

Depressive disorders in late life

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“The pain of depression is quite unimaginable to those who have not suffered it...”

Darkness Visible. A Memoir of Madness.

William Styron. 1990

- A. Five (or more) of the following symptoms have been present during the same 2- week period and represent a change from previous functioning; at least one of the symptoms is either **(1) depressed mood or (2) loss of interest or pleasure**.
- Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

- Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful).
- Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others).
- Significant weight loss when not dieting or weight gain (e.g., a change of more than 5 percent of body weight in a month), or decrease or increase in appetite nearly every day.
- Insomnia or hypersomnia nearly every day.
- Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

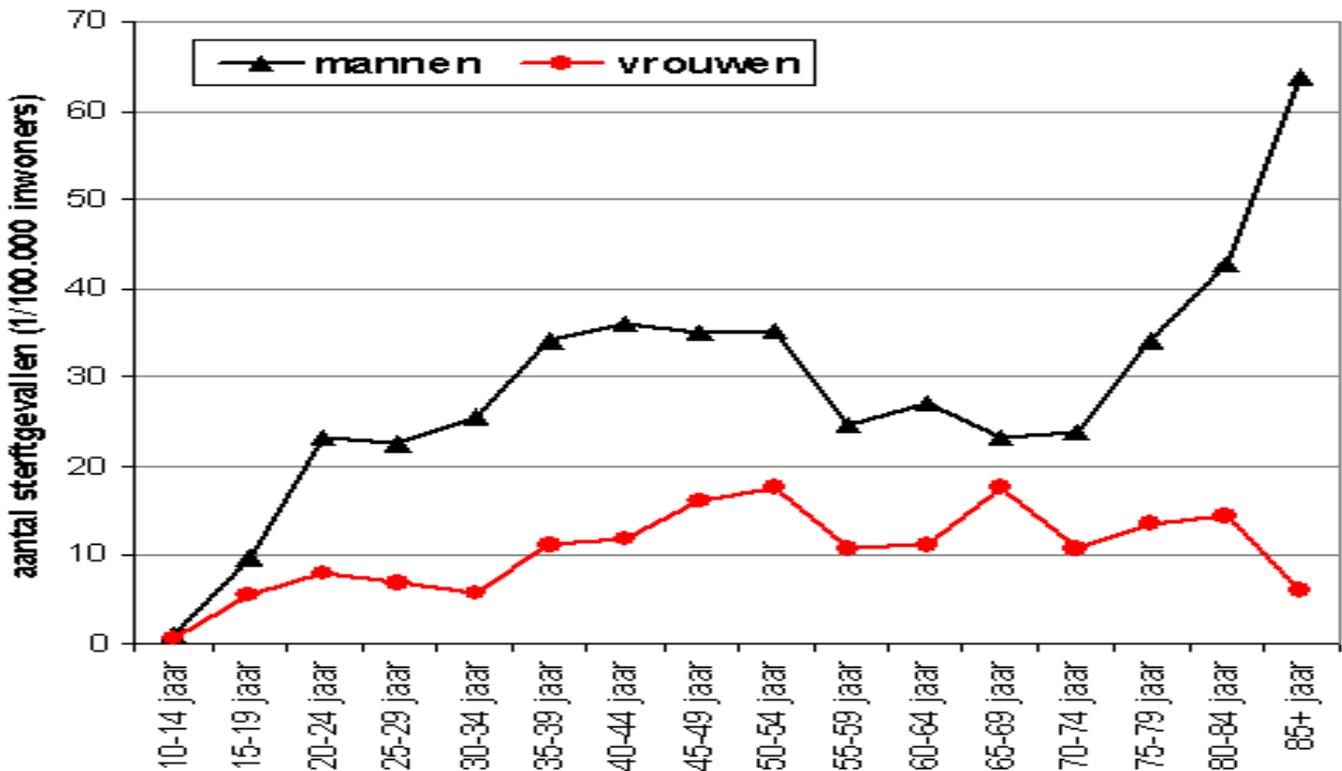
- Fatigue or loss of energy nearly every day.
- Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
- Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
- Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
- B. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.
- C. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

A few topics to consider...

- heterogeneous presentation due to comorbidity (psychiatric, somatic, neurodegenerative)
- DSM V: uses an exclusive approach (probable medical condition causing a symptom)
- probably the current classification systems used in most community studies overlook many of the late-life depressions
- 'clinical significant depression' is associated with worsened medical comorbidity, disability and increased health care utilization
- depression: a spectrum disease (* series of dichotomous diseases): symptom * syndrome * disease

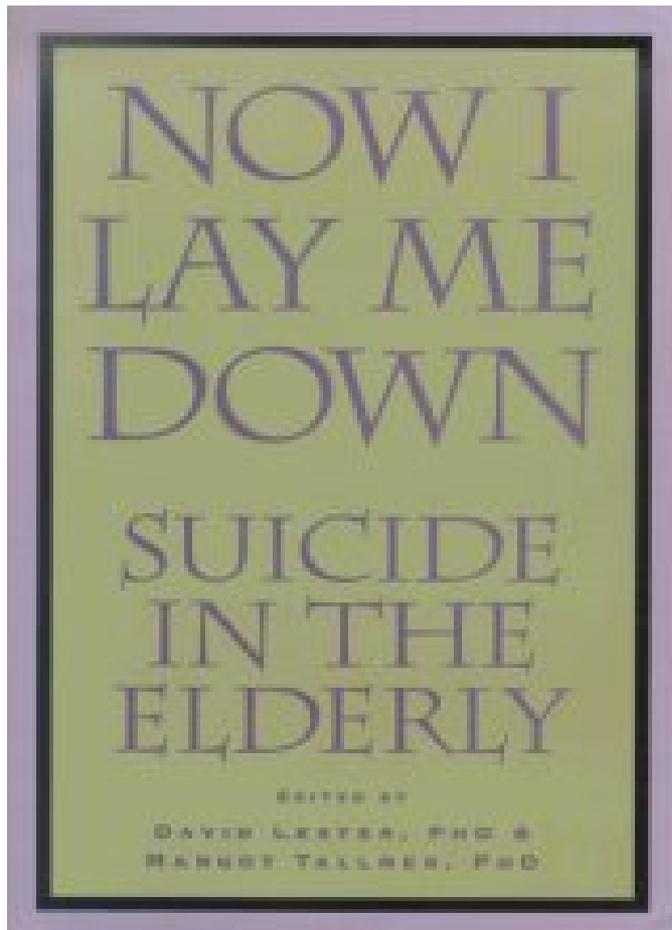
- prevalence of depressive symptoms > prevalence of major depression (in both younger and older populations)
- major depression: $\pm 2\%$ of community dwelling elderly subjects (* 3 à 6% in younger adults)
- ‘clinically significant depressive’ symptoms:
 - $\pm 15\%$ of an elderly population living in the community
 - 20 to 40% in residential care, nursing homes and hospital wards

Leeftijdsspecifieke sterftcijfers voor suïcide (per 100.000 inw.), Vlaams Gewest, 2008



Riskfactors

- history of psychiatric problems:
major depression, alcohol abuse, PTSD, history of suicide attempt, personality disorder
- somatic disease: complex interaction between functional loss, anticipation of functional loss, personality * direct 'attack' on identity and life style
'One never gets used to pain and urinary incontinence...'
- age related life events
- awareness of cognitive deterioration



The illusion of the choice?

Case report

Maria

- 78 yr, married, 2 children
- housewife; administration in business of husband
- no personal nor family psychiatric history
- no psychosocial problems

January 2011:

- Maria is transferred from the department of cardiology to old age psychiatry because of 'hysterical behaviour'

On admission:

- agitated, angry at the transfer; feels not being taken seriously
- very occupied by intestines and convinced she 'smells badly'
- lost about 15 kg last 2 year
- complains of bad sleeping
- denies depression
- no major cognitive deficits

Heteroanamnesis (husband)

- 'all went wrong' after the CABG (2007)
- shortly after the operation Maria gets convinced her intestines were 'touched' * medical shopping and several admissions into hospital
- weight loss, loss of interest in grandchildren, household
- she even succeeded in forcing a surgeon to 're-open' to have everything 'controlled'

- diagnosis of major depression with psychotic symptoms
- ECT (6 sessions bifrontal)
- after 3 sessions her husband describes a 'miracle'
- after 5 weeks she goes home completely recovered (on nortriptyline en aripiprazole)

Older patients with depression are little different to younger adults, although:

compared to younger adults some symptoms are more frequent:

- more somatic complaints and hypochondriasis
- more psychomotor disturbances (retardation or agitation)
- more psychotic symptoms
- more melancholia
- more feelings of guilt
- more reported insomnia

some symptoms are less prominent:

- less irritability
- less hypersomnia

Diagnostic difficulties

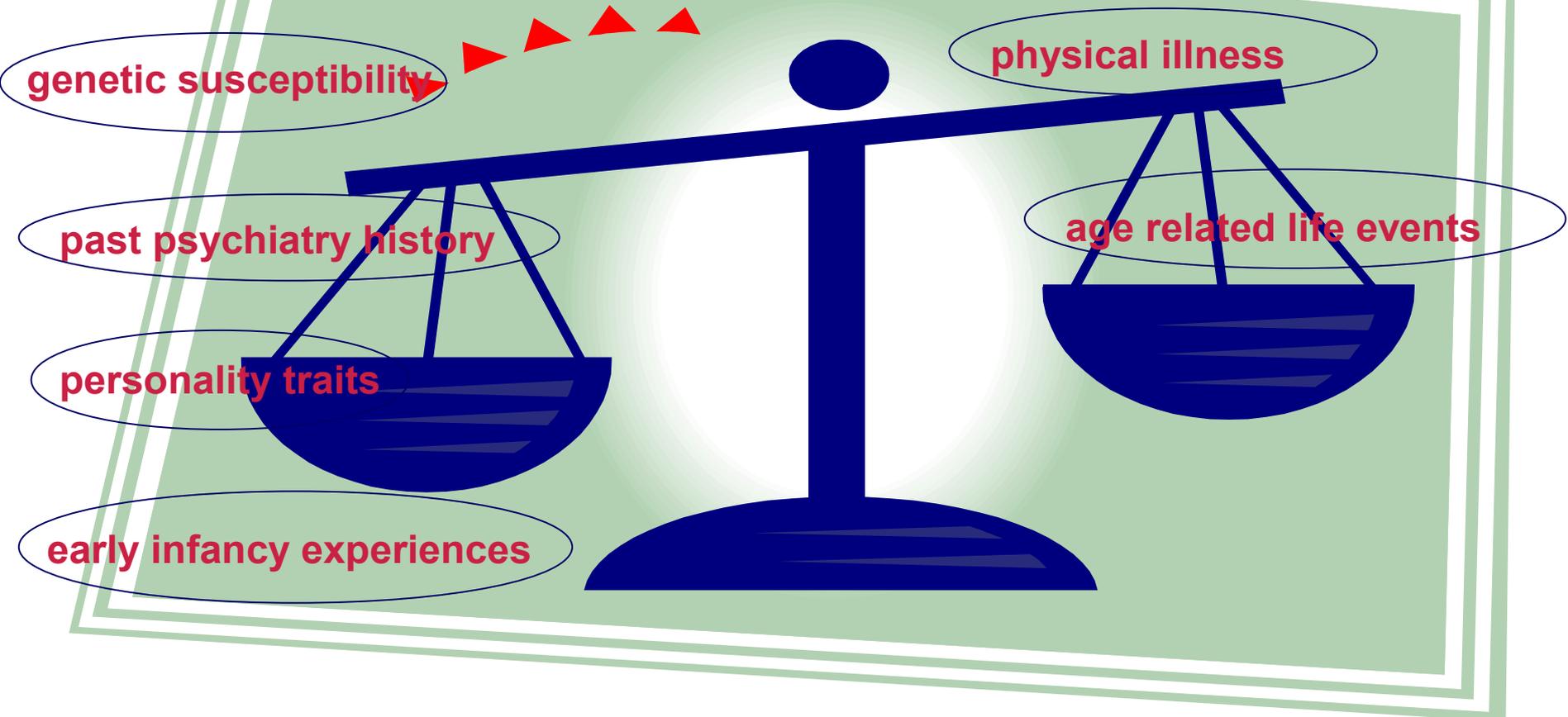
- overlap of symptoms (somatic disorder * physical symptoms of depression)
- pain is a frequent and unrecognized symptom of depression
- tendency of older people to minimize sadness
- late onset neurotic symptoms (anxiety, hysteria) may mask depression
- behavioural symptoms (e.g. alcohol abuse, abrupt onset of incontinence) may mask depression
- deliberate selfharm which seems medically trivial (e.g. overdose)
- prominent cognitive symptoms

Older persons do not usually mask depressive symptoms more than younger persons if only the clinician asks for the presence of a depressed mood

Blazer, 1993

Predisposing factors

Precipitating factors



'after seventy years, all is trouble and sorrow...'
Burton, The Anatomy of Melancholy, 1621

Age related life events

- change in social function
- social isolation, poverty, poor social support
- moving into residential setting
- loss of significant 'other' (including pets) – bereavement
-lack of intimate relationships
- chronic caregiving
- non-events
- sensory loss, cognitive decline, physical illness and disability

Vink, 2008; Blazer, 2005; Lenze, 2001; Prince, 1998; Robert, 1997

Healthy, normally functioning older adults are at no greater risk for depression than younger adults. What seem to be age-related effects on depression are attributable to physical health problems and disability

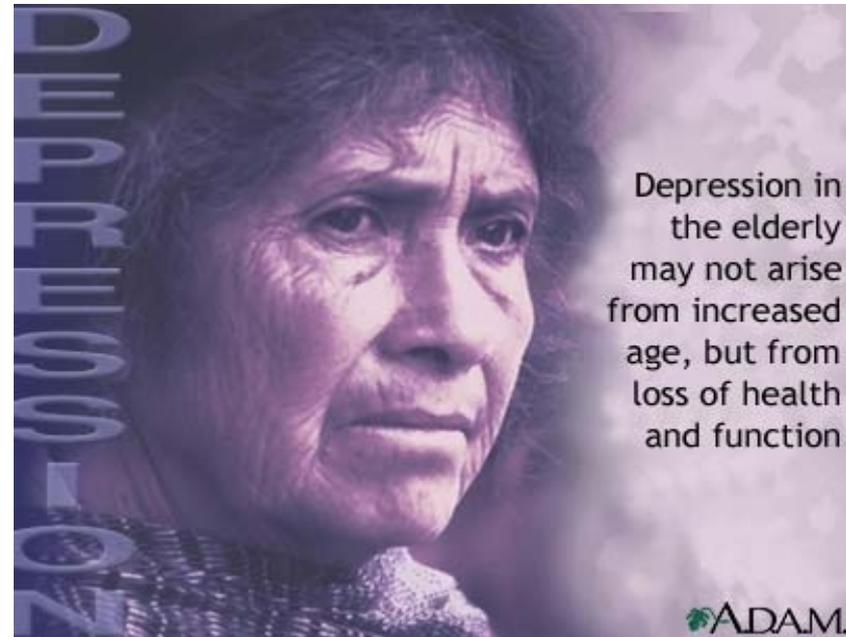
Roberts et al, Am J Psychiatry, 1997

The majority of these cases are not recognized or properly treated

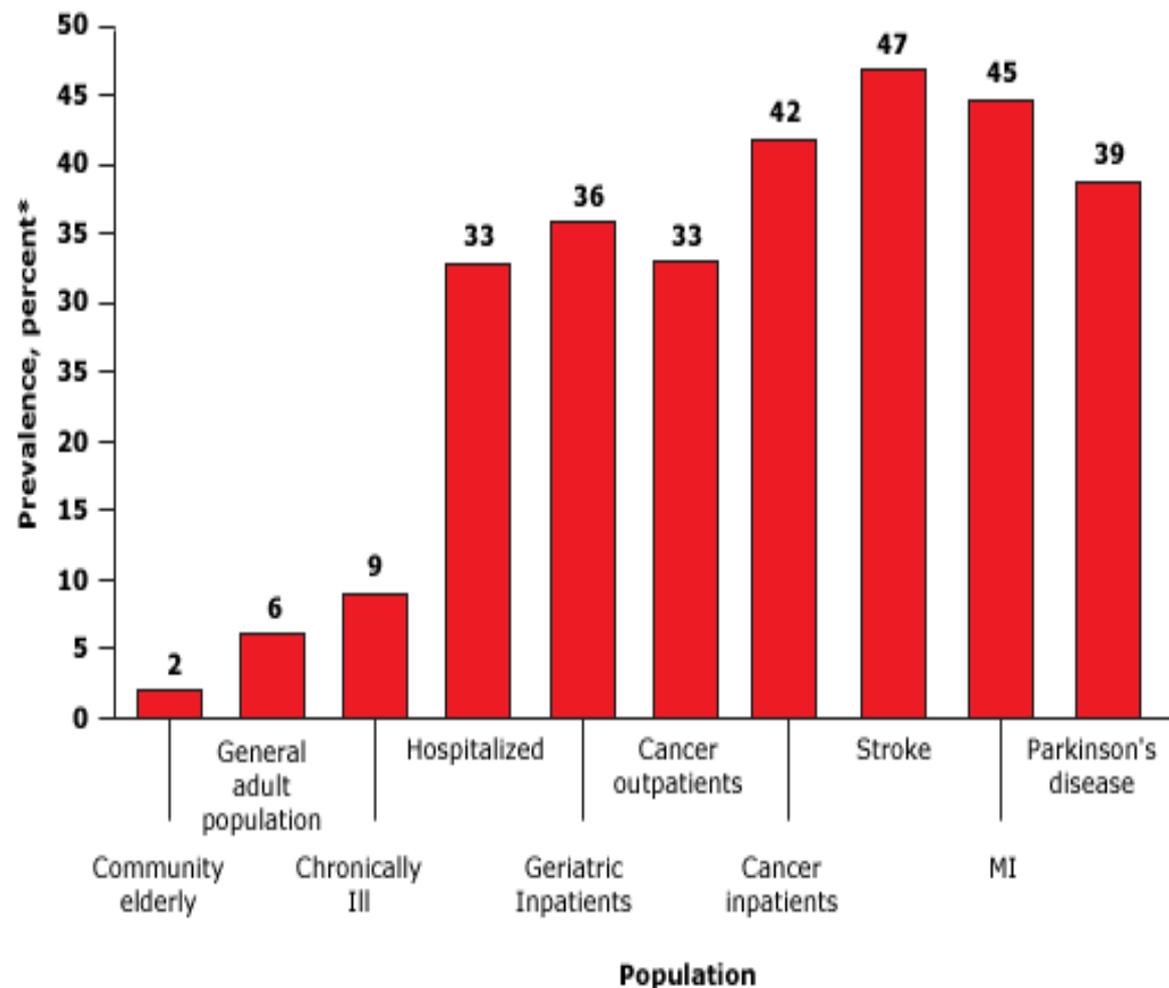
Whooley, JAMA, 2006, Healing the Broken-Hearted

Late-life depression: independent risk factor for disability

Lenze et al, Am J Geriatr Psychiatry 2001



Prevalence of depressive disorders in various patient populations



* Prevalence range varies according to study.

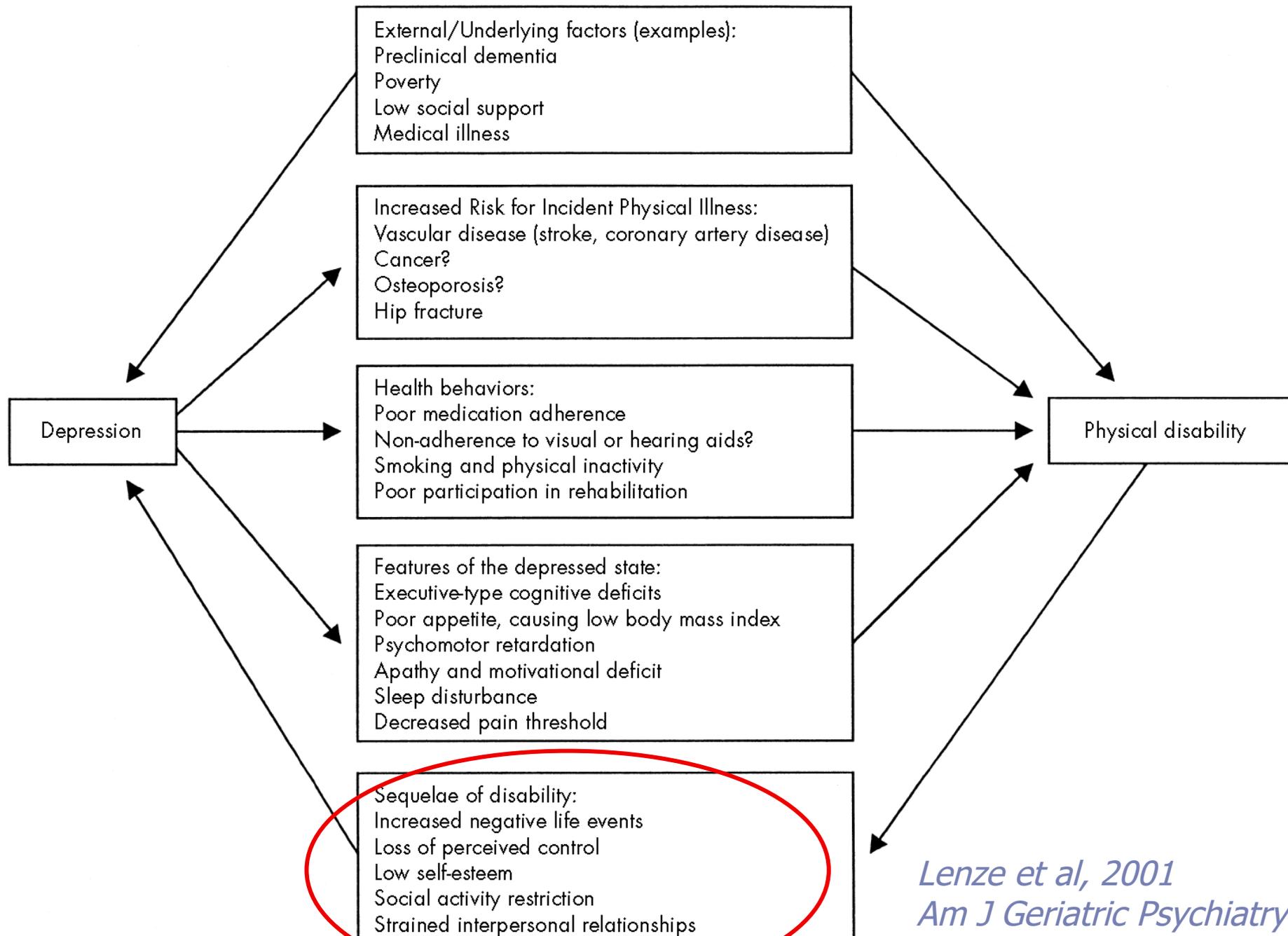
Data from Birrer, RB, Vemuri, SP. Depression in later life: a diagnostic and therapeutic challenge. *Am Fam Physician* 2004; 69:2375

Mechanisms whereby physical illness may lead to depression

- altered serotonergic brain systems (Parkinson's disease, dementia, stroke)
- organic depressive disorder:
 - hypo/hyperthyroidism; hypercalcemia; Cushing's disease, anaemia; CNS tumor; occult carcinoma; chronic infections (AIDS, brucellosis,..); systemic lupus
 - medication: non-selective β blockers, methyldopa, clonidine, nifedipine, calcium channel agents, digoxin, steroids, opioids, levodopa, neuroleptics, benzodiazepines, interferon
 - (alcohol)
- disability: **'the meaning of being ill'**: *'the disadvantage in society'*

Dhondt, 2003; Lenze, 2001; Prince, 1998; Robert, 1997

1. Model of depression and disability



*Lenze et al, 2001
Am J Geriatric Psychiatry*

...subtle cerebral changes may make aging persons increasingly liable to affective disturbances... Post, '68

- damage to frontal subcortical circuitry due to either neurodegenerative or cerebrovascular disease, is implicated in some subtypes of late-life depression
- changes in mono amine system with advancing age * increased susceptibility for depression in late life? ≈ inconsistent findings
- neuro endocrine changes with e.g. dysregulation of HPA axis may lead to increased susceptibility for depression in late life
- changes in immune and inflammatory systems may make older people more vulnerable for depression (?)

Alexopoulos, 2003 ; Baldwin, 2005; Karlsson, 1990; Leonard, 2007

- Vascular depression hypothesis
 - Less depressive ideation
 - More psychomotor retardation, apathy and poorer insight
 - More cognitive impairment (executive dysfunction)
 - Greater disability
 - High rate of structural brain abnormalities in white matter and basal ganglia
 - Poorer response to antidepressant treatment and ECT

Alexopoulos, 1997; Krishnan, 2004; Alexopoulos, 2004

Vascular depression: a valid concept?

- No clear correlation with traditional vascular riskfactors
- Temporal link between vascular lesions and depression unclear
- Direction of causality unclear

Vascular depression: clinical relevance?

- Worse outcome of classical antidepressant strategies
- Importance of screening (and treating) each depressive patient (young or old) on vascular riskfactors
- Antidepressant therapy should aim at improving underlying vascular problems as well as mood

- motivational problem with loss of focused behaviour and cognition and loss of emotional responses
- great impact on daily functioning
- negative impact on comorbid disease
- high association with neurodegenerative diseases (Alzheimer's, Parkinson's) and stroke (Re hemisphere)
- poor therapeutic possibilities: cholinesterase inhibitors? ginkgo biloba? dopaminergic strategies? methylfenidaat?
- poor prognosis

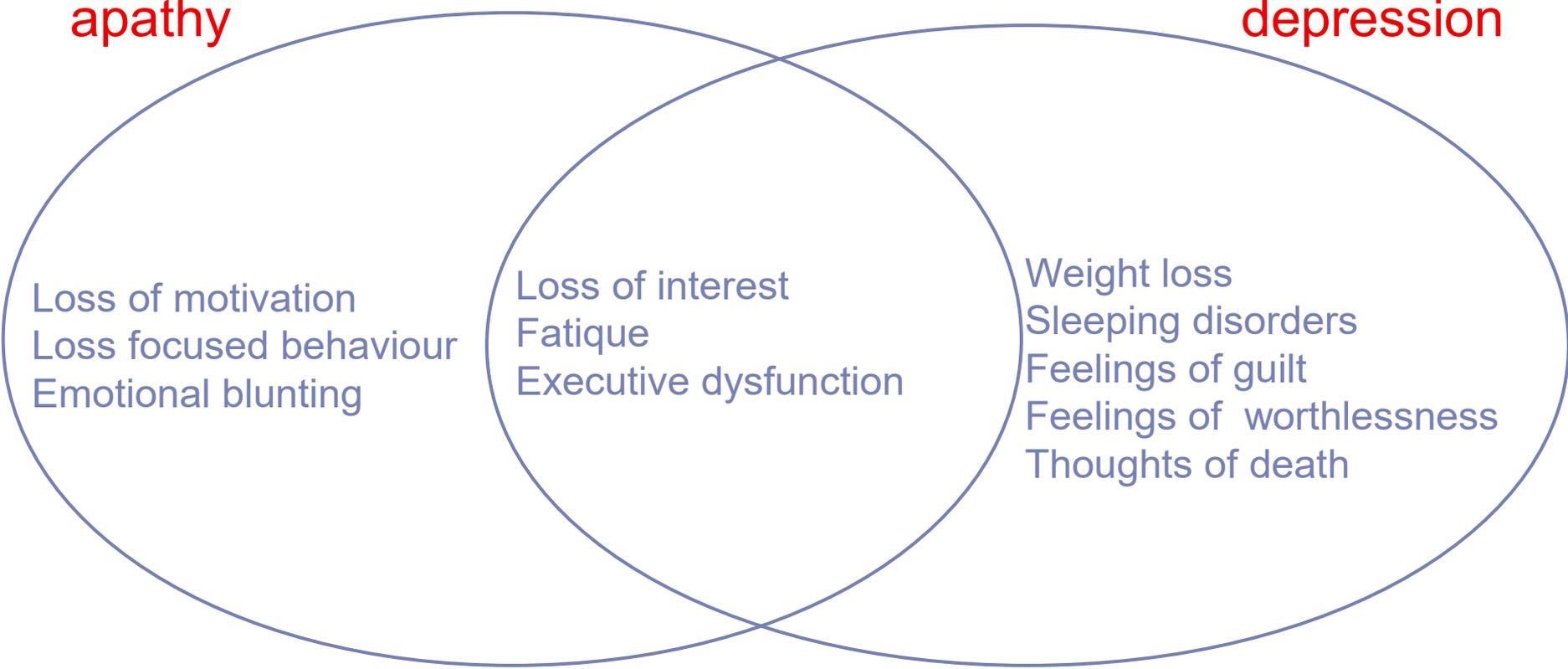
apathy

depression

Loss of motivation
Loss focused behaviour
Emotional blunting

Loss of interest
Fatigue
Executive dysfunction

Weight loss
Sleeping disorders
Feelings of guilt
Feelings of worthlessness
Thoughts of death



- Cognitive symptoms are frequent in depression in older and younger adults
- Former literature focused on differential diagnosis between late life depression and dementia (*'pseudodementia'*) in order not to miss a *'reversible dementia'*
- Neuropsychological deficits in late life depression:
 - executive dysfunctioning (planning, initiation, task persistence)
 - speed of information processing
 - attention deficits
- Executive dysfunctioning ✳ poorer response to antidepressant treatment?
- Neuropsychological deficits reversible after recovery from depression?
- Growing evidence for depression as a risk factor of later dementia
- When depressed and MMSE < 24/30: at-risk group for later dementia

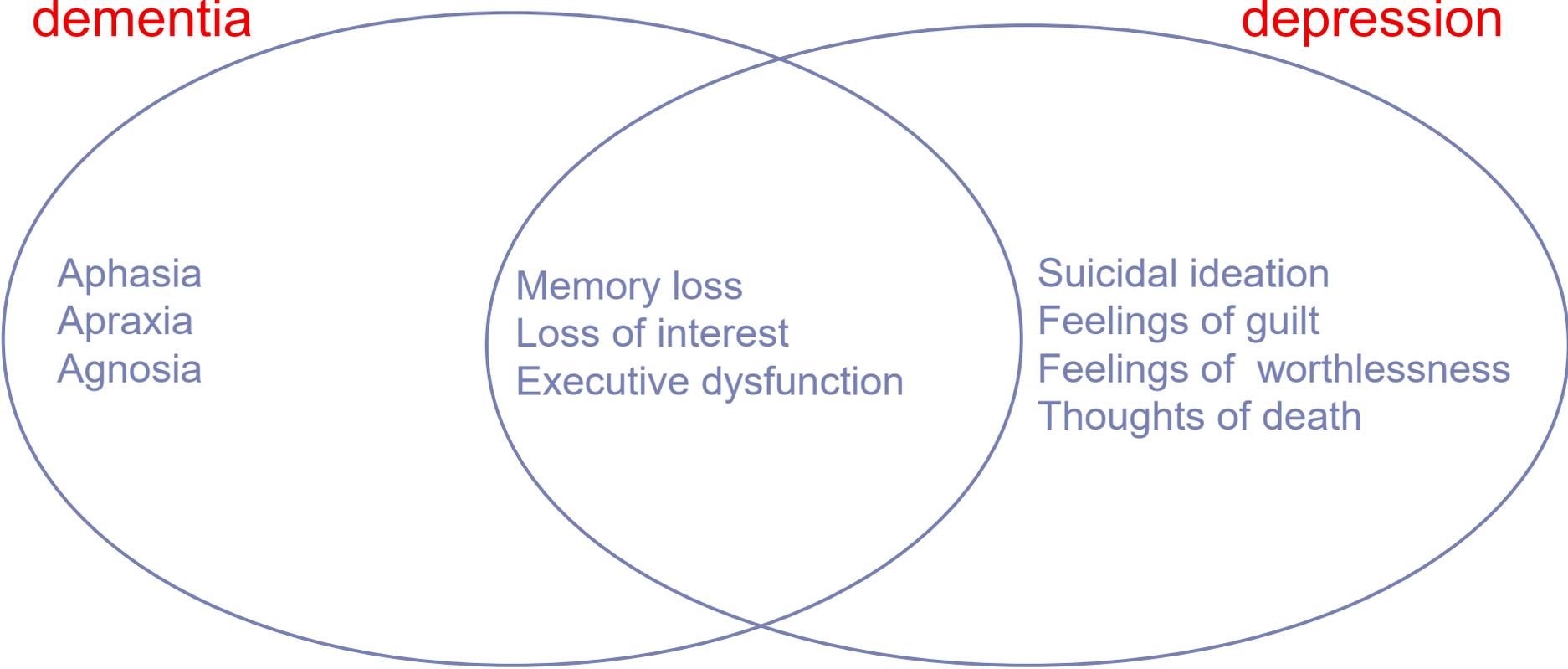
dementia

depression

Aphasia
Apraxia
Agnosia

Memory loss
Loss of interest
Executive dysfunction

Suicidal ideation
Feelings of guilt
Feelings of worthlessness
Thoughts of death



- adjusted criteria for depression in dementia: focus on social isolation, withdrawal, reduced positive affect
- great impact on overall performance
- major concern of caregivers
- often difficult differential diagnosis with apathy

Olin, 2002

- affiliation and belonging
- positive life events (eg birth of a grandchild)
- healthy life styles
- adaptive coping styles and psychological resilience
(the ability to make sense of events and accept one's existence)
- wisdom in late life
(wisdom: accumulation of knowledge, understanding, judgment and the capacity of being able to place matters in a context)

Blazer, 2005; Arian, 2005

- clinical history with, if possible, information from a proxy
- assessment for suicidality, including ideation
- assessment for hopelessness, insomnia
- psychiatric history (individual and family)
- alcohol (abuse?) and nutritional evaluation
- physical examination and drug evaluation (*cfr organic mood disorder*)
- cognitive screening test (*MMSE*)
- depression screening questionnaire (*Geriatric Depression Scale*)
- evaluation of current supporting systems

GDS: 30 questions; shorter version: 15 questions

5-item version:

- Are you basically satisfied with your life?
- Do you often get bored?
- Do you often feel helpless?
- Do you prefer to stay at home rather than going out and doing new things?
- Do you feel pretty worthless the way you are now?

Cut-off for 'possible depression' in 5 item version: $> \text{ or } = 2$

('no' to question 1 or 'yes' to questions 2 through 5)

Validation of the five-item geriatric depression scale in elderly subjects

Rinaldi et al J Am Geriatr Soc. 2003;51(5):694.

- Full blood count
- Urea and electrolytes
- Calcium
- Thyroid function
- B12 and folate
- Liver function
- CT (brain), EEG, serology: if clinically indicated

- depressive disorder is prone to persistence across all age groups
- in late life: remission comparable to younger adults but greater risk of relapse
 - 1/3 full remission, 1/3 remission with recurrence, 1/3 chronic intermittent course
- associated with high 'family burden'
- worse outcome of medical comorbidity
- independent risk factor for mortality, independent of suicide
- outcome from medical ward poorer than those under psychiatric care
- great risk of relapse * need for continuation of treatment

Depression in late life: treatment issues

Public perceptions of mental illness

71%: due to emotional weakness

65%: caused by bad parenting

45%: victim's fault

43%: incurable

35%: consequence of sinful behavior

10%: has a biological basis; involves brain

80%: depression in the elderly: quite normal

- **'frailty':**
geriatric syndrome: poor mobility, sensorial deficits, loneliness, chronic diseases, cognitive decline, depressed mood, growing dependency
- growing group of elderly where 'well-being' and 'quality of life' are often difficult to define
- often negative public perception

'Major depression in the very old can be treated as successfully as in early old age'

Gildengers, 2002

General principles:

- holistic approach with attention for (eventual) underlying somatic disease, psychosocial problems, global functioning (eg mobility, ...), spiritual aspects, ...
- psycho-education is of major importance (de-stigmatisation, depression as a disease, treatment issues, life style, ...)
- non-specific factors play a major role in recovery:
'tender loving care'
- empowerment of the older individual as main goal in our approach

'stepped care' model:

- minor depression and dysthymia: minor interventions (merely life style adjustment) and *watchful waiting*
- if insufficient effect (eg after 3 months): more focused psycho- or pharmacotherapy to be added
- major depression with / without psychotic symptoms: antidepressant therapy / ECT

Antidepressants:

- more than 100 RCT's showing efficacy of antidepressive medication in an elderly population
- effect comparable to younger adults
- equal efficacy of TCA and SSRI
- SSRI's seem to be better tolerated
- tailoring pharmacologic choices to the individual patient
- careful watching for side effects
- somatic complaints too often interpreted as side effect
- dose: start low, go slow but go!
- continue for at least 1 yr after remission (1st episode)

- 1st choice for psychotic depression, severe depression with life-threatening refusal of medication, food or fluids
- safe in older people
- response rate: 80% in psychotic depression
- some discussion about delivery of ECT (unilateral, bifrontal, bitemporal): efficacy and cognitive complaints have to be considered
- CI: feochromocytoma, recent MI, unstable angina pectoris, recent stroke, intracerebral overpressure

- indication: acute mania, maintenance therapy in bipolar disorder
- very few studies on use of lithium in late life
- although: quite large cohort of older people using lithium, well tolerated
- dosage adjustment: mean dose: 300 to 600 mg/d
- toxicity at 'normal' bloodlevels * lower bloodlevels preferred: 0,4 to 0,6
- adverse effects: nausea, tremor, dysarthria, ataxia, delirious, hypothyreosis, ↑ weight, risk of renal impairment
- drug interactions: ↑ risk on Li – intoxication with:
thiazide diuretics, ACE inhibitors, furosemide, NSAID's

Psychotherapy and combined psychotherapy/pharmacotherapy for late life depression

- Cognitive-behavioral therapy and interpersonal psychotherapy combined with antidepressant medication have the largest base of evidence in support of their efficacy for late life depression
- In mild depression, there is support for interpersonal psychotherapy, brief dynamic therapy and life review treatments
- Need for further research (evidence based model * series with experimental design)

Multidisciplinary approach is essential

*'In geriatric care we don't need collaboration, we need **unity**'*

Tom Arie, Nottingham, 1980 Mental Health Care for the Elderly'

'I believe the time has come for psychiatry to join geriatric medicine in order to recapture its roots and deliver optimal care to the old and oldest old'

Dan Blazer, Am J Psychiatry 2000

Anxiety disorders in late life

Diagnostic criteria for generalized anxiety disorder

1. Excessive anxiety and worry about a number of events or activities, occurring more days than not for at least six months, that are out of proportion to the likelihood or impact of feared events.
2. The worry is pervasive and difficult to control.
3. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms present for more days than not for the past six months):
 - Restlessness or feeling keyed up or on edge
 - Being easily fatigued
 - Difficulty concentrating or mind going blank
 - Irritability
 - Muscle tension
 - Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)
4. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Adapted from Diagnostic and Statistical Manual of Mental Disorders, 4th Ed, Primary Care Version (DSM-IV-PC). American Psychiatric Association, Washington, DC 1995.

- generalized anxiety disorder
- panic disorder (with or without agoraphobia)
- agoraphobia without history of panic disorder
- social phobia
- specific phobia
- obsessive-compulsive disorder (OCD)
- post-traumatic stress disorder (PTSD)
- anxiety due to a general medical condition
- substance-induced anxiety disorder

Prevalence of anxiety disorders in late life compared to general population

	General population	60+
Panic disorder	2,2%	1 - 2%
OCD	0,9%	0,6%
PTSD	0,4%	0,9%
Phobia	± 7%	4%
GAD	1,2%	1 - 7,3%
All anxiety disorders	12,4%	10%

Bryant, 2008; Beekman, 1998; Beekman, 2000

Poor detection in spite of high prevalence and highly negative impact on quality of life, health, functional deterioration

Due to:

- tendency of older people not to talk about anxiety
- high co-morbidity with somatic disorders
- main focus of health care, research, public interest, ...on dementia and depression

‘Older adults with anxiety disorders worry less than younger adults about work, future, .. but more about medical illness and falls’

Kastenschmidt and Kennedy, Mount Sinai Journal of Medicine, 2011

Case report: Eric

- 76yr, lives alone, wife died 1 yr ago
- since his wife died, he feels anxious and lonely at home
- he's afraid about failing in organizing the household and thinks he will never be able to manage on his own
- he panics at 'unusual' situations (eg when taxes to pay, wedding of granddaughter, ...)
- highly irritable, doesn't sleep well and feels very restless
- when he's at his daughter's home, he seems to feel 'safe'

≈ *generalized anxiety disorder*

Case report: Suzanne

- 74yr, married, complains of dizziness since years
- no somatic explanation for her symptoms despite numerous visits to GP and specialist
- more and more she avoids to go out on her own because of fear of falling
- when her husband stimulates her to go into town by bus, she starts sweating and complaining of palpitations

≈ phobia with symptoms of panic disorder

Case report: Dora

- 69yr, lives alone, husband died 8yr ago
- sees GP regularly different 'vague' symptoms (abdominal pain, insomnia, headache,...)
- after some hesitation she tells GP she's avoiding to go out because she feels unsafe, she sees 'danger' everywhere
- further exploration reveals the fact that she has been violated by an uncle at the age of 14
- since her husband died she 'sees' nearly everyday what happened at that time (flash backs)

≈ post traumatic stress disorder

The acquisition and subsequent loss or elaboration of symptoms of anxiety is determined by vulnerability of patient, factors responsible for destabilisation and the measures taken (or not) by patient and / or doctor

- genetic factors contribute to vulnerability in younger adults
- physical illness, institutionalisation, bereavement are major factors of destabilisation *'nothing is the same anymore'*
- previous traumatic experiences: early parental loss, sexual abuse, war trauma, ... highly associated with anxiety (all ages)
- quality of current relationships

- anxiety – like symptoms due to medical conditions and medication

Physical causes of anxiety-like symptoms

Cardiovascular
Angina pectoris, arrhythmias, heart failure, hypertension, hypovolemia, myocardial infarction, syncope (multiple causes), valvular disease, vascular collapse (shock)
Dietary
Caffeine, monosodium glutamate (Chinese restaurant syndrome), vitamin-deficiency diseases
Drug-related
Akathisia (secondary to antipsychotic drugs), anticholinergic toxicity, digitalis toxicity, hallucinogens, hypotensive agents, stimulants (amphetamines, cocaine, related drugs), withdrawal syndromes (alcohol, sedative-hypnotics), bronchodilators (theophylline, sympathomimetics)
Hematologic
Anemias
Immunologic
Anaphylaxis, systemic lupus erythematosus
Metabolic
Hyperadrenalism (Cushing's disease), hyperkalemia, hyperthermia, hyperthyroidism, hypocalcemia, hypoglycemia, hyponatremia, hypothyroidism, menopause, porphyria (acute intermittent)
Neurologic
Encephalopathies (infectious, metabolic, toxic), essential tremor, intracranial mass lesions, postconcussive syndrome, seizure disorders (especially of the temporal lobe), vertigo
Respiratory
Asthma, chronic obstructive pulmonary disease, pneumonia, pneumothorax, pulmonary edema, pulmonary embolism
Secreting tumors
Carcinoid, insulinoma, pheochromocytoma

Adapted from: Rosenbaum, JF, *N Engl J Med* 1982; 306:401.

Drugs that cause anxiety-like symptoms

Stimulants	Anticholinergics
Amphetamine	Benztropine mesylate (Cogentin)
Aminophylline	Diphenhydramine (Benadryl)
Caffeine	Meperidine (Demerol)
Cocaine	Oxybutynin (Ditropan)
Methylphenidate	Propantheline (Pro-Banthine)
Theophylline	Tricyclics
Sympathomimetics	Trihexyphenidyl (Artane)
Ephedrine	Dopaminergics
Epinephrine	Amantadine
Phenylpropanolamine	Bromocriptine
Pseudoephedrine	Levodopa (L-dopa)
Drug withdrawal	Levodopa-carbidopa (Sinemet)
Barbiturates	Metoclopramide
Benzodiazepines	Neuroleptics
Narcotics	Miscellaneous
Alcohol	Baclofen
Sedatives	Cycloserine
	Hallucinogens
	Indomethacin

Adapted from Goldberg, RJ. Practical Guide to the Care of the Psychiatric Patient. Mosby Year Book, St. Louis 1995.

- perception of 'loss of control' or 'loosing the track' is a major individual treath in early stage dementia and results often in feelings of anxiety
- anxiety in dementia can show itself in very different manners: agression, paranoia, emotionality, withdrawal, hostility, ...
- anxiety symptoms in late life may be a 1st symptom of dementia

- 'memory loss' phobia

Treatment of late life anxiety anno 2011:

1. *doing nothing*
2. *benzodiazepines, muscle relaxants, referral to specialty medical clinics (usually worse than doing nothing)*
3. *antidepressant monotherapy*

Lenze, Am J Geriatr Psychiatry, 2011

Defining who needs treatment: major concern

Therapeutic possibilities:

- cognitive behavioral therapy (CBT) effective, also in older populations
- SSRI and dual reuptake antidepressants effective
- relaxation, mindfulness, bibliotherapy, stepped care prevention, ... all promising but lack of research

Solution focused psychotherapy in an elderly population

It's the key that matters, not the nature of the lock...

Steve De Shazer

Main principles:

- focus on mental health
- 'empowerment' versus negative self esteem
- client and doctor are both experts
 - older adults: experts in surviving
 - older adults know very well what's good for them
 - focus on resources of patient, utilisation of what they bring us
- introduction of hope
- focus on present and future rather than endlessly exploring the past
- preconceive realistic goals
- cooperation with the 'system' of the client

De Shazer, Isebaert, in 'The Bruges model' , 2002



The largest part of the elderly, even older than 85, seem to live quite satisfied and happily, and this in spite of many handicaps and disabilities

Von Faber, 2001