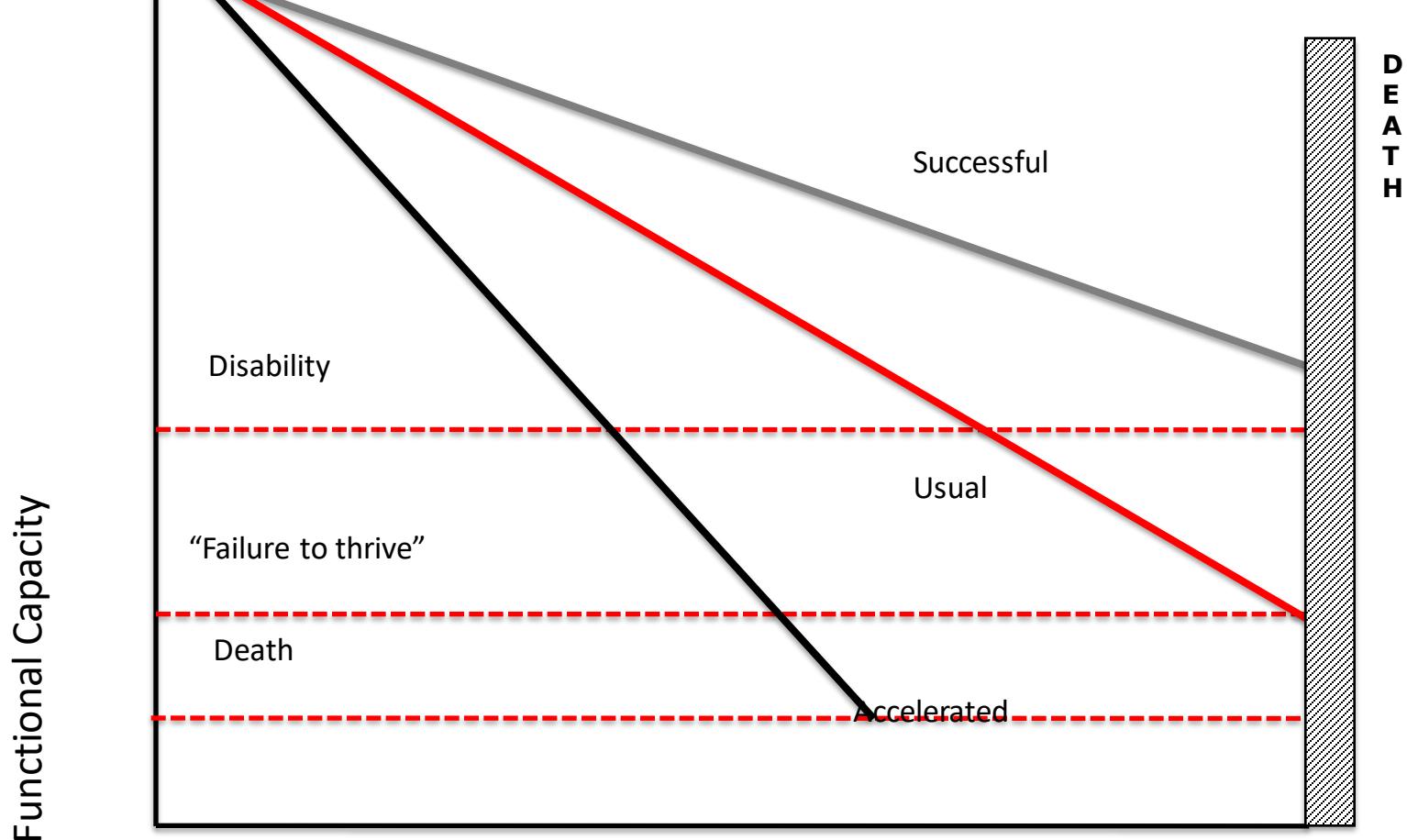
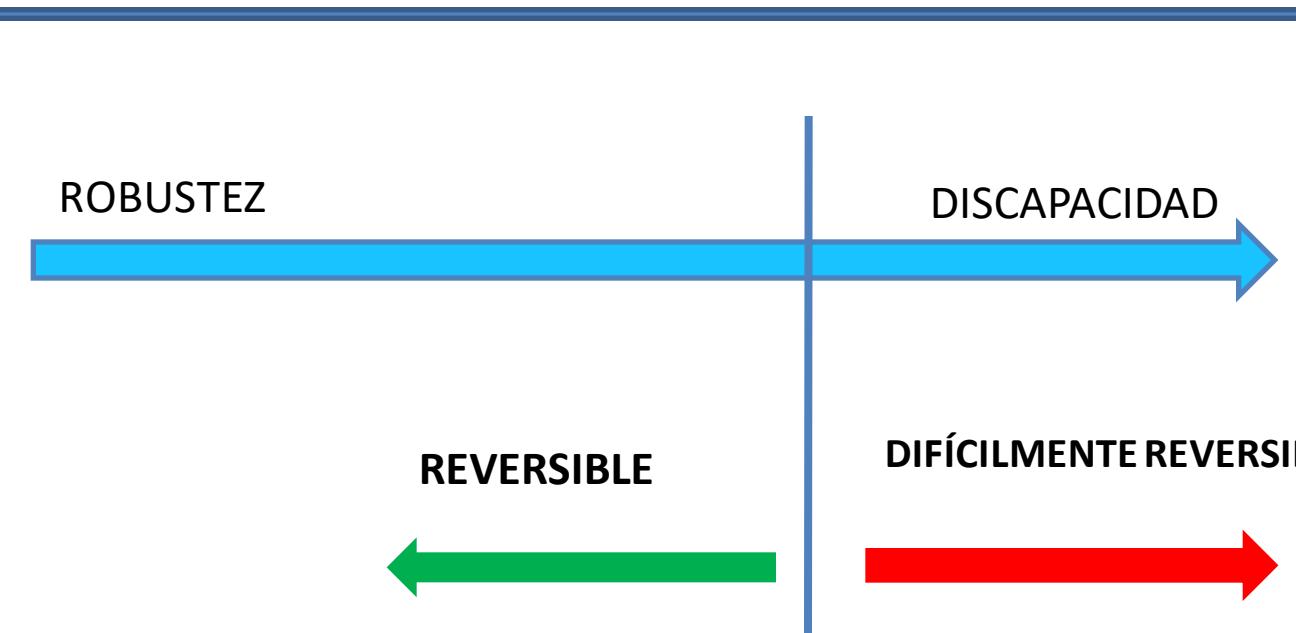


Figure 2. Effects of aging and illness on muscle mass

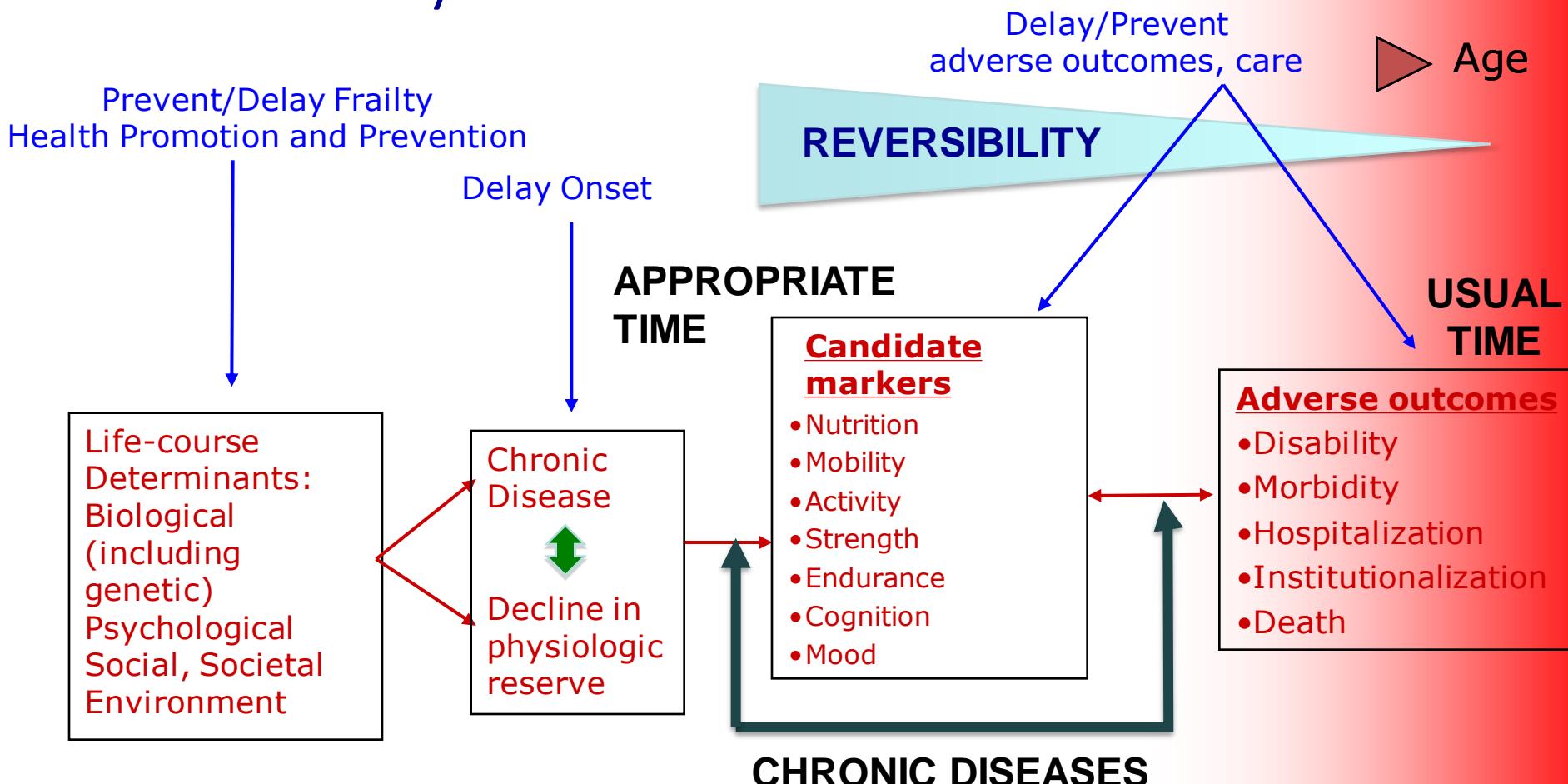


Pérdida progresiva de la capacidad para responder a las demandas



*Ferrucci et al., 2002; Gill, Gahbauer, Allore, & Han, 2006; Strandberg & Pitkala, 2007;
Xue, 2011; Pahor et al., 2014*

Frailty: a Complex Syndrome of Increased Vulnerability



Frailty in the clinical scenario

The aim of health care has changed substantially—after centuries of trying to live longer, the time for living better has come. This change in focus has two main

*Leocadio Rodriguez-Mañas, Linda P Fried
Lancet, March 2015

Envejecer... pero a qué precio?

INDEPENDIENTE-ROBUSTO



???????

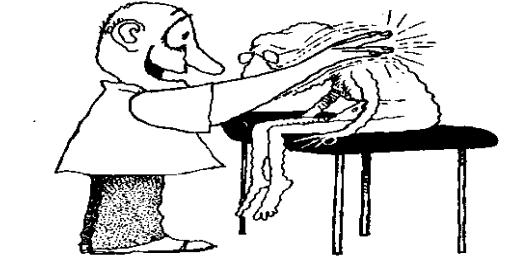
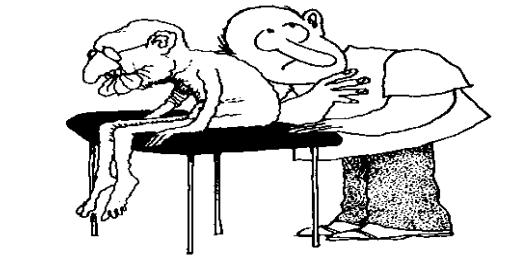
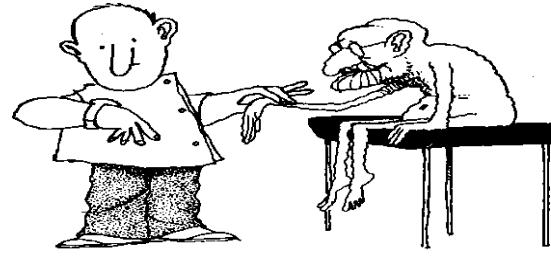
FRAGILIDAD



DEPENDIENTE-DISCAPACIDAD

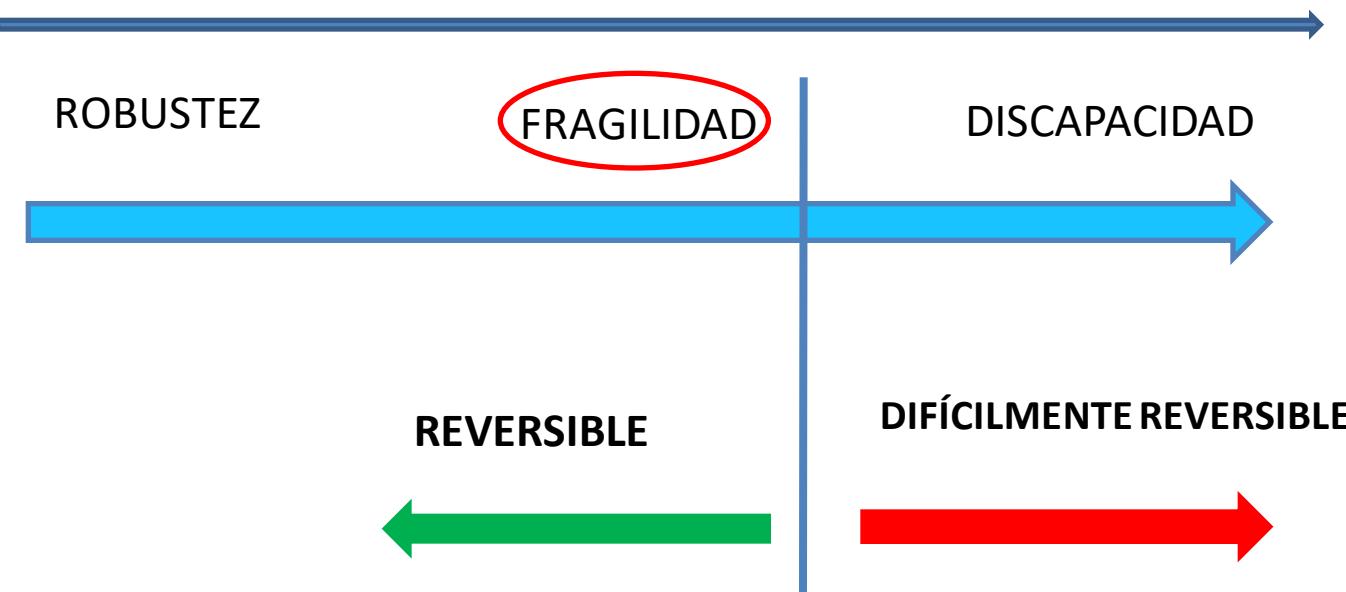
ciberfes

Necesitamos
diagnosticar
las situaciones
que preceden la
discapacidad
para intervenir
“a tiempo”

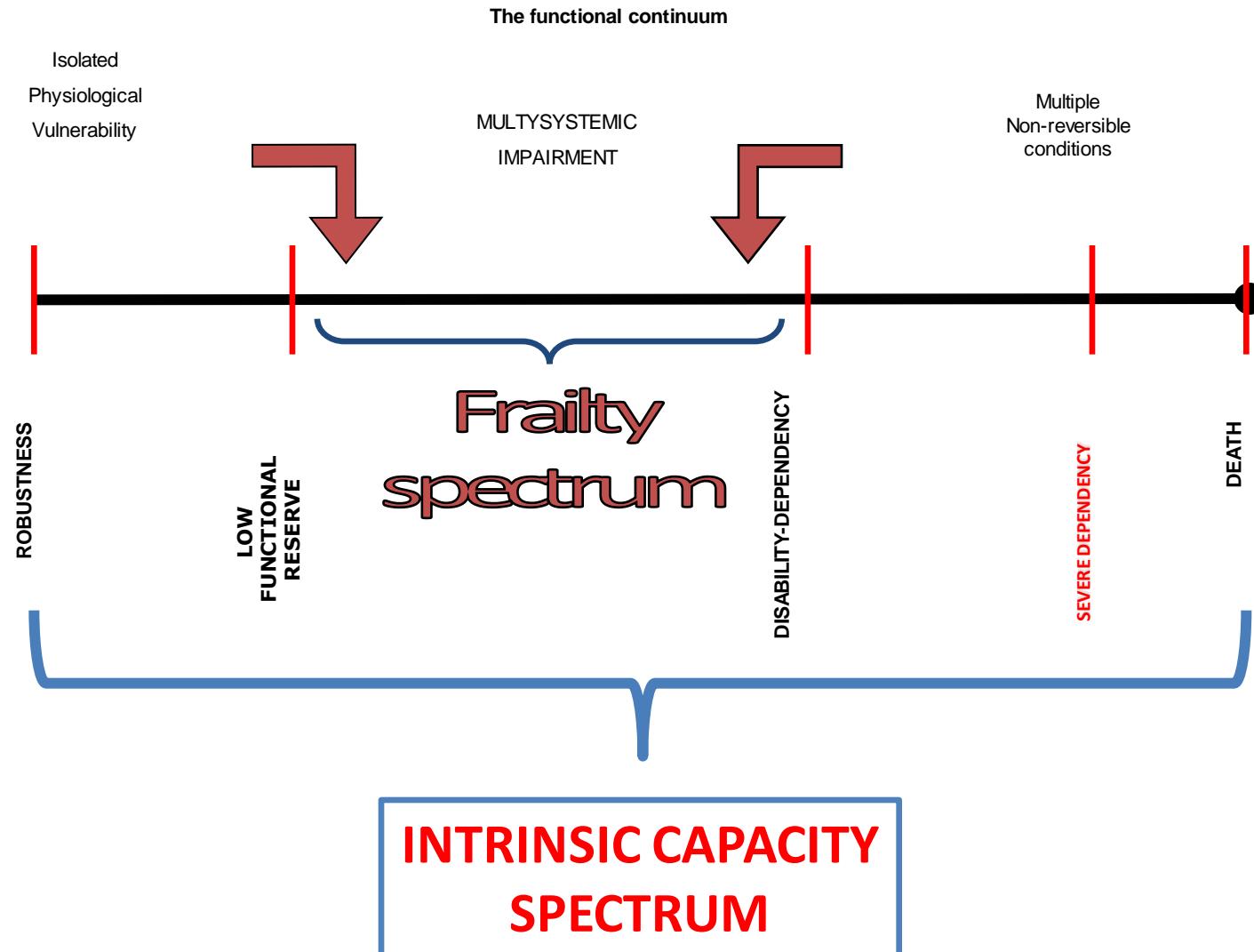


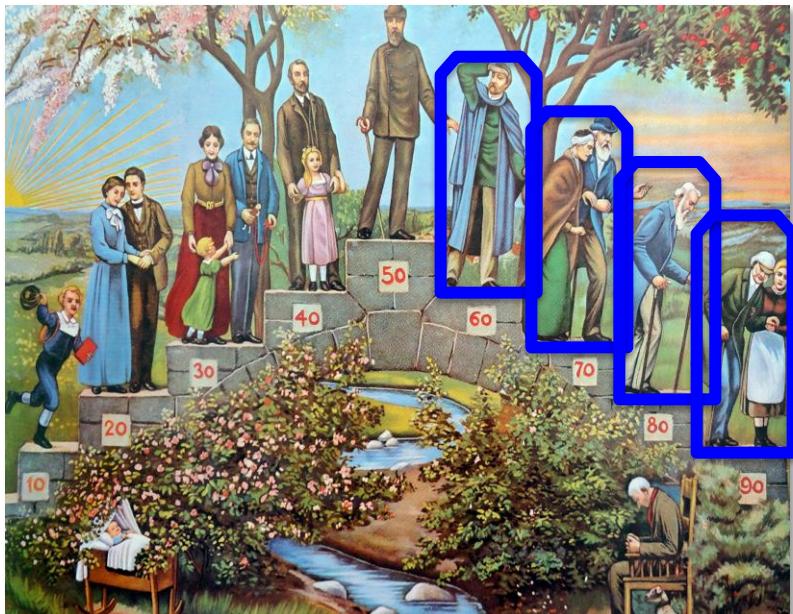
SÍNDROME DE FRAGILIDAD

Pérdida progresiva de la capacidad para responder a las demandas



*Ferrucci et al., 2002; Gill, Gahbauer, Allore, & Han, 2006; Strandberg & Pitkala, 2007;
Xue, 2011; Pahor et al., 2014*





+

MULTIPLE DISEASES CONDITIONS

FRAILTY

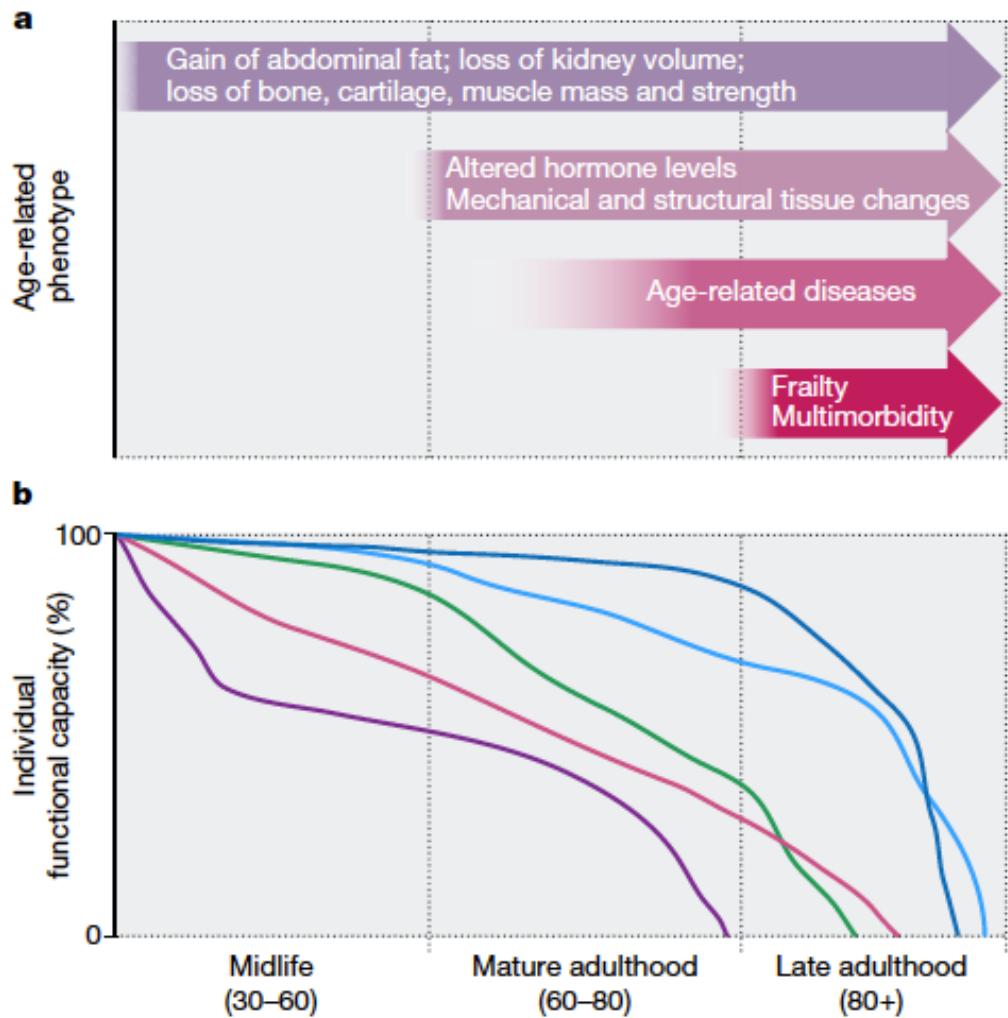


Fig. 3 | Schematic representation of the timing and progression of age-related phenotypes in adult humans. a, Age-related phenotypes include



*“When the facts change, I
change my mind. What do you do,
sir?”*

John Maynard Keynes

TITLE: THE THIRD TRANSITION – the Clinical Evolution oriented to the Contemporary Older Patient

Authors and affiliation

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Alan J Sinclair, MD, PhD

Diabetes Frail Ltd, UK and University of Aston, UK

JAMDA, 2017

**DEMOGRAPHIC
TRANSITION**



**EPIDEMIOLOGIC
TRANSITION**



**CLINICAL
TRANSITION**

Frailty as a dynamic functional state

CARE FOCUSED ON

Preventing
frailty

Preventing
Disability
Treating
Frailty

Preventing
Disability
Treating
Functional
Decline

Preventing
Dependency
Treating
Disability

Managing
Dependency

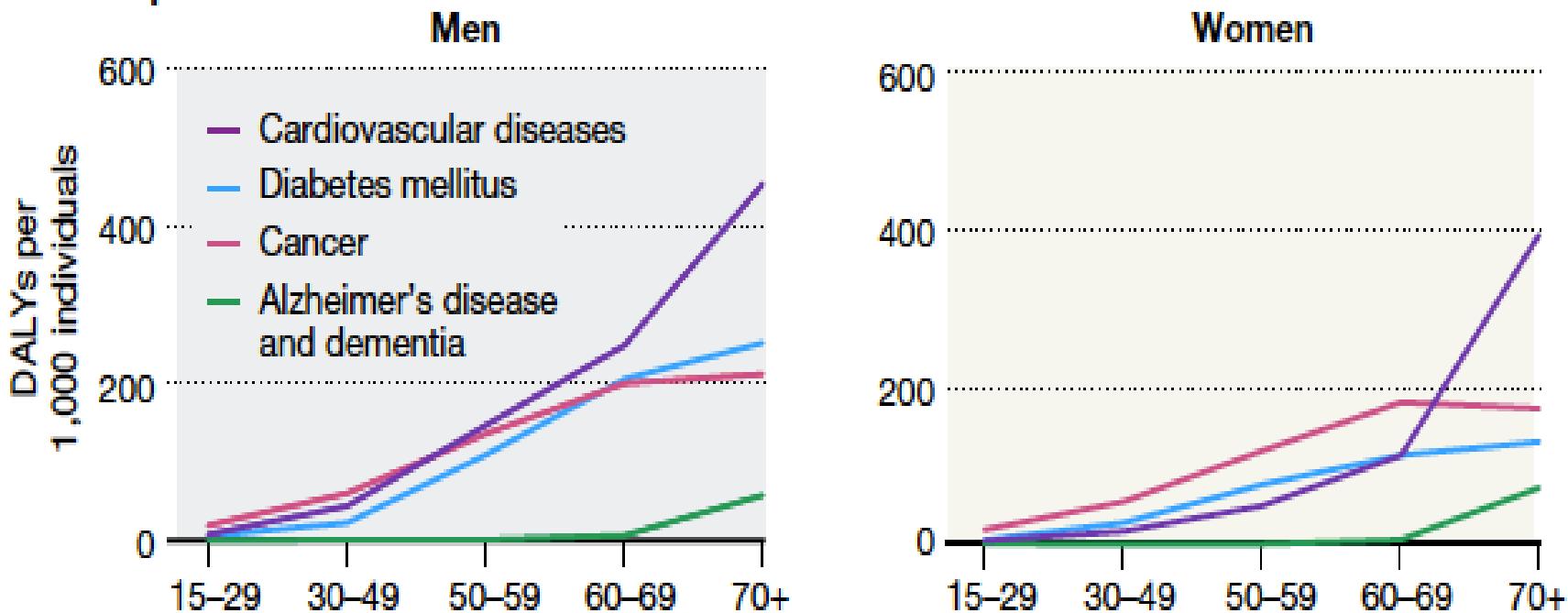
Potential reversibility of
functional decline

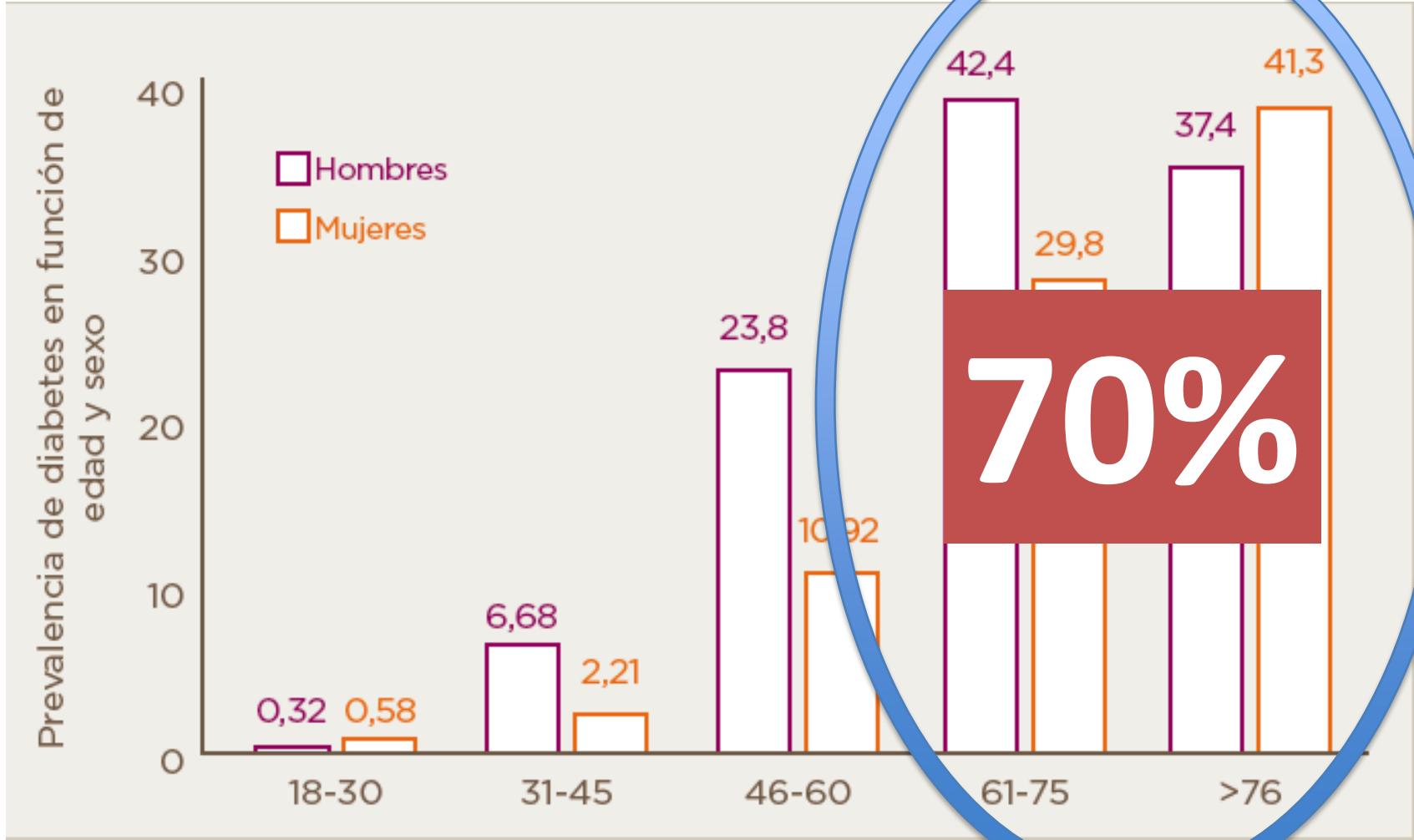
	Robust	Frail	Functional Limitation	Disability	Dependency
Definition					
Interventions to improve quality and outcomes - and prevent or delay further functional decline	What How Where ?	What How Where ?	What How Where ?	What How Where ?	What How Where ?

Facing up to the global challenges of ageing

Linda Partridge^{1,2*}, Joris Deelen^{1,3} & P. Eline Slagboom^{1,2*}

a Europe





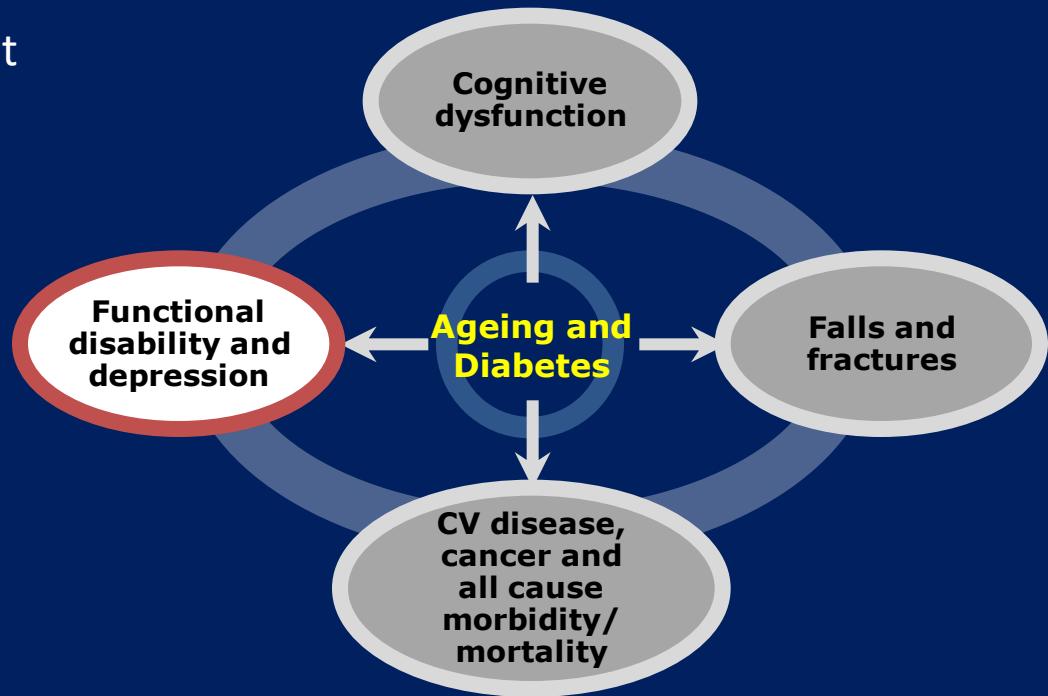
Gomez Huelgas R et al., Rev Clin Esp 2018

	1988-94	1995-99	2000-04	2005-09	2010-15	Average 10-year difference	10-year percentage change	p value for linear trend
Diabetes								
Sex								
Men	30.8 (25.7 to 35.9)	29.3 (26.2 to 32.5)	25.3 (23.0 to 27.6)	21.8 (20.1 to 23.4)	20.4 (19.1 to 21.7)	-5.2 (-7.0 to -3.4)	-12.4 (-22.9 to -0.4)	<0.0001
Women	19.3 (16.1 to 22.5)	22.4 (20.4 to 24.8)	22.0 (20.0 to 24.2)	18.3 (17.0 to 19.6)	16.7 (15.6 to 17.8)	-2.1 (-3.4 to -0.8)	-3.3 (-14.8 to 9.8)	0.0141
Age (years)								
20-44	5.1 (2.1 to 8.1)	3.5 (1.5 to 5.5)	5.3 (3.0 to 7.6)	5.3 (3.3 to 7.6)	4.9 (3.4 to 6.3)	0.4 (-0.8 to 1.7)	9.2 (-16.4 to 42.8)	0.7297
45-64	17.5 (12.2 to 22.7)	18.9 (15.6 to 22.1)	18.0 (15.4 to 20.5)	13.8 (12.3 to 15.2)	13.8 (12.3 to 15.2)	-2.9 (-5.0 to -0.8)	-16.1 (-25.4 to -5.8)	0.0408
65-74	47.2 (29.7 to 54.8)	51.4 (44.9 to 58.0)	37.1 (22.7 to 41.5)	20.6 (7.6 to 22.5)	26.5 (24.4 to 28.7)	-11.4 (-14.7 to -8.2)	-25.9 (-31.3 to -20.1)	<0.0001
≥75	90.0 (74.8 to 105.2)	91.9 (82.3 to 101.4)	87.8 (80.9 to 94.6)	74.9 (70.3 to 79.5)	68.3 (64.7 to 71.9)	-12.1 (-17.8 to -6.3)	-13.5 (-18.9 to -7.7)	0.0004
Ethnic origin								
Non-Hispanic white	24.8 (21.5 to 28.1)	27.1 (24.8 to 29.5)	23.9 (22.0 to 25.8)	20.6 (19.2 to 22.0)	19.2 (18.1 to 20.3)	-3.4 (-4.7 to -2.0)	-6.0 (-16.7 to 6.0)	<0.0001
Non-Hispanic black	26.8 (19.9 to 33.6)	19.0 (15.6 to 22.5)	24.7 (21.3 to 28.2)	21.3 (18.7 to 23.9)	17.8 (16.1 to 19.4)	-3.2 (-5.7 to -0.7)	-6.1 (-19.3 to 2.0)	0.0357
Other	20.5 (10.7 to 30.4)	20.0 (15.1 to 25.0)	20.0 (16.6 to 23.3)	13.6 (11.9 to 15.3)	13.3 (11.9 to 14.7)	-4.5 (-7.8 to -1.2)	-16.1 (-31.0 to 2.0)	0.0507
Without diabetes								
Sex								
Men	14.3 (13.6 to 15.1)	13.7 (13.1 to 14.3)	12.9 (12.4 to 13.4)	12.1 (11.7 to 12.4)	11.4 (11.1 to 11.7)	-1.4 (-1.7 to -1.0)	-3.6 (-7.9 to -0.2)	<0.0001
Women	9.0 (8.5-9.5)	9.2 (8.8-9.6)	9.0 (8.6-9.3)	8.5 (8.2-8.7)	8.4 (8.2-8.7)	-0.3 (-0.6 to -0.1)	3.6 (-0.6 to 7.9)	0.0065
Age (years)								
20-44	1.1 (1.0 to 1.3)	1.4 (1.2 to 1.5)	1.4 (1.2 to 1.5)	1.4 (1.3 to 1.5)	1.5 (1.3 to 1.6)	0.1 (0.1 to 0.2)	12.3 (5.5 to 19.6)	0.0011
45-64	5.2 (4.7 to 5.7)	4.3 (4.0 to 4.6)	4.4 (4.1 to 4.7)	4.5 (4.3 to 4.7)	4.5 (4.3 to 4.7)	-0.2 (-0.5 to 0.0)	-3.9 (-8.5 to 1.0)	0.0561
65-74	10.4 (7.6 to 21.2)	17.0 (16.6 to 19.1)	15.0 (14.0 to 16.9)	12.2 (12.4 to 14.0)	12.0 (11.4 to 12.7)	-3.6 (-4.4 to -2.7)	-19.8 (-23.7 to -15.7)	<0.0001
≥75	58.3 (55.1 to 61.5)	59.7 (57.2 to 62.1)	57.8 (55.7 to 60.0)	54.2 (52.6 to 55.8)	52.4 (50.9 to 53.9)	-3.0 (-4.6 to -1.5)	-4.5 (-7.0 to -1.9)	<0.0001
Ethnic origin								
Non-Hispanic white	11.1 (10.5 to 11.6)	11.1 (10.7 to 11.5)	10.4 (10.1 to 10.7)	9.9 (9.6 to 10.1)	9.6 (9.3 to 9.9)	-0.7 (-1.0 to -0.5)	-0.1 (-3.3 to 3.5)	<0.0001
Non-Hispanic black	15.2 (13.7 to 16.6)	13.0 (11.9 to 14.0)	14.1 (13.0 to 15.2)	12.5 (11.7 to 13.3)	11.2 (10.5 to 11.9)	-1.5 (-2.2 to -0.9)	-4.5 (-10.3 to 1.3)	<0.0001
Other	9.8 (7.6 to 12.0)	9.7 (8.6 to 10.9)	9.9 (9.0 to 10.8)	9.0 (8.4 to 9.6)	9.2 (8.7 to 9.8)	-0.3 (-1.2 to 0.5)	3.7 (-5.5 to 13.8)	0.4719

Data are deaths per 1000 person-years (95% CIs) unless stated otherwise, adjusted for sex, age group, and ethnic origin.

The frail, elderly patient with diabetes

- Older persons with diabetes are at higher risk than those without diabetes of:
 - Cancer mortality and vascular deaths
 - **Functional disability**
 - Geriatric syndromes: depression
 - Falls and fractures
 - 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.



Original Study

Diabetes and Risk of Frailty and Its Potential Mechanisms:
A Prospective Cohort Study of Older Adults

Esther García-Esquinas PhD ^{a,*}, Auxiliadora Graciani PhD ^a, Pilar Guallar-Castillón PhD ^a,
 Esther López-García PhD ^a, Leocadio Rodríguez-Mañas PhD ^b,
 Fernando Rodríguez-Artalejo PhD ^a

^aDepartamento de Medicina Preventiva y Salud Pública, Universidad Autónoma de Madrid / IdiPaz, and CIBER of Epidemiology and Public Health (CIBERESP), Madrid, Spain
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Diabetes is associated with higher risk of frailty after 3.5 yrs of follow-up. This risk is explained by,

- ✓ Unhealthy behaviour
- ✓ Poor glycemic control
- ✓ Altered serum lipid profile (HDL)

Only levels of HbA1c > 8% provides an increase risk of frailty/functional decline in older adults

Kalyani et al., Diabetes Care 2010
 Kalyani et al., JAGS 2012

Table 3

ORs (95% CIs) of Frailty in Diabetic Versus Nondiabetic Individuals With Progressive Adjustment for Possible Mechanism of the Association

	OR (95% CI)
Adjusted for age, sex, and educational level (basic model)	2.18 (1.42–3.37)
Additionally adjusted for health behaviors and morbidity	
Basic model and lifestyle factors (smoking, alcohol consumption, time spent watching TV, recreational activity, MEDAS, energy intake)	2.01 (1.28–3.16)
Basic model and abdominal obesity	1.96 (1.26–3.03)
Basic model and lifestyle factors and abdominal obesity (model 1)	1.83 (1.16–2.90)
Additionally adjusted for morbidity	
Model 1 and cardiovascular disease (heart disease, stroke, heart failure), cancer, chronic respiratory disease, arthritis, osteoarthritis, fracture (model 2)	1.76 (1.10–2.82)
Additionally adjusted for cardiometabolic biomarkers	
Model 2 and hs-CRP	1.71 (1.06–2.76)
Model 2 and fibrinogen	1.75 (1.09–2.80)
Model 2 and leptin	1.80 (1.12–2.88)
Model 2 and systolic blood pressure	1.79 (1.11–2.87)
Model 2 and HDL-cholesterol	1.64 (1.00–2.69)
Model 2 and HDL-cholesterol, triglycerides and LDL-cholesterol	1.47 (0.89–2.43)
Model 2 and HbA1c	1.51 (0.83–2.74)
Model 2 and all the above mediators (model 3)	1.32 (0.70–2.49)
Additionally adjusted for treatment of diabetes and of cardiovascular risk factors	
Model 3 and diabetes nutritional therapy	1.64 (0.77–3.49)
Model 3 and with oral antidiabetic drugs	1.01 (0.46–2.20)
Model 3 and insulin	1.29 (0.68–2.45)
Model 3 and treatment with nutritional therapy, oral antidiabetics, and/or insulin	1.28 (0.57–2.91)
Model 3 and antihypertensive drug treatment	1.35 (0.72–2.55)
Model 3 and lipid-lowering drug treatment	1.35 (0.72–2.55)
Model 3 and all the above treatments (model 4)	1.32 (0.58–2.98)

Analyses were based on 76 frailty cases among 1404 nondiabetic individuals and 39 frailty cases among 346 diabetic individuals.

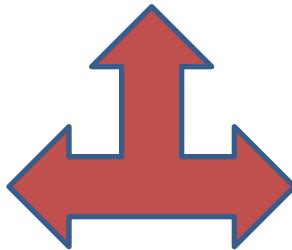
Note: Bold values are statistically significant $P < .05$.

COGNITIVE FUNCTION AND MOOD

DM: ↑ RISK OF COGNITIVE IMPAIRMENT AND DEMENTIA

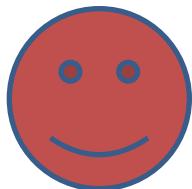
COGNITIVE IMPAIRMENT:

- Poor adherence to treatment
- ↑ hypoglycemias and < resolution capacity



DEPRESSION:

- Poor glycemic control
- Poor adherence to treatment
- Disabling disease and poor quality of life



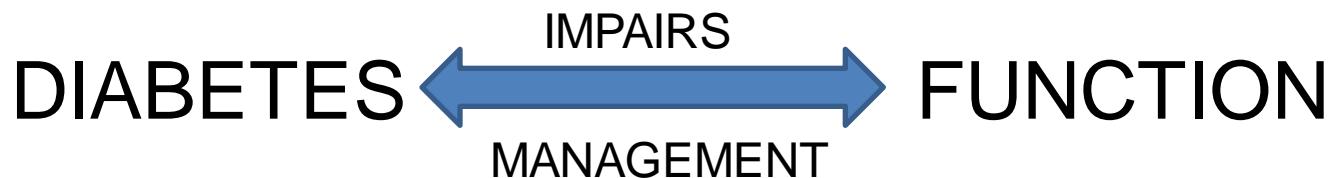
ASSESSMENT OF COGNITIVE FUNCTION



BENEFITS

- To detect dementia in the earliest stages
- To fit medication to the condition of the patient
- Optimise CVRF control
- Improvement in quality of life of both the patient and the carer and the costs associated to the disease

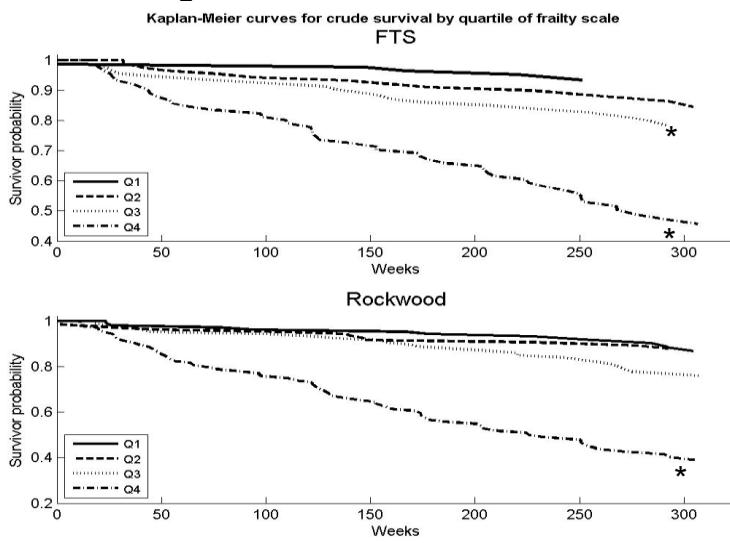
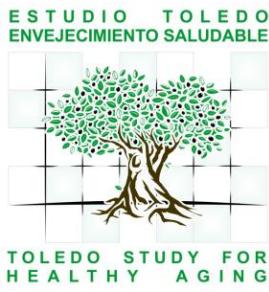
DIABETES AND FUNCTION



Frailty, but not disease, accounts for the excess of mortality and disability risks, in older people with DM (Toledo Study of Healthy Ageing)

Variable	Model 1. Death with Charlson					
	FTS			Rockwood FS		
	HR	LL	UL	HR	LL	UL
Age	1,068	1,022	1,116	1,075	1,037	1,114
Sex (female)	0,510	0,328	0,795	0,540	0,366	0,797
Charlson Index	1,009	0,894	1,138	0,987	0,882	1,104
Disability	1,292	0,748	2,231	1,095	0,653	1,839
Frailty I.*	1,042	1,025	1,059	1,063	1,041	1,085
Frailty I.**	1,229	1,134	1,333	1,356	1,222	1,503
Frailty I.***	1,511	1,286	1,776	1,838	1,494	2,260

Variable	Model 3: Incident disability with Charlson					
	FTS			Rockwood FS		
	OR	LL	UL	OR	LL	UL
Age	1,051	0,980	1,127	1,092	1,026	1,161
Sex (female)	1,475	0,759	2,868	2,077	1,152	3,744
Charlson Index	1,129	0,951	1,341	1,042	0,879	1,235
Frailty I.*	1,031	1,005	1,058	1,053	1,012	1,095
Frailty I.**	1,165	1,025	1,325	1,292	1,060	1,576
Frailty I.***	1,358	1,050	1,757	1,670	1,123	2,482



VIEWPOINT

Incorporating Lag Time to Benefit Into Prevention Decisions for Older Adults

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Prevention holds the promise of maintaining good health by testing, diagnosing, and treating conditions before they cause symptoms. However, prevention can harm as well as help when tests or treatments for asymptomatic conditions cause immediate complications. "Lag time to benefit" is defined as the time between a preventive intervention (when complications and harms are most likely) to the time when improved health outcomes are seen.¹ Just as different interventions have different magnitudes of benefit, different preventive interventions have different lag times to benefit, ranging from 6 months for statin therapy for secondary prevention to more than 10 years for prostate cancer screening.² Many standardized measures such as relative risk, odds ratio, and absolute risk reduction quantify the magnitude of benefit ("How much will it help?"). However, the measures and methodologies to calculate a lag time to benefit ("When will it help?") are underdeveloped and often not reported.

This Viewpoint will describe how guidelines are already using age as a crude marker for life expectancy and show how explicitly accounting for life expectancy could improve prevention decisions. To help clinicians apply this framework, the Viewpoint will outline ways to determine lag time to benefit and life expectancy, highlighting how online life expectancy calculators (eg, <http://epronosis.ucsf.edu>) may facilitate prediction of life expectancy. The Viewpoint also will demonstrate how this framework could be applied for a hypothetical patient during a Medicare Annual Wellness visit.

When Will It Help?
For older adults, the question "When will it help?" is just as important as "How much will it help?" If an older adult's life expectancy is substantially shorter than the lag time to benefit for a preventive intervention, administering that intervention exposes them to the immediate risks of the intervention with little likelihood of surviving long

and falls, but decreased cardiovascular outcomes occur many months or years later. Glycemic treatment for diabetes can cause immediate hypoglycemia, with the hope of preventing vascular complications many years in the future. Given immediate risks and delayed benefits, treatments for asymptomatic conditions should also be targeted to older patients whose life expectancy is greater than the lag time to benefit.

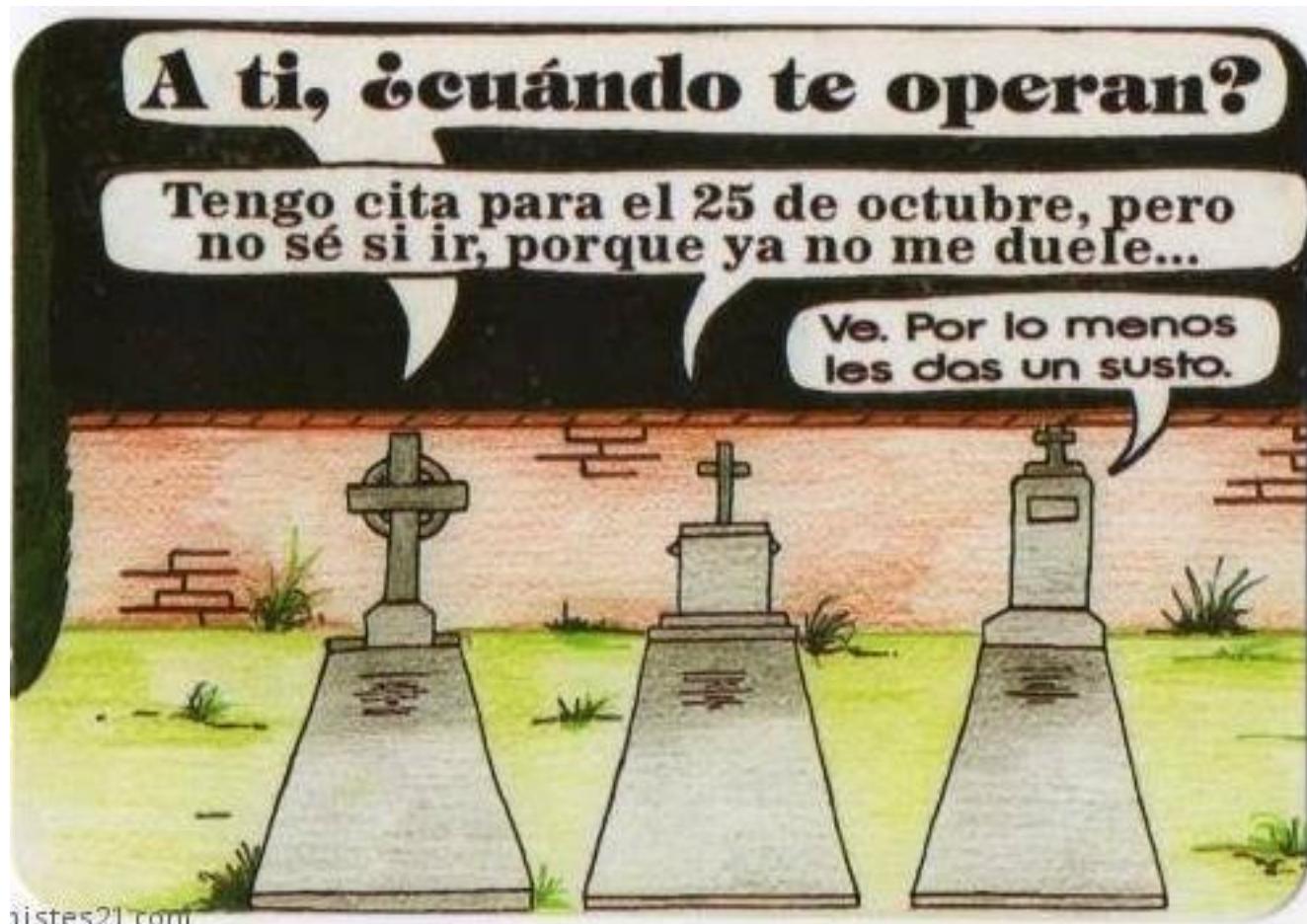
Juxtaposing an older patient's life expectancy and the lag time to benefit may help clinicians identify which patients are more likely to be helped by a preventive intervention and which patients are more likely to be harmed. A general approach involves the following: (1) estimate the patient's life expectancy; (2) estimate the preventive intervention's lag time to benefit; (3A) if life expectancy is much greater than lag time to benefit, the intervention may help and should generally be recommended; (3B) if life expectancy is much less than lag time to benefit, the intervention is more likely to harm and generally should not be recommended; (3C) if life expectancy and lag time to benefit are roughly equivalent, the benefits vs harms of the preventive intervention are a "close call," and patient preferences (eg, the degree of importance placed on the potential benefits and harms) should play the dominant role in decision making.

Moving Beyond Age as a Crude Marker for Life Expectancy

Many guidelines use age as the main criterion for recommending preventive interventions, with the specific age threshold determined by the average life expectancy for the selected age group. For example, the US Preventive Services Task Force recommends routine colorectal cancer screening for older adults aged 50 to 75 years.⁴ One reason for the threshold of 75 years is that the average life expectancy for 75-year-old US adults (11.1 years in 2000)⁵ is similar to the lag time to benefit for colorectal cancer screening

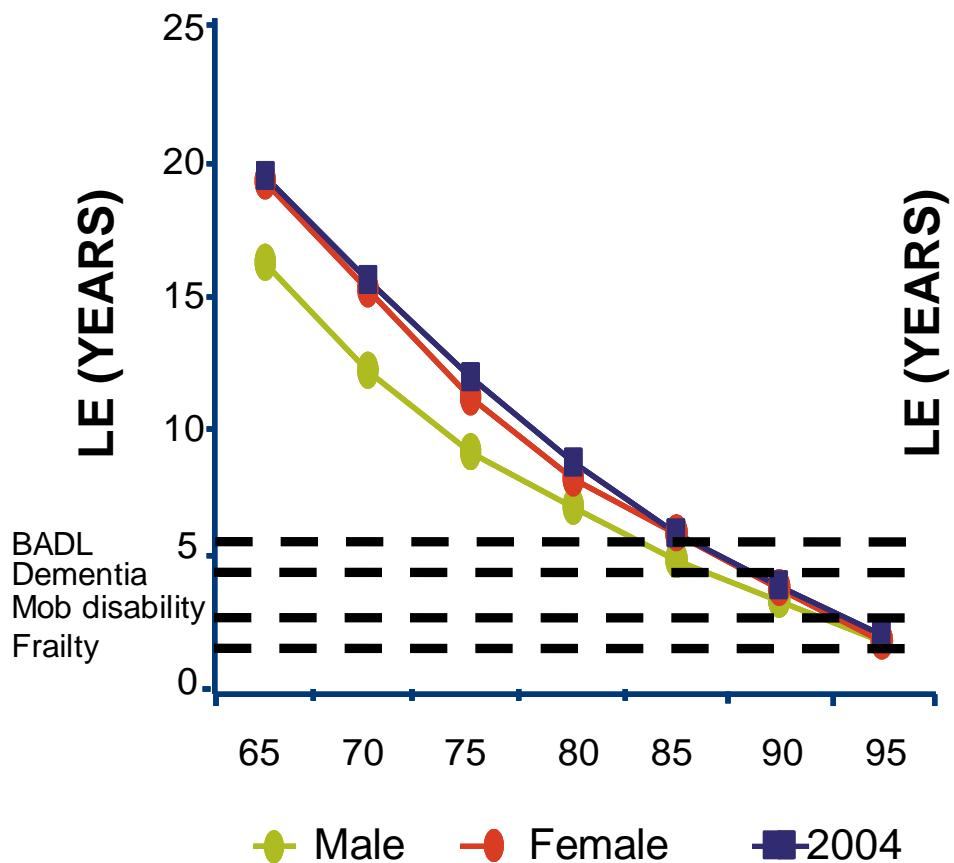
tomatic conditions cause immediate complications. "Lag time to benefit" is defined as the time between a preventive intervention (when complications and harms are most likely) to the time when improved health outcomes are seen.¹ Just as different interventions have dif-

Lo que ha de ocurrir despues de la muerte....

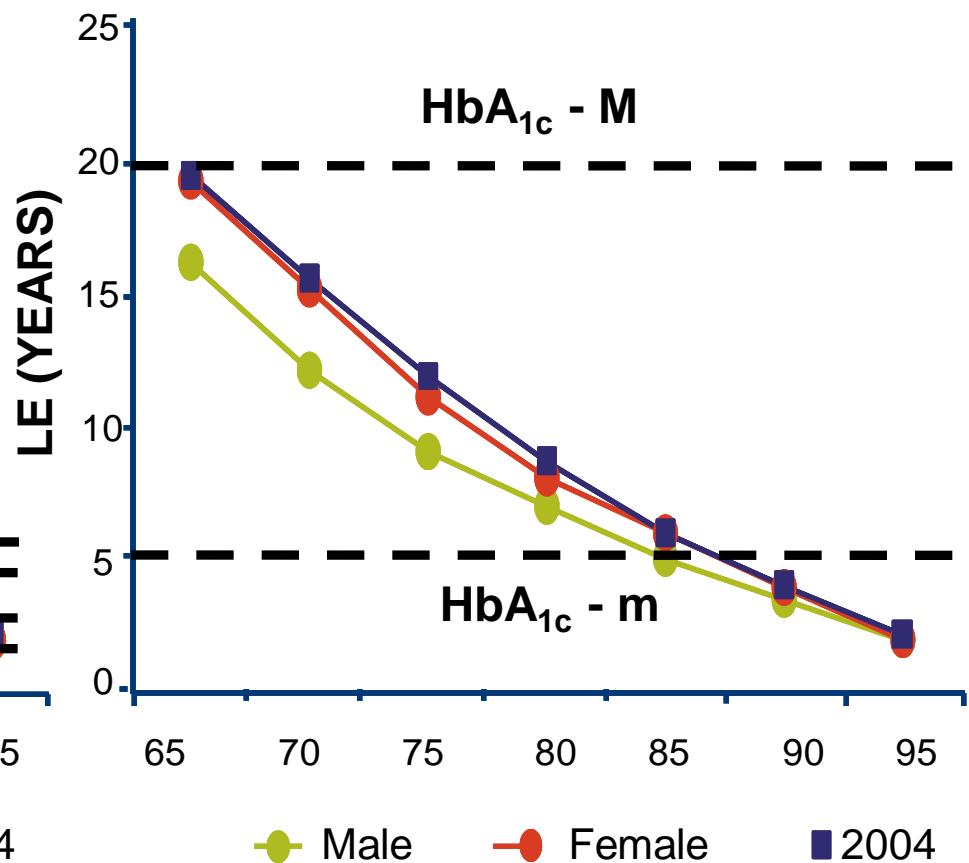


....simplemente, no ocurre

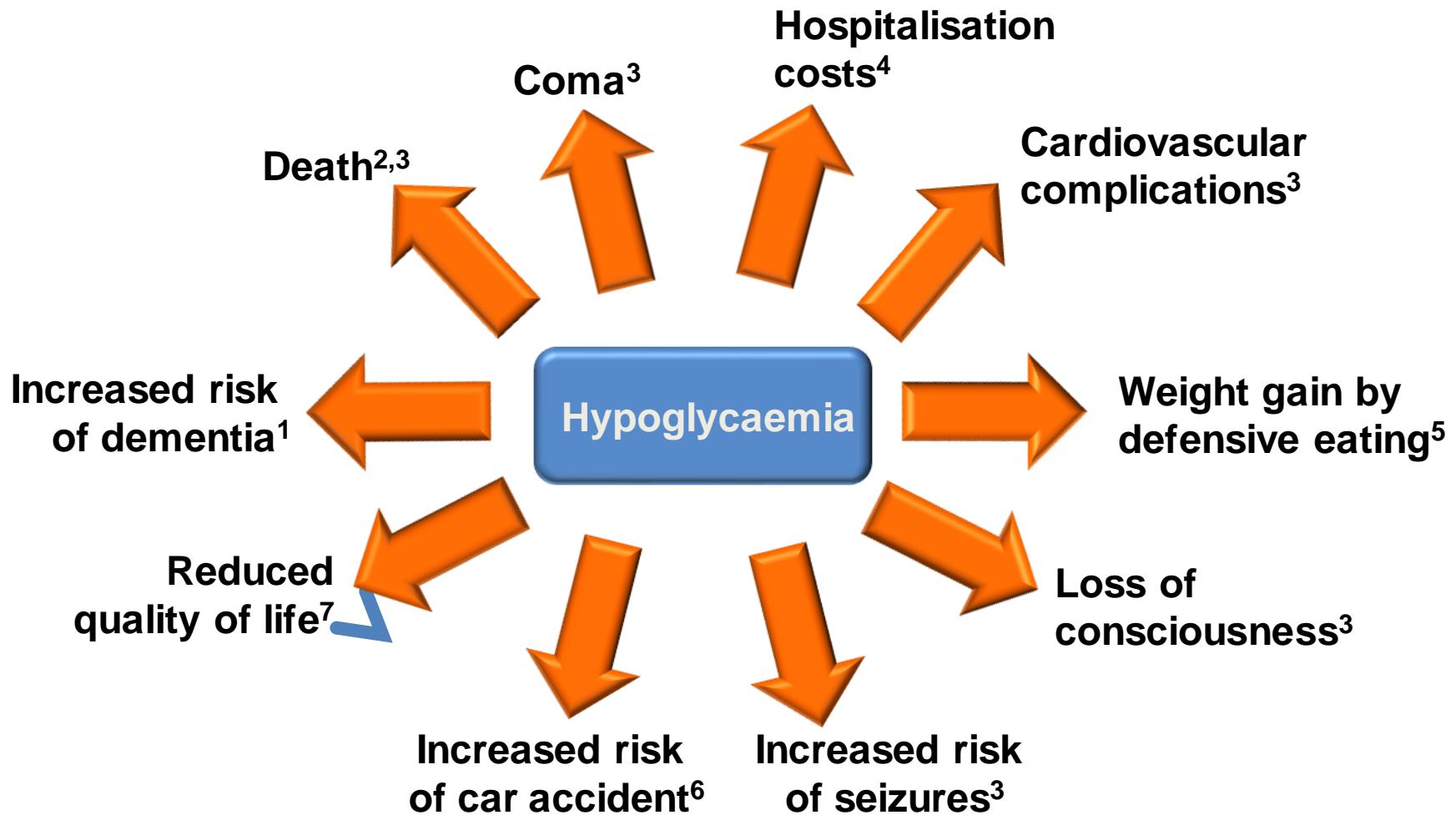
Time for functional decline



Time for benefit (CV disease) from interventions in people with Type 2 DM



The consequences of hypoglycaemia



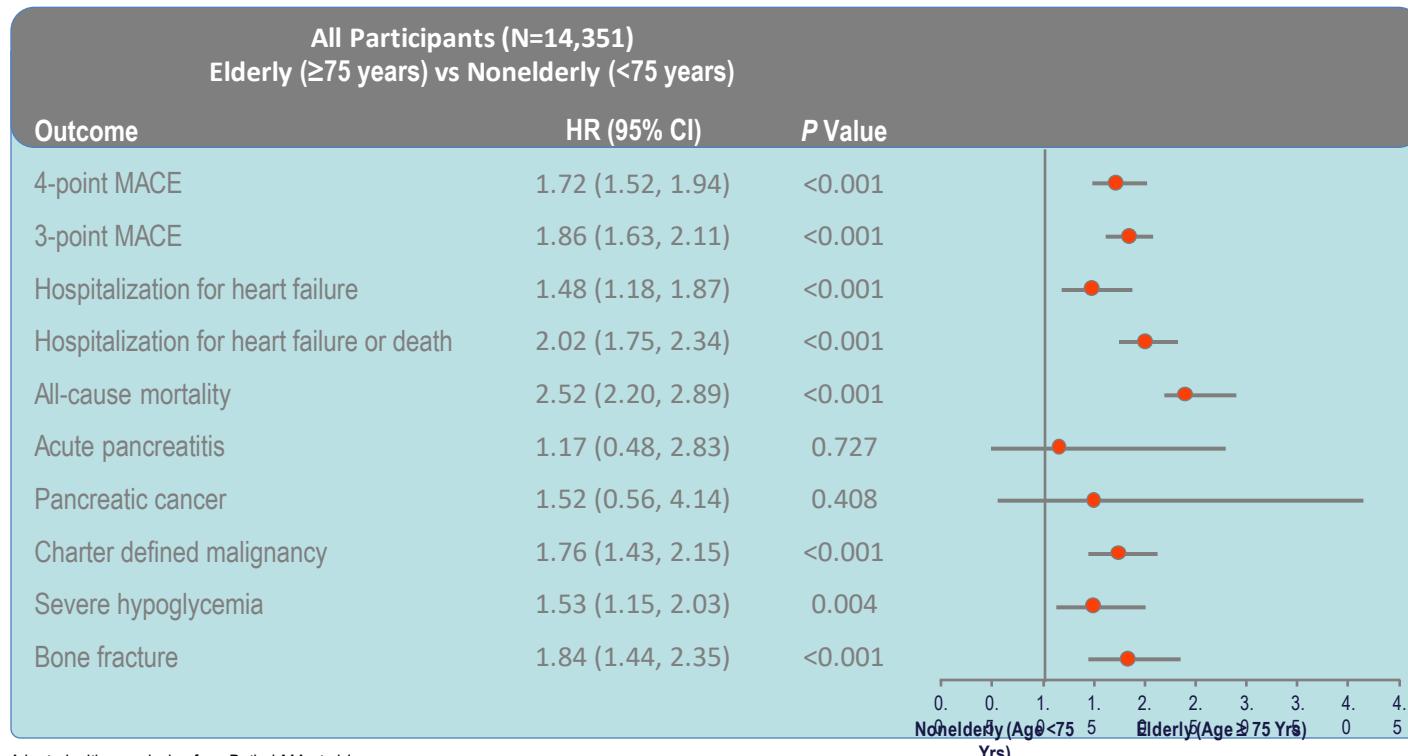
¹Whitmer RA, et al. *JAMA*. 2009; 301: 1565– 72; ²Bonds DE, et al. *BMJ*. 2010; 340: b4909;

³Barnett AH. *Curr Med Res Opin*. 2010; 26: 1333–1342; ⁴Jönsson L, et al. *Value Health*. 2006; 9: 193–198;

⁵Foley JE, Jordan J. *Vasc Health Risk Manag*. 2010; 6: 541–548; ⁶Begg IS, et al. *Can J Diabetes*. 2003; 27: 128–140;

⁷McEwan P, et al. *Diabetes Obes Metab*. 2010; 12: 431–436.

Safety of Sitagliptin in Elderly Patients With T2DM in TECOS: Primary and Key Secondary Outcomes in the Elderly vs Nonelderly Cohorts¹



Adapted with permission from Bethel MA et al.¹

T2DM = type 2 diabetes mellitus; TECOS = Trial Evaluating Cardiovascular Outcomes With Sitagliptin; HR = hazard ratio; CI = confidence interval; MACE = major adverse cardiovascular events.

1. Bethel MA et al. *Diabetes Care*. 2017. doi: 10.2337/dc16-1135.



Safety of Sitagliptin in Elderly Patients With T2DM in TECOS: Primary and Key Secondary Outcomes in the Elderly Cohort by Treatment Group¹



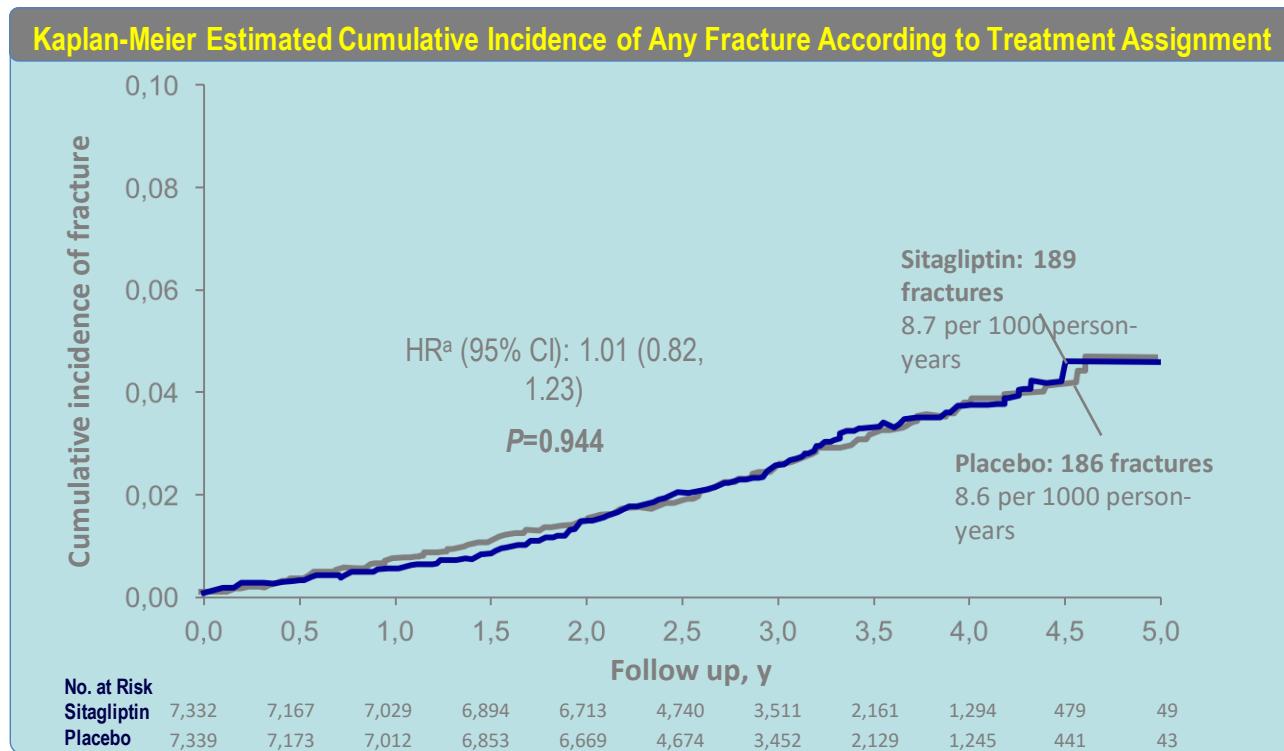
Adapted with permission from Bethel MA et al.¹

T2DM = type 2 diabetes mellitus; TECOS = Trial Evaluating Cardiovascular Outcomes With Sitagliptin; HR = hazard ratio; CI = confidence interval; MACE = major adverse cardiovascular events.

1. Bethel MA et al. *Diabetes Care*. 2017. doi: 10.2337/dc16-1135.



Sitagliptin and Risk of Fractures in T2DM in TECOS: Cumulative Incidence of Fracture¹



Adapted with permission from Josse RG et al.¹

^aUnadjusted HR.

T2DM = type 2 diabetes mellitus; TECOS = Trial Evaluating Cardiovascular Outcomes With Sitagliptin; HR = hazard ratio; CI = confidence interval.

1. Josse RG et al. *Diabetes Obes Metab*. 2017;19:78–86.



DM ALONG THE TIME



1922



Focus on

- Type 1 DM
- Children/Young people
- To Save lives
- Starvation

PRE-TREATMENT



POST-TREATMENT

¡¡FIRST TREATMENT WITH INSULIN!!

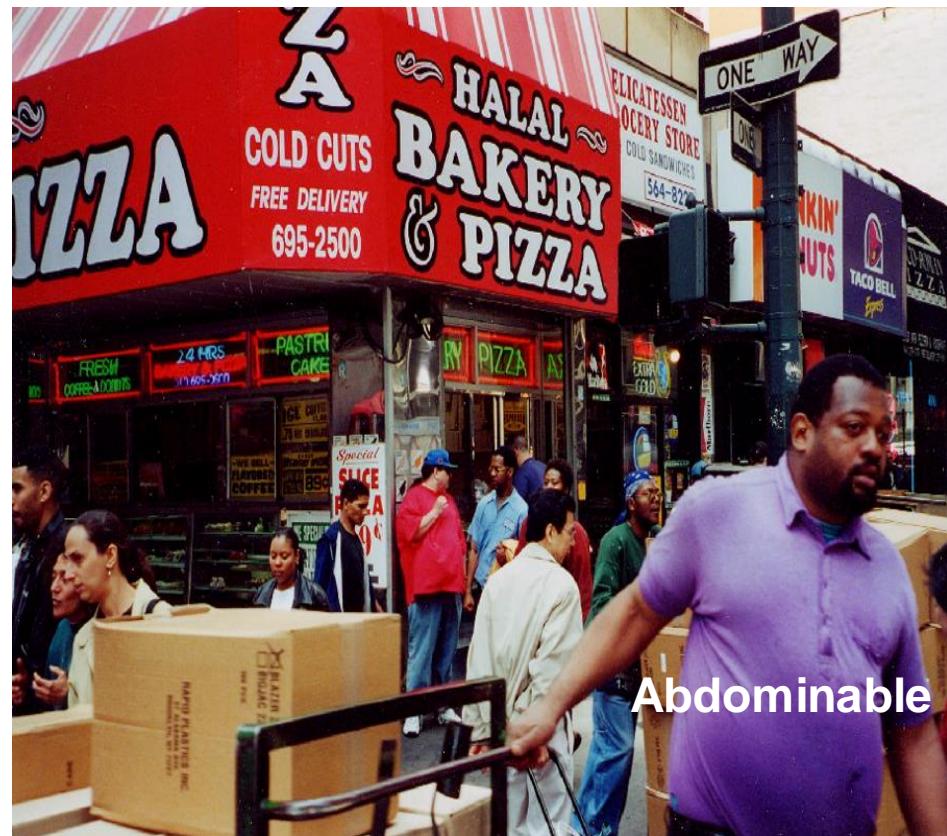
DM ALONG THE TIME



1976

Focus on

- Type 2 DM
- Middle-age people
- To Save lives
- CVD



Abdominable

DM ALONG THE TIME

¡LA DECIMOTERCERA!



2018



Focus on

- Type 2 DM
- Older adults
- To avoid disability
- To avoid dependency



OBJETIVOS

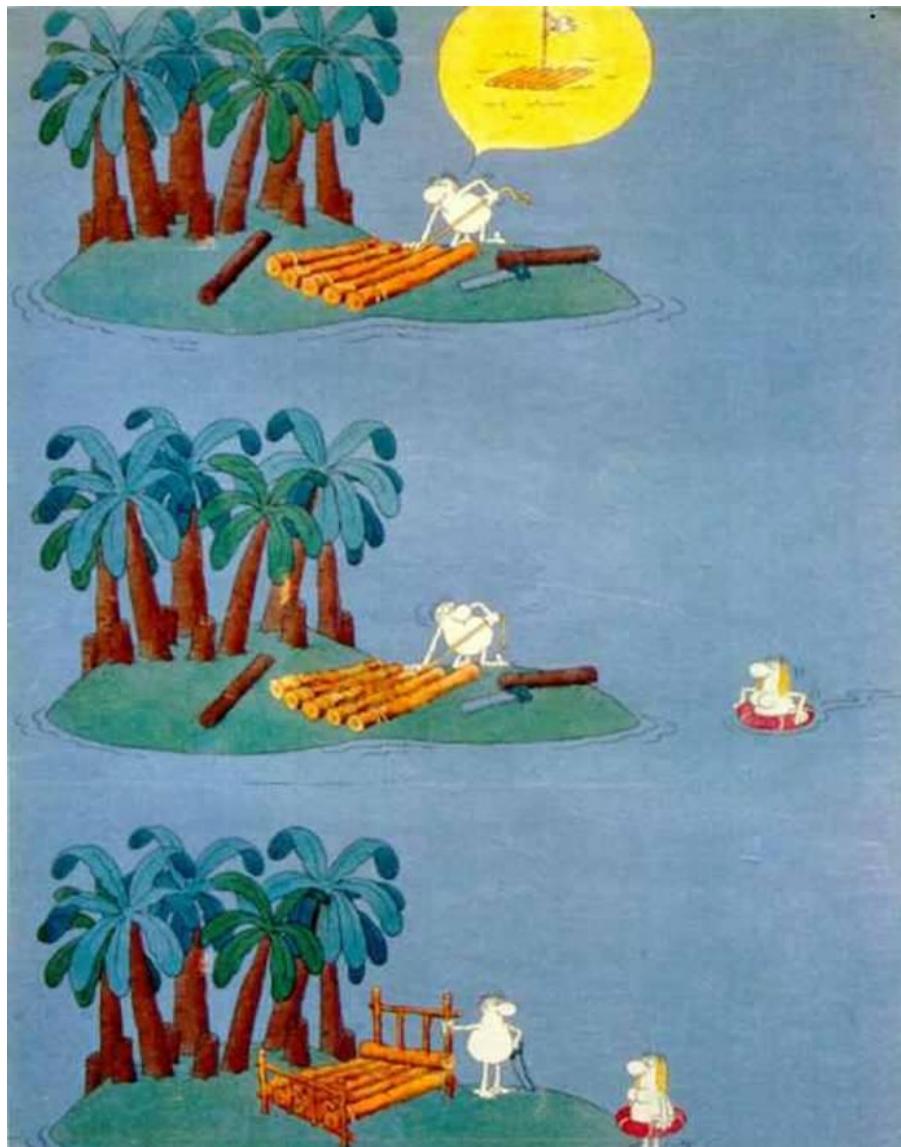
nuevos retos, nuevas situaciones,
SIGNIFICAN

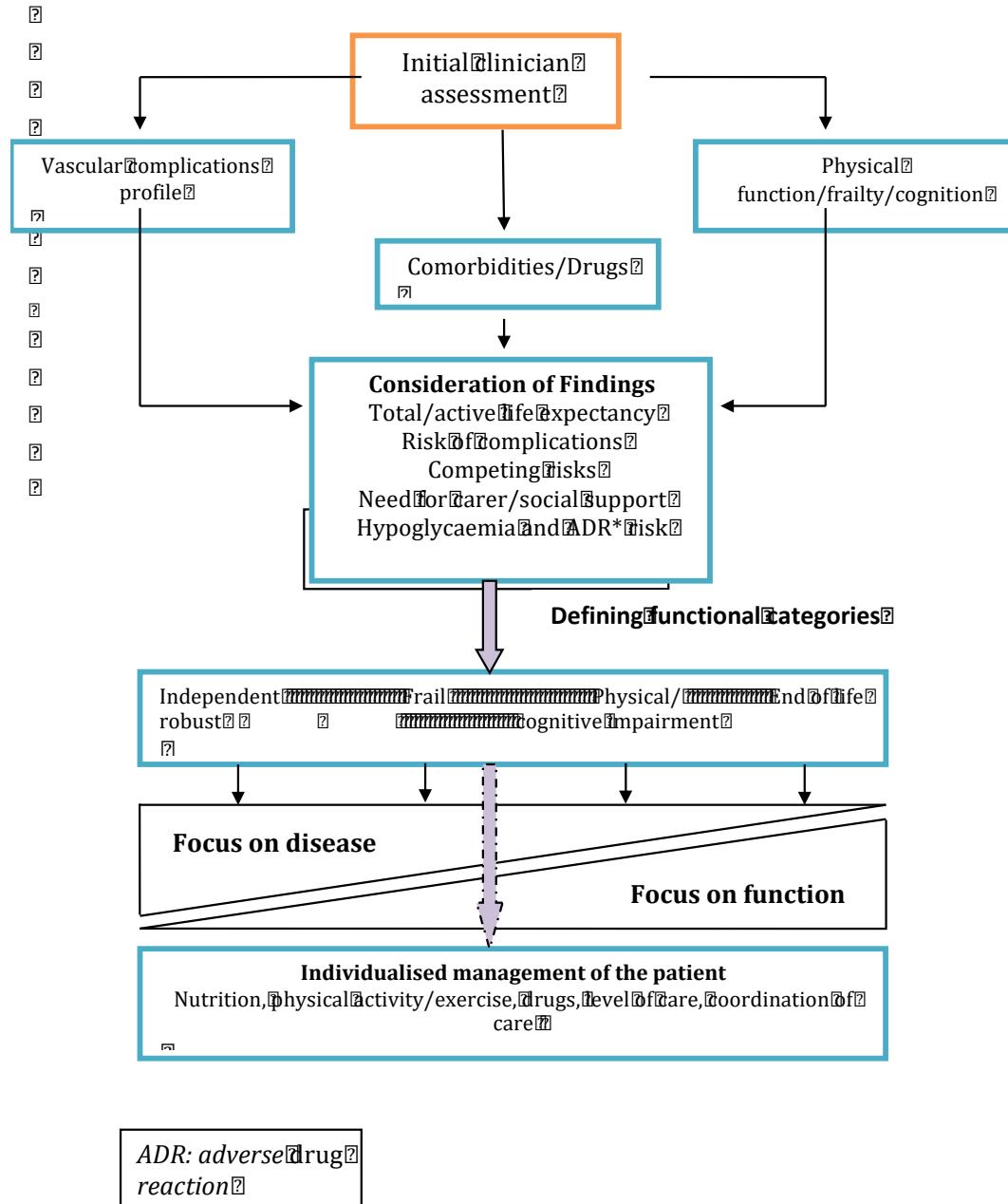
nuevos servicios con nuevos objetivos

- ✓ Para evitar las consecuencias de la DM sobre la función
- ✓ En el marco temporal adecuado

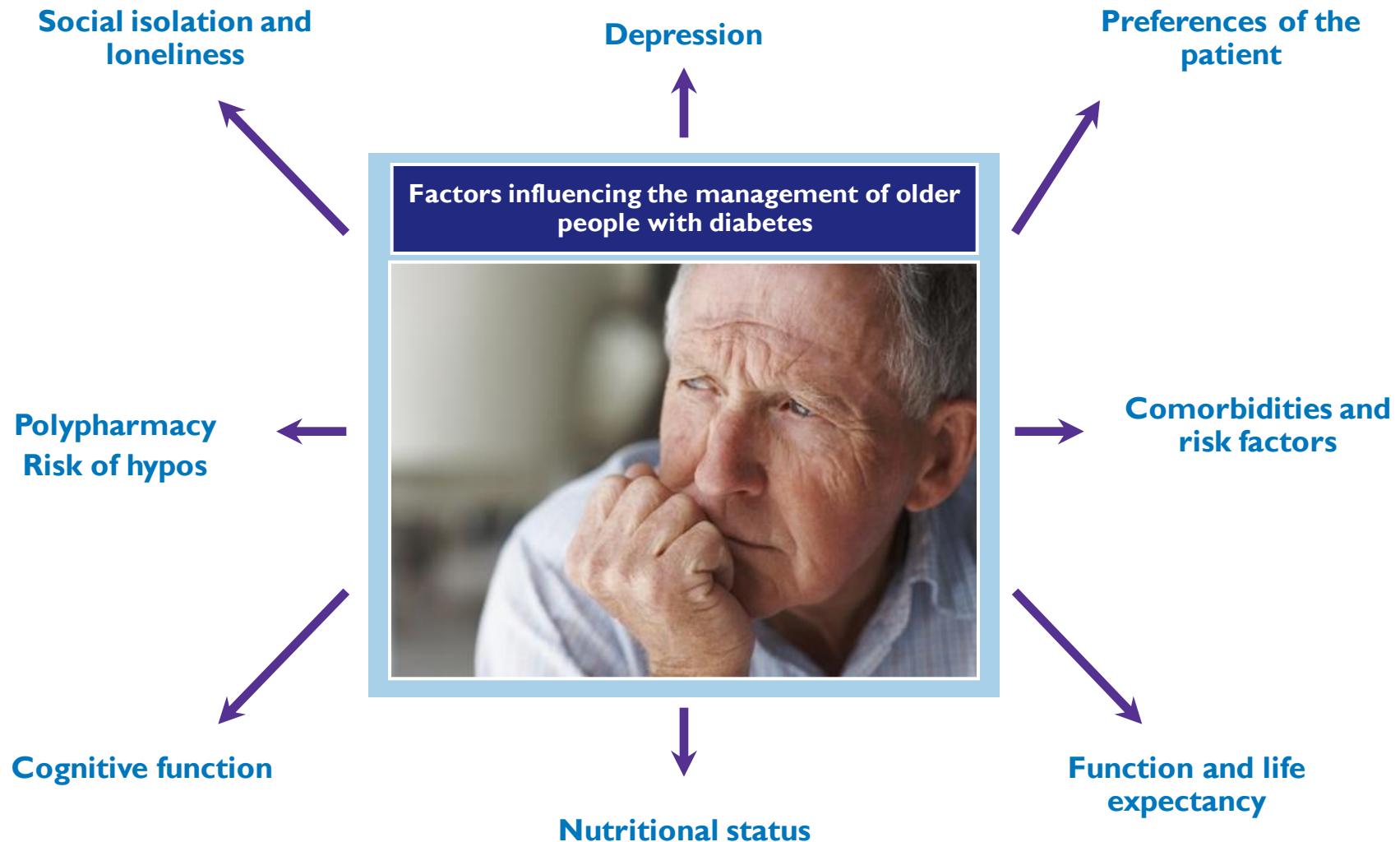
Pero tambien

- ✓ Para evitar consecuencias no deseadas de los tratamientos





Clinical assessment of older people with DM



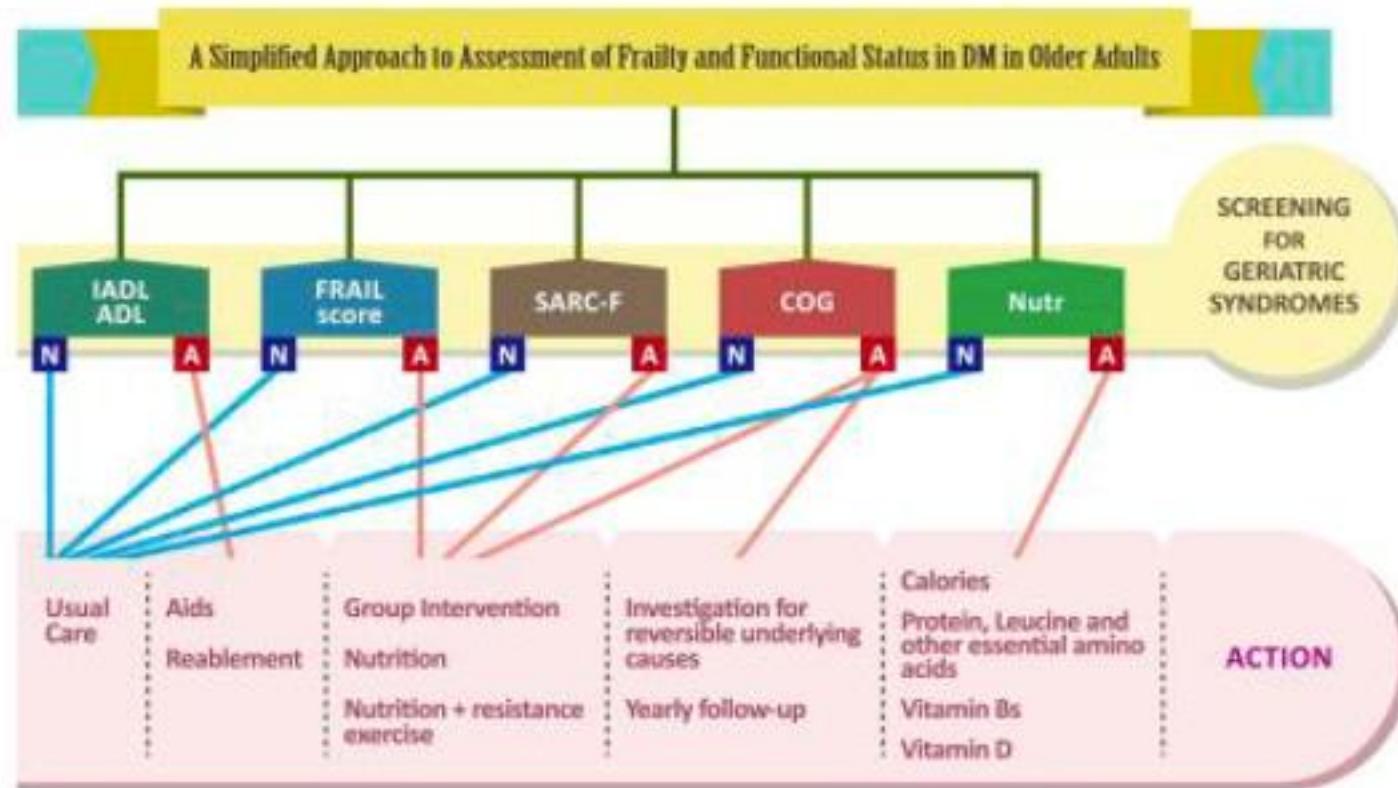
INDIVIDUALIZATION OF TARGETS AND TREATMENT

- LIFE STYLE MODIFICATIONS (PE and NUTRITION)
- DRUGS ALLOWING TO ACHIEVE THE TARGETS BUT...
- WITH THE LOWEST RISK OF ADVERSE REACTIONS
 - HYPOS
 - FALLS/FRACTURES



2 - Assessment Algorithms

2 (A): Simplified Version



N=Normal; A=Abnormal;

DM=diabetes mellitus; IADL=instrumental activities of daily living; ADL=activities of daily living;

SARC=sarcopenia; COG=cognitive impairment; Nutr=nutrition.

AGS-ADA (2012)

Table 1—A framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Patient characteristics/ health status	Rationale	Reasonable A1C goal (A lower goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden)	Fasting or preprandial glucose (mg/dL)	Bedtime glucose (mg/dL)	Blood pressure (mmHg)	Lipids
Healthy (Few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5%	90–130	90–110	<140/80	Skin unless contraindicated or not tolerated
Complex/intermediate (Multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild to moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90–150	100–110	<140/80	Skin unless contraindicated or not tolerated
Very complex/poor health (Long-term care or end-stage chronic illnesses** or moderate to severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%†	100–180	110–200	<150/90	Consider likelihood of benefit with statin (secondary prevention moreso than primary)

4.2. Glucose regulation [37-44]

4.2.1. Targets

1. For older patients with type 2 diabetes, with single system involvement (free of other major co-morbidities), a target HbA_{1c} range of 7-7.5% should be aimed for (DCC T aligned). Evidence level 1+, Grade of recommendation A. The precise target agreed will depend on existing cardiovascular risk, presence of microvascular complications, and ability of individual to self-manage.

2. For frail (dependent; multisystem disease; care home residency including those with dementia) patients where the hypoglycaemia risk is high and symptom control and avoidance of metabolic decompensation is paramount, the target HbA_{1c} range should be 7.6-8.5%. Evidence level 1+, Grade of recommendation A.

IAGG-Experts-EDWPOP (2012)

Glucose Targets

Consensus statements

- (1) The clinician must consider individual comorbidities, and cognitive and functional status when determining what glucose goals should be agreed with the patient and/or carer.
- (2) In general, on treatment, an HbA_{1c} target range of 53 to 59 mmol/mol (HbA_{1c} 7.0%–7.5 %) should be aimed for.
- (3) To reduce the risk of hypoglycemia, no patient should have a fasting glucose on treatment of less than 6.0 mmol/L; "Not below 6."
- (4) No patient should commence glucose-lowering therapy with drugs until the fasting glucose level is consistently 7 mmol/L or higher; "Not before 7."
- (5) Low blood glucose states (levels of glucose of <5.0 mmol/L) should be strictly avoided.
- (6) A random glucose level higher than 11.0 mmol/L should be avoided to minimize symptoms and reduce the risk of other diabetes-related complications.

These values are a guide to treatment and in cases of functional dependence, care home residency, dementia, end-of-life care, and other high dependency states, they may need adjusting to reduce the risk of hypoglycemia and to enhance patient safety.

EDWPOP (2011)

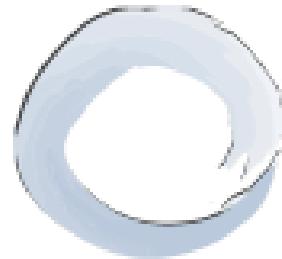
IDF GUIDELINES-DECEMBER 2013

The following chapter structure has been adopted:

- **Recommendations:**

Specific recommendations are made for each of the functional categories detailed in *Chapter 4: Functional categories of older people with diabetes*.

General
Category 1: Functionally Independent
Category 2: Functionally Dependent:
Sub-category A: Frail
Sub-category B: Dementia
Category 3: End of Life Care



INTERNATIONAL DIABETES FEDERATION
**MANAGING OLDER PEOPLE
WITH TYPE 2 DIABETES**
GLOBAL GUIDELINE



Table 2. General glycaemic targets according to functional category*

Functional category	General glycated haemoglobin target
Functionally Independent	7.0-7.5% / 53-59 mmol/mol
Functionally dependent	7.0-8.0% / 53-64 mmol/mol
• Frail	• Up to 8.5% / 70 mmol/mol
• Dementia	• Up to 8.5% / 70 mmol/mol
End of life	Avoid symptomatic hyperglycaemia

Standards of Medical Care in Diabetes—2016

Table 2—Framework for considering diabetes management goals

	Special considerations	Rationale	A1C	Fasting and premeal blood glucose targets	Glucose monitoring
Community-dwelling patients at skilled nursing facility for short rehabilitation	<ul style="list-style-type: none"> • Rehabilitation potential • Goal to discharge home 	<ul style="list-style-type: none"> • Need optimal glycemic control after recent acute illness 	<ul style="list-style-type: none"> • Avoid relying on A1C due to recent acute illness • Follow current glucose trends 	<ul style="list-style-type: none"> • 100–200 mg/dL 	<ul style="list-style-type: none"> • Monitoring frequency based on complexity of regimen
Patients residing in LTC	<ul style="list-style-type: none"> • Limited life expectancy • Frequent changes in health impacting glucose levels 	<ul style="list-style-type: none"> • Limited benefits of intensive glycemic control • Focus needs to be on better quality of life 	<ul style="list-style-type: none"> • <8.5% (69 mmol/mol) • Use caution in interpreting A1C due to presence of many conditions that interfere with A1C levels 	<ul style="list-style-type: none"> • 100–200 mg/dL 	<ul style="list-style-type: none"> • Monitoring frequency based on complexity of regimen and risk of hypoglycemia
Patients at end of life	<ul style="list-style-type: none"> • Avoid invasive diagnostic or therapeutic procedures that have little benefit 	<ul style="list-style-type: none"> • No benefit of glycemic control except avoiding symptomatic hyperglycemia 	<ul style="list-style-type: none"> • No role of A1C 	<ul style="list-style-type: none"> • Avoid symptomatic hyperglycemia 	<ul style="list-style-type: none"> • Monitoring periodically only to avoid symptomatic hyperglycemia

Overtreatment of hyperglycemia in older people

Figure 1. Achieved Glycemic Control Among Older US Adults With Diabetes Mellitus Across 3 Health Status Categories

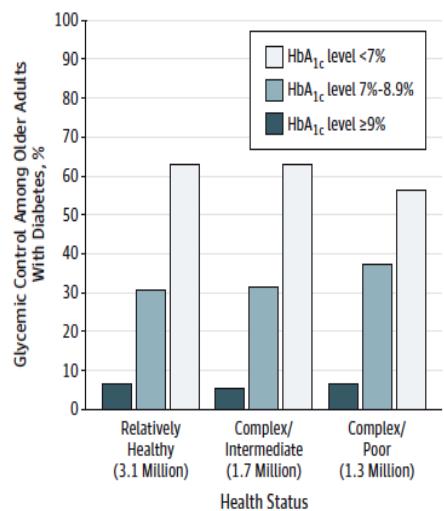
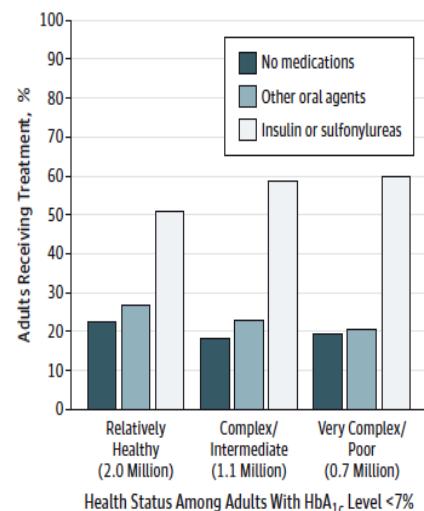
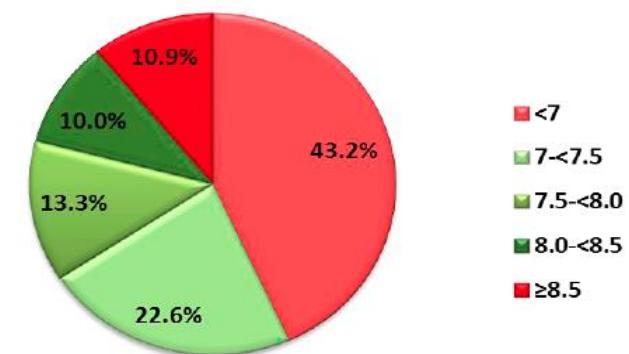


Figure 2. Treatment of Older US Adults With Diabetes Mellitus With an HbA_{1c} Level of Less Than 7% Across Health Status Categories



Distribution of the values of HbA_{1c} in 7269 patients ≥ 65 yrs.



UNITED STATES OF AMERICA

Lipska KJ et al, JAMA 2015

SPAIN

Formiga F et al, JNHA 2017

LIFESTYLE MEASURES

Then, at each step, if not at individualized target HbA_{1c}

Consider as first line therapy

Metformin

Sulfonylurea
or DPP-4 inhibitor

Acarbose or
Glinides or
Insulin or
SGLT2 inhibitors or
Thiazolidinedione

Consider as second line - dual therapy by adding to first line therapy

Sulfonylurea
or DPP-4 inhibitor

Metformin
(if not used first line)

Acarbose or
Glinides or
GLP-1RA or
Insulin or
SGLT2 inhibitors or
Thiazolidinedione

Consider as third line - triple oral therapy, insulin or GLP-1RA

DPP-4 inhibitor
or Sulfonylurea

Basal insulin
or Pre-mix insulin

GLP-1RA

Acarbose or
Glinides or
SGLT2 inhibitors or
Thiazolidinedione

Subsequent options

Change oral agent
or
Basal insulin
or
Pre-mix insulin

or

GLP-1RA
or
Basal +
Meal-time insulin



Usual approach



Alternative approaches



Other options
(alphabetical order)

Considerations:

- Functional capacity
- Frailty
- Dementia
- End of life

Medication Choice:

- Renal function
- SU with low hypoglycaemia risk
- Medication side effect profile
- Potential harms of medications which induce weight loss
- Cost
- Availability
- Local prescribing rules
- Discontinue ineffective treatment

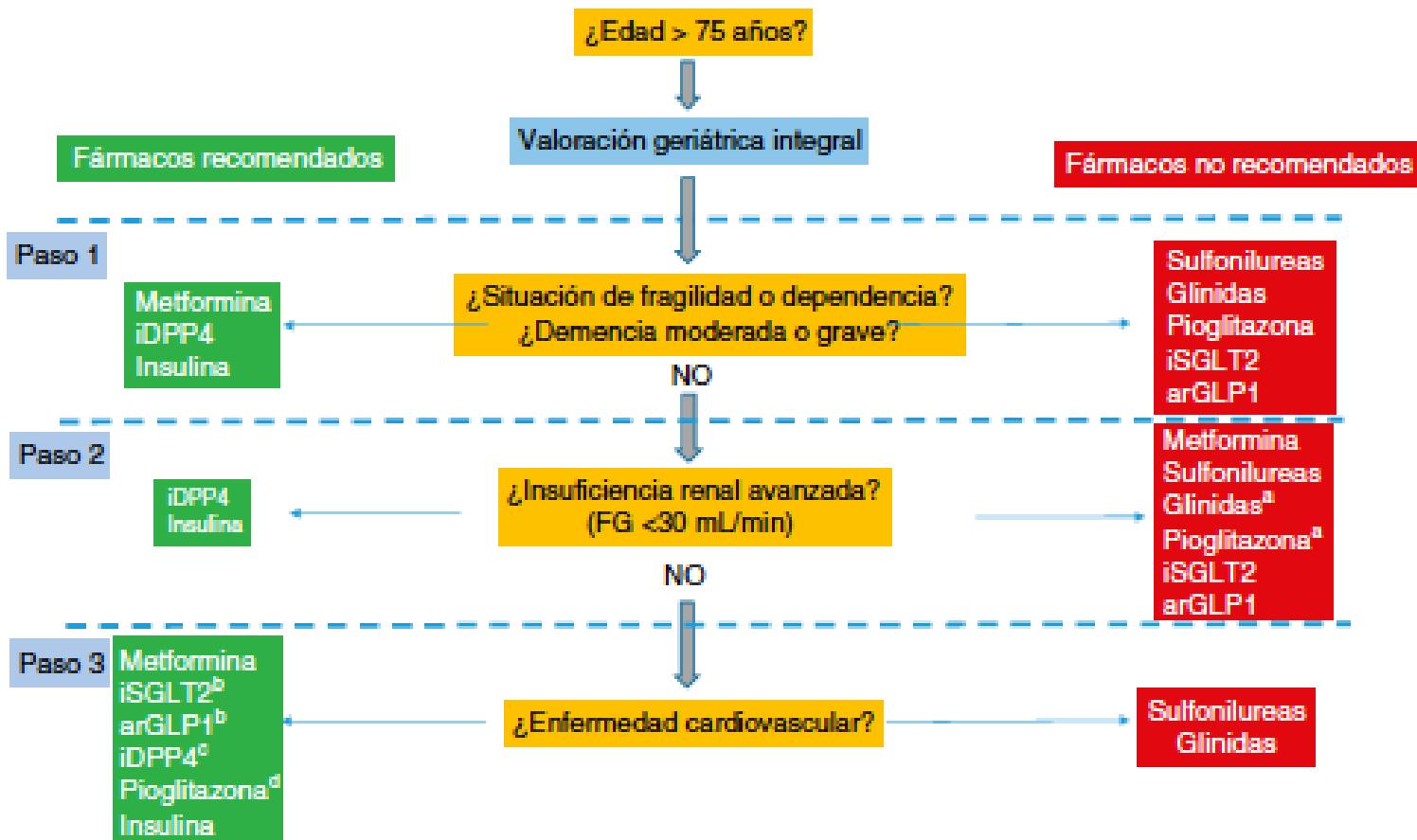
DPP-4 dipeptidyl peptidase 4

GLP-1 RA glucagon-like peptide-1 receptor antagonist

HbA_{1c} glycated haemoglobin

SGLT2 sodium glucose co-transporter 2

SU sulfonylurea



arGLP1: agonistas del receptor del *glucagon-like peptide-1*; iDPP4: inhibidores de la dipeptidil peptidasa-4; iSGLT2: inhibidores del cotransportador sodio-glucosa tipo 2.

^a Repaglinida y pioglitazona pueden emplearse en pacientes con FG < 30 ml/min, pero su uso no es recomendable por el riesgo de efectos adversos: hipoglucemias (repaglinida); retención hidrosalina, insuficiencia cardiaca y fracturas (pioglitazona).

^b Empagliflozina, canagliflozina y liraglutida han demostrado reducción de la morbilidad cardiovascular en pacientes con diabetes tipo 2 de alto riesgo vascular.

^c Saxagliptina deben evitarse en pacientes con insuficiencia cardiaca.

^d Pioglitazona está contraindicada en pacientes con insuficiencia cardiaca o en riesgo de fracturas.

Lack of Evidence-Based Practice in Treating Older People with Diabetes

A cause for concern?



- *No large-scale intervention studies in older people which focus on functional outcomes*
- Extrapolated evidence of benefit for glucose-lowering only – UKPDS data; Steno-2; EMPAREG
- No evidence to support glucose-lowering in residents (patients) of nursing homes
- *No longer term studies in frail older subjects*



Modified from Sinclair AJ



A RANDOMIZED CLINICAL TRIAL TO
EVALUATE THE EFFECTIVENESS OF A
MULTI-MODAL INTERVENTION IN OLDER
PEOPLE WITH TYPE 2 DIABETES ON **FRAILTY**
AND QUALITY OF LIFE: THE **MID-FRAIL**
STUDY



Professor Leocadio Rodriguez-Mañas
Project Co-ordinator

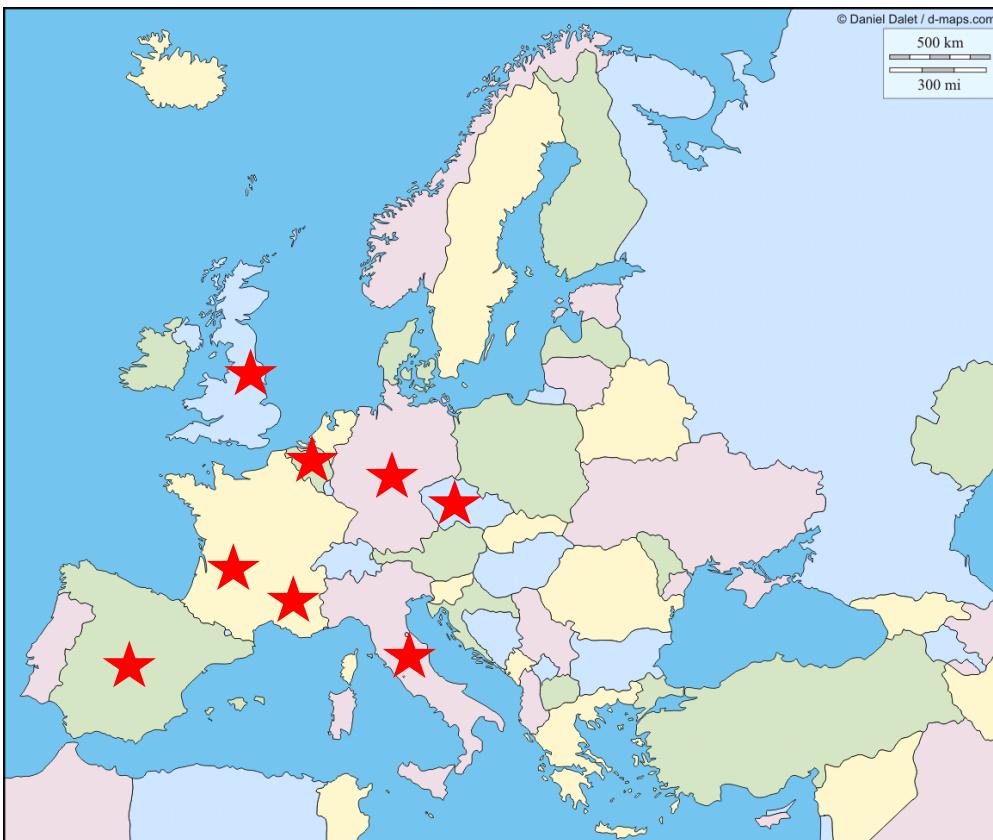
Professor Alan Sinclair
Scientific Co-ordinator

- Multi-modal Intervention (fitted clinical targets, education, diet and exercise) in older people with Diabetes to improve **frailty** and quality of life.





COUNTRIES



Spain
United Kingdom
France (Toulouse
and Bordeaux)
Italy
Belgium
Czech Republic
Germany



PRIMARY OBJECTIVE

To evaluate, in comparison with usual clinical practice, the **effectiveness of a multi-modal intervention (education, adequate of HbA1c and BP targets and strength exercise program)** in frail and pre-frail subjects aged ≥ 70 years with T2D in terms of the difference in function 12 months post randomization, according to changes in score on the SPPB

INTERVENTION GROUP (IG)

- ✓ **Exercise program (Resistance exercise MMII):** Twice *week (16 weeks)



*Seated bench
press*



*Leg
extension*

Midfrail-study	Number of exercises	% MVC	Series; RM	Frequency	Rest
	2	40%-80%	1-3 serie; 6-12 RM	2 days/week	1'30"

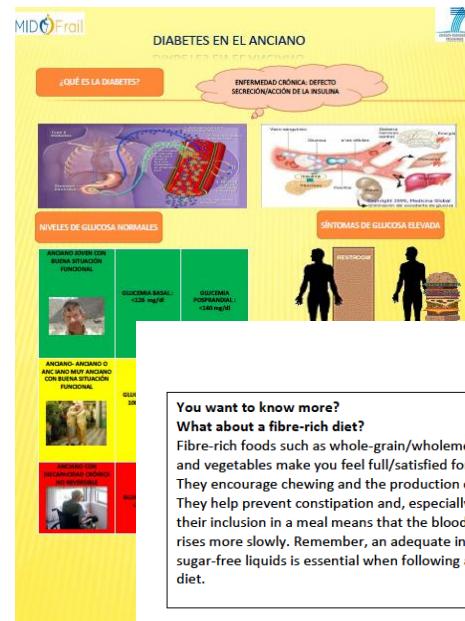
Enhancing nutritional status and diabetes knowledge – part of the MID-Frail 3-steps programme



For Older People with Diabetes

Prepared by:

Andrej Zeyfang, Irene Feucht, Leocadio Rodriguez Mañas and Alan Sinclair



If you have previously been unwell or not eating adequately, the main course portions should be increased as a protein-rich diet is needed.

If for any reason you need a high protein diet, it is also possible to eat or drink supplements bought at your pharmacy.

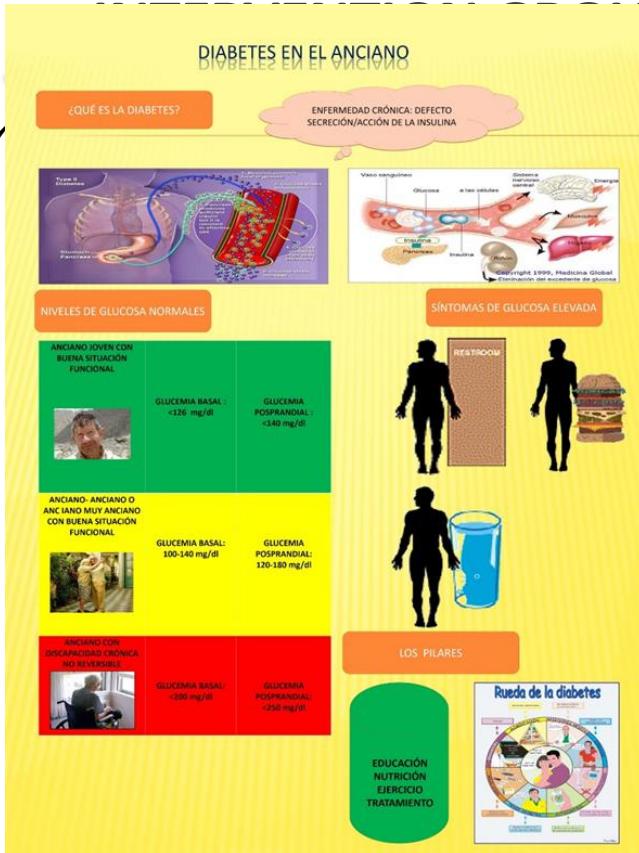
Please remember to drink sufficient fluids every day. One and a half litres is a good quantity for most persons. If you have a heart problem which does not prevent your participation in the study, weigh yourself daily and ask your GP about your fluid requirements.

What is my personal goal?



You want to know more? Shall I use sweeteners or diet products?

Low calorie sweeteners can be used to sweeten coffee or tea. Sweeteners are a better choice than sugar, because they do not influence the blood glucose level and do not contain calories. Calorie-rich sugar substitutes such as fructose or sorbitol can cause diarrhea and do not bring any benefits to people with diabetes. Diet products including sugar-free biscuits/cakes, ice cream, sweets and chocolate are not necessary. They are expensive, affect metabolism and also often contain large amounts of fat.



INTERVENTION (IG)

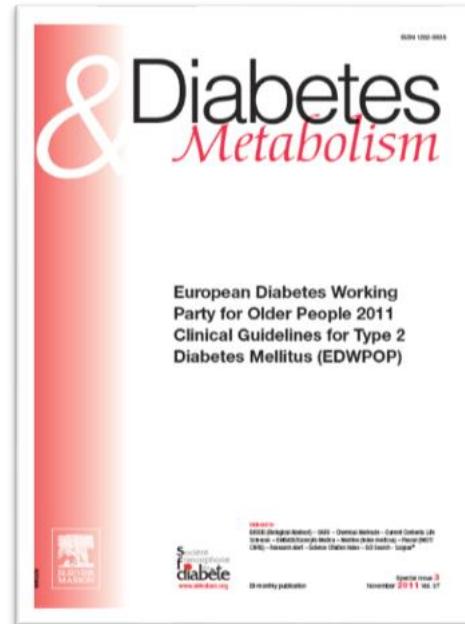
Optimisation of glycaemic and blood pressure control

HbA1c: 7-8% (9.6-11.6 mmol/L)

BP <150/90 mmHg

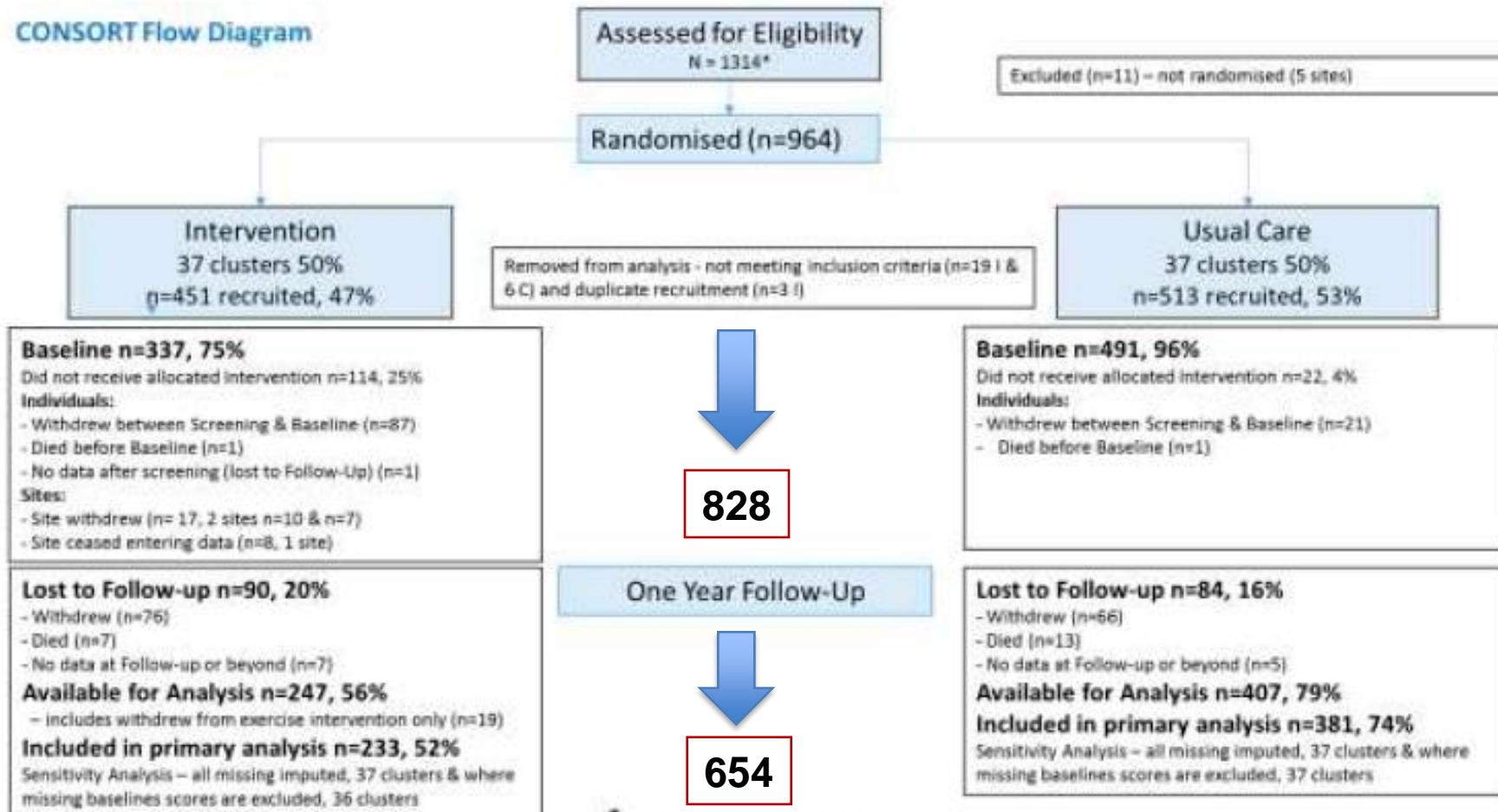
USUAL CLINICAL PRACTICE (UCG)

Level of routine care a patient with diabetes will normally be expected to receive from his/her local healthcare system



Mean Age: 78 yr
 Females: 49.1%
 Diagnoses: 5.7/patient
 Years since diagnosis: 16.7

CONSORT Flow Diagram



$\approx p < 0.01$ vs UCG
 $* P < 0.01$ vs baseline

SPPB Changes



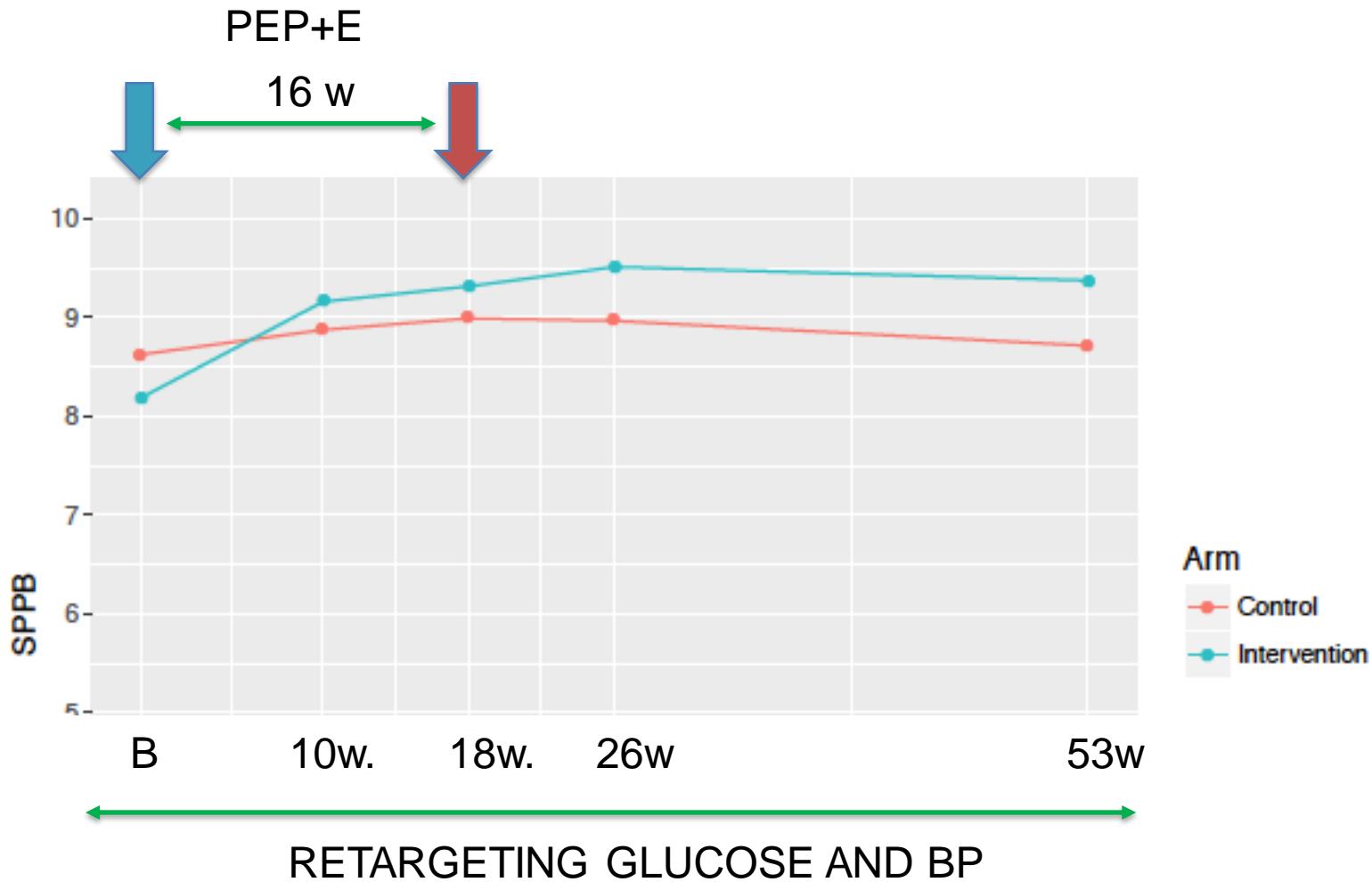
MAIN RESULTS

340 (not improve) vs 291 improve at least 1)

Variable	OR	95% CI	p-value
Woman	1,13	0,82-1,57	0,45
Age*	1,00	0,97-1,03	0,99
Frailty	1,43	1,01-2,03	0,04
Intervention (IG)	2,16	1,55-3,01	<0,01
Educational level*	0,96	0,93-0,99	<0,01

*Variable in years

MAIN RESULTS



TOTAL COSTS

Table 15. Mean annual total care cost by groups. (EUR 2016 per patient)

	Intervention (n=236)	Usual care (n=387)
	Mean (SD)	Mean (SD)
Intervention Costs	331.75 (127.75)	0
Primary Care Costs	506.14 (1,699.07)	611.50 (1,832.78)
Medical visits, specialist	244.73 (275.51)	265.68 (316.56)
Medical test/examinations	142.69 (201.15)	140.84 (179.58)
Hospitalizations	 540.93 (2,113.08)	1,176.75 (3,736.92)
Health-care cost	 1,766.25 (3,159.89)	2,194.78 (4,914.18)
ΔFormal care cost	 -18.22 (3,245.17)	166.33 (3,829.40)
ΔInformal care costs	-255.90 (6,297.36)	-194.23 (2,100.05)
Δ Non healthcare cost	 -274.12 (6,387.03)	-27.89 (4,323.04)
Total Care cost (HC Cost + Δ non HC Cost)	 1,492.12 (7,455.79)	2,166.88 (6,736.83)

8. Note: SD: standard deviation

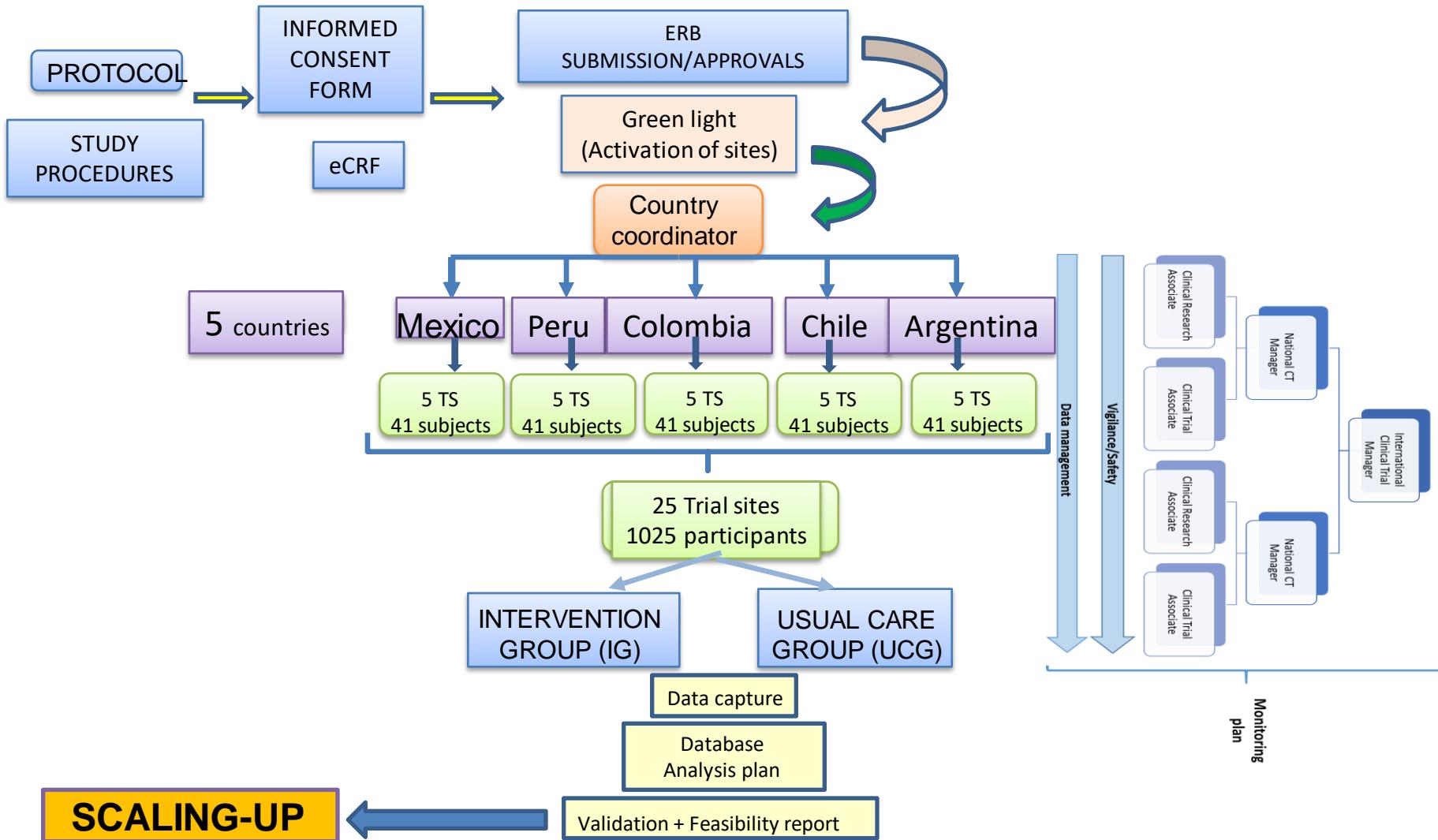
COST-EFFECTIVENESS

Table 18. Cost Effectiveness Analysis. Base Case (EUR 2016)

	N	Δ Costs	Δ Outcomes	Incremental ratio (interventions vs usual care)
Health care perspective				
CEA (outcome: SPPB score)	613	-428,02	0,92272	Intervention dominates control
CEA (outcome: % people with improvement in SPPB \geq one point)	613	-428,02	15,52%	Intervention dominates control
CUA (outcome: QALY)	538	-461,00	0,05276	Intervention dominates control
Social perspective				
CEA (outcome: SPPB score)	613	-610,19	0,92272	Intervention dominates control
CEA (outcome: % people with improvement in SPPB \geq one point)	613	-610,19	15,52%	Intervention dominates control
CUA (outcome: QALY)	538	-711,96	0,05276	Intervention dominates control

DIABFRAIL-LATAM

H2020



Exercise and Aging



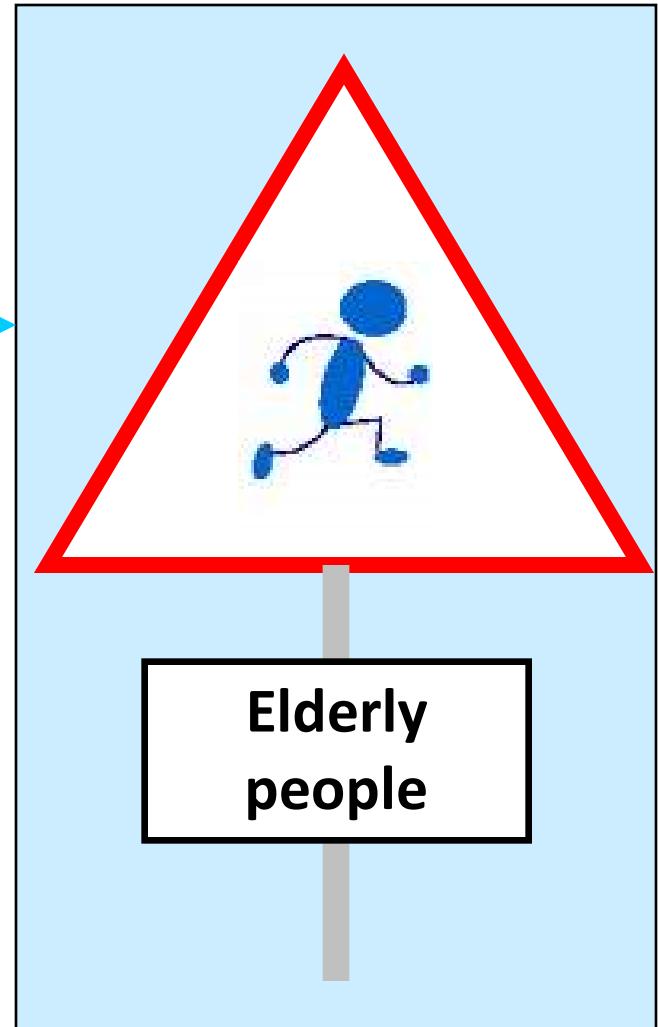
Aging and Sarcopenia



Mitochondriogenesis and Aging



Exercise, Mitochondriogenesis and Aging



MUCHAS GRACIAS



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