Angststoornissen op leeftijd

Aandachtspunten voor diagnostiek en behandeling

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Symposium, KU Leuven, 17-10-2019

Prevalence of late-life anxiety disorders[1-3]

	LASA[1] (55+, 6M)	NCS-R[2] (55+, 12M)	ESA[3] (65+, 12M)
• Generalised anxiety disorder	7.3 %	2.0 %	1.2 %
• Social phobia	3.1%	3.5 %	0.1 %
• Specific phobia	-	6.5 %	2.0 %
• Panic disorder +/- agoraphobia	1.0 %	1.3 %	0.6 %
• Agoraphobia	-	0.8 %	0.3 %
• Post-traumatic stress disorder	0.9 %	2.1 %	-
• Obsessive compulsive disorder	0.6 %	-	1.5 %
Any anxiety disorder	**10.2 %**	**11.6 %**	**5.6 %**

[1] Beekman et al, Int J Geriatr Psychiatry 1998
[2] Byers et al, Arch Gen Psychiatry 2010
[3] Preville et al, Can J Psychiatry 2008

Meta-analysis (n=16) late-life (65+) anxiety disorders[1]

Anxiety disorder	Pooled prevalence		Age Effects	Sex effects
	12-month	Life-time		
• Generalized anxiety #	1.3 %	3.1 %	None	F > M
• Specific phobia	4.2 %	7.0%	↓ by age	-
• Social phobia	1.1 %	1.6 %	None	F > M
• Panic disorder	0.8 %	1.6 %	None	-
• Agoraphobia	0.5 %	1.2 %	-	F > M
• Obsessive-compulsive #	0.6 %	0.6 %	-	-
• Post-traumatic stress #	1.6 %	3.4 %	-	-

[1] Grenier et al, Int J Geriatr Psychiatry 2019

I made a backup disk. Then I realized I wanted a backup of the backup. Then I decided, just to be safe, to make a backup of _that_ backup….
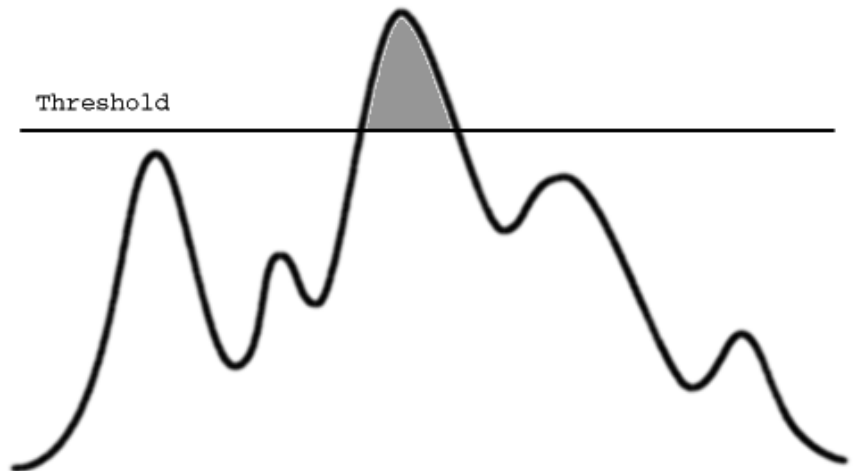
No, I'm not backing up our files - I'm just assuming that the N.S.A. is making copies.

Subthreshold anxiety disorders in old age

Subthreshold =

- Not meeting the number of symptoms required for a diagnosis

- Not reporting significant impairment or distress

Threshold

Impairment not operationalized in the DSM

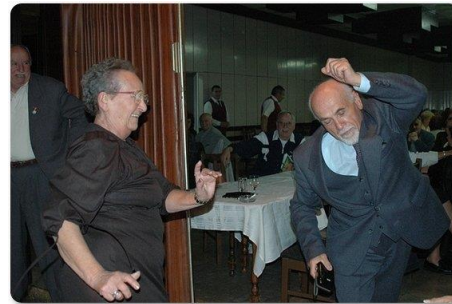Self-rated disability in four areas of functioning related to ageing

ADL

Domestic tasks

Social activities

Relationships

↓

↓

↓

↓

Dressing
Eating
Bed transfer
Etc

Preparing meals
House maintenance
Etc

Dancing
Etc

Family members
Friends
Etc

It's all about perception
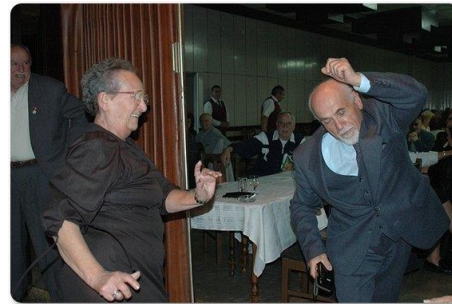
Older adults are less likely to perceive themselves as disabled than younger adults

ADL   Domestic tasks   Social activities   Relationships
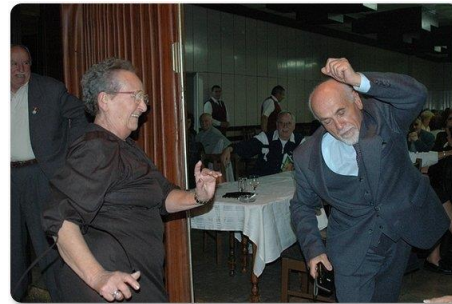
It's all about perception

Older adults are less likely to perceive themselves as disabled than younger adults**, but…. for me it is easy to understand why….**

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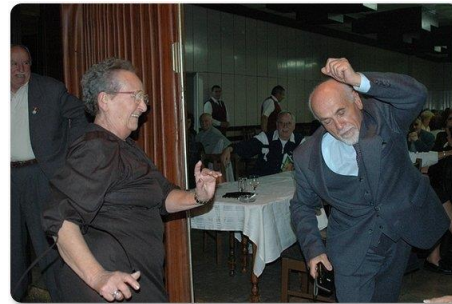
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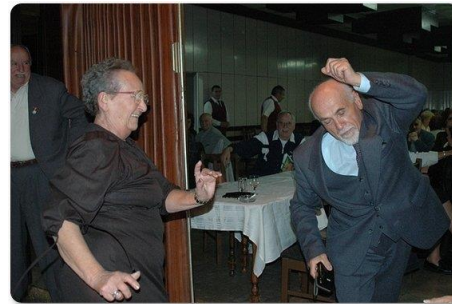
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ADL

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It's all about perception
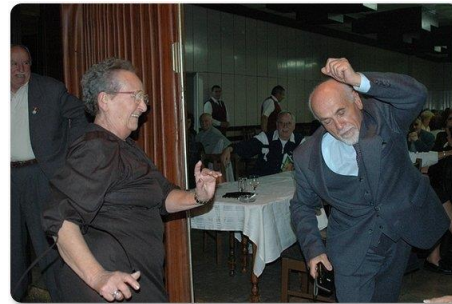
Older adults are less likely to perceive themselves as disabled than younger adults**, but…. for me it is easy to understand why….**

ADL   Domestic tasks   Social activities   Relationships

Prevalence of subthreshold AD in later life[1]

	DSM-IV criteria	Full symptoms, no impairment	Less symptoms, sig. impairment
• GAD	1.2 %	0.2 %	2.8 %
• SocP	0.1 %	0.1 %	1.2 %
• SpecP	2.0 %	3.1 %	4.7 %
• PD +/- AGO	0.6 %	0.2 %	2.4 %
• AGO	0.3 %	0.9 %	3.3 %
• OCD	1.5 %	-	1.6 %
Any AD	**5.6 %**	**4.6 %**	**15.9 %**

[1] Grenier et al, Am J Geriatr Psychiatry 2011

For screening, see http://gai.net.au

Geriatric Anxiety Inventory (GAI)[1]

- 20-item screening questionnaire

- Robust in case of MCI/nursing homes[2]

- Well-validated in over 10 countries worldwide[3]

- Validated 5- and 6-item versions available

Dutch ROM-GPS study (n=977):

- Associated with *any* anxiety disorder in 60+ patients in mental health care.

- Can replace disorder specific scales (PSWQ, Liebowitz scale, MI)

[1] Pachana et al, Int Psychogeriatr 2007

[2] Boddice et al, Nurs Older People 2008

[3] Molde,…., Oude Voshaar & Pachana, J Gerontol B Psychol Sci Soc Sci 2019

Diagnostic complexities

1. State or trait issue

   a) Age of onset

   b) Personality

2. Expression of anxiety symptoms in later life

   a) Agoraphobic cognitions

   b) Avoidance behaviour

[1] Mohlman et al, Int J Geriatr Psychiatry 2011

Anxiety in later life: State or trait?

Clinically difficult to tease apart due to long-standing anxiety problems
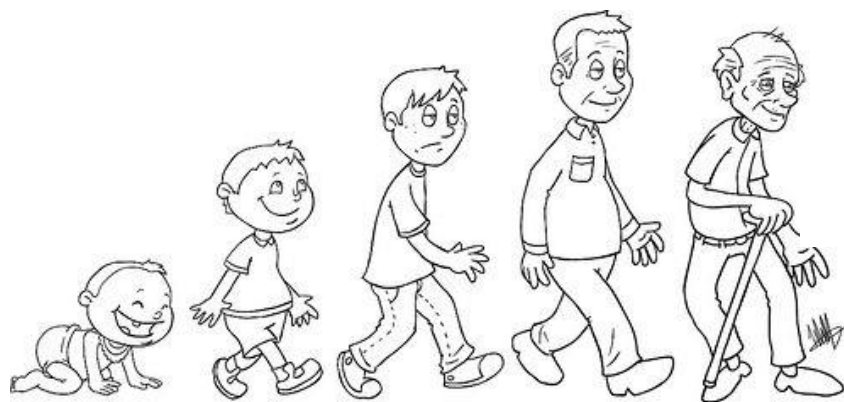
Kessler et al (2005)[1]	Age of onset (years)		
	Median	95th perc.	99th perc.
• Panic disorder	24	56	63
• Agoraphobia	20	51	54
• Specific phobia	7	41	64
• GAD	13	66	75
Any anxiety disorder	**11 years**	**51 years**	**65 years**

[1] Kessler et al, Arch Gen Psychiatry 2008

Comorbidity with personality disorders

- Prevalence of personality disorders (meta-analysis of 125 studies)[1]:

  – 49% among persons suffering from anxiety disorder

  – 15% in the general population

	All	Cluster		
Anxiety disorder:	**PD**	**A**	**B**	**C**
• Panic disorder with AGO	**41 %**	14 %	16 %	22 %
• Panic disorder without AGO	**47 %**	11 %	20 %	38 %
• Social phobia	**48 %**	9 %	6 %	46 %
• Generalized anxiety disorder	**47 %**	7 %	14 %	36 %
• Posttraumatic stress disorder	**35 %**	29 %	27 %	63 %
• Obsessive-compulsive disorder	**52 %**	13 %	15 %	34 %

[1] Friborg et al, J Affect Disord 2012

Personality versus AD in later life

- Personality disorder and anxiety disorders[1]:

  - Duration of illness does not moderate association with personality disorders.

  - Except: Social phobia – Avoidant personality disorder

- Neuroticism and GAD (3899 twin pairs aged 55-74 years)[2]:

  - Heritability of life-time GAD: .27

  - Heritability of neuroticism: .47

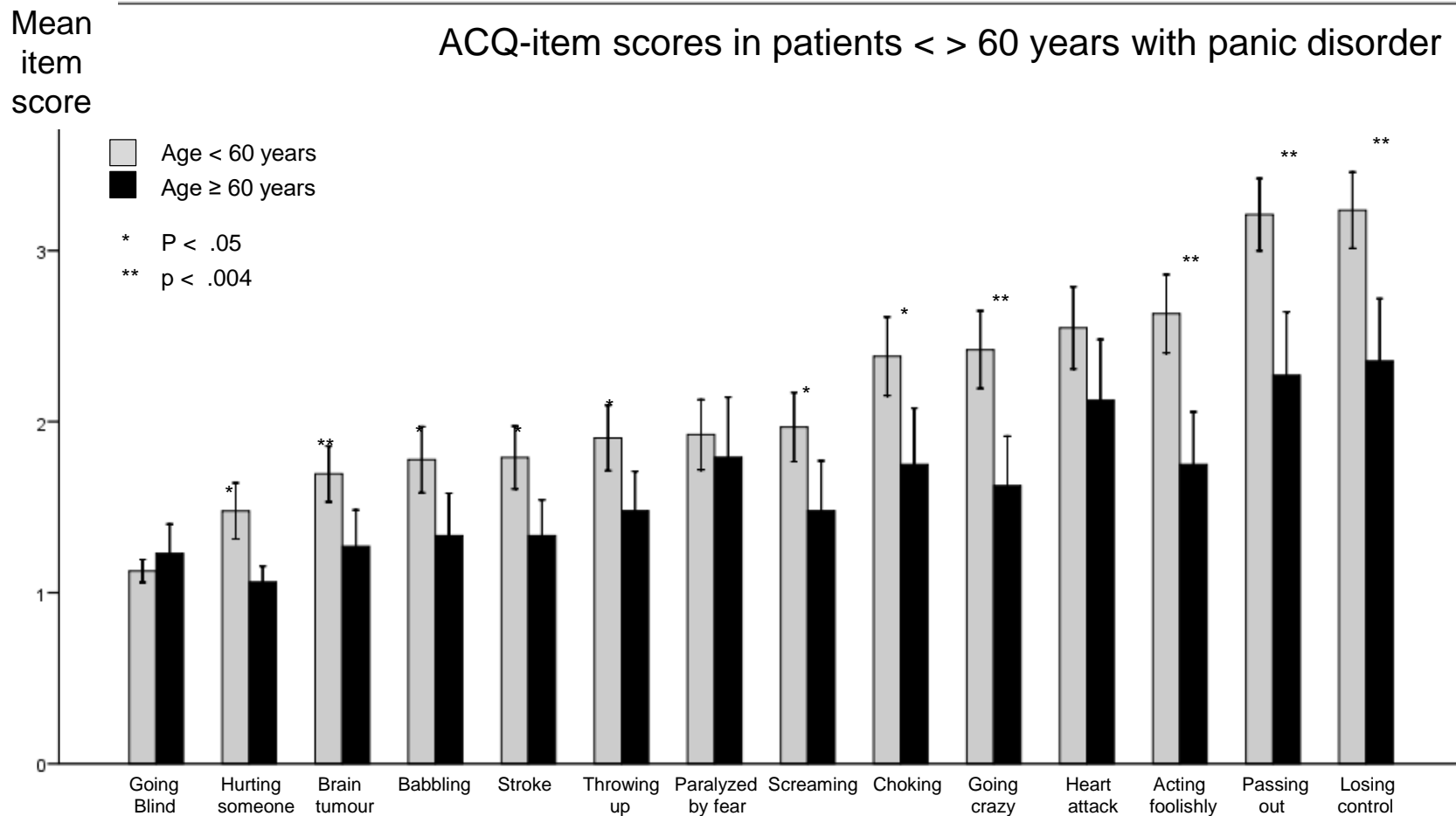 - One third of genetic influence shared between GAD and neuroticism

[1] Friborg et al, 2006, 2012
[2] MacKintosh et al, Twin Res Hum Genet 2006

Expression of anxiety in later life

Expression of agoraphobic cognitions

ACQ-item scores in patients < > 60 years with panic disorder

Avoidance behaviour in late-life[1]

Examples of maladaptive avoidance behaviour typical for later life

[1] Mohlman et al, Int J Geriatr Psychiatry 2011

Anxiety in a medical context

Consider always anxiety in medical patients (beyond DSM)

Examples of my own studies to the clinical relevance:

- Fear of falling

- Cardiac anxiety

- Fear of dementia

Fear of falling[1]

Falls:

- 30% of older people fall; half of them (15%) more than once.

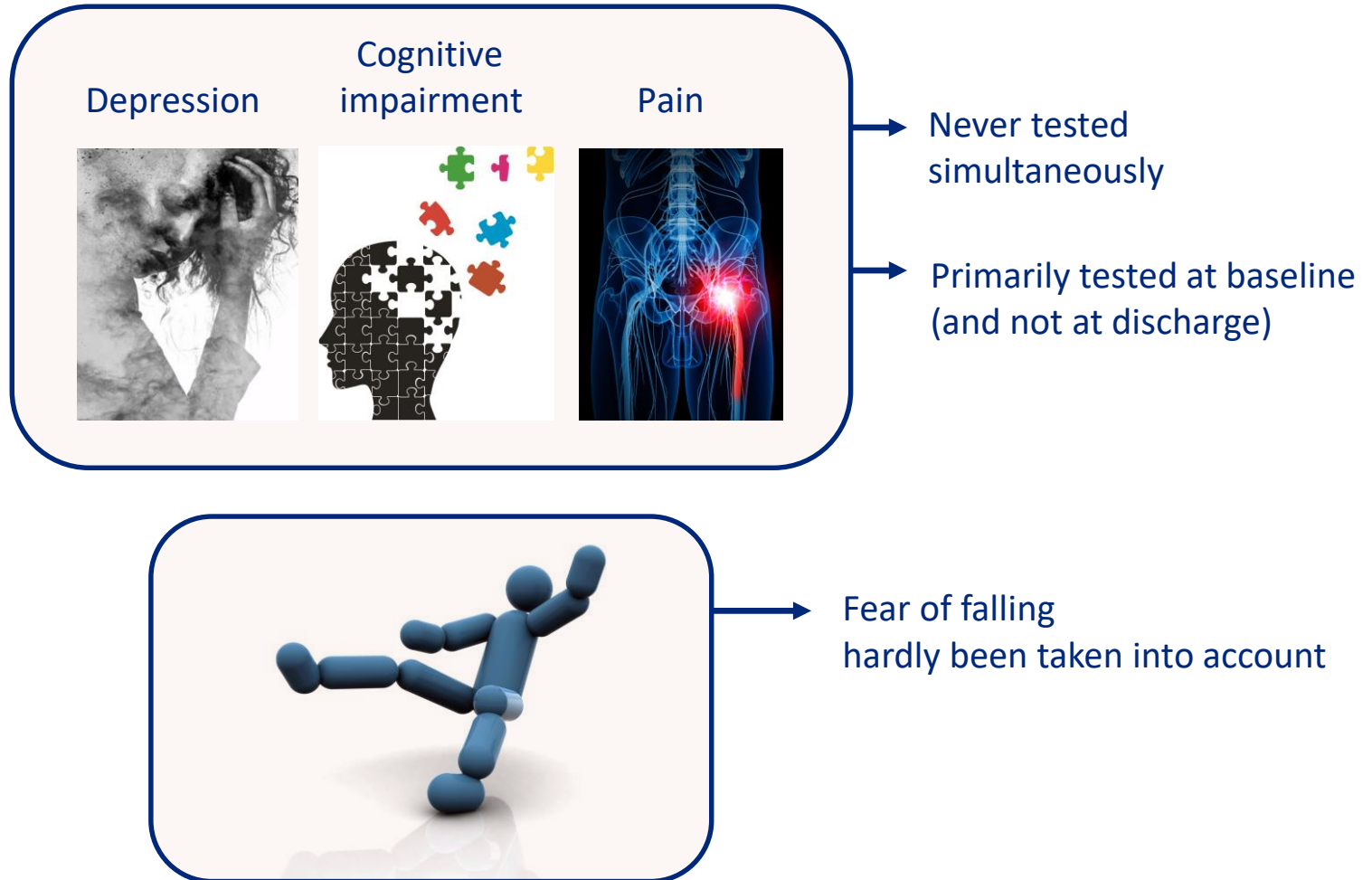- 33% experience functional decline after a fall.

Fear of falling:

- 20-40% of older persons after a fall.
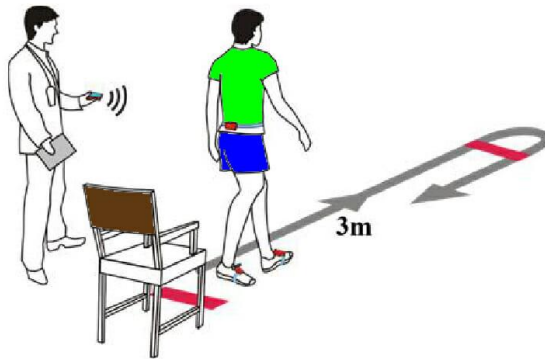
- 10-20% of older people who never fell.

[1] Scheffer et al, Age Ageing 2008

Psychopathology in hip fracture surgery[1]

N=293

GDS ≥7 → Treatment study (n=121) → CBT, TAU

GDS ≤6 → Prevention study (n=172 → CBT, TAU
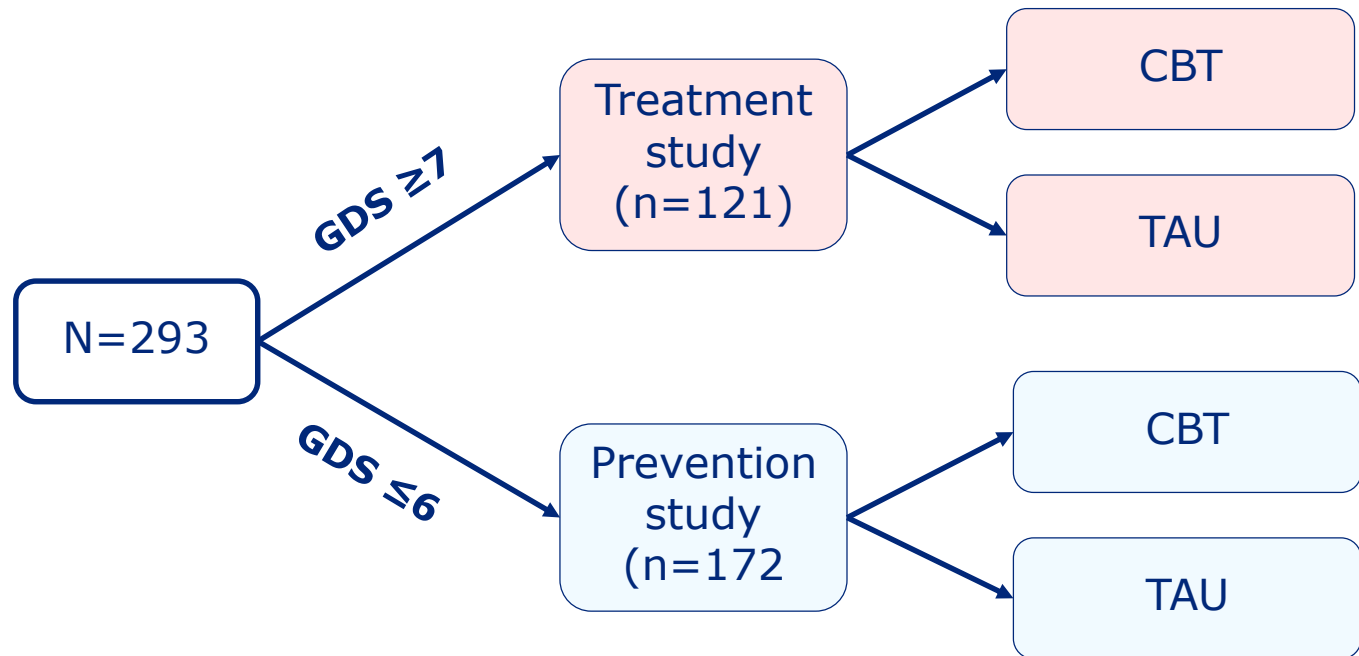
Two parallel RCTs on treatment and prevention of depression

[1] Burns et al, JAGS 2007

Psychological determinants of functional recovery[1]

Depression

Cognitive impairment

Pain

→ Never tested simultaneously

→ Primarily tested at baseline (and not at discharge)

→ Fear of falling hardly been taken into account

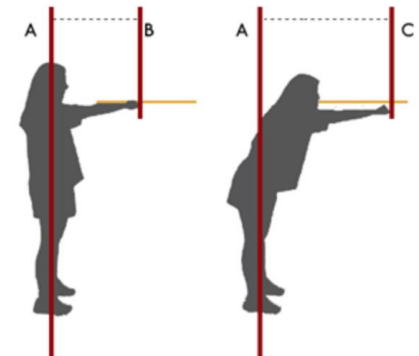[1] Oude Voshaar, Psychol Med 2006

Assessment of functional recovery at 6 months[1]

Get-up-and-go test
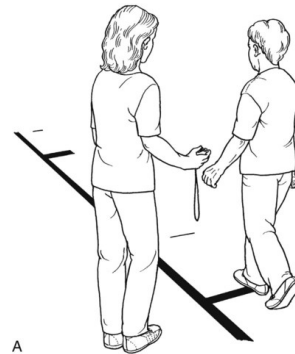
Gait speed

Functional reach

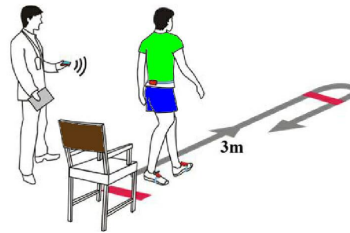[1] Oude Voshaar, Psychol Med 2006
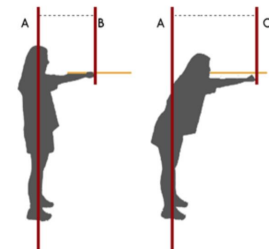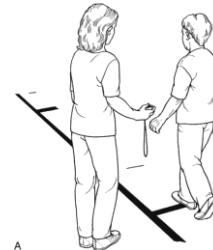
	OR [95% CI]	p	OR [95% CI]	p		
• **MMSE**	0.86 [0.77–0.96]	.009	0.85 (0.76–0.95)	.005	-	*ns*
• Depression (baseline)	1.16 [1.02–1.32]	.03	1.22 (1.07–1.40)	.003	0.85 (0.72–1.01)	.07
• Depression (6 weeks)	1.14 [0.99–1.30]	.07	1.15 (1.01–1.32)	.04	-	*ns*
• Fear of falling (baseline)	0.89 [0.80–0.99]	.04	-	*ns*	-	*ns*
• **Fear of falling (6 weeks)**	0.75 [0.64–0.88]	.001	0.73 (0.62–0.86)	.001	1.32 (1.08–1.60)	.006
• Pain (baseline)	-	*ns*	-	*ns*	-	*ns*
• Pain (6 weeks)	1.16 [1.01–1.35]	.04	-	*ns*	-	*ns*

[1] Oude Voshaar, Psychol Med 2006
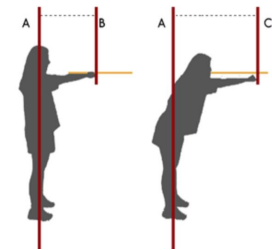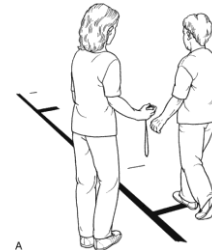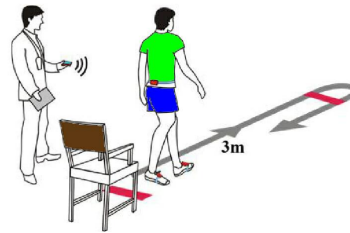
	OR [95% CI]	p	OR [95% CI]	p	OR [95% CI]	p
• **MMSE**	0.87 [0.77–0.98]	.02	0.87 [0.77–0.98]	.02	-	*ns*
• Depression (baseline)	-	*ns*	-	*ns*	-	*ns*
• Depression (6 weeks)	-	*ns*	-	*ns*	-	*ns*
• Fear of falling (baseline)	-	*ns*	-	*ns*	-	*ns*
• **Fear of falling (6 weeks)**	0.77 [0.65–0.91]	.002	0.75 [0.63–0.88]	.001	1.32 [1.08–1.60]	.006
• Pain (baseline)	-	*ns*	-	*ns*	-	*ns*
• Pain (6 weeks)	-	*ns*	-	*ns*	-	*ns*

[1] Oude Voshaar, Psychol Med 2006

Cardiac anxiety: Scared to death!

The impact of (cardiac) anxiety on vascular health

Meta-analyses of anxiety

as risk factor for vascular health[1,2]

Anxiety in cardiac patients (12 studies, 5750 patients, 2.6 years follow-up)[2]

- $OR_{\text{all-cause mortality}}$ = 1.5 [95% CI: 1.0 – 2.1], p=.04

- $OR_{\text{cardiac mortality}}$ = 1.2 [95% CI: 1.0 – 1.5], p=.02

- $OR_{\text{new cardiac events}}$ = 1.7 [95% CI: 1.3 – 2.2], p=.001

[1] Roest et al, J Am Coll Cardiol 2010
[2] Roest et al, Psychosom Med 2010

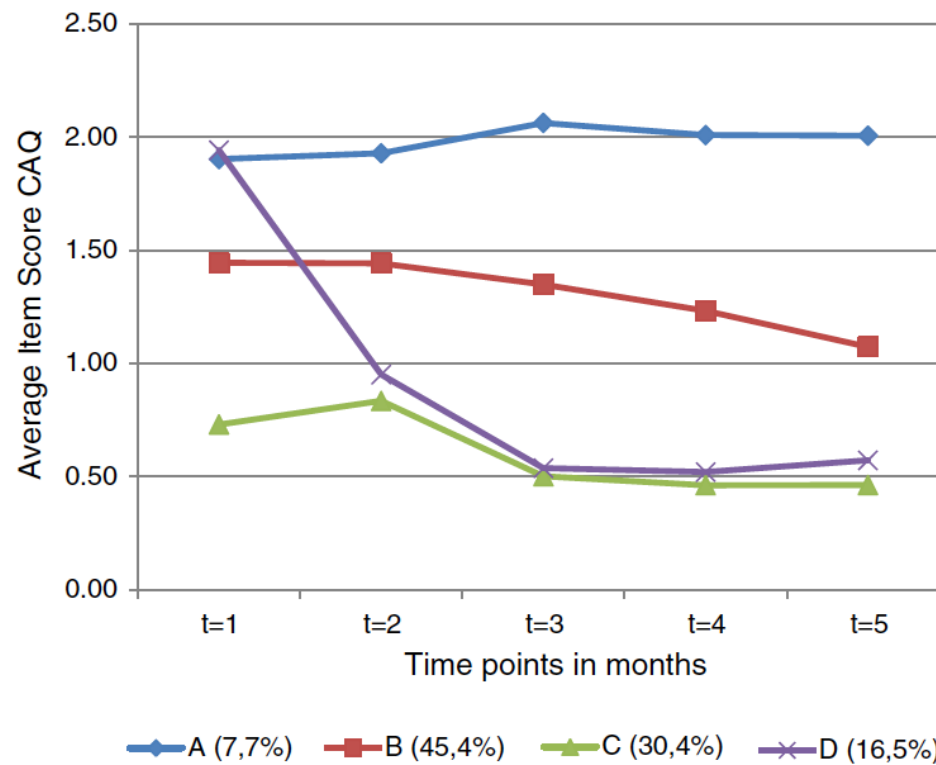# The concept of cardiac anxiety (by Eiffert et al)[1]

CAQ: an 18-item self-report questionnaire:

1. Specific fears about heart sensations

2. Heart-focussed attention/monitoring

3. Avoidance behaviour

Dutch validation study in acute cardiac patients (n=237)[1]:

4. Safety seeking behaviour

Latent Class Growth Analysis of CAQ over time[1]

[1] Van Beek, Oude Voshaar, et al. J Psychosom Res 2012

Five year follow-up data: CAQ sum score[1]

	Hazard Rate [95% CI]*, p-value	
	Baseline (n=77/193)	4 months after discharge (n=67/189)
CAQ sum score	**1.59 [1.04-2.43], p=0.033**	**1.77 [1.04-3.02], p=0.036**
• Fear		
• **Avoidance**		
• Attention		
• Safety seeking		

* Adjusted for age, sexe, LVEF, h/o MI, depressive symptom severity

[1] Van Beek, Oude Voshaar, et al. Br J Psychiatry 2016

Five year follow-up data: CAQ sum score[1]

	Hazard Rate [95% CI]*, p-value	
	Baseline (n=77/193)	4 months after discharge (n=67/189)
CAQ sum score	**1.59 [1.04-2.43], p=0.033**	**1.77 [1.04-3.02], p=0.036**
• Fear	1.32 [0.92-1.90], p=0.143	1.09 [0.78-1.53], p=0.616
• **Avoidance**	**1.23 [1.00-1.53], p=0.050**	**1.41 [1.07-1.86], p=0.014**
• Attention	1.04 [0.74-1.45], p=0.843	1.45 [0.92-2.28], p=0.111
• Safety seeking	1.25 [0.96-1.62], p=0.093	1.07 [0.78-1.46], p=0.690

* Adjusted for age, sexe, LVEF, h/o MI, depressive symptom severity, cardiac rehabiliation

[1] Van Beek, Oude Voshaar, et al. Br J Psychiatry 2016

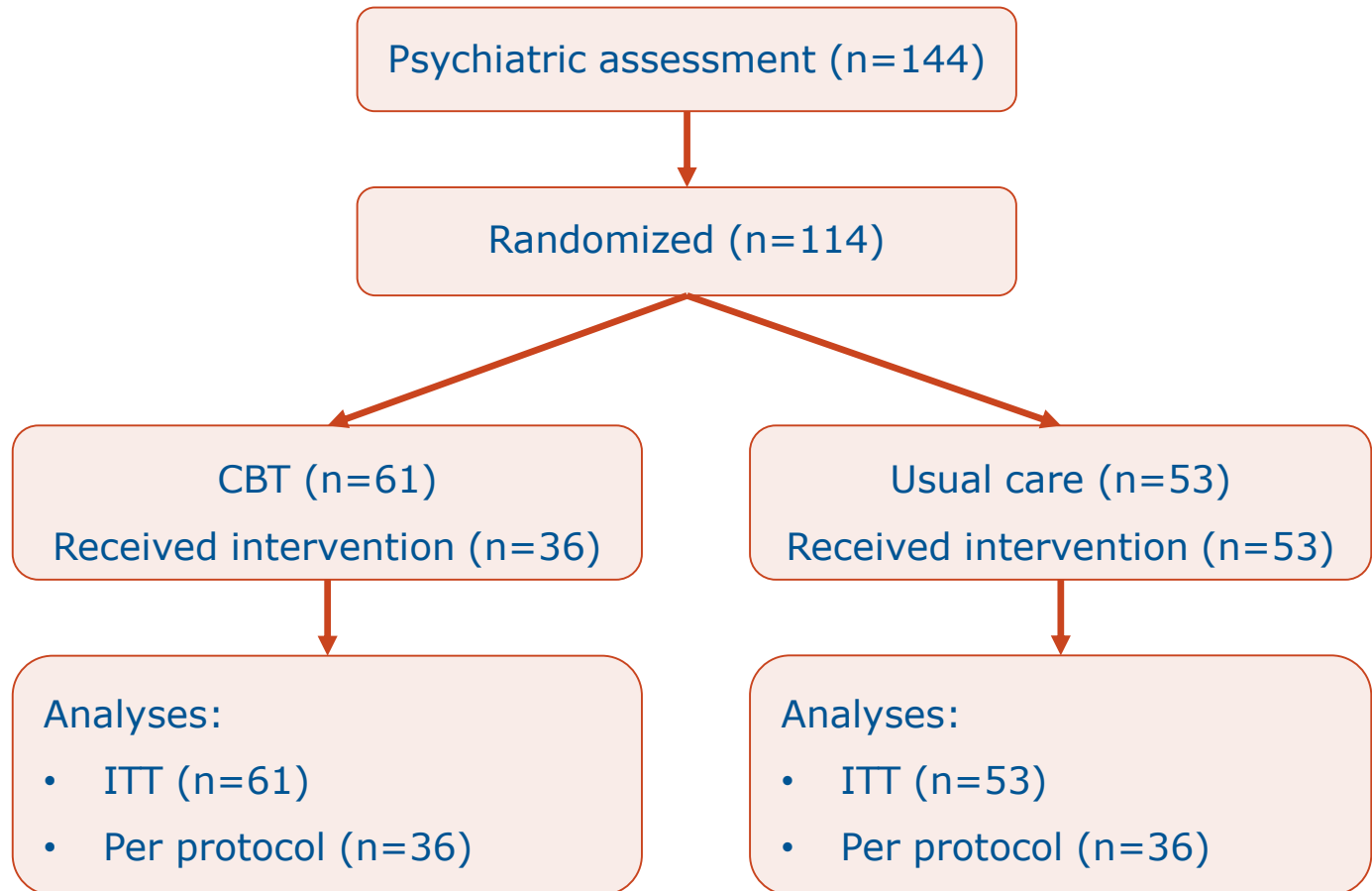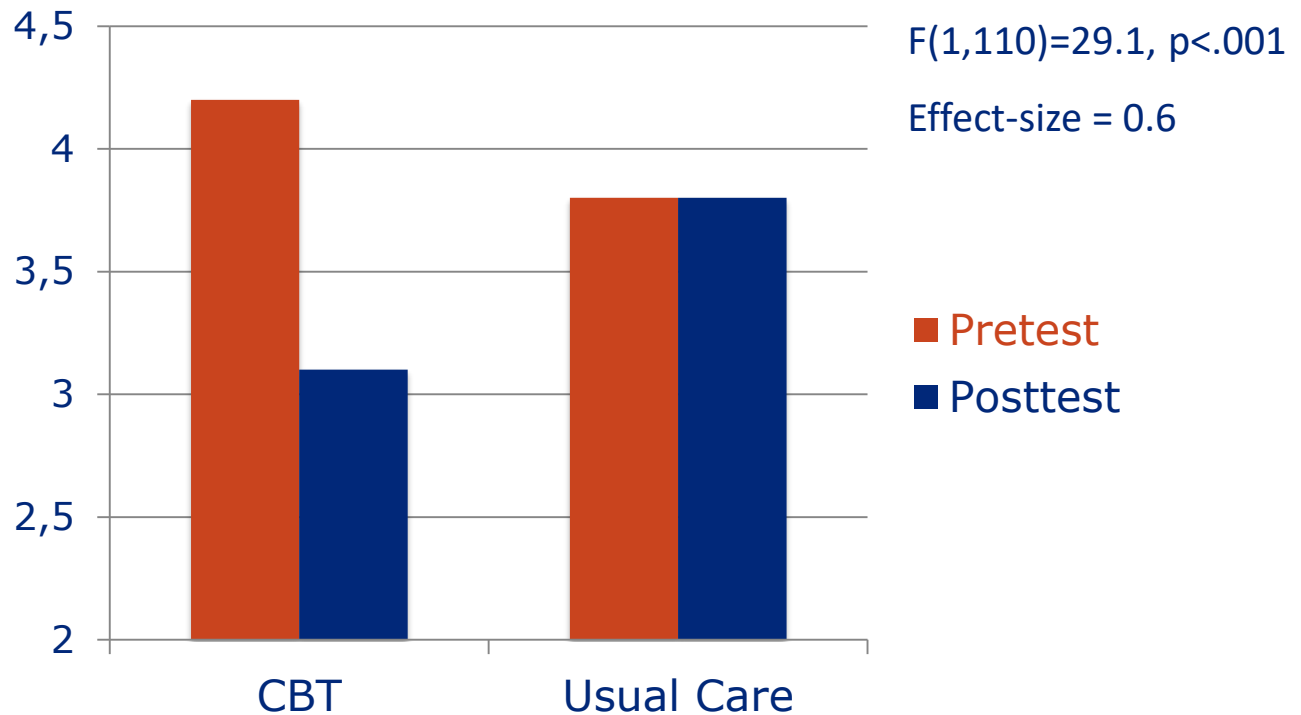# Chest pain at the ED[1,2]

NO cardiac cause
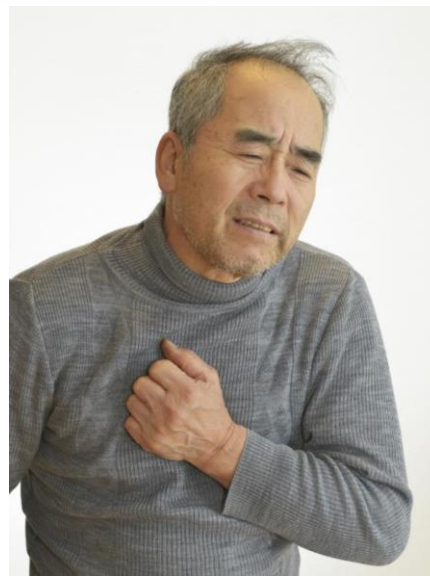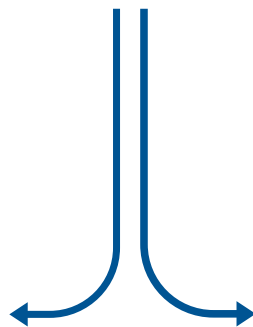
Cardiac cause

[1] Mayou, J Psychosom Res 1998
[2] Karlson et al, J Inter Med 1991
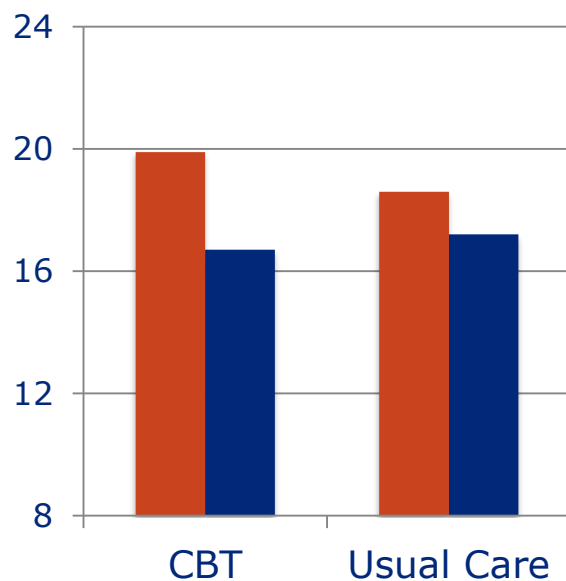
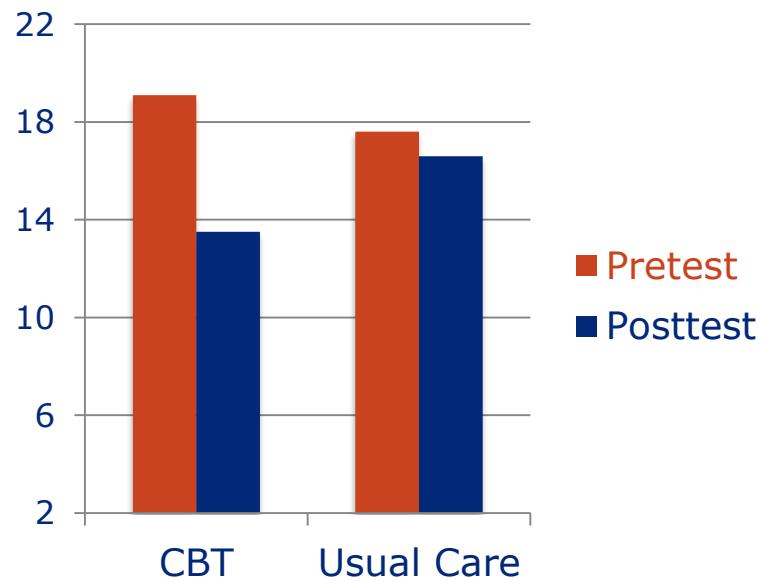# Patient recruitment and attrition

ITT results primary outcome (CGI)

F(1,110)=29.1, p<.001

Effect-size = 0.6

Effect comparably on secondary outcomes

HADS-anxiety

HAM-Depression

F(1,110)=5.3, p=.024

F(1,110)=11.1, p=.001

Systematic review & meta-analysis[1,2]

Objective:	No. of studies	RR	[95% CI]
Community studies[1]:			
• Cognitive decline	7	n.a.	
• Cognitive impairment	4	1.77	[1.38 – 2.26]*
• Dementia	6	1.61	[1.00 – 2.58]*
Memory clinics:			
• Conversion of MCI[1]	6	1.21	[0.90 – 1.63]
• Conversion of MCI[2]	7	1.18	[1.07 – 1.31]*

* p-value < .05

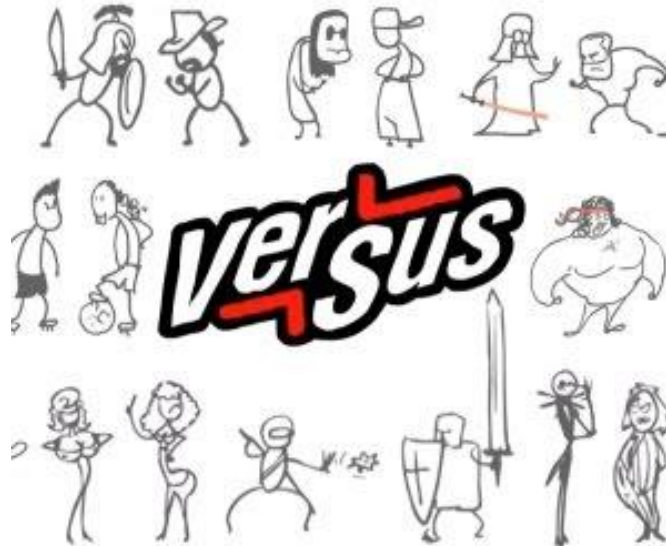[1] Gulpers, Oude Voshaar, et al, AJGP 2016
[2] Li et al, Int J Geriatr Psychiatry 2017

Treatment of late-life anxiety (disorders)

1. Comparison old versus young

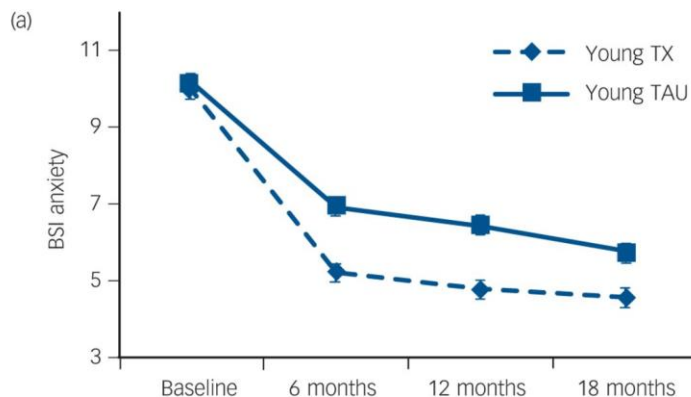2. Meta-analyses on late-life anxiety

3. Important treatment studies

Old versus young: Direct comparisons

RCT: CALM trial (n=1004)
Coordinated Anxiety Learning and Management

Younger Patients (18-59 yrs)

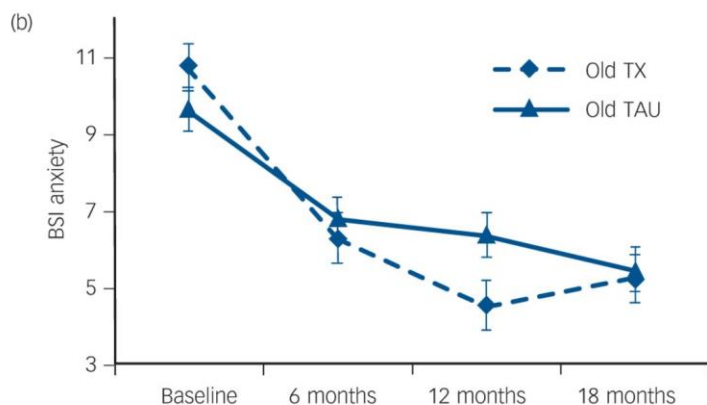Older Patients (60-75 yrs)

Inclusion
- Young adults (n=870)
- Old adults (n=134)

Effect among older patients:
- Intervention favours TAU
- Effect extinguished at 18 months
- No impact on remission

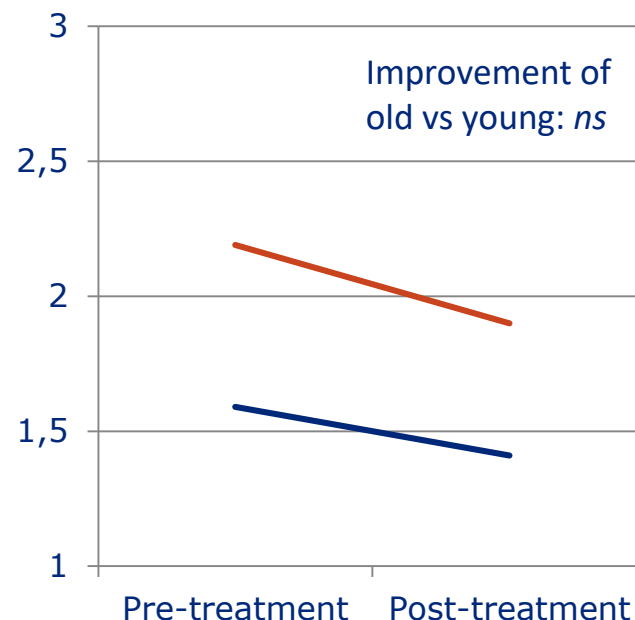Wetherell et al, Br J Psychiatry 2013

Effect of age on effectiveness of CBT for PD

Older patients (60+, n=31) - **younger patients** (18-60 years, n=141)

Mobility Inventory
Avoidance scale (MI-A)

Improvement of
old vs young: p=.035
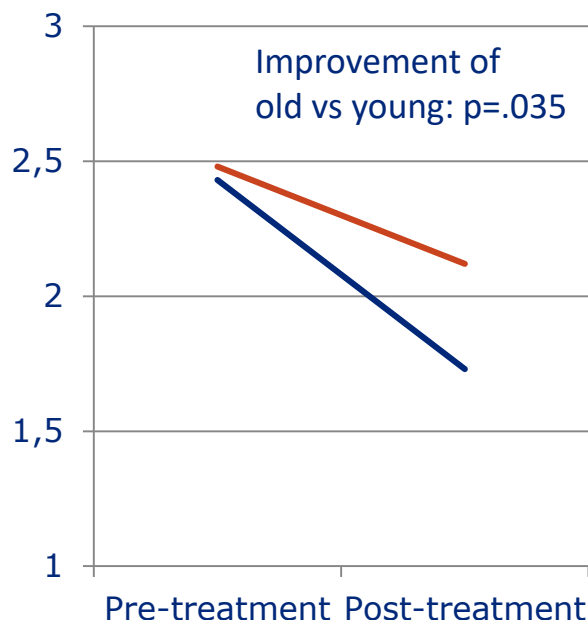
Agoraphobic Cognitions
Questionnaire (ACQ)

Improvement of
old vs young: *ns*

Case 1: SSRI with CBT or nursing home admission?

76 years old lady with an early-onset GAD, late-onset PD triggered by an TIA, complicated by secondary depression.

Referred for 2nd opinion due to institutionalisation

Previous treatment:

- SSRI: not effective due to early side-effects
- P.r.n. benzodiazepines
- CBT, day treatment, inatient care not effective.

Casus 2: Paniek in de (strand?)tent

Vrouw, 82 jaar, paniekstoornis, 10 jaar huisgebonden

Diagnose: Subthreshold/atypische paniekaanvallen

Doel: Remissie paniekstoornis

Vakantie Costa Brava

Meta-analyses for LLA: heterogeneity![1,2,3,4]

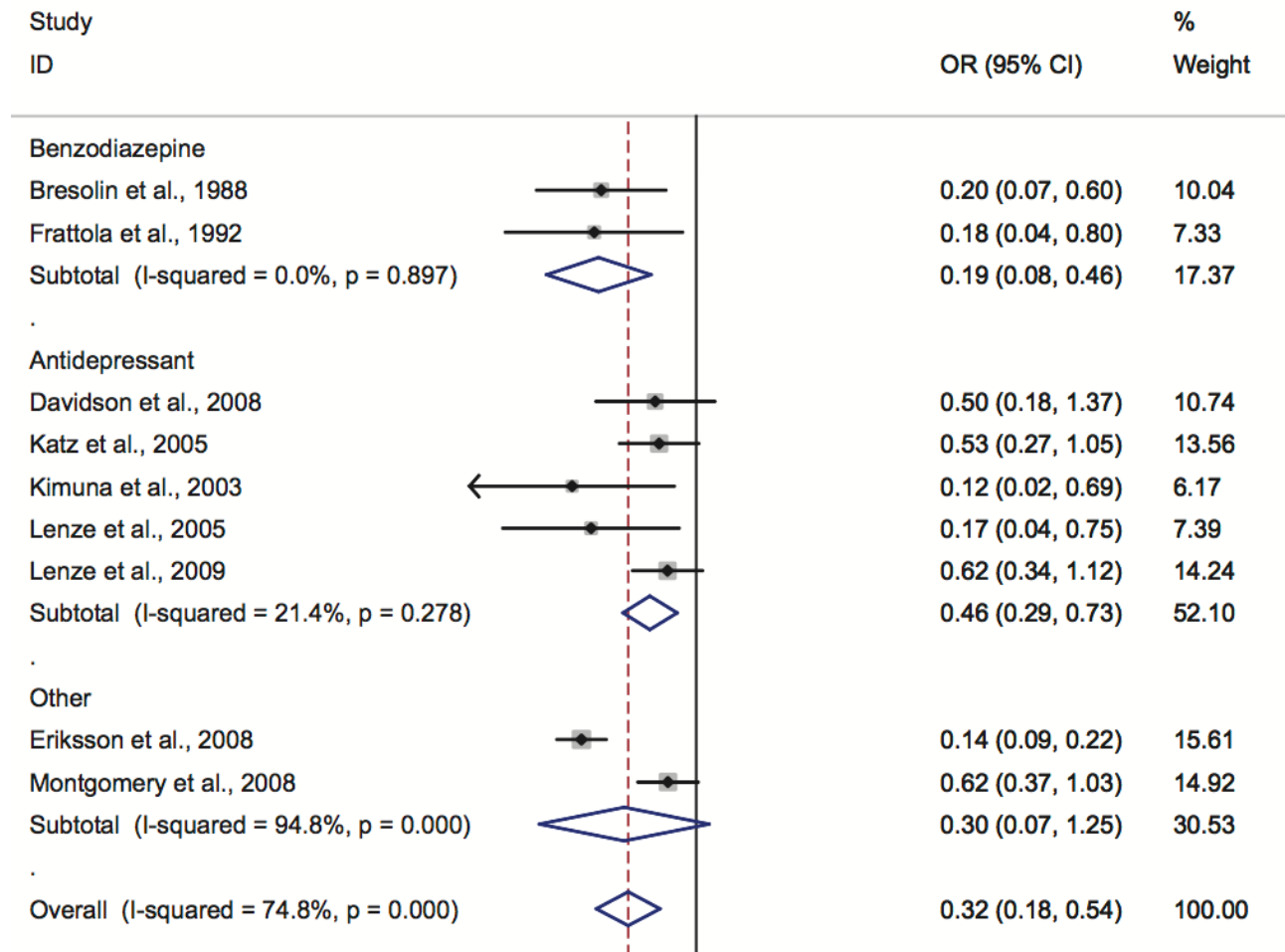| Authors	year	Studies (n)	Participants (n)	RCT only	Psycho-therapy	Pharmaco-therapy
Pinquart & Duberstein[1]	2007	32	2484	No	Yes, all	Yes
Hendriks & Oude Voshaar[2]	2008	7	396	Yes	Yes, CBT	No
Goncalves & Byrne[3]	2011	20	2373	Yes	Yes, all	Yes
Gouldt et al[4]	2012	12	665	Yes	Yes, CBT	No

[1] Pinquart & Duberstein, Am J Geriatr Psychiatry 2007

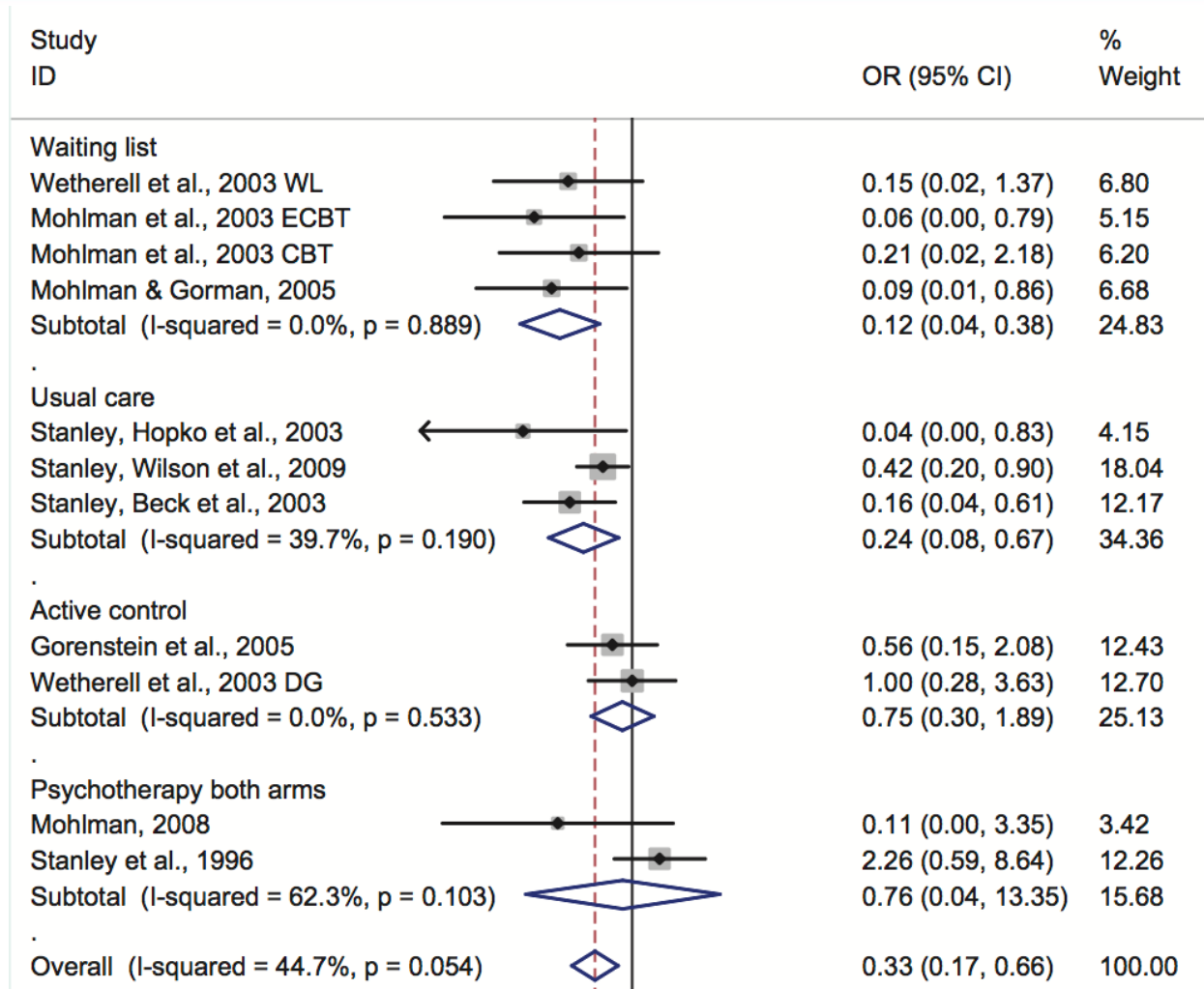[2] Hendriks, Oude Voshaar et al, Acta Psychiatr Scand 2008

[3] Goncalves & Byrne, J Anxiety Disord 2011

[4] Gould et al, J Am Geriatr Soc 2012

Goncalves & Byrne, J Anx Disord 2011

Study ID	OR (95% CI)	% Weight
Benzodiazepine		
Bresolin et al., 1988	0.20 (0.07, 0.60)	10.04
Frattola et al., 1992	0.18 (0.04, 0.80)	7.33
Subtotal (I-squared = 0.0%, p = 0.897)	0.19 (0.08, 0.46)	17.37
.		
Antidepressant		
Davidson et al., 2008	0.50 (0.18, 1.37)	10.74
Katz et al., 2005	0.53 (0.27, 1.05)	13.56
Kimuna et al., 2003	0.12 (0.02, 0.69)	6.17
Lenze et al., 2005	0.17 (0.04, 0.75)	7.39
Lenze et al., 2009	0.62 (0.34, 1.12)	14.24
Subtotal (I-squared = 21.4%, p = 0.278)	0.46 (0.29, 0.73)	52.10
.		
Other		
Eriksson et al., 2008	0.14 (0.09, 0.22)	15.61
Montgomery et al., 2008	0.62 (0.37, 1.03)	14.92
Subtotal (I-squared = 94.8%, p = 0.000)	0.30 (0.07, 1.25)	30.53
.		
Overall (I-squared = 74.8%, p = 0.000)	0.32 (0.18, 0.54)	100.00

umcg

Goncalves & Byrne, J Anx Disord 2011

Study ID		OR (95% CI)	% Weight
Waiting list			
Wetherell et al., 2003 WL		0.15 (0.02, 1.37)	6.80
Mohlman et al., 2003 ECBT		0.06 (0.00, 0.79)	5.15
Mohlman et al., 2003 CBT		0.21 (0.02, 2.18)	6.20
Mohlman & Gorman, 2005		0.09 (0.01, 0.86)	6.68
Subtotal (I-squared = 0.0%, p = 0.889)		0.12 (0.04, 0.38)	24.83
Usual care			
Stanley, Hopko et al., 2003		0.04 (0.00, 0.83)	4.15
Stanley, Wilson et al., 2009		0.42 (0.20, 0.90)	18.04
Stanley, Beck et al., 2003		0.16 (0.04, 0.61)	12.17
Subtotal (I-squared = 39.7%, p = 0.190)		0.24 (0.08, 0.67)	34.36
Active control			
Gorenstein et al., 2005		0.56 (0.15, 2.08)	12.43
Wetherell et al., 2003 DG		1.00 (0.28, 3.63)	12.70
Subtotal (I-squared = 0.0%, p = 0.533)		0.75 (0.30, 1.89)	25.13
Psychotherapy both arms			
Mohlman, 2008		0.11 (0.00, 3.35)	3.42
Stanley et al., 1996		2.26 (0.59, 8.64)	12.26
Subtotal (I-squared = 62.3%, p = 0.103)		0.76 (0.04, 13.35)	15.68
Overall (I-squared = 44.7%, p = 0.054)		0.33 (0.17, 0.66)	100.00

Meta-analyse CBT for late-life anxiety[1]

Follow-up (months)	Type of control	Studies (n)	Participants (n)	ES	[95% CI]	P-value
0	Non-active	7	215	0.66	[0.38 – 0.94]	<.001
0	Active	7	348	0.20	[-0.01 – 0.42]	.06
3	Active	3	164	0.40	[-0.12 – 0.91]	.13
6	Active	4	202	0.29	[0.01 – 0.57]	.04
12	Active	3	172	0.21	[-0.35 – 0.76]	.47

1. Gould et al, Am J Geriatr Psychiatry 2012

Important (new?) studies in later life

- Hendriks et al, Acta Psychiatr Scand 2010

- Wetherell, Am J Psychiatry 2013

- Brenes et al, JAMA Psychiatry 2015

Panic disorder in later life

A randomized controlled study of paroxetine and cognitive-behavioural therapy for late-life panic disorder

Hendriks G-J, Keijsers GPJ, Kampman M, Oude Voshaar RC, Verbraak MJPM, Broekman TG, Hoogduin CAL. A randomized controlled study of paroxetine and cognitive-behavioural therapy for late-life panic disorder.

Objective: To examine the effectiveness of paroxetine and cognitive-behavioural therapy (CBT) in elderly patients suffering from panic disorder with or without agoraphobia (PD(A)).
Method: Forty-nine patients aged 60+ years with confirmed PD(A)

G.-J. Hendriks[1,2,3], G. P. J. Keijsers[2], M. Kampman[1], R. C. Oude Voshaar[3], M. J. P. M. Verbraak[2,4], T. G. Broekman[5], C. A. L. Hoogduin[2]

[1]Forum GGz Nijmegen, Department for Anxiety Disorders ``Overwaal'', Nijmegen, [2]Radboud University Nijmegen, Behavioural Science Institute, Nijmegen,

RCT: Panic disorder in later life (n=49)

Changes in MI (avoidance)
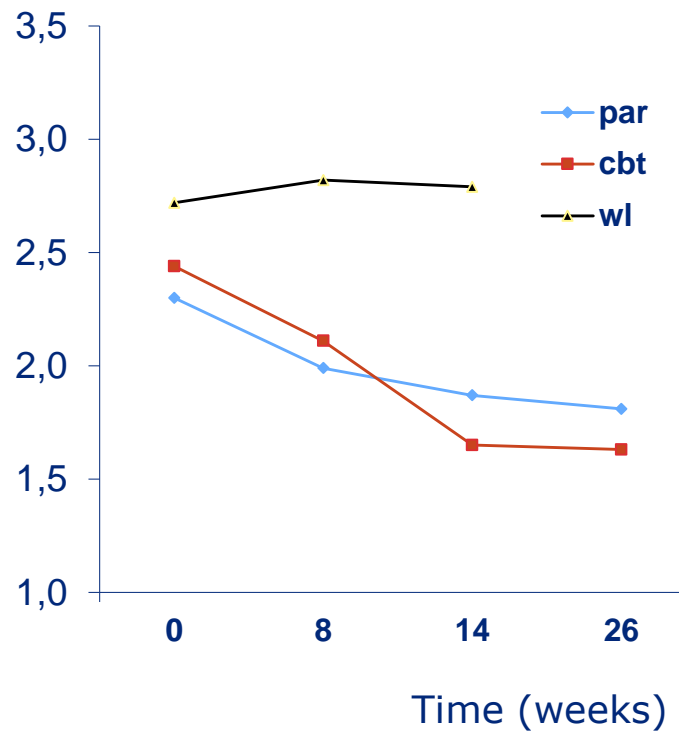
Changes in ACQ (cognitions)
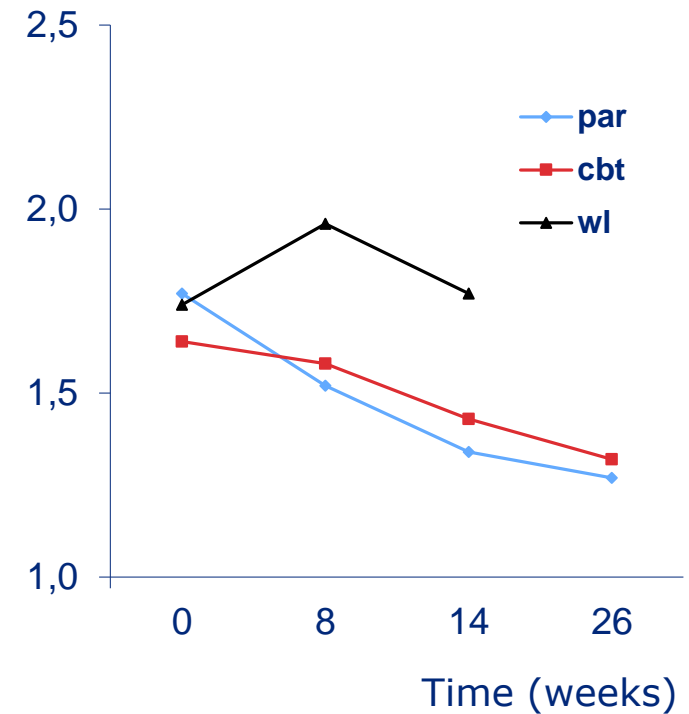
Age of onset

Differential effects of paroxetine and CBT
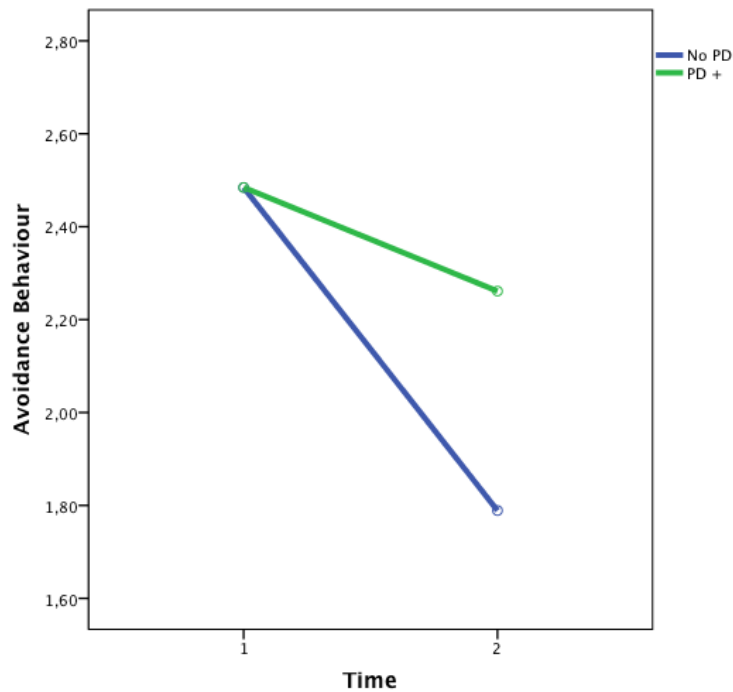## on avoidance behaviour in late-life panic disorder

[1] Hendriks et al, Int J Geriatr Psychiatry 2011
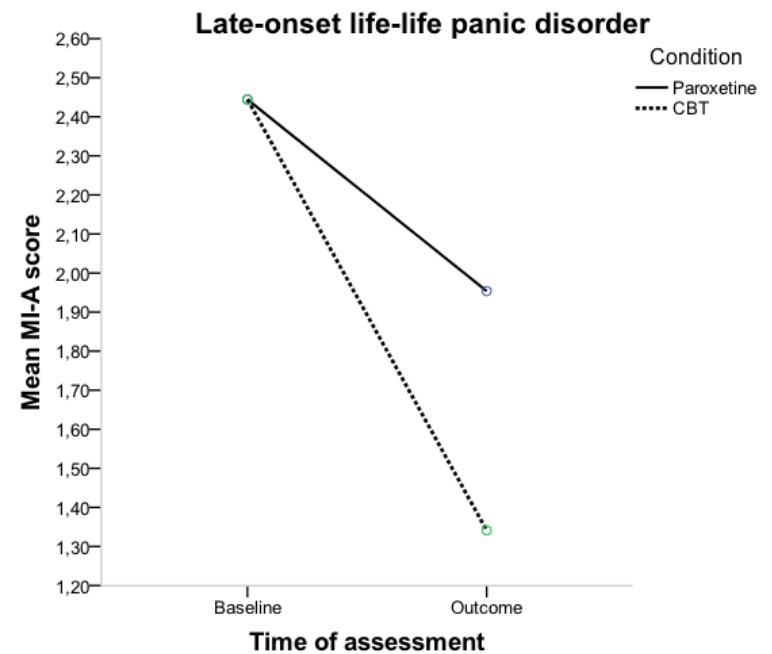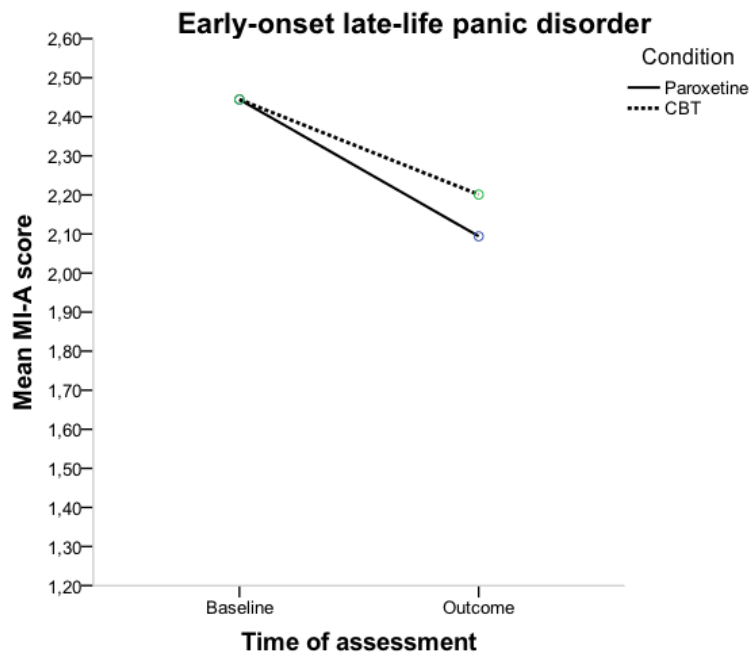
Age of onset

Differential effects of paroxetine and CBT

on agoraphobic cognitions in late-life panic disorder

[1] Hendriks et al, Int J Geriatr Psychiatry 2011
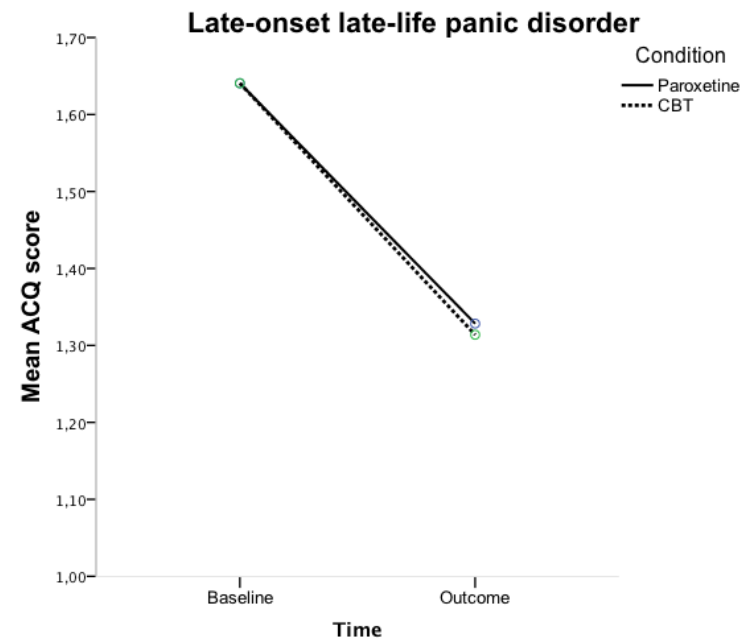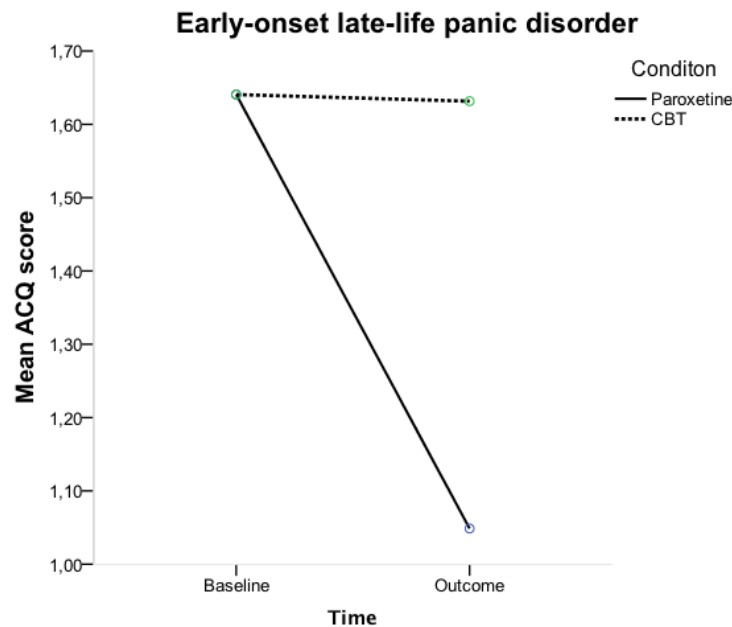
Personality disorders & late-life panic disorder

Paroxetine

CBT
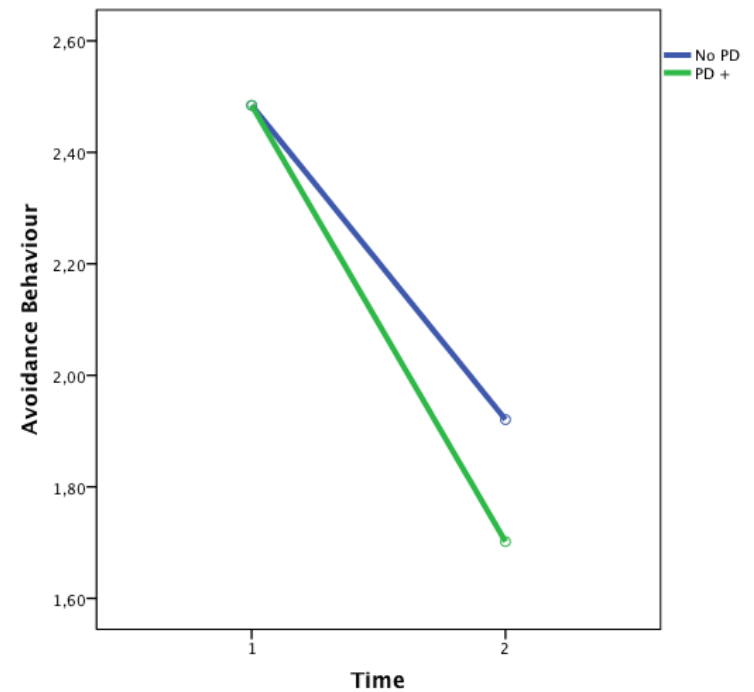
Conclusions late-life panic disorders

- CBT and paroxetine equally effective in later life

  – Early-onset: SSRI preferred over CBT

  – Late-onset: CBT preferred over paroxetine

- Experiences with treatment:

  – Atypical panic attacks deserve more attention

  – Exposure should be done thoroughly, also in oldest-old

RCT: Escitalopram augmented with CBT[1]

Background:

- SSRI are first choice for GAD in daily practice

- Efficacy decreases with age in GAD

- CBT is also less effective with age

- SSRI & CBT involve different mechanisms

- A sequential approach reflects clinical practice

Objective:

- Does CBT following escitalopram treatment boost responses and prevent relapse?

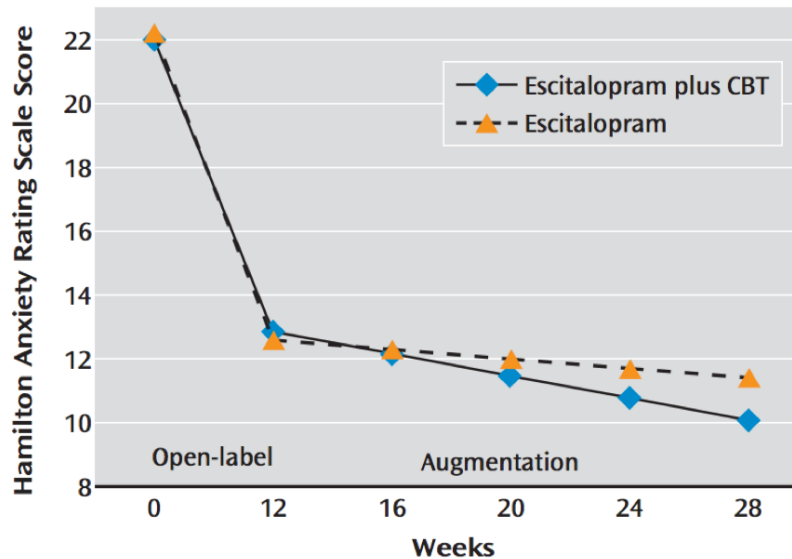[1] Wetherell et al, Am J Psychiatry 2013
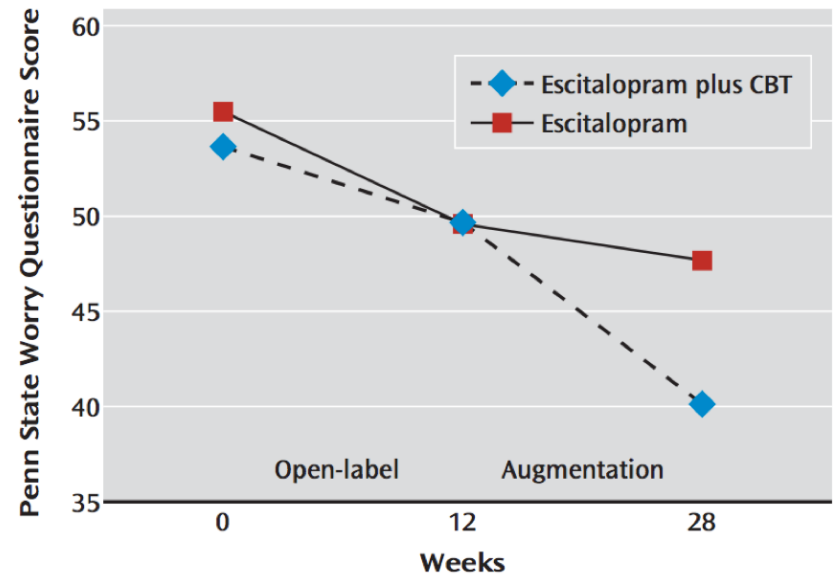
RCT: Flowchart[1]
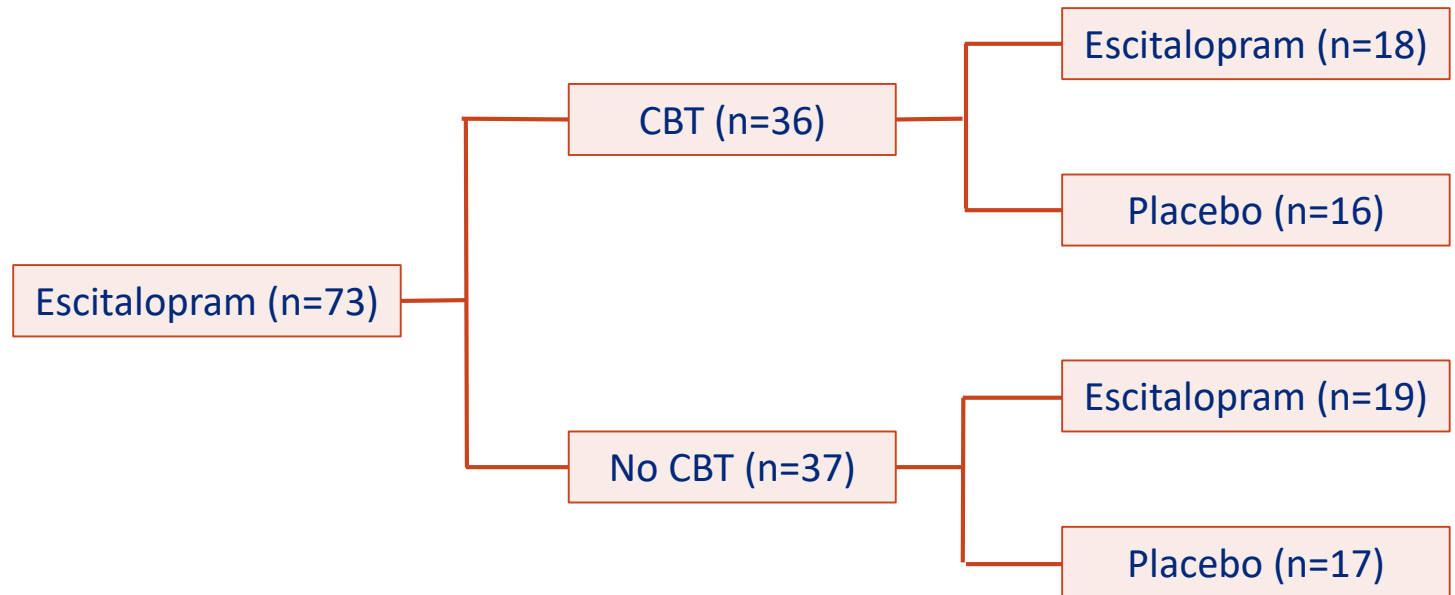
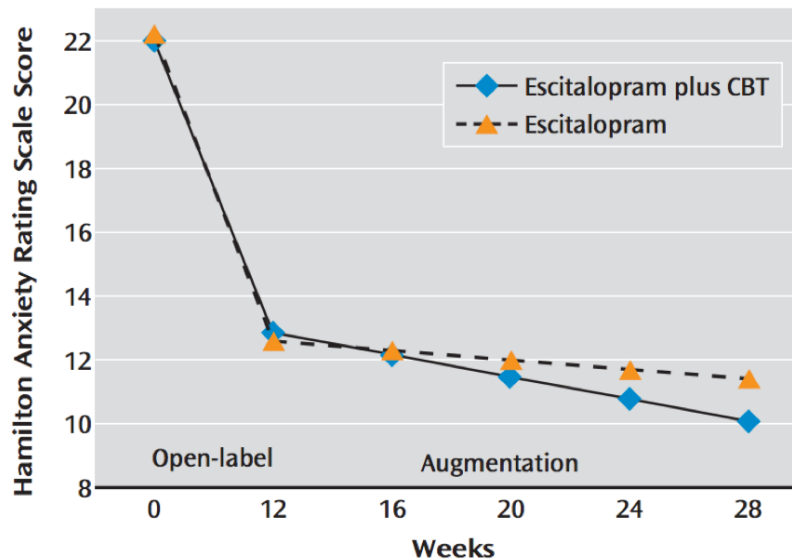[1] Wetherell et al, Am J Psychiatry 2013

Results: Escitalopram & CBT augmentation[1]

[1] Wetherell et al, Am J Psychiatry 2013

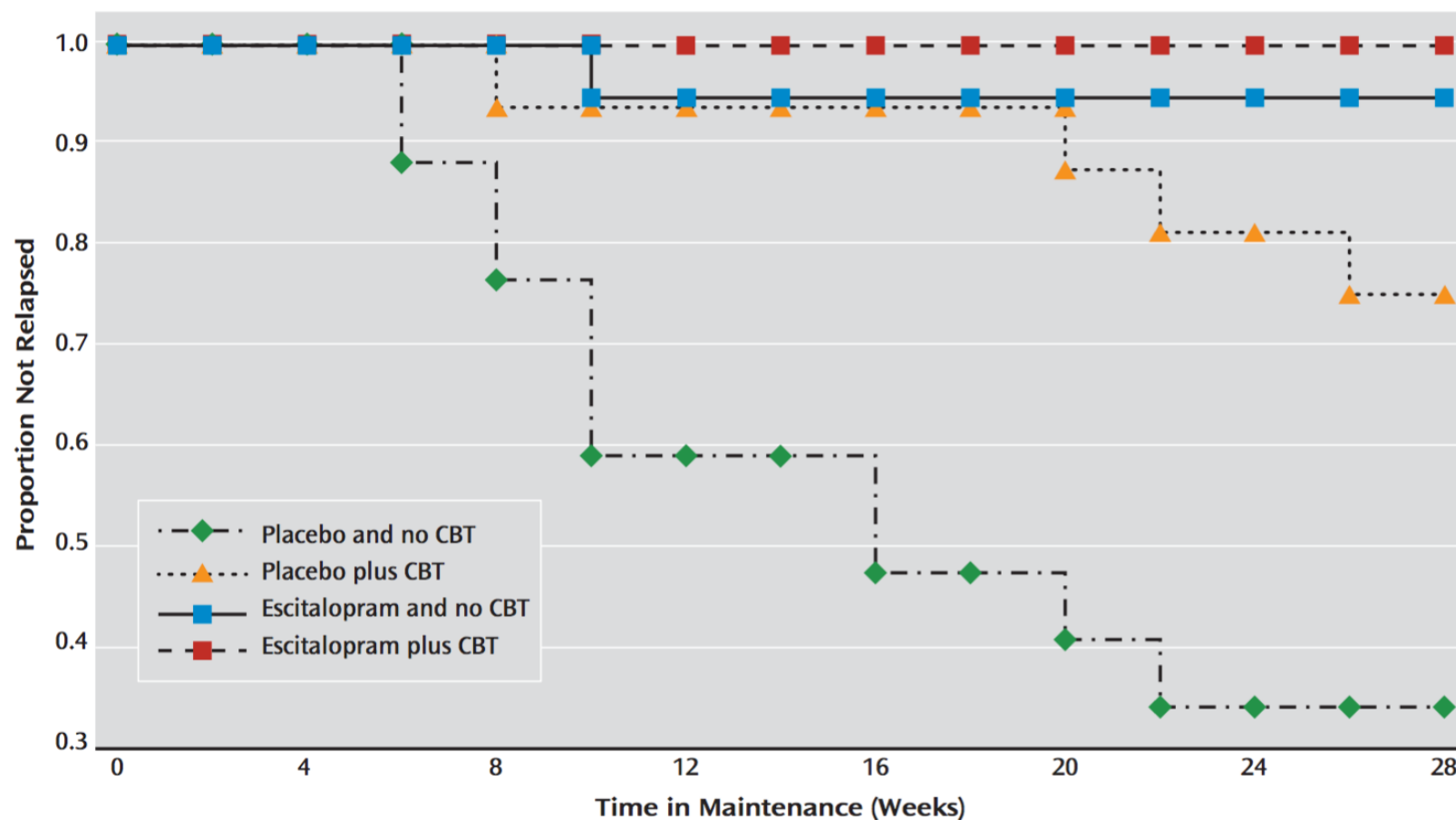Adding CBT to medication reduces worry

(but not somatic anxiety symptoms)

[1] Wetherell et al, Am J Psychiatry 2013

FIGURE 3. Kaplan-Meier Survival Curve for Relapse in Older Adults With Generalized Anxiety Disorder Who Received Maintenance Escitalopram, Cognitive-Behavioral Therapy (CBT), Both, or Pill Placebo (N=70)

[1] Wetherell et al, Am J Psychiatry 2013
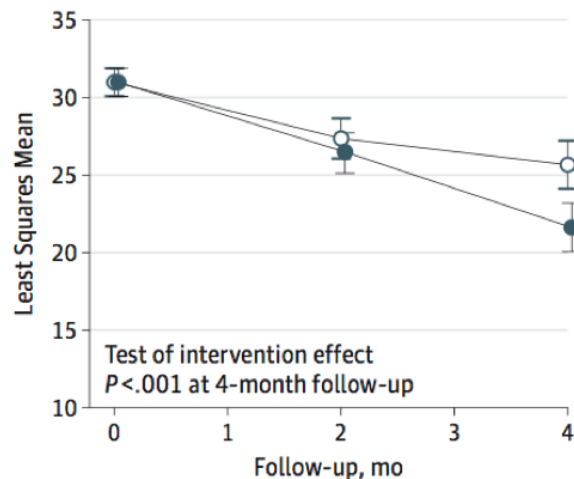
Telephone-delivered CBT for GAD[1]

Is telephone-delivered CBT (CBT-T) superior to non-directive supportive therapy (NST-T) for GAD in later life four months post-randomisation?
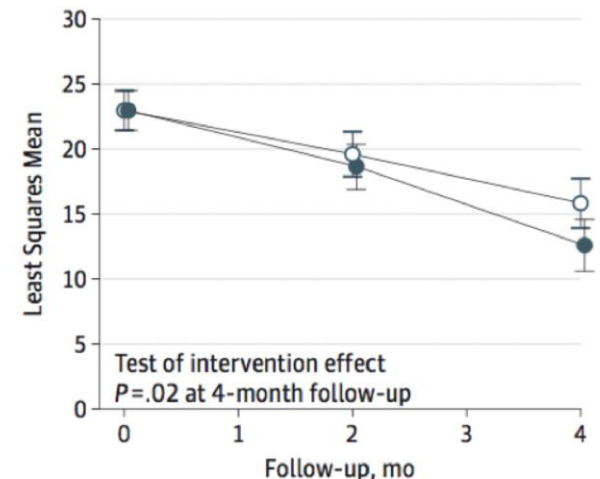
[1] Brenes et al, JAMA Psychiatry 2015

Primary & secondary outcome RCT (n=141)

A | Penn State Worry Questionnaire—Abbreviated

B | Beck Depression Inventory

[1] Brenes et al, JAMA Psychiatry 2015

Take home messages

- Highly prevalent, but poorly recognised

  - More attention for subthreshold anxiety, especially panic attacks

- Pay attention to anxiety related to somatic morbidity

  - E.g. cardiac anxiety, fear of falling, fear of dementia.

- CBT can be equally effective in older vs younger life.

- Personality pathology and age of onset might be important profiling factors