Health Education England

MRCPsych General Adult Module

Depression
(Semester 1)

Developing people
for health and
healthcare

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GA Module: Depression - 1

Aims and Objectives

The overall aim is for the trainee to gain an overview of depression.

By the end of the sessions, trainee should have:

- Developed an understanding of the clinical presentation of depression
- Developed an understanding of aetiological theories and epidemiology of depression

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GA Module: Depression - 1

Expert Led Session

Depression – 1

Aetiological theories and epidemiology

Facts about Depression

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- Major depression is thought to be the **second leading cause** of disability worldwide and a major contributor to the burden of suicide and ischemic heart disease.[1]

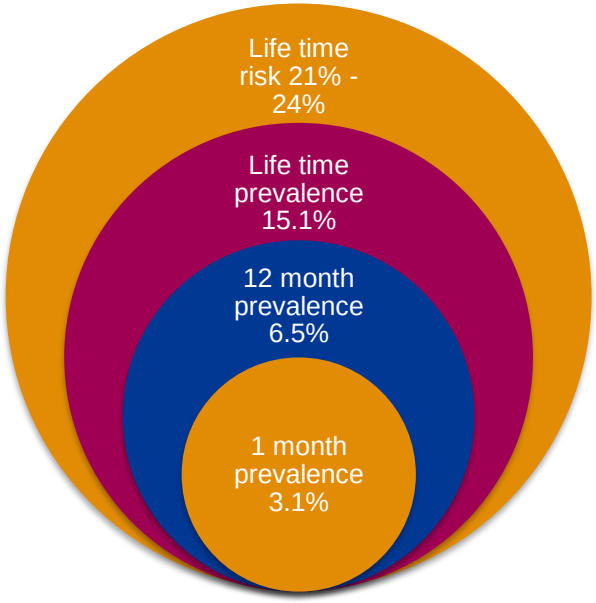
- In 2013, depression was the **second leading cause of years lived with a disability worldwide**, behind lower back pain.[2]

- Mental health and behavioural problems (e.g. depression, anxiety and drug use) are reported to cause over **40 million years** of disability in 20 to 29-year-olds.[3]

1 Whiteford, H. A. et al. (2013) Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. The Lancet. 382 (9904). pp. 1575-1586
2 Ferrari, A.J., Charlson, F.J., Norman, R.E., Patten, S.B., Freedman, G., Murray, C.J.L.,& Whiteford, H.A., (2013). Burden of Depressive Disorders by Country, Sex, Age, and Year: Findings from the Global Burden of Disease study 2010. PLOS Medicine, 10(11).
3 Lozano, R. et al. (2012) Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010. a systematic analysis for the global burden of disease study 2010. The Lancet. 380(9859), pp. 2095–2128.

Epidemiology

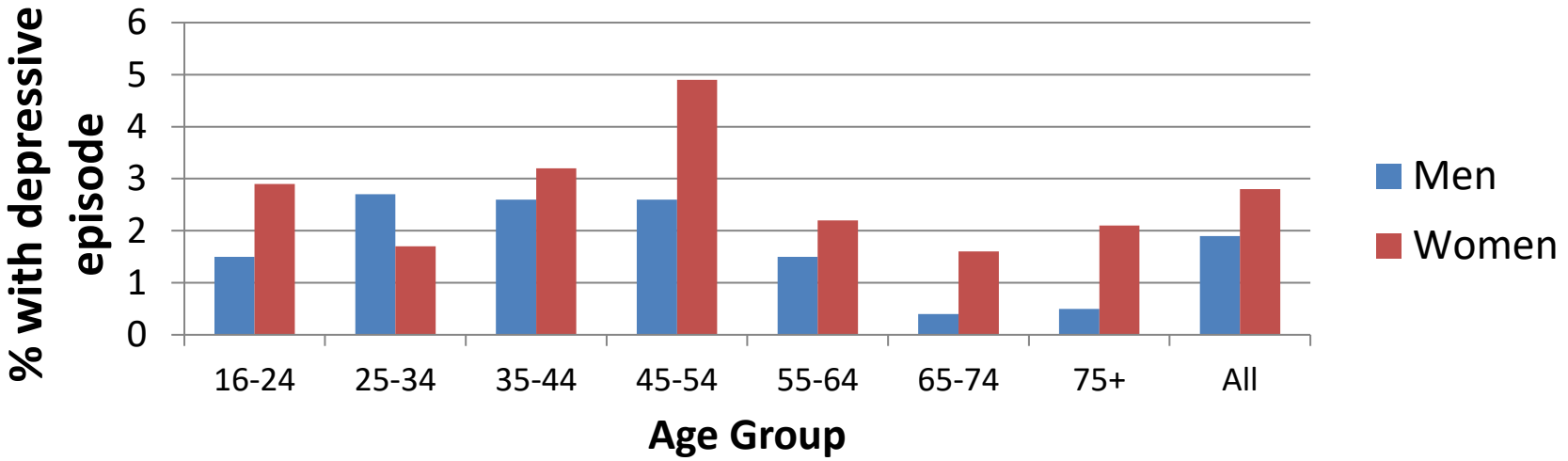
- Mixed anxiety and depression is the most common mental disorder in Britain[1]
- Depression affects 1 in 5 older people[1]
- 8-12% of the population experience depression in any year[2]
- Point (1-month), 12-month, and lifetime estimates for **major depressive disorder** in community surveys of the European Union[3]



1 Mental health Foundation – www.mentalhealth.org.uk
2 The Office for National Statistics Psychiatric Morbidity report, 2001
3. Wittchen HU, Jacobi F. Size and burden of mental disorders in Europe—a critical review and appraisal of 27 studies. Eur Neuropsychopharmacol. 2005;15: 357-376.

Epidemiology

- Prevalence of depression in England
- More common in women in most age groups
  - Most cases with depression emerged between the ages of 12 and 25 years, with a significant gender difference apparent at around age 14 years



- Approximately 2% of men and 3% of women in England are suffering from depression in a given week.

Epidemiology

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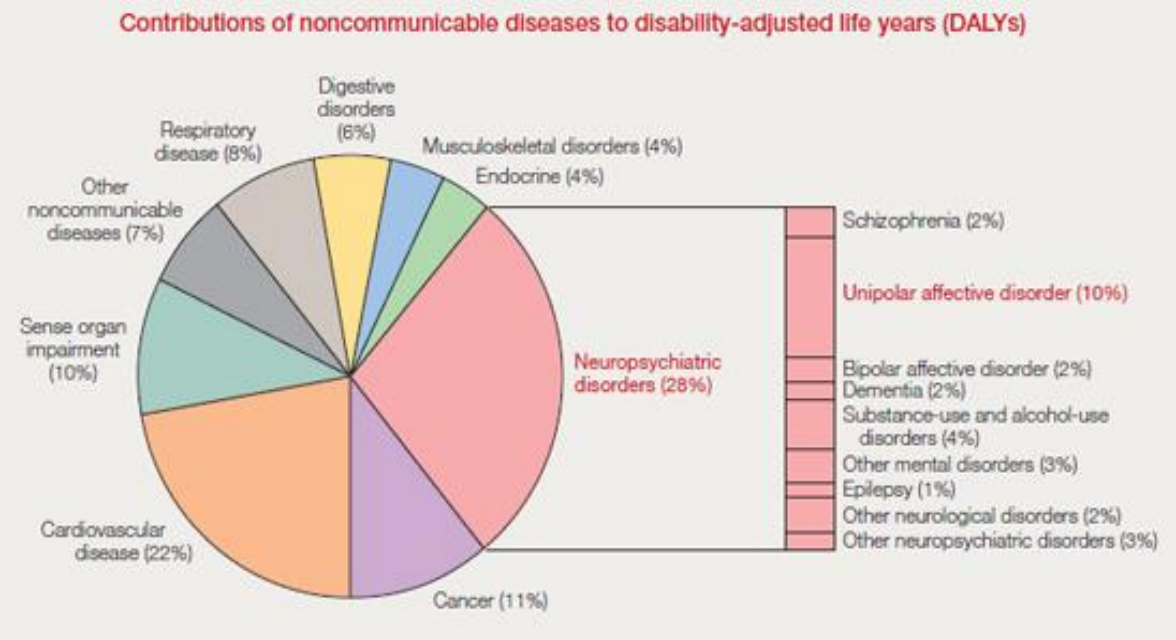
WHO - General Health Care Study, 14 countries[4]

- Frequency of depression in the community
  - 2.6% in Nagasaki to 16.9% in Manchester and 29.5% in Santiago
- 4th most important contributor to the global burden of disease



4. World Health Organisation – www.who.int

Epidemiology

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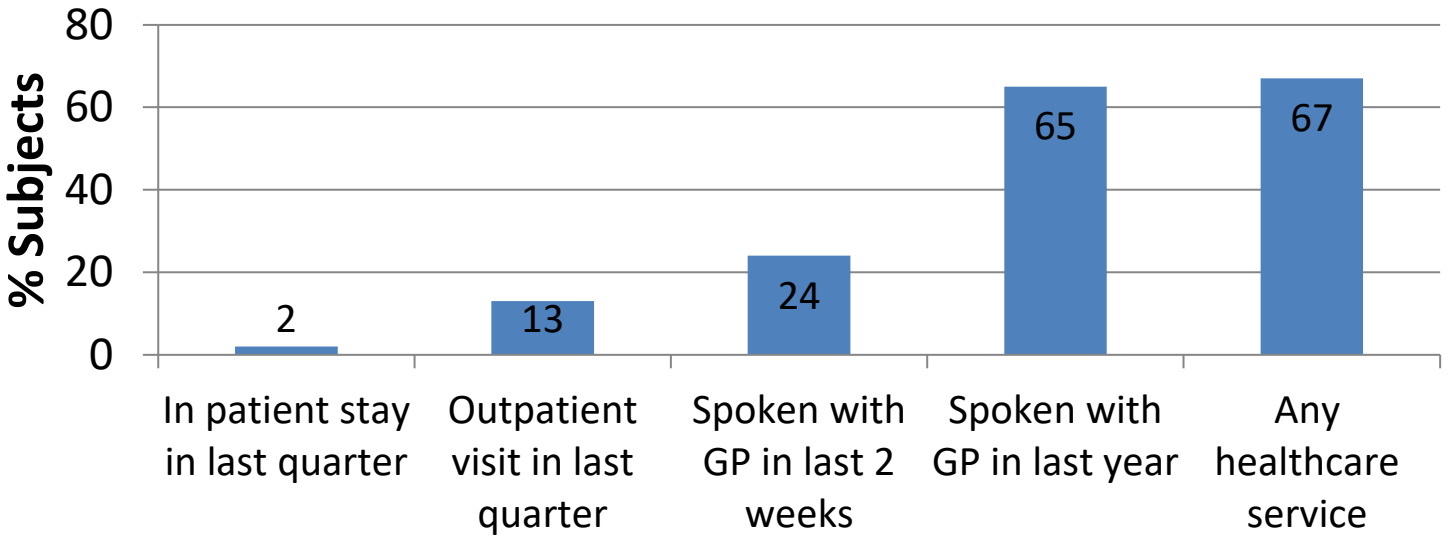
- Health care services used for depressive episode.[5]



- 7.2% of consecutive adult attendees in general practice had a depressive disorder[6]

5. Adult Psychiatric Morbidity in England 2007 NHS information centre for health and social care 2009
6. Ostler K et al. B J Psychiatry 2001;178: 12-17

Epidemiology

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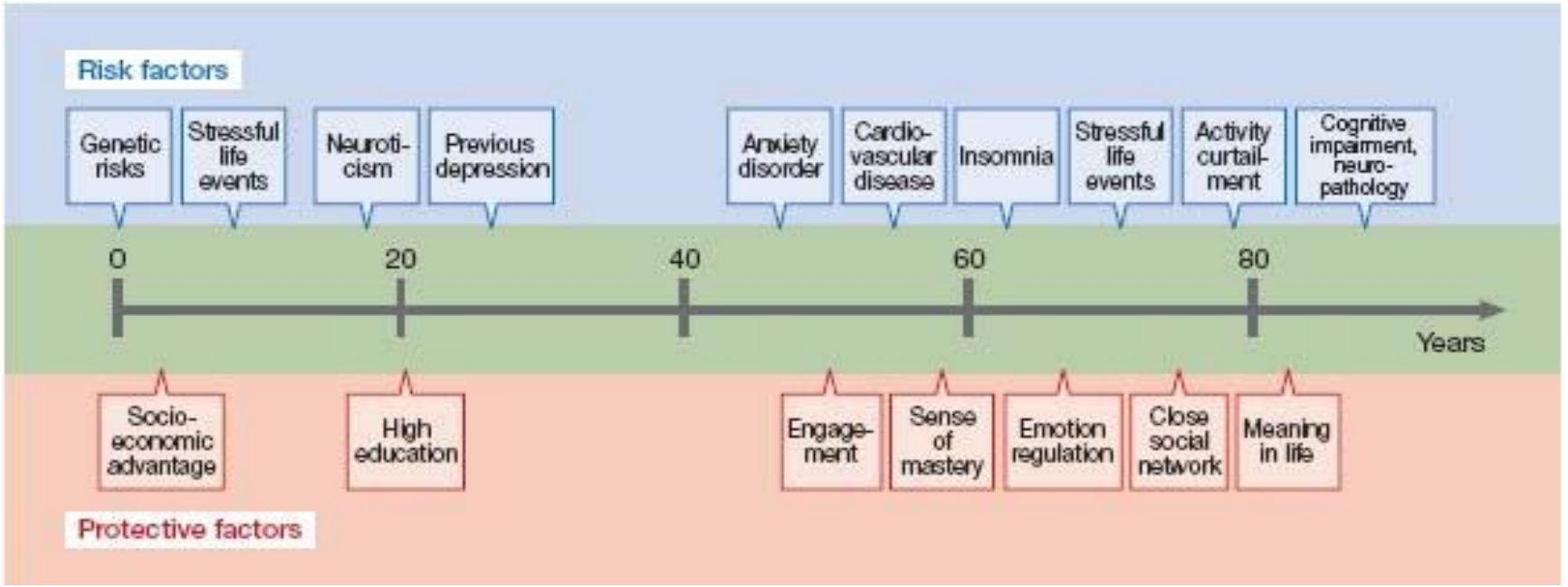
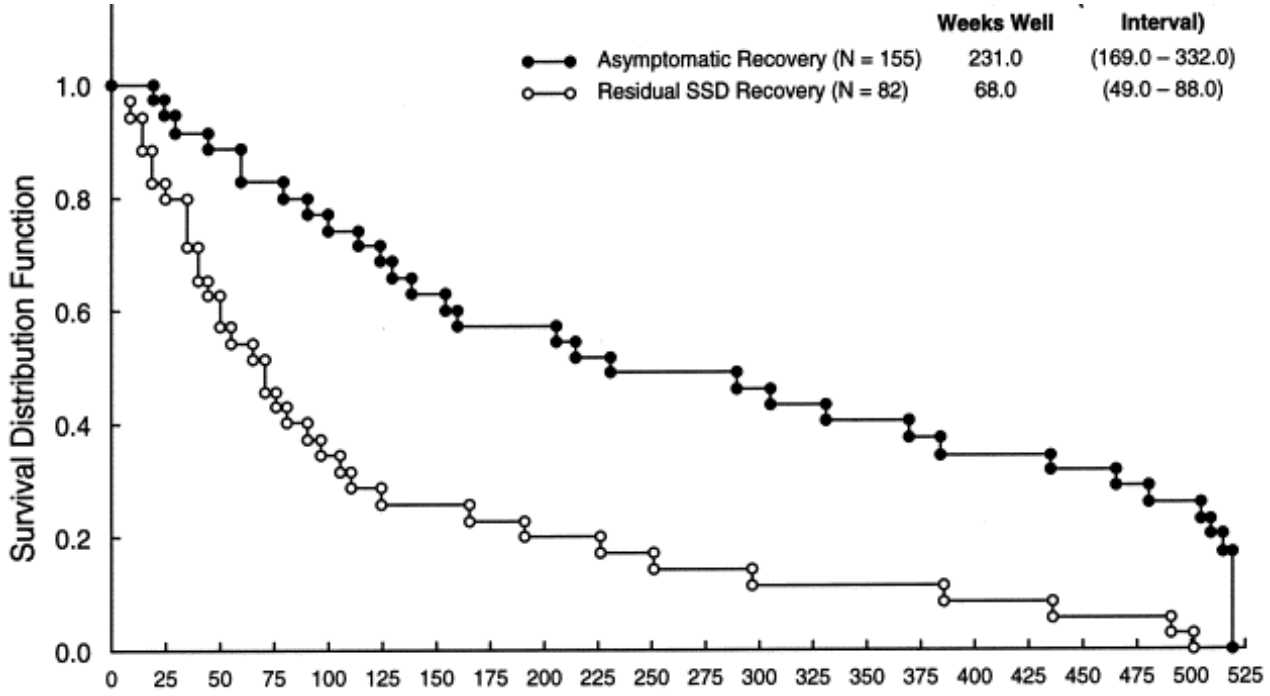
Risk factor and Resilience model for depression over the human lifespan.[7]



7. Fiske A, Wetherell JL, Gatz M. Annu Rev Clin Psychol. 2009;5:363-389

Epidemiology



Survival analysis of weeks to *major depressive episode* relapse (MDE): comparing patients with unipolar major depressive disorder who recovered from intake MDE with residual subsyndromal depressive symptoms vs. asymptomatic status. Wilcoxon Chi Square Test of Difference=47.96; $P<0.0001$

Epidemiology

Why Is Achieving Remission Important?

- Residual symptoms put patients at high risk of relapse and recurrence
  - Patients with residual symptoms after medication treatment are 3.5 times more likely to relapse compared to those fully recovered (Judd et al, 1998)
  - This risk is greater than the risk associated with having ≥ 3 prior depressive episodes
  - Similar finding exists after response to cognitive therapy

Epidemiology

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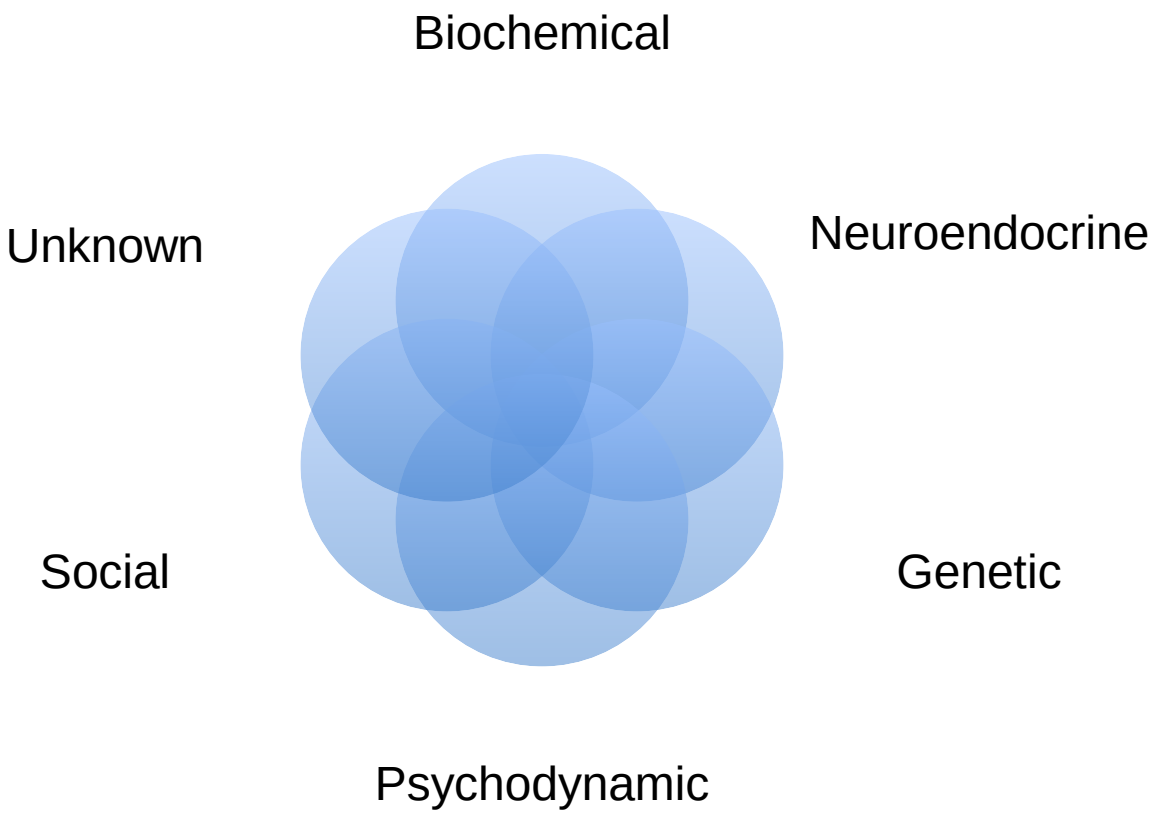
- Considerable cross-cultural similarities in depressive symptomatology with[4]
  - low mood, anhedonia, anxiety, lack of energy in most cultures.
- Cross-cultural differences do exist[4]: for example,
  - feelings of guilt are one of the major symptoms of depression in Western countries
  - Somatic complaints were more common in Asians.
- Depression is common in patients with physical illness.[8]

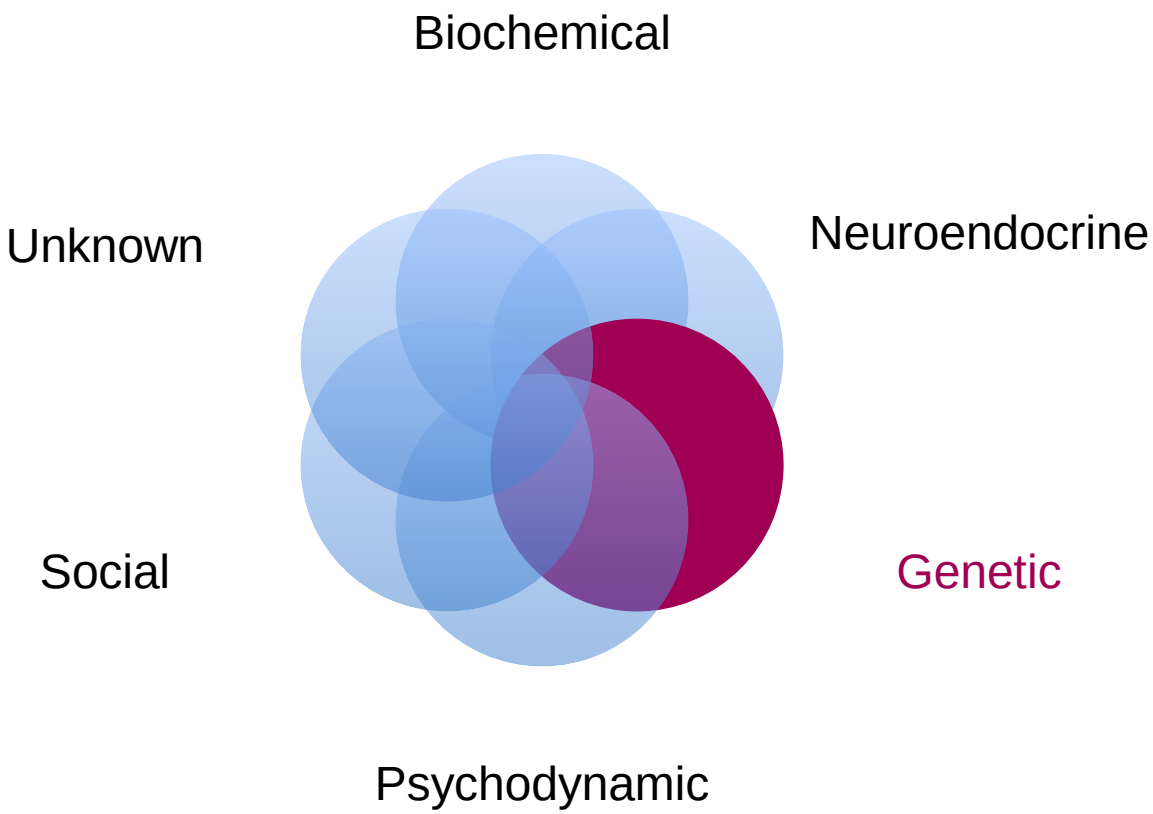
Disease	Prevalence
Older cancer patients	25%
Post Stroke patients	5-50%
Post MI patients	30%
Alzheimer's dementia pts	33%
Parkinsons patients	50%

4. World Health Organisation – www.who.int
8. Rao Mprimary Psychiatry vol 15:No 9 2008

Aetiology of depression



Aetiology


Biochemical
Unknown
Neuroendocrine
Social
Genetic
Psychodynamic

Aetiology - Genetics

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MDD-RU Major depressive disorder – recurrent unipolar

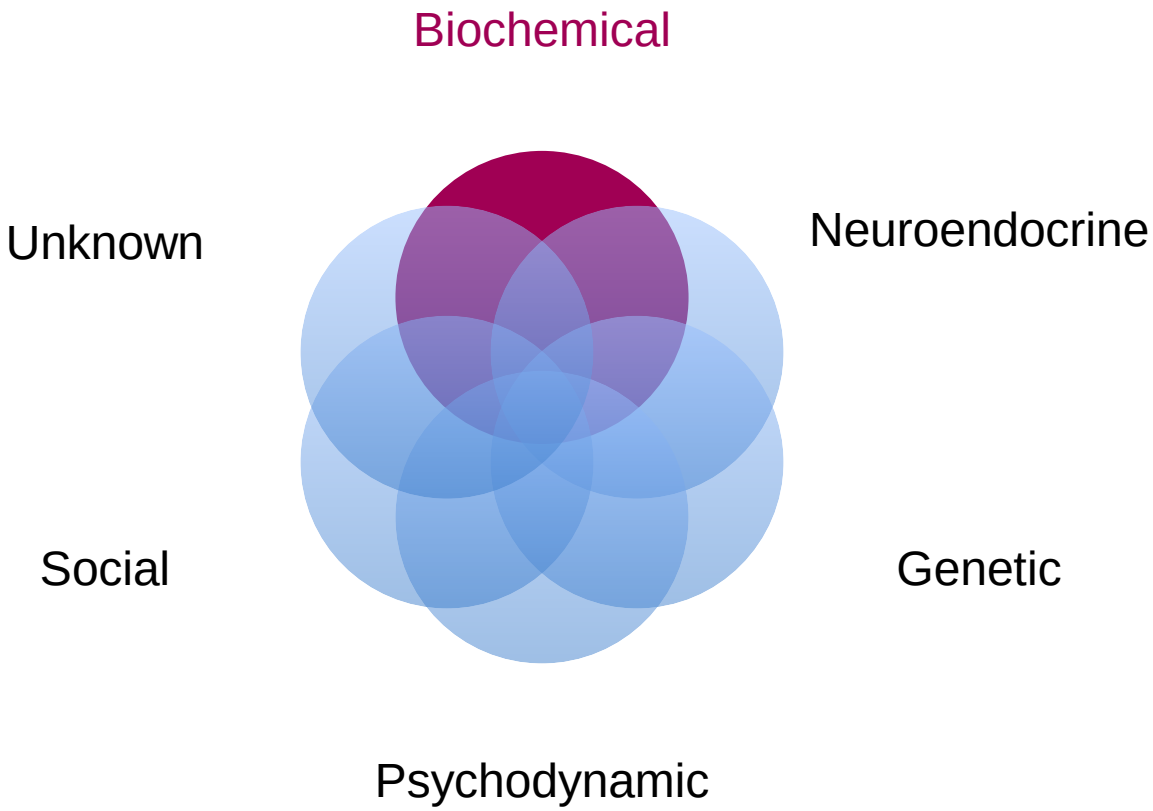
- Twin studies - heritability at 37% [10]
- 2 – 4 fold increased risk among first-degree relatives Heritable phenotype - early onset and a high degree of recurrence
- There is no universal susceptibility gene - several candidate genes have been suggested to be implicated[11]

Serotonin	Brain-derived neurotrophic factor	Other
Serotonin transporter gene: 5HTT/SLC6A4	BDNF gene: Val66Met polymorphism	APOE (apolipoprotein E)
Serotonin receptor gene: HTR2A		GNB3 (guanine nucleotide-binding protein β-3),
Tryptophan Hydroxylase gene: TPH2 -polymorphism (Arg441His)		MTHFR (methylene tetrahydrofolate reductase),

10. Genetic epidemiology of major depression: review and meta-analysis. Sullivan PF, Neale MC, Kendler KS Am J Psychiatry. 2000 Oct; 157(10):1552-62

11. Overview of the genetics in major Depressive Disorder Curr Psychiatry Rep Dec 2010. 12(6), 539-546

Aetiology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Aetiology – Biochemical

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Signal transmission through the neural synapse

Neurotransmitters	Availability + metabolism	Decreased serotonin, Dopamine and Noradrenaline
Receptors	Number or density	5-HT_2 upregulation, Increased presynaptic a2-adrenergic receptors
	Affinity + sensitivity	5-HT_{1A} desensitisation
Post receptor systems	Number + activity of G proteins	increase of G protein
	2^{nd} messenger systems	Hypofunction of the AC-cAMP kinases pathway
	Transcription factors	Decrease expression of BDNF and CREB (cAMP response element binding protein)

Aetiology

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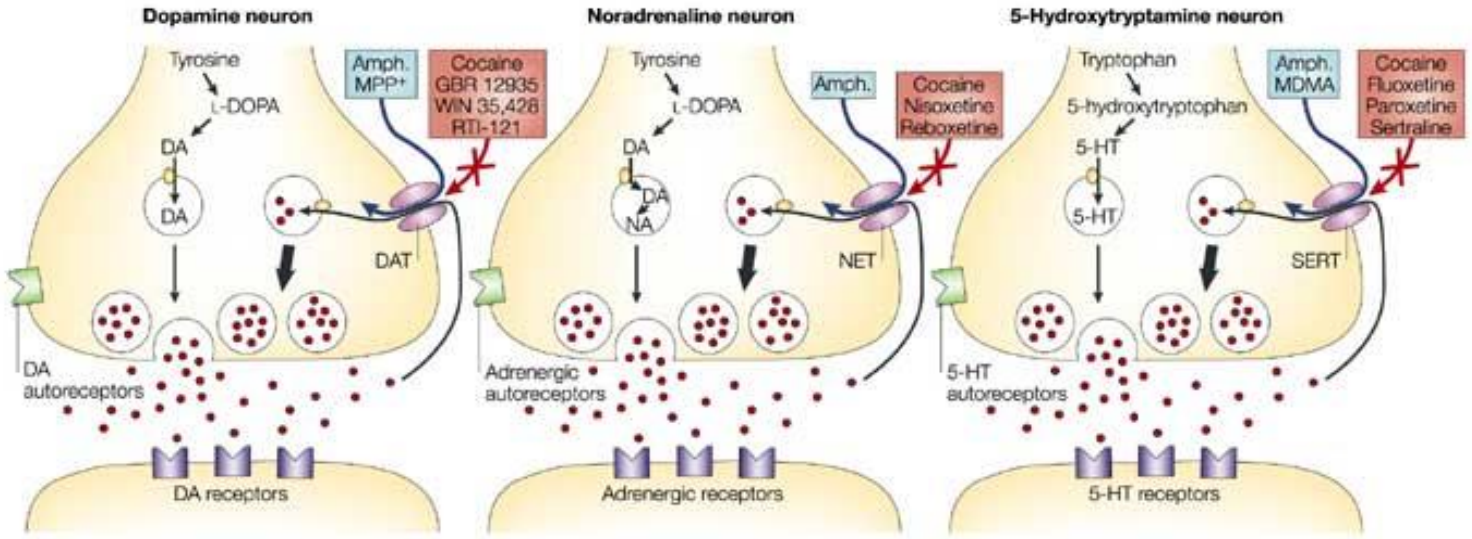
Biochemical

- Monoamine theory of depression
  - Decreased Serotonin, Dopamine, and Noradrenaline

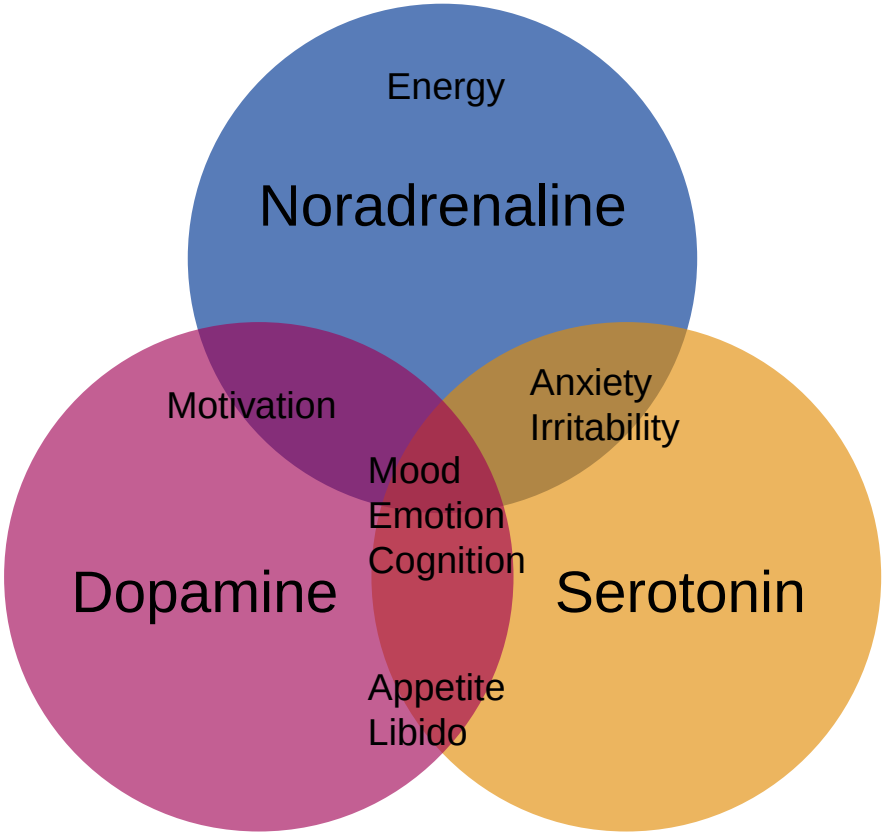


- Decreased GABA
- Increased Glutamate

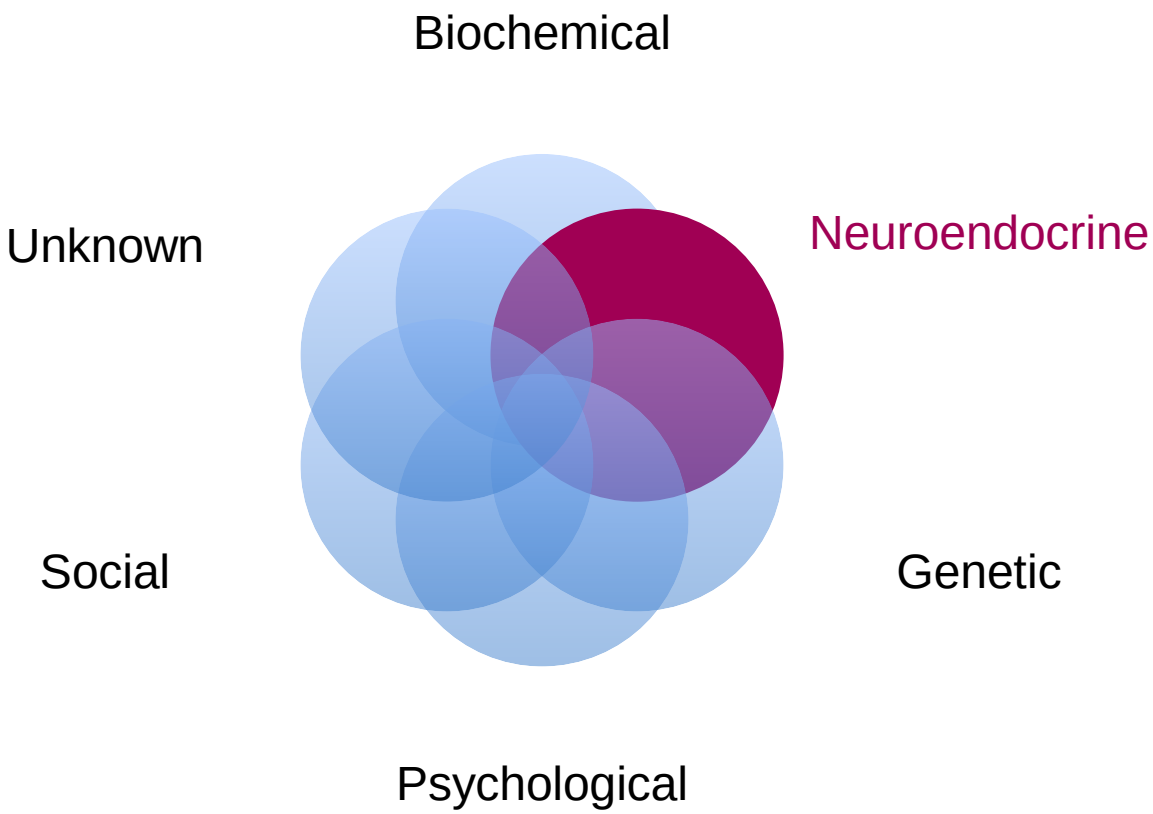
Aetiology

Biochemical

- Evidence for theory – Antidepressant mechanism of action
- Neurochemicals associated with the phenotypic presentation of depression



Aetiology

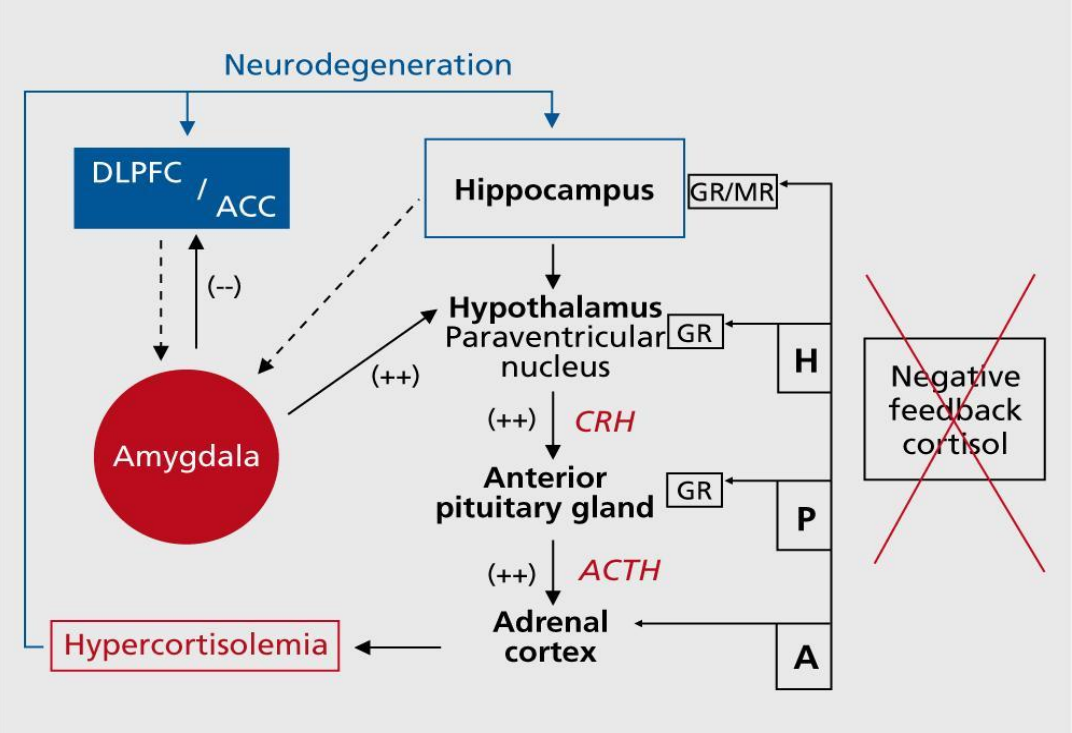

Biochemical
Unknown
Neuroendocrine
Social
Genetic
Psychological

Aetiology - Neuroendocrine

Increased function of the hypothalamic-pituitary-adrenal (HPA) axis

Abnormalities of the HPA axis in patients with depression
Cortisol hypersecretion
Decreased glucocorticoid receptor sensitivity
Abnormal circadian rhythms of cortisol
Increased CSF corticotrophin releasing factor
Increased circulating ACTH
Increased adrenal gland size

Aetiology



- Diminished activity in the prefrontal cortex (DLPFC and dorsal ACC)
- Enhanced activity in the amygdala
- Hyperactivity in limbic areas results in higher neural activities at the hypothalamic level, evoking higher corticotrophin-releasing hormone (CRH) secretions, resulting in elevations of cortisol levels.

Hypercortisolemia due to:
Hippocampal dysfunction -reduction of the inhibitory regulation of the HPA axis.

Aetiology - Other biological theories

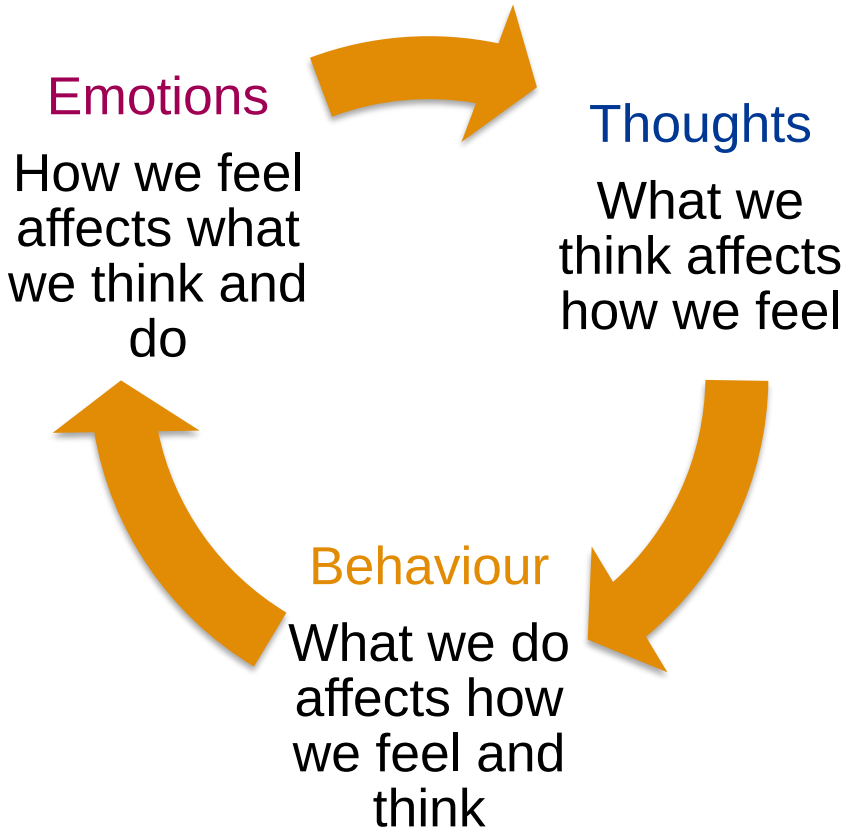
- Endothelial dysfunction and platelet activation
- Pro inflammatory states

- Structural and functional brain changes
  - Neuroimaging
    - Limbic activation – subgenual cingulate, amygdala, anterior insula
    - Neocortical deactivation – prefrontal cortex, inferior parietal
    - Basal ganglia deactivation – caudate and putamen

Aetiology - Psychological

- Cognitive triad – Becks
- Errors in logic

  Depressed people often draw illogical conclusions when they evaluate themselves



Aetiology - Social

Independent and additive effect

- Social isolation
- Lack of social support
- Stressful life experiences
- Financial stress , unemployment
- Chronic health problems
- Childhood trauma and abuse
- Substance misuse

Summary

- Biochemical
- Neuroendocrine
- Genetic
- Psychological
- Social
- Other?

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Any Questions?

Thank you…. MCQs are next....

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MCQ

1. Which of the following is not a well-recognised symptom of depressive illness:

A. Ruminations of guilt
B. Thought broadcast
C. Irritability
D. Thoughts of worthlessness
E. Hypersomnia

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MCQ

The correct answer is: B. Thought broadcast

- Explanation: Psychosis in a depression is almost always mood congruent, and in the elderly is often nihilistic ('I am dead', 'My intestines don't work'). It is unusual to have a first rank symptom like thought broadcast which is more suited to a primary psychosis like Schizophrenia.
- Course links: GA Depression LAPs and Mood Disorders in the Elderly LAP.

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MCQ

2. David has chronic back pain and depression, which is not responding to SSRI antidepressants. Which one of the following is the best antidepressant of choice in this situation?

A. Vortioxetine
B. Trazodone
C. Venlafaxine
D. Bupropion
E. Amitriptyline

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MCQ

- **The correct answer is: E. Amitriptyline**
- Explanation: As this patient has not responded to SSRIs, tricyclic antidepressants like Amitriptyline would be a good choice. Amitriptyline is also prescribed frequently for the treatment of neuropathic pain.
- Course links: Psychopharmacology Academic Day.

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MCQ

3. Which of the following factors is NOT associated with risk of repetition of attempted suicide?

A. No previous psychiatric treatment
B. Alcohol or drug abuse
C. Previous attempts at self harm
D. Personality disorder
E. Criminal record

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MCQ

The correct answer is: A. No previous psychiatric treatment

- Explanation: There are a number of risk factors for repetition of attempted suicide, these include previous attempts, having a criminal record, pre-existing EUPD and the use of alcohol/drugs.
- Course links: Self Harm LAP

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MCQ

4. Which of the following medications has RCT evidence for reduction of suicide rate?

A. Citalopram
B. Imipramine
C. Aripiprazole
D. Bupropion
E. Lithium carbonate

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MCQ

The correct answer is: E. Lithium carbonate

- Explanation: There is RCT evidence that links the use of Lithium with a reduction in the suicide rate.
- Course links: Self Harm LAP and Psychopharmacology Academic Day.

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MCQ

5. Which ONE of the antidepressants below is safest to use in an individual who becomes depressed following a myocardial infarction, as concluded from the SADHART trial?

A. Fluoxetine
B. Mirtazapine
C. Amitriptyline
D. Sertraline
E. Citalopram

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MCQ

The correct answer is: D. Sertraline

- Explanation: (Ref - Glassman AH, et al. "Sertraline treatment of major depression in patients with acute MI or unstable angina". *Journal of the American Medical Association*. 2002. **288**(6):701-709)
- Course links: General Adult Psychiatry: Session 2 - Depression I and the Psychopharmacology Academic Day.

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Any Questions?

Thank you….