DEPRESSION IN OLDER PEOPLE

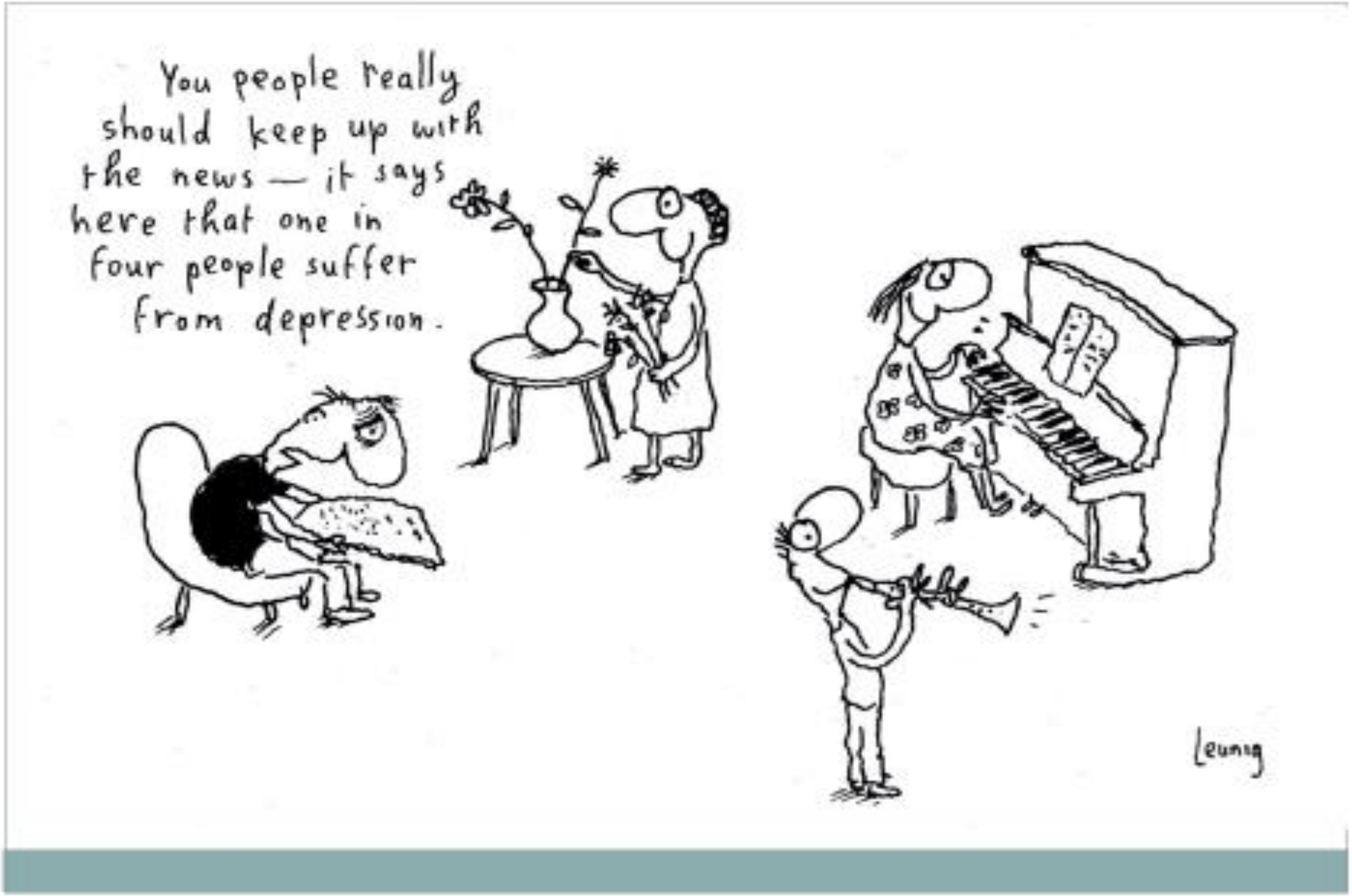
Dr Petra Muir – April 2021

Burden of Illness:

- 7.5% of all YLD – **all ages**[WHO -2017]
- Depression remains the single most important predictor of suicide in older people
- Increases risk of hospitalisation
- Increases healthcare costs
- Adds to disability and poor recovery from co-morbid illness
- Independent predictor of mortality

Epidemiology of Depression in Older People:

- Prevalence in general community >65 - **4% depressive syndrome (not normal)**
  - 20% depressive symptoms
- Prevalence in Aged Care – 5-25 %
- Depression in A.D. – up to 50% (CG Gottfries 2001)
- Post Stroke Depression – 20% – 50% (varying criteria)
- Contributes to increased mortality post Myocardial Infarct
- Males >85 at highest risk of death from DSH – 33 / 100,000
- Males 75-79 largest decrease in death
  - from **21.4**/100,000 (2016) to **15.5**/100,000 (2017)
- Treatment response rate for Depression in >65 – reported as up to 90%


You people really should keep up with the news — it says here that one in four people suffer from depression.
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Aetiology / Risk Factors:

Age Related Stressors

- **Social isolation**
- Lack of belonging
- Loss spouse/partner/**close other**
- Poor health
- Increasing physical disability
- Loss of Role / purpose
- Feeling a burden
- Increased need for personal assistance
- **Move to institutional care**
- Loss of independence
- **Elder abuse**

Other risk Factors

- Adverse childhood experiences
- **Physical illness**
  - Parkinson's Disease
  - Huntington's Disease
  - Stroke
  - Obstructive Sleep Apnoea
  - Thyroid Disease
  - Cancer – incl. paraneoplastic syndrome
  - Severe / Chronic Pain
- Iatrogenic
  - Medications
- Alcohol
- Dementia
  - Alzheimer's
  - Vascular
- Autism Spectrum Disorder
- **Sleep disorders 1.5 fold** (Benkert, R et al 2014)
  - Insomnia (Ford et al 1989)

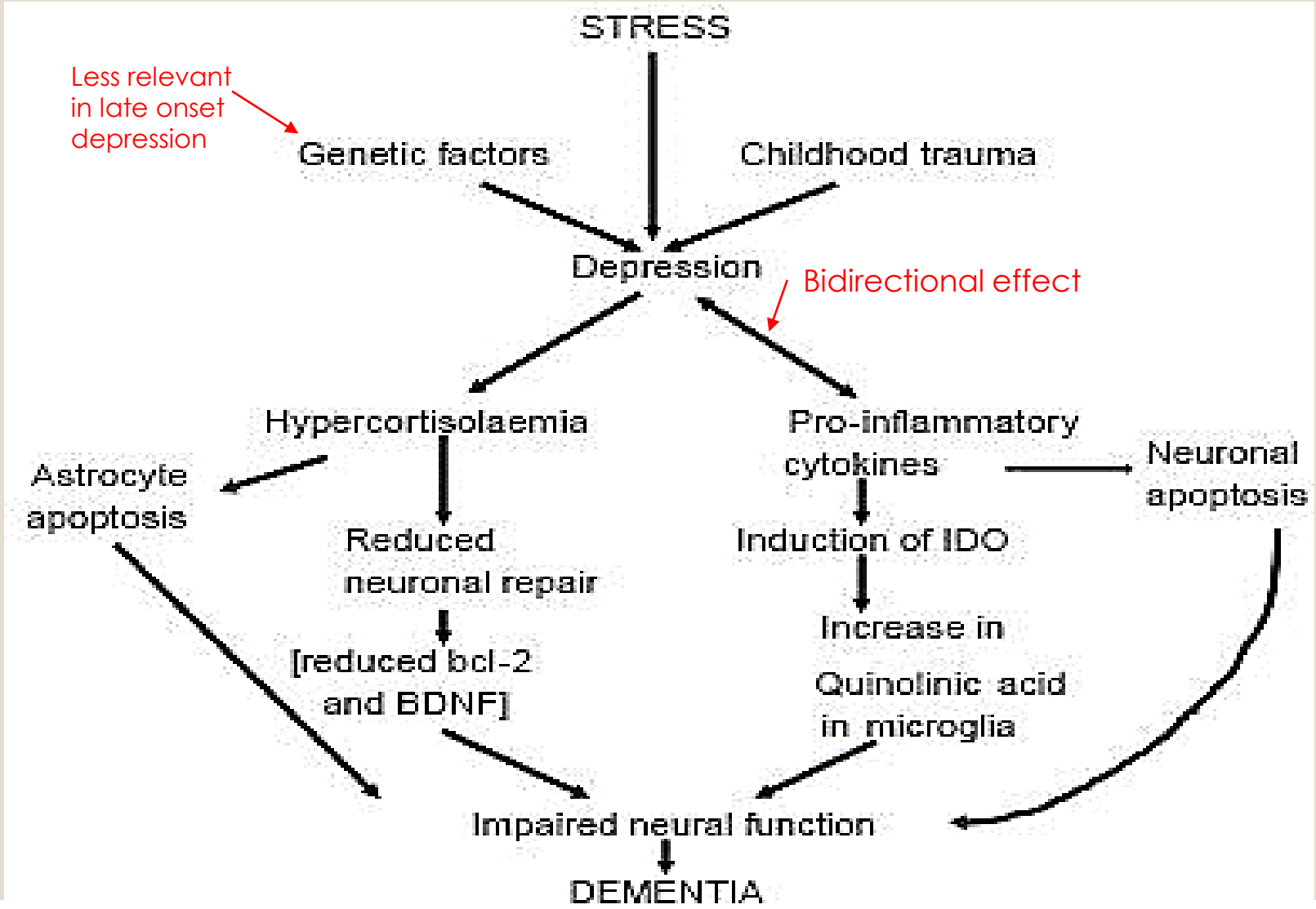
Aetiology Studies:

- Statistically significant association between **elder abuse, total financial dependence, lack of social support**, and **depression** among the elderly patients (Nisha, Catherin et al 2016)
- **Adverse Childhood Experiences:** Data from the U.S. CDC's 2010 Behavioural Risk Factor Surveillance Survey (BRFSS)
  - sample consisted of 8,051 adults aged 60 years and over
  - 53% women, 83% Caucasian
  - Six different types of ACE were included in the study: (not neglect/emotional abuse)
    - parents being physically abusive to each other,
    - being physically harmed by a parent,
    - being sworn at by the parent,
    - being touched sexually by an adult,
    - being forced to sexually touch an adult,
    - being forced into a sexual encounter.
  - *Depression was significantly correlated with **repeated** ACEs of all types*

Aetiology Studies (cont.):

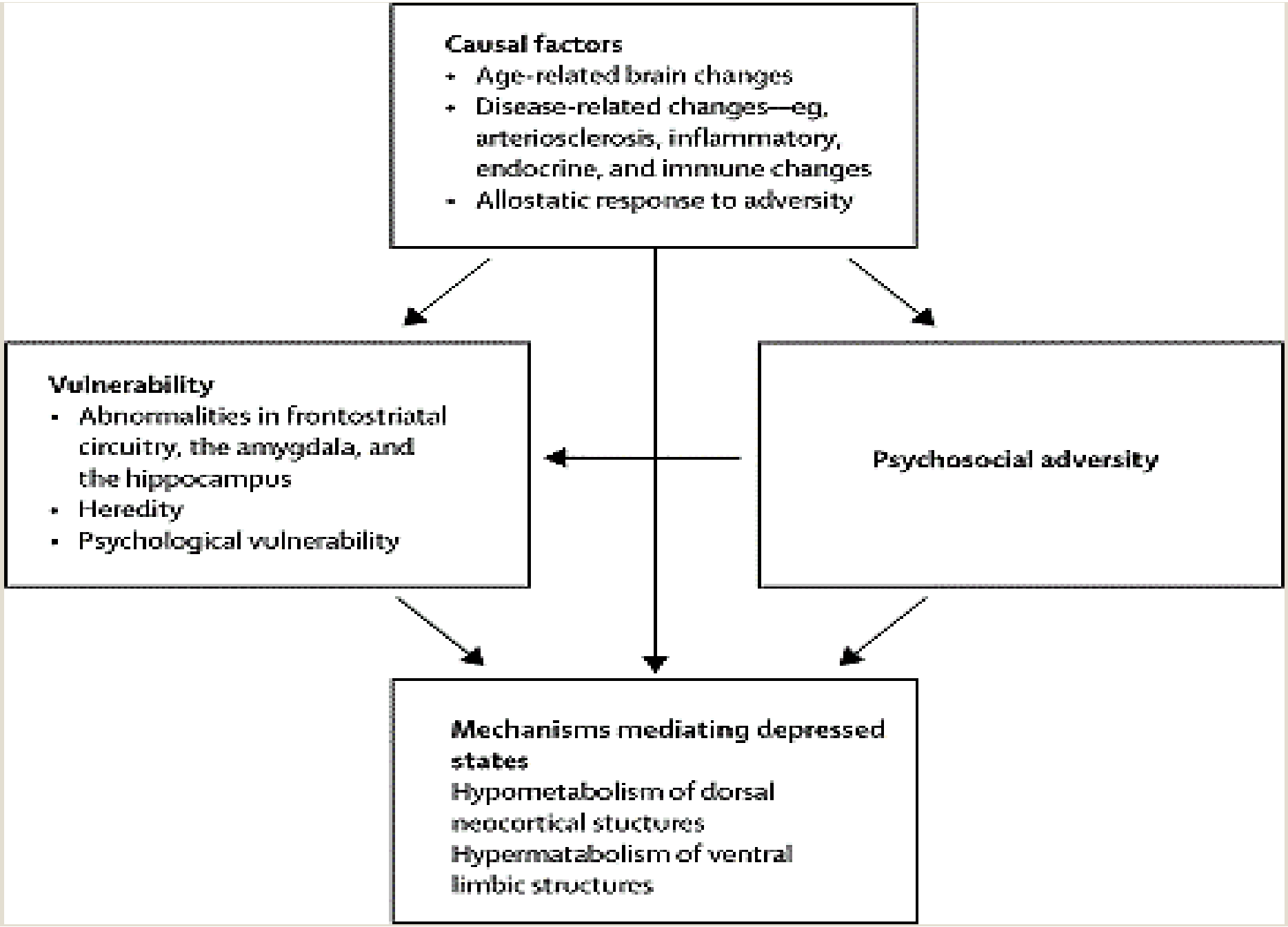
- Prevalence of **autism spectrum disorder (ASD)** characteristics in older adults with and without depressive disorders study in the Netherlands (2016):
  - Older persons (aged 60-90 years) with (N = 259) and without (N = 114) a depressive disorder
  - DSM-IV criteria for Depression;
  - abbreviated Autism Spectrum Quotient with a cut-off score of 70.
  - 31% showed elevated ASD characteristics vs 6% in comparison group
  - High ASD characteristics were also associated with **more comorbid anxiety disorders**
- Geriatric depression study in **advanced cancer patients** (Mystakidou, K et al 2013):
  - Sample of 92 advanced cancer patients > 65 years
  - prevalence of depression was found to be 67.4%.
  - with metastases were found to be 2.2-fold more likely to have depression
  - with moderate / severe cognitive impairment were found to be 3.61-fold more likely to be depressed
- **Strong independent predictors** of depression in elderly with cancer:
  - Pain, ↓ physical activity (even walking), sadness, ↓ social activity & reduced enjoyment of life

Depression and Dementia:

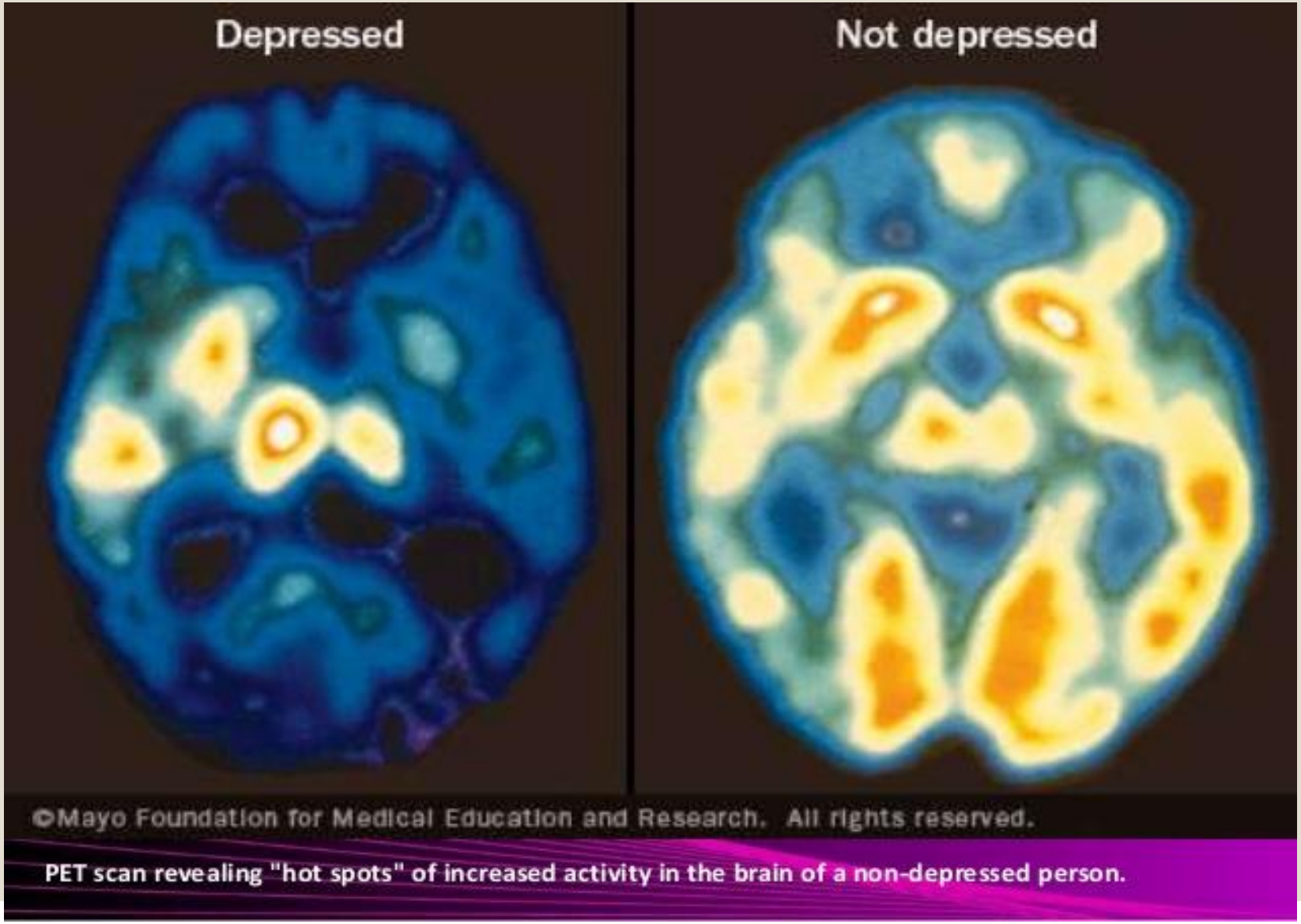


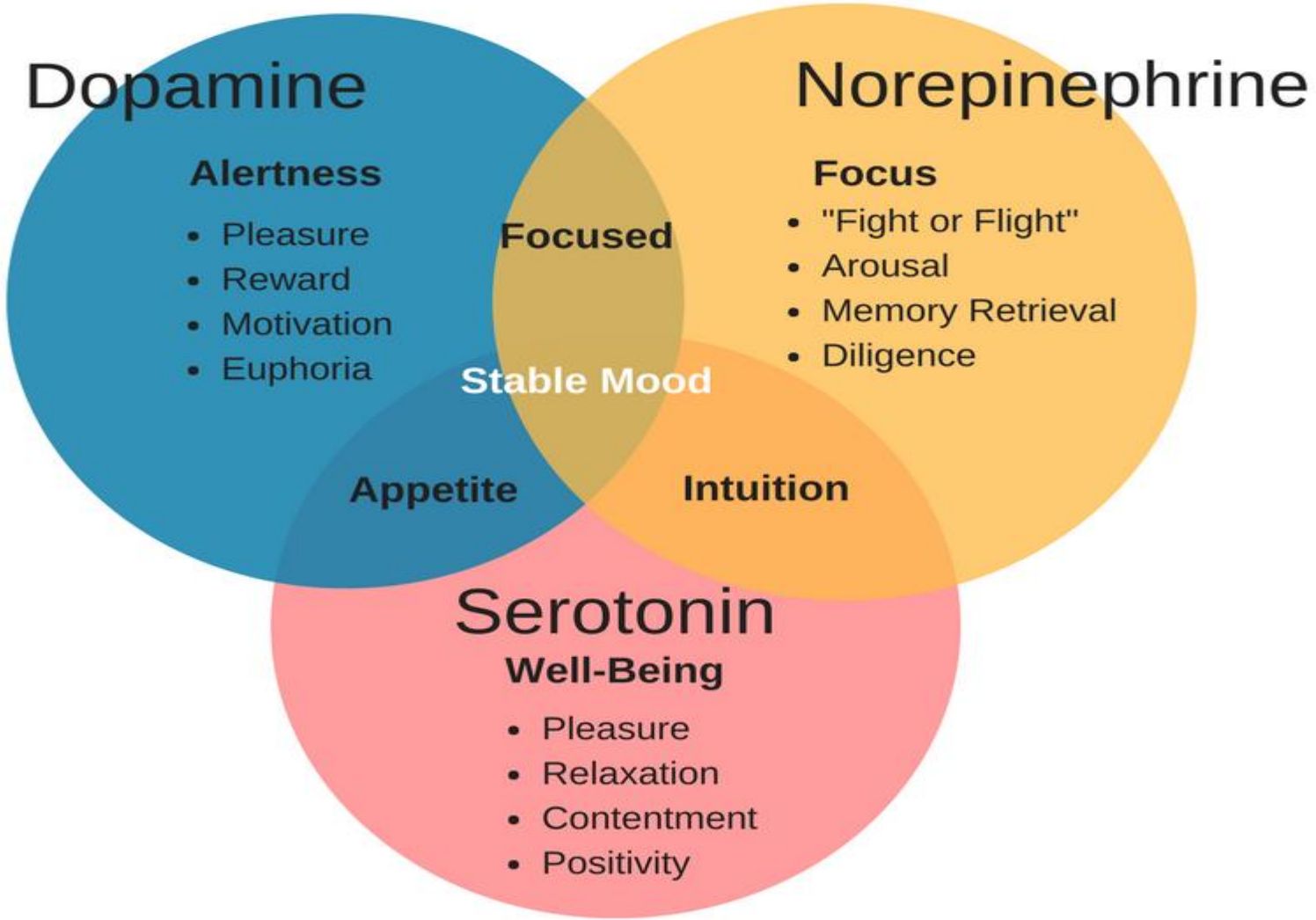
Pathophysiology of Depression:

- Neurotransmitter Theories
- Endocrine theories
- Genetics – less important in late onset depression
- Regional Brain Networks


Causal factors
• Age-related brain changes
• Disease-related changes—eg, arteriosclerosis, inflammatory, endocrine, and immune changes
• Allostatic response to adversity
Vulnerability
• Abnormalities in frontostriatal circuitry, the amygdala, and the hippocampus
• Heredity
• Psychological vulnerability
Psychosocial adversity
Mechanisms mediating depressed states
Hypometabolism of dorsal neocortical stuctures
Hypermatabolism of ventral limbic structures

Functional Imaging: hypoactivity




Dopamine
Alertness
Pleasure
Reward
Motivation
Euphoria
Norepinephrine
Focus
"Fight or Flight"
Arousal
Memory Retrieval
Diligence
Focused
Stable Mood
Appetite
Intuition
Serotonin
Well-Being
Pleasure
Relaxation
Contentment
Positivity

Diagnosis: DSM-5

- The individual must be experiencing five or more symptoms during the same 2-week period and at least one of the symptoms should be either (1) depressed mood or (2) loss of interest or pleasure.

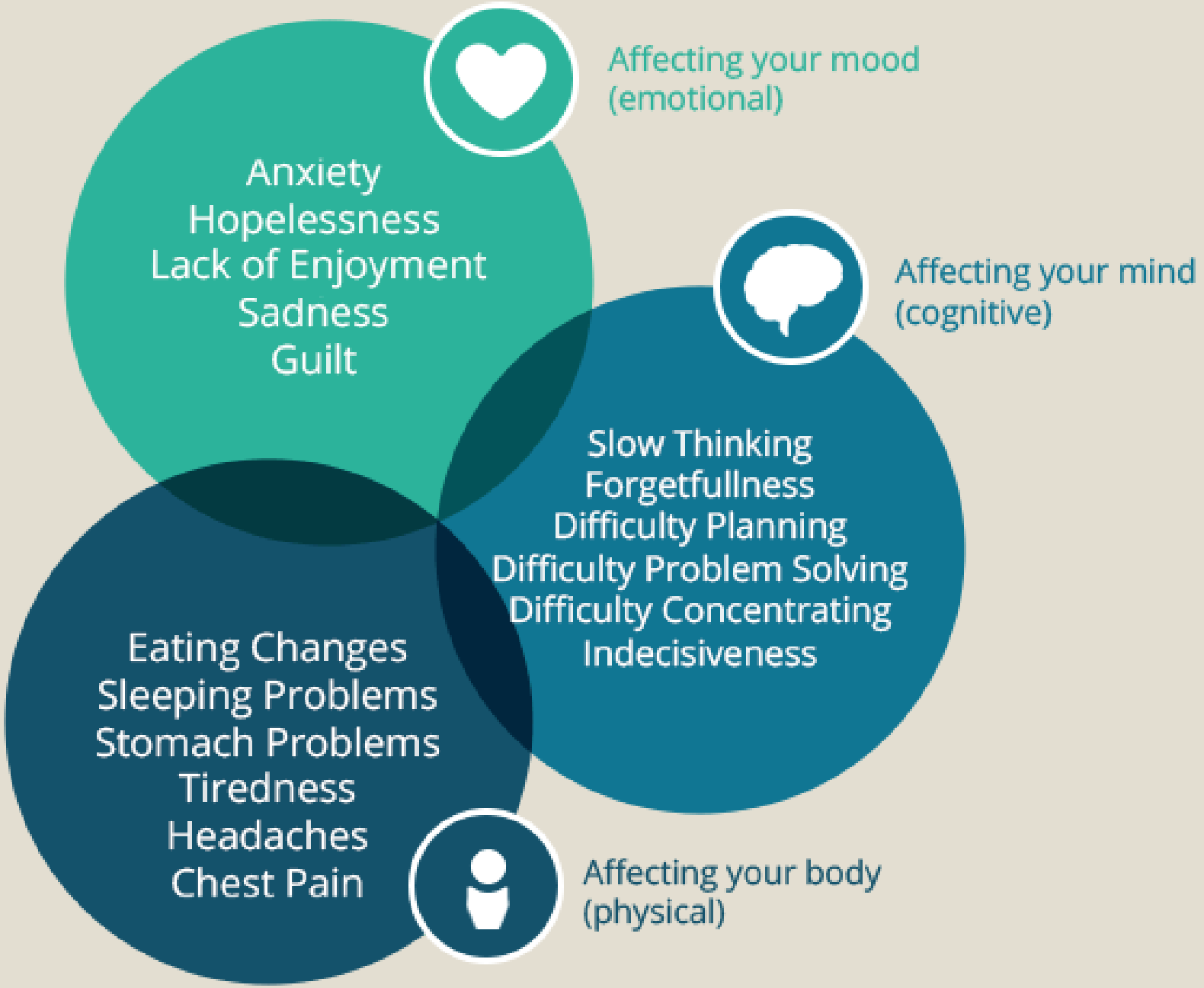
- 1. Depressed mood most of the day, nearly every day.
- 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day.
- 3. Significant weight loss when not dieting or weight gain, or decrease or increase in appetite nearly every day.
- 4. A slowing down of thought and a reduction of physical movement (observable by others, not merely subjective feelings of restlessness or being slowed down).
- 5. Fatigue or loss of energy nearly every day.
- 6. Feelings of worthlessness or excessive or inappropriate guilt nearly every day.
- 7. Diminished ability to think or concentrate, or indecisiveness, nearly every day.
- 8. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

DSM-5 criteria (cont.)

- To receive a diagnosis of depression, these symptoms must cause the individual
  - clinically significant distress or
  - impairment in social, occupational, or other important areas of functioning.
  - The symptoms must also not be a result of substance abuse or
  - another medical condition.

- With Mixed Features – This specifier allows for the presence of manic symptoms as part of the depression diagnosis in patients who do not meet the full criteria for a manic episode.

- With Anxious Distress – The presence of anxiety in patients may affect prognosis, treatment options, and the patient's response to them. Clinicians will need to assess whether or not the individual experiencing depression also presents with anxious distress.


Affecting your mood
(emotional)
Anxiety
Hopelessness
Lack of Enjoyment
Sadness
Guilt
Affecting your mind
(cognitive)
Slow Thinking
Forgetfullness
Difficulty Planning
Difficulty Problem Solving
Difficulty Concentrating
Indecisiveness
Eating Changes
Sleeping Problems
Stomach Problems
Tiredness
Headaches
Chest Pain
Affecting your body
(physical)

Clinical Features:

- Depressed mood.
- Anhedonia.
- Psychomotor **agitation**/retardation.
  - Flattened affect.
- Fatigue/amotivation.
- Worthlessness/guilt.
- Impaired concentration.
- **Helplessness**
- **Cognitive complaints** /Pseudo-dementia.
- **Somatic pre-occupation**.
- Delusions.
  - Mood congruent.
  - Nihilistic.
  - Somatic.
- Melancholia “black bile”.
- Catatonia

Screening Tools:

- Geriatric Depression Scale
  - 4,5,10,12,15,& 30 item versions
  - Cut-off >11 for depression in 30 item scale
  - Good cross cultural validity
  - Not valid in severe dementia

- Cornell Scale for Depression in Dementia
  - 19 items
  - Mixed observation / informant components
  - 30 mins to administer
  - Cut-off > 8 points = significant depression

- Geriatric Suicide Ideation Scale
  - Developed in Canada (Dr Marnin Heisel)
  - 5,10 & 31 item versions
  - Validated in cognitively intact
  - Community dwelling individuals

  - Four factors
    - Suicide ideation
    - Death Ideation
    - Loss of worth
    - Perceived meaning in life

  - Hospital Anxiety & Depression Scale
    -HADS

Depression & Physical Illness – a two way street :

- Depression is a risk factor for
  - stroke, cardiac mortality (1.8fold) & possibly cancer.
- Depression increases disability, impairs rehabilitation & can worsen prognosis e.g. post AMI.
- Depression risk doubled in diabetes mellitus (lifetime prev. 75%)
- Disability is a risk factor for depression.
- Chronic illness impairs prognosis in depression.
- Sensory impairment is associated with depression.
- Comorbidity with both AD and PD.

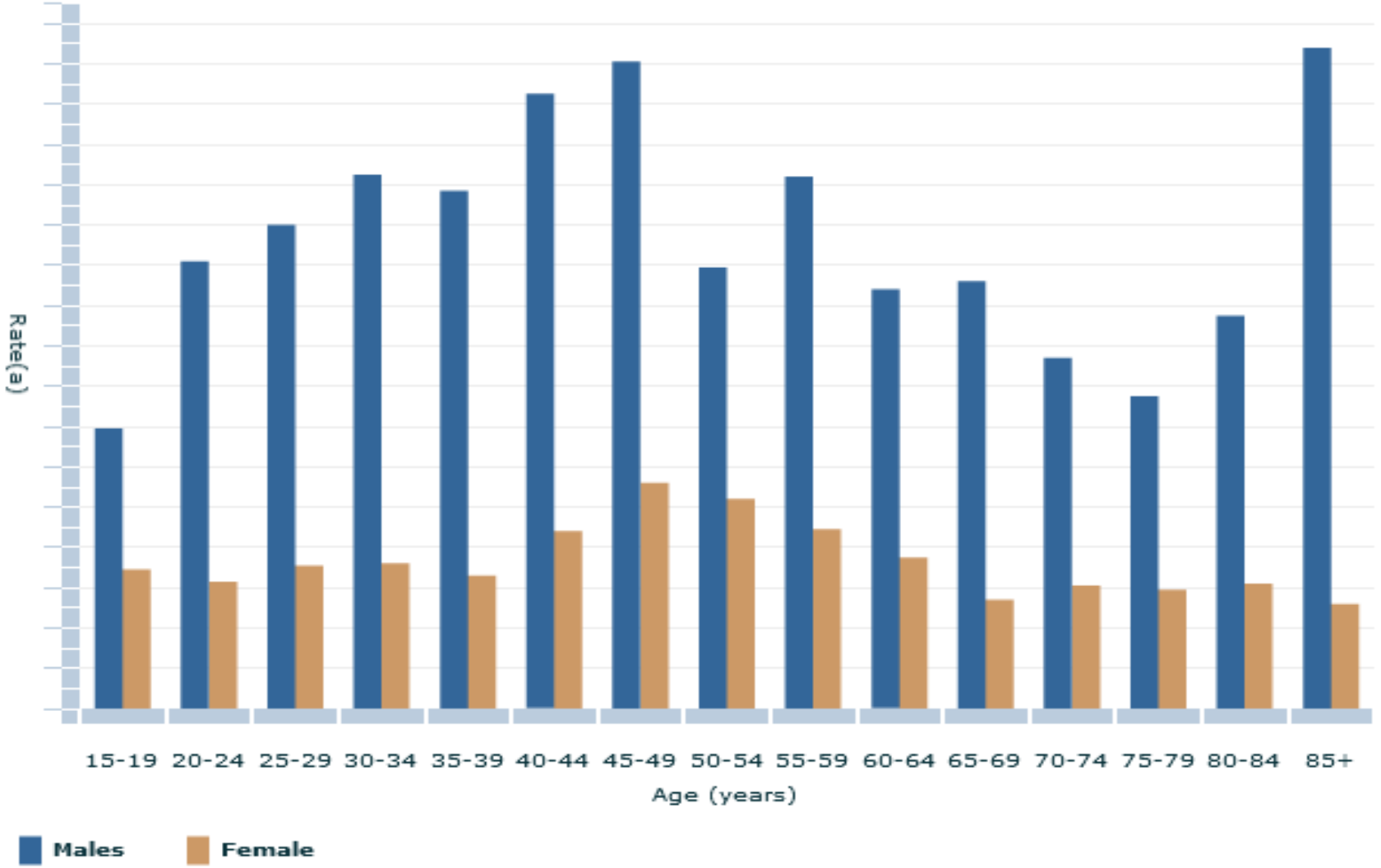
- A two way street or…a closed loop? To find the exit signs - need to provide optimal treatment of both depression and physical illness.

Depression and Suicide:

- **Gender paradox**
  - Female > Male – suicidal ideation
  - Male > Female – completed suicide
- **Increased risk**
  - Moderate - severe depression
  - Social isolation
  - Anxiety
  - Hopelessness
  - Insomnia
  - Alcohol use
  - Past history of attempted self harm
  - Family history of suicide

- **Self-neglect** may be a de-facto means of suicide

Age-specific death rates for intentional self-harm, by sex, 2017 (a)(b)(c)



Save Chart Image

Australian Bureau of Statistics

Recognition & Appropriate Treatment :

- Frequent comorbidity of anxiety (3.2-14.2%) EPA 2021-Gabriella Stoppe
- Severity may be underestimated in frail oldest old
- Physical comorbidities excluded from epidemiological studies
- Physical illness may mask symptoms
- Insufficient evidence of phenomenological differences between younger and older adults - Haigh, EAP et al. The American Journal of Geriatric Psychiatry. Vol.26, 2018, pp. 107-122

- "Almost half of those with depression received potentially inappropriate drug treatment with anxiolytics or hypnotics" Karlsson, Bjorn et al. The American Journal of Geriatric Psychiatry. Vol.24(8), 2016, pp. 615-623.

Aims of Treatment:

- Remission of *all* symptoms (if possible)
- Reduce suffering
- Risk reduction
- Improve function
- Prevent relapse

Prevention in Primary Care:

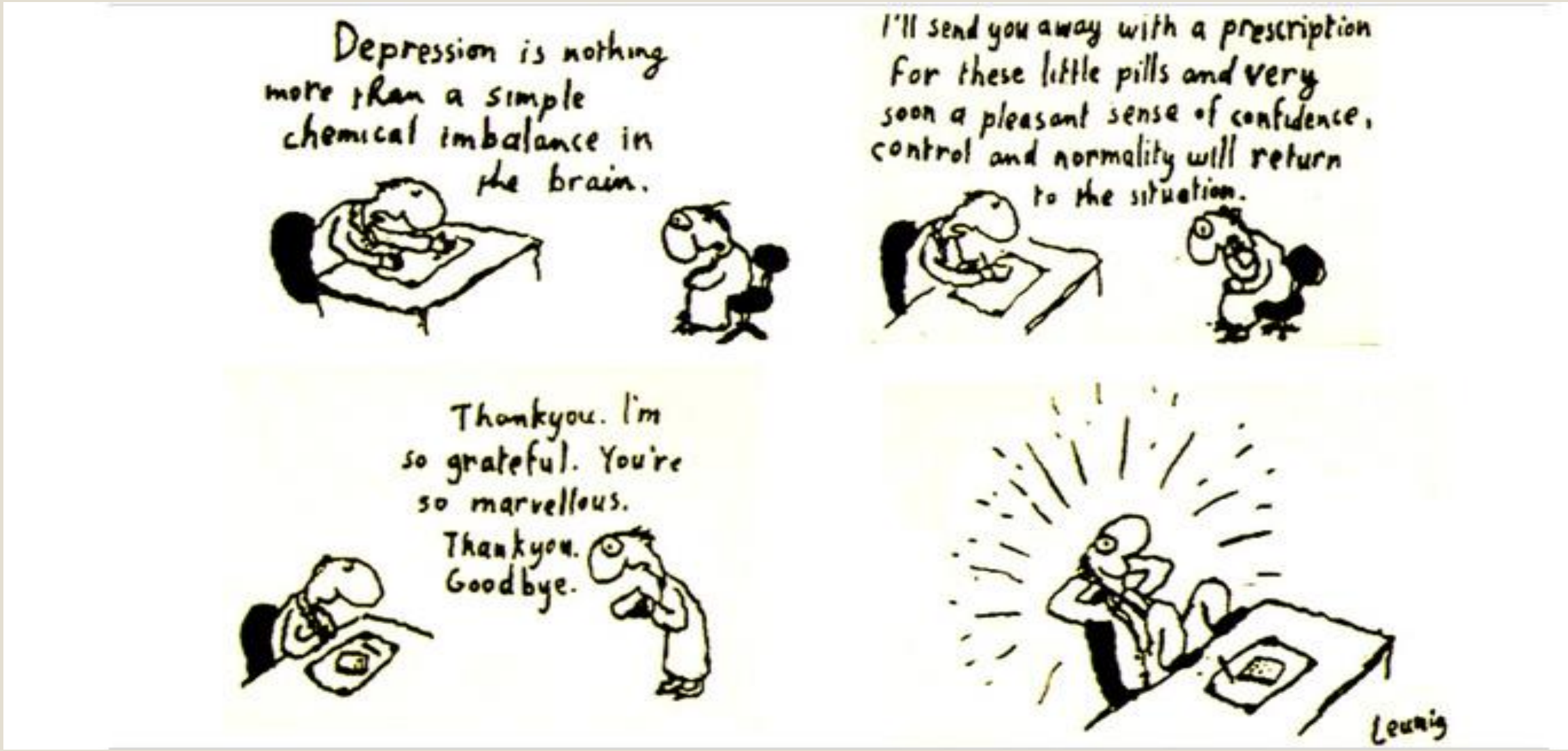
- Study:-
- Van't Veer-Tazelar et al, American Journ of Geriatric Psychiatry 2011; Vol 19 pp 230-239

- Inclusion of patients with subclinical symptoms
- Randomisation to prevention or "treatment as usual"
- Prevention therapy: watchful waiting, minimal supportive CBT, problem solving strategies, medication when required.
- At one year follow-up, the cumulative incidence of depression could be reduced by 50%. NNT:5

Treatment Timeline & Duration:

- Acute treatment phase –attain remission
  - weeks to months
- Continuation phase – prevent relapse
  - If 1st episode consider tapering at 1 year
  - If 2nd episode continue for 1-2 years
- Maintenance phase – prevent recurrence
  - If > 3 episodes consider indefinite treatment
  - Avoid suspending treatment too soon - ↑ risk relapse

The value of treatment...



Treatment Approach:

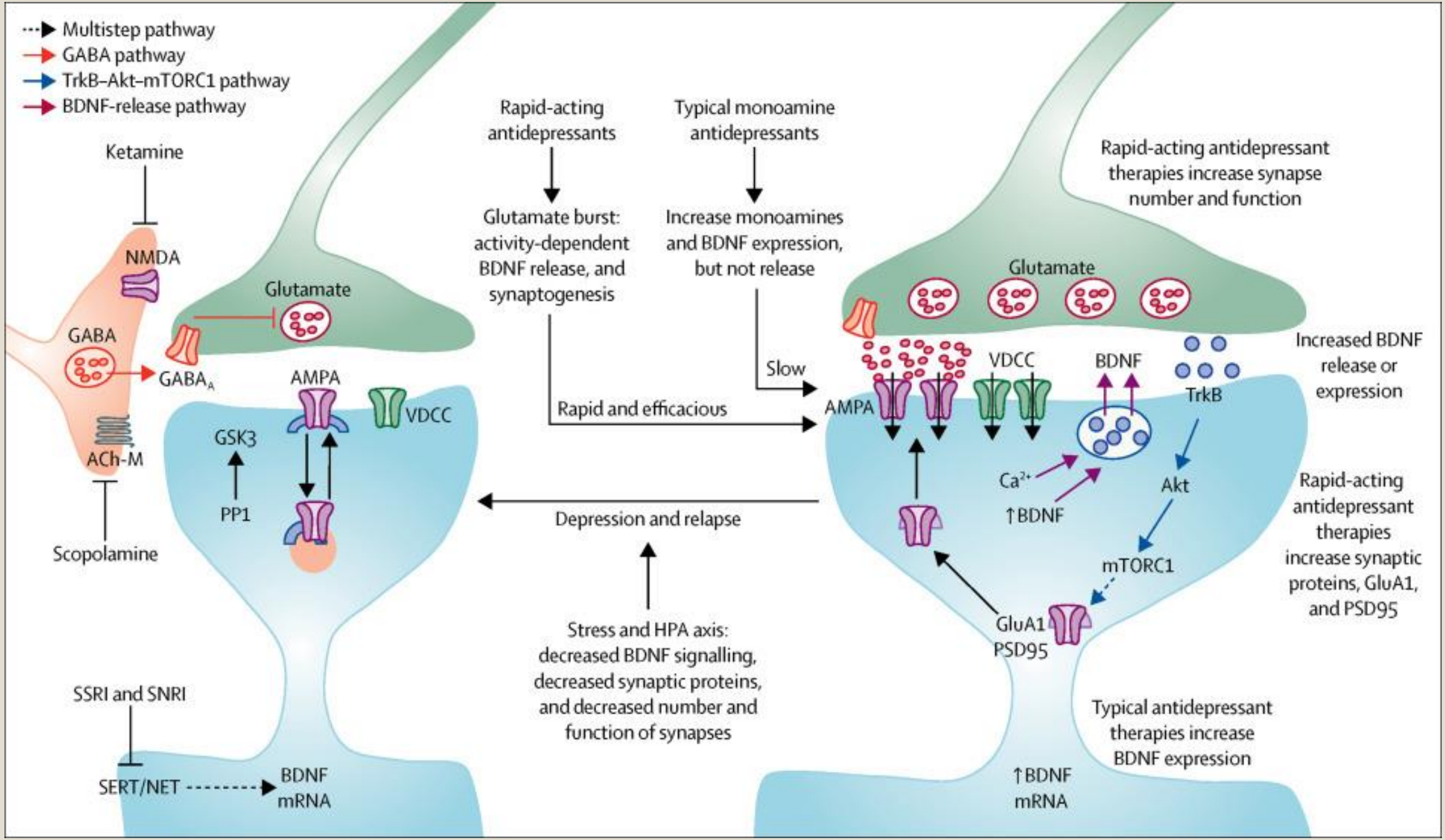
- Multi-modal and multi-disciplinary approach
  - Risk assessment and monitoring
  - Treat co-morbid physical illness
  - Provide education and support to patient and carers
  - Minimise effect of disability
  - Review and cease inappropriate medication
  - Address social issues eg. Isolation/loneliness
  - Initiate appropriate treatment with antidepressant and/or psychotherapy

Treatments & Level of Evidence:

- Psycho-education (II a)
- Physical Treatments
  - Antidepressants **(I a)**
  - ECT **(I a)**
  - Transcranial Magnetic Stimulation (III)
- Psychological Treatments
  - CBT & IPT **(1 a)**
  - Psychodynamic therapy (1 b)
  - Problem solving and self help (II b)
  - Supportive and Family therapy (III)
- Meta-analysis & Systematic Review 2008
  - Psychotherapy is efficacious and comparable or superior to drug therapy - Wilson KC et al Cochrane Database Syst Rev 2008

Matching Type and Treatment (I a – II a)

- Psychotic Depression: Antidepressant + antipsychotic… or ECT
- Severe non-psychotic depression: antidepressant + psychotherapy
- Moderate Depression: antidepressant or CBT or IPT
- Dysthymia: antidepressant +/- psychotherapy
- Recent onset minor depression: “watchful waiting” + problem solving
- Persistent minor depression: antidepressant
- Grief: If persistent depression – psychotherapy and antidepressant as needed


Multistep pathway
GABA pathway
TrkB–Akt–mTORC1 pathway
BDNF-release pathway
Ketamine
NMDA
Glutamate
GABA
GABA$_A$
AMPA
VDCC
GSK3
PP1
ACh-M
Scopolamine
SSRI and SNRI
SERT/NET
BDNF mRNA
Rapid-acting antidepressants
Glutamate burst: activity-dependent BDNF release, and synaptogenesis
Typical monoamine antidepressants
Increase monoamines and BDNF expression, but not release
Slow
Rapid and efficacious
Depression and relapse
Stress and HPA axis: decreased BDNF signalling, decreased synaptic proteins, and decreased number and function of synapses
Rapid-acting antidepressant therapies increase synapse number and function
Glutamate
AMPA
VDCC
BDNF
TrkB
Increased BDNF release or expression
Ca^{2+}
↑BDNF
Akt
mTORC1
GluA1
PSD95
Rapid-acting antidepressant therapies increase synaptic proteins, GluA1, and PSD95
Typical antidepressant therapies increase BDNF expression
↑BDNF mRNA

Antidepressants:

- **Tricyclics** amitriptyline, nortriptyline, clomipramine, doxepin
- **SSRIs** sertraline, citalopram, escitalopram, fluoxetine, paroxetine
- **SNRIs** venlafaxine, desvenlafaxine, duloxetine
- **MAOIs** Phenelzine, tranylcypromine, moclobemide
- **NaRIs** Reboxetine, Atomoxetine
- **NaSSA** Mirtazapine, Mianserin
- **Stimulants** Methylphenidate, Dexamphetamine
- **Atypical** Agomelatine, Bupropion, Vortioxetine

Factors to consider in Treatment:

- Age related pharmacokinetics
  - Lower volume of distribution, declining renal and hepatic function,
  - ↑ permeability of BBB
- Specific symptoms of depression
  - Insomnia, agitation
- Previous response to treatment
- Tolerability
- Safety
- Adverse effect profile
  - Cardiotoxicity, hypotension, hyponatraemia, anticholinergic, sexual dysfunction
- Drug interactions
- Medication adherence
- Co-morbidity
  - Anxiety, psychosis, personality disorder, suicide risk

Which antidepressants if also…

- Anxious – 1st sertraline; 2nd duloxetine / desvenlafaxine
- Insomnia – 1st mirtazapine (7.5-15mg more sedating);
  - 2nd agomelatine (if baseline LFTs are ok)
- High suicide risk – SSRI's have better safety in DSP - limit dose availability & ↑ supervision
- Sexual dysfunction – mirtazapine, vortioxetine and bupropion cause less dysfunction
- Severe cardiac disease – lower doses of sertraline or mirtazapine (monitor postural BP)
- Psychosis – combine antidepressant with low dose risperidone 0.5mg / or aripiprazole 5mg
- Avoiding sedation – e.g. work / driving – SSRI's and SNRI's
- Renal impairment >= Stage 4 – avoid mirtazapine or use very low dose 15-30mg & monitor BP
- Hypotension / Hypertension – SSRI's best. Mirtazapine (↓ BP), venlafaxine (↑ BP)
- On anticoagulants – Minimise SSRI's due to ↑ bleeding risk OR start a PPI
- Polypharmacy – where possible de-prescribe duplicates in class, NSAIDS, anti-hypertensives and benzodiazepines

A note about treatment in the "Very Old"

- Baseline antidepressant treatment does not seem to be independently associated with increased mortality risk. (Bostrom, Gustaf et al**; Antidepressant use and mortality in very old people.** Int. Psychogeriatrics July 2016)

Possible Errors:

- Benzodiazepines – ↓ effect of antidepressants; ↑ risk falls & cog impairment
- Baseline & monitor bloods should include U/E/CR to check sodium & renal function
- NB. check vitamin D as def. can cause depression / suicidal thoughts
- Review effectiveness and tolerability (Weeks 2, 4 and 8 – sooner if high risk)
- Non adherence - particularly with cognitive impairment / early adverse effects
- Rapid dose escalation ↑ risk of adverse effects
- Starting dose too high (↑ adverse effects incl. agitation/insomnia/ GI Sx's)

Lithium

- Good efficacy in depression…BUT
- High potential for morbidity & mortality
  - Need to check levels every 2-3 months or sooner if concerned
  - Maintain good hydration status to minimise risk of toxicity & renal impairment
  - Use diuretics with caution
- Educate patient and carers re prevention & signs / symptoms of lithium toxicity
- Acute and chronic toxicity can occur separately or together

- Acute toxicity (can escalate over a few days)
  - Nausea / vomiting / diarrhoea/abdominal pain (any or all)
  - Signs of dehydration
- Chronic neurotoxicity (usually emerges over several weeks to months)
  - Muscle weakness / nystagmus / tremor / hyperreflexia / dysarthria
  - Fatigue / Sedation / hypotension
- Confusion / Coma & ultimately death
- Lithium levels are a guide but clinical picture is paramount.

How about a nice cup of tea?

Emerging and other treatments

- Ketamine (subcutaneous)
  - Australian pilot study in older people by Duncan George et al 2017
  - Small sample size, excluded acute SI, multiple other treatments
  - Concluded there is preliminary evidence for efficacy and safety in elderly with treatment resistant depression.
  - Not currently approved by TGA (off-label only)
  - RANZCP (2019) noted significant gaps in knowledge about dosage, treatment protocols, effectiveness and long term safety.
- Esketamine nasal spray
  - Not yet available in Australia
- Pramipexole, magnetic seizure therapy, vagus nerve stimulation & deep brain stimulation
  - All still experimental

Neurostimulation:

- ECT is most effective of all treatments in the elderly
  - 80% response rate
  - 1st line option in psychotic depression
  - Effective in the 'old' old (Tew et al 1999)
  - Effective in depression + dementia but risk of delirium is higher
  - Rapid onset of benefit so preferred in urgent scenarios
    - Severe suicide risk
    - Cessation of fluid and nutritional intake
    - Risk of medical deterioration due to non-adherence to critical medications
    - Usually requires hospitalisation to initiate and stabilise
    - outpatient ECT possible for continuation and maintenance phases

  - Limited evidence of benefit for TMS in moderate to severe depression
    - May be emerging evidence of benefit in mild to moderate depression
    - Expensive

Prognosis / Outcome Studies:

- Meta-analysis of hospital based studies (Cole & Bellavance 1997)
  - 60% remained well or had treatable relapses/recurrences.
  - 15 – 20% develop chronic symptoms but majority of these remained well or had treatable relapse / recurrence.
- Community studies <33% had good outcome.
  - In three studies use of antidepressants only in 4%, 9% & 33%.
- Majority of studies show that with appropriate treatment the outcome for elderly people is as good as or better than younger depressed patients.

Geriatric Depression Scale: Short Form

Choose the best answer for how you have felt over the past week:

1. Are you basically satisfied with your life? YES / NO
2. Have you dropped many of your activities and interests? YES / NO
3. Do you feel that your life is empty? YES / NO
4. Do you often get bored? YES / NO
5. Are you in good spirits most of the time? YES / NO
6. Are you afraid that something bad is going to happen to you? YES / NO
7. Do you feel happy most of the time? YES / NO
8. Do you often feel helpless? YES / NO
9. Do you prefer to stay at home, rather than going out and doing new things? YES / NO
10. Do you feel you have more problems with memory than most? YES / NO
11. Do you think it is wonderful to be alive now? YES / NO
12. Do you feel pretty worthless the way you are now? YES / NO
13. Do you feel full of energy? YES / NO
14. Do you feel that your situation is hopeless? YES / NO
15. Do you think that most people are better off than you are? YES / NO

Answers in bold indicate depression. Score 1 point for each bolded answer.

A score > 5 points is suggestive of depression.
A score ≥ 10 points is almost always indicative of depression.
A score > 5 points should warrant a follow-up comprehensive assessment.

Source: http://www.stanford.edu/~yesavage/GDS.html

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:

Total score: Depression (D) _____ Anxiety (A) _____

0-7 = Normal

8-10 = Borderline abnormal (borderline case)

11-21 = Abnormal (case)

NAME _____ AGE_____ SEX_____ DATE _____

Cornell Scale for Depression in Dementia

Ratings should be based on symptoms and signs occurring during the week before interview. No score should be given if symptoms result from physical disability or illness.

SCORING SYSTEM

a = Unable to evaluate **0 = Absent**

1 = Mild to Intermittent **2 = Severe**

Score greater than 12 = Probable Depression

	a	0	1	2
A. MOOD-RELATED SIGNS				
1. Anxiety; anxious expression, rumination, worrying				
2. Sadness; sad expression, sad voice, tearfulness				
3. Lack of reaction to pleasant events				
4. Irritability; annoyed, short tempered				
B. BEHAVIORAL DISTURBANCE	a	0	1	2
5. Agitation; restlessness, hand wringing, hair pulling				
6. Retardation; slow movements, slow speech, slow reactions				
7. Multiple physical complaints *(score 0 if gastrointestinal symptoms only)*				
8. Loss of interest; less involved in usual activities *(score 0 only if change occurred acutely, i.e., in less than one month)*				
C. PHYSICAL SIGNS	a	0	1	2
9. Appetite loss; eating less than usual				
10. Weight loss *(score 2 if greater than 5 pounds in one month)*				
11. Lack of energy; fatigues easily, unable to sustain activities				
D. CYCLIC FUNCTIONS	a	0	1	2
12. Diurnal variation of mood; symptoms worse in the morning				
13. Difficulty falling asleep; later than usual for this individual				
14. Multiple awakenings during sleep				
15. Early morning awakening; earlier than usual for this individual				
E. IDEATIONAL DISTURBANCE	a	0	1	2
16. Suicidal; feels life is not worth living				
17. Poor self-esteem; self-blame, self-depreciation, feelings of failure				
18. Pessimism; anticipation of the worst				
19. Mood congruent delusions; delusions of poverty, illness or loss				

NOTES/CURRENT MEDICATIONS:

ASSESSOR:

Score

Instruction for use: (Cornell Dementia Depression Assessment Tool)

1. The same CNA (certified nursing assistant) should conduct the interviewed each time to assure consistency in the response.
2. The assessment should be based on the patient's normal weekly routine.
3. If uncertain of answers, questioning other caregivers may further define the answer.
4. Answer all questions by placing a check in the column under the appropriately numbered answer. (a=unable to evaluate, 0=absent, 1=mild to intermittent, 2=severe).
5. Add the total score for all numbers checked for each question.
6. Place the total score in the **"SCORE"** box and record any subjective observation notes in the **"Notes/Current Medications"** section.
7. Scores totaling twelve (12) points or more indicate probable depression.

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