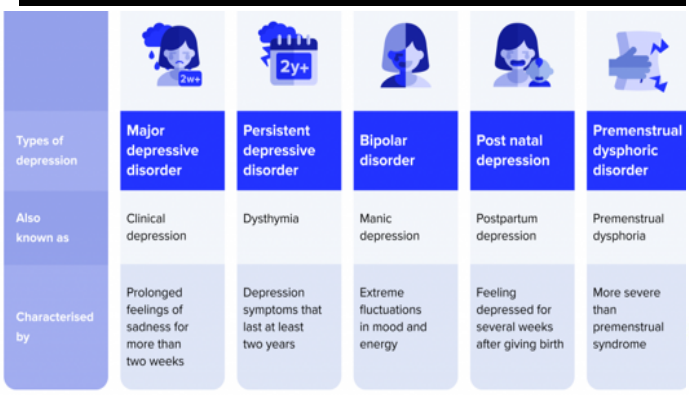
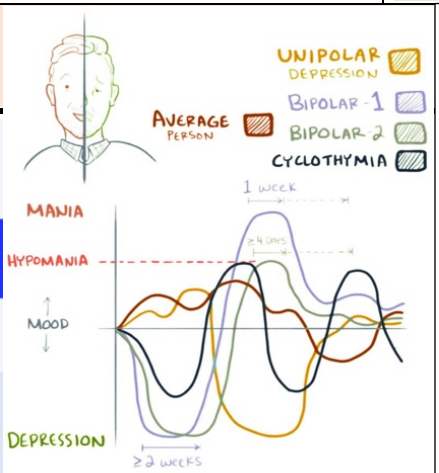
THE PERSON WITH MOOD OR ANXIETY SYMPTOMS

	Depression	GAD	Bipolar Disorder
Define /Sx	**5 or more symptoms in same 2-week period with At least one (1)** ➢ **Low mood** (pervasive sadness) **OR anhedonia** **PLUS (diurnal pattern of – e.g. worse AM/better PM)** ➢ Suicidal ideation ➢ Interest loss ➢ XS Guilt / worthlessness ➢ Energy loss ➢ Poor concentration ➢ Loss of appetite + >5% wt loss ➢ Psychomotor retardation ➢ Sleep disturbance (insomnia, hypersomnia)	**Group of disorders** *(GAD, panic disorder, social anxiety, separation anxiety, specific phobia, PTSD, agorophobia)* Uncontrolled XS worry/anxiety on most days for 6/12 months with **≥ 3 out of 6 symptoms BELOW** causing significant impairments to ADLs, social and occupational life **I** rritability **C** oncentration impaired – circumstantial thoughts **A** nxiety, nervousness, worry on most days **N** o control over worry **T** ime > 6/12 **R** estlessness **E** nergy decrease **S** leep impaired **T** ension in muscles	"mania and melancholy" **"difficult to dx as need manic episode"** **Mania = feeling amazing!! NO sleep needed!** **Bipolar I = Major depression + mania** **Criteria for mania** ➢ **>** 1 week of elevated mood **plus 3 Sx** ➢ **>** 1 week of irritable **plus 4 Sx** **D** istractability **I** ndiscretion / impulsive / irritable –, XS spend, sex, substance (**impaired function)** **G** randiosity – ?special powers or talents, ?new hobbies, interest, hobbies **F** light of ideas (distractibility) – *pressured speech (rapid speech), clanging, word salad, alogia* **A** ctivity **increased energy (goal-directed)** **S** leep deficit – **no sleep** **T** alkativeness (*racing thoughts)*
Types.	Function impaired during episode BUT not b/w episodes (1) **Unipolar depression** (**NO** mania or hypomania) • **Melancholic depression** (*early AM waking, psychomotor agitation, diurnal mood variation*) • **Atypical** depression (*sleep a lot and eat a lot*) • **Depression due to general medical condition or substance misuse** (CS, cannabis, Roaccutane, SSRI) • **Dysthmia = (> 2 years) persistent depressive disorder** (longer-lasting, less depressive symptoms with minimal fxn impairment) • **Catatonic depression ➔ ECT needed** • **Normal bereavement ➔ low mood <6/12 post trauma event** *(2) **Bipolar depression*** ➢ *mania and/or hypomania Sx present in life*	AND • NOT due to drugs or substance absue • NOT due to other mental health illness	**Bipolar II = milder hypomania** ➢ Depressed mood for 2 weeks ➢ Hypomania Sx (elation) > at least 4 days ➢ **NO** impaired function ➢ **Lower Lows – higher suicide risk**
Cause.	**Biological cause** • **Early childhood** (pre-term, dev. trauma, TBI) • **CO-morbidities** (e.g. low Vit D, CVD, hypothyroidism, chronic pain, inflammation) ➔ **higher relapse risk** • **Meds** (steroids, chemotherapy, anti-psychotics) **Psychological cause** • **Recent** childhood (stressors, loss job) • Past trauma and losses (previous abuse) **Social cause** • Poverty , homelessness and rural vs urban	**Biological cause** • **NO specific biological markers** • **HPA axis abnormalities [**CRH release increased by amygdala] • **Anxiety inherited** (possible epigenetic, intergeneration effects) • **Biology of arousal** –resting tachycardia, hyperventilation • **Personality (**?OCPD, OCD)	**1% of population** • **FHx** • **Childhood traumatic events** • **Acquired brain injury** (3x more likely to develop) • **Hypermania causes** = steroids (anabolic, CS, isoniazid)
DDx.	• ***Adjustment disorder*** *(specific traumatic event with no physical & emotional symptoms of clinical depression)* • ***anxiety, substance use disorder*** • ***PTSD*** • ***Personality disorder (e.g. borderline)*** • *negative affect of* ***schizoaffective disorder*** • ***Bereavement/grief = abnormal if after 4/12 post-event*** • ***Organic causes (****hypothyroid****, T2DM, PD, post-stroke/MI)***	• **Performance anxiety** • **Trauma** (PTSD) • **Panic disorder** (cannot leave house) - **DISABLING IRRATIONAL FEAR** • **Panic attack ➔** Abnormal intense fear of losing control, losing your mind or dying • **Agoraphobia** *(fear of the market place, going out)* → avoid many situations • **Social phobia ➔** Fear of criticism	• **Substance induced bipolar** (e.g. stimulant, steroids, anti-depressant) • **Schizophrenia & its subtypes** • ***Personality disorder (e.g. cluster B types → borderline, histrionic)*** • ***Organic causes (****thyroid storm, pheo)*
Ix	• **DASS21** *(anxiety, stress, depression cause of low mood)* • **Edinburgh Post-natal depression** *Exclude ddx:* ➢ *FBC, EUC, CMP, CRP, Fe, B12, folate, TFT, vitamin D* ➢ *ECG → CT/MRI brain*	*Exclude ddx:* ➢ *FBC, EUC, CMP, CRP, Fe, B12, folate, TFT, vitamin D* ➢ *ECG:*	• MSE, thyroid, CV, Resp exam • FBC, EUC, LFT, CRP, TFT, BSL • Urine drug screen and B-HCG • Li concentration • CT or MRI brain +/- EEG
Mx	**Lifestyle (1st line = mild)** • Better diet, regular exercise • Improve sleep hygiene • Avoid smoking, drugs, alcohol • Address social issues – work, finances, housing • Address co-morbidities (DM, RA, OA, Chronic pain, cancer) • **GPMP needed + safety planning (when to go to ED)** **Refer to: (2nd line = mod)** • CBT or psychodynamic psychotherapy • Case worker, significant other, NGOs (black dog, lifeline) **Medication** • **SSRI** (fluoxetine (child), sertraline (adult)) • **SNRI** > **mirtazapine** (if poor appetite), **TCAs** **Invasive (If psychosis present)** • If Rx resistant ➔ ECT, TMS	**Non-pharm** • Cognitive behavioural therapy (e.g. graded exposure + minimise avoidance behaviour) • **Muscle relaxation** (mindfulness, clench and relax from bottom to top) • **Abdominal breathing** (box breathing) • **Breath counting** **Pharm** 1. SSRI – fluoxetine, paroxetine 2. SNRI - venlafaxine 3. MAOi / mirtazapine *Acute agitation / risk of suicide* • **BZD** (GABA agonists) potent anxiolytics, → beware of tolerance / Dependence **If unresponsive / refractory** • ?ECT (less effective than for MDD)	**Acute episodes** 1. **Involuntary Ax** (scheduled under MH act 2007) → call on-call psych reg for mania 2. **Once-off Anti-psychotics** (haloperidol, olanzapine or risperidone) 3. **Add Mood stabiliser** (Li, Na val or lamotrigine) acutely + prophylactically 4. **Check blood/urine for illicit drugs** **AVOID** ➢ **Anti-depressant** = may trigger mania ➢ **BZDs – falls, sedation in elderly** **Beware of Li Toxicity (esp. long-term use)** • **Acute** = fine tremor, urinary freq., polydipsia (DI), ankle oedema, GI (N/D) ➔ seizures • **Long** = CKD, hypo/hyperthyroidism, HPTH • **Cause** = due to changing Na levels → **dehydration, low salt diet, Addison's** ***Monitoring:*** • Check **Li levels EUC/CMP, TFT** weekly for 3/12 • **Avoid ACEi/ARB, NSAID, diuretics, SSRI, metronidazole** (increase Li toxicity) **CI for Li use: AKI →** Change to: • **Lamotrigine** (BD tablet) ➔ inconvenient, SJS • **Valproate (**OD tablet**)** ➔ check LFT.
Barriers	1) **Stigma** 2) **Lack of resources (**E.G. remote communities) 3) **Lack of trained clinician's** 4) **Incorrect or missed diagnosis (***incorrectly prescribed)*		





Assessing suicide risk

- All patients are "**high risk**", as suicide risk fluctuates
- We are **NOT** independent observers of suicide risk (it is interaction between pt and dr)
- **Suicide risk assessment (is BAD)** = can **never** be a basis for clinical decisions, because the **base rate is too low** + known **risk factors are too common**, to identify a person at risk of suicide
- **Game theory (b/w dr and pt)= Aim** to provide a **good standard** of patient-specific care **NOT to predict what will happen**
- Address **modifiable RF** (untreated mental illness, substance use etc)
- Mobilise support networks → instill hope
- Avoid behaviour or service responses that might trigger suicide

MAJOR DEPRESSIVE DISORDER

- Major depression – clinical diagnosis
- Major depressive disorder – One of more episodes of major depression

	Examples		Investigations
Medical causes	**Endocrine**	Hypo/hyperthyroid, Addison's, Cushing's, DM	➢ **MMSE, DASS21, MAS, GAD-7, PC-PTSD-5** ➢ **Bloods** = FBC, EUC, LFT, BSL, Fe studies, B12, folate ➢ **Hormone screen** = LH/FSH, ACTH, TSH, GH, PrL ➢ **Viral serology** (extended panel) ➢ **Imaging** = CT abdo, brain (CVA) ➢ **Deficiency – Fe, B12, Folate, B1, B3** ➢ Urine Tox screen
	Chronic disease	Cancer, CCF, COPD, chronic pain, post-partum, hearing loss	
	Metabolic	Hypercalcemia, anaemia	
	Neuro	• **Parkinson's, MS, TBI, dementia** • CVA (STROKE), complex partial seizure	
	Viral	Hepatitis, EBV, HIV	
Iatrogenic causes	**Meds**	• Corticosteroids, oral COCP/POP, • Anti-HTN, statins, anti-psychotics, • PD meds , maxolon	
	Euphoria	Cannabis, opioids, stimulants, inhalants	
	Irritable/ Agitation	Caffeine, cannabis, tobacco withdrawal	
	Environment	Job loss, relationship breakdown, social isolation	

Management options for mild, moderate and major depressive disorder

	Mild	Mod	Severe
Signs (ICD-10 criteria)	2 core or main ***plus*** at least 2/9 cognitive symptoms(> 2 wks)	2 core or main ***plus*** at least 3/9 cognitive symptoms (> 2 wks) More likely social and work affected	two core or main ***plus*** at least 4/9 cognitive cognitive symptoms (> 2 wks)
Somatic Sx	Marked appetite loss, weight loss, loss of libido, diurnal variation of mood, psychomotor agitation		
Education	• Psychoeducation about family commitments, chronic disease Mx and depression → Relapse prevention plan • Risk outcomes assessment +assess social support		
Non-pharm	• **Lifestyle** (Diet / exercise / sleep / reduce smoking and alcohol or medications that affect mood • **Psych Intervention** e.g. CBT, family focused therapy, mindfulness • **Manage co-morbidities –** hearing, vision, pain, constipation		
Pharm	None *suggest SSRI if counselling ineffective	MUST TAKE FOR AT LEAST 3/12 for effect (LAG TIME) Check Na+ levels before commencing • **1st line = SSRI** → ***sertraline/*Zoloft**, fluoxetine/Prozac, escitalopram (lexipro) • **2nd line = SNRI** (venlafaxine, duloxetine) → more effective but more A/E • **3rd line = mirtazapine** (will cause wt gain, sedation)	
Referral Ind.	• Primary care Mx	• Specialist service referral . • ECT (if meds fail) – risk of retrograde amnesia • CI = UA and CVA	• **ADMIT -** (+++ self-harm, suicidal • Outreach or crisis team (e.g. Local MH support line -1800 011 511) • Suicide ideation • Ineffective meds • Psychotic/manic episode

Alternatives:

- **Increasing** dosage of anti-depressant

*Avoid TCA – risk of OD

- Adding **2nd line** agent
- **Switch** to other agent OR psychologist
- **ECT** – needs patient consent

Major complications of depression:

1. **Suicide**: the risk of suicide in patients with depression is four times higher than in patients without depression
2. **PMHx of substance abuse = BIGGEST RF for suicidal attempts**
3. **Chronic disease (e.g. DM, HIV, HD, CF) →** prolongs depression
4. **Reduced QoL**: patients may struggle with employment and relationships
5. **Beware of psych referral mismatch**
6. Antidepressant A/E: **↓sexual dysfunction, risk of self-harm, weight gain, hyponatraemia + agitation, insomnia**

Rationale of creating a GP mental health treatment plan (GPMHP) inc. financial benefits for patient

Purpose of GPMHP	• GP identifies what type of health care you will require to improve/manage mental health condition • Details what you and your doctor have agreed you are aiming to achieve.
Rationale	• claim up to 10 sessions each calendar year with a Medicare registered mental health professional • (i.e. psychologist, psychiatrist, social worker or occupational therapist) for an initial 6 sessions, with the possibility of 4 more after a review
Requirements	GP appointment + Medicare card + ID
Cost	Free
Savings	Medicare rebate may provide more then 50% off compared to out-of-pocket
Referral	Patient's choice
Length of GPMHP	• Mental Health Care Plan gives twenty sessions partially covered by Medicare until 30 June 2022. • MHCP referral covers up to six mental health sessions at a time – need to revisit GP for another referral
Barriers to Rx depression	• Stigma (social and cultural) • Financial + logistical (seek counselling and paying for meds) • Misconception about psych meds (i.e. A/E, addiction)

Identify RF for suicide	Protective factors for suicide
• Access to weapons (handguns) • Chronic disease • Substance abuse • Male • Low SES • FHx of suicide	• Married • Dependents • Fear of social disapproval • Coping skills • Fear of suicide

ANXIETY DISORDERS – the "fear of uncertainty"

Emotional symptoms	Somatic Symptoms	Behavioural symptoms	Cognitive symptoms
"**Persistent feeling of the patient"** ➢ Worry ➢ Fear ➢ Nervousness ➢ Anticipatory anxiety (catastrophising) ➢ Retrospective anxiety	**Persistent** • SOB, tachycardia • Dry mouth (xerostomia) • Muscle tension, trismus, tremor • Abdo discomfort "butterflies", N/V, urgency • Blushing, hot flushes, diaphoresis • Lightheaded, dizzy, vertigo • **Derealisation** (feelings of unreality • **Depersonalisation** (being detached from one self) • **Paraesthesia (peripheral**	**Persistent** • **Cessation or reduced of activities** o *Non-participation* o *Stop exercising* • **Avoidance:** o *Overt – e.g. only catch train with trusted friend* o *Covert (safety) behaviour* • **Adopt specific activities** o *drug/alcohol use* o ***XS preparation** (can only leave home with Xanax)* o constantly seeking reassurance that something is safe to do • *Complicated by* o *Suicidal ideation*	**"mental representations of an idea of belief"** ➢ *What do you fear will happen?* ➢ *"What goes through your mind when you get anxious?* **Thoughts, images or self-talk (beliefs about beliefs)** ➢ Specific feared situations ➢ Constant catastrophising ➢ Focused on risk mitigation (e.g. *belief that worrying makes me a better doctor? Not cooking makes me a bad mother"* **Systematic habits of thinking** ➢ **Overestimating risks** - *I'll fail this subject, and I'll have to repeat the entire year. My career will be ruined before it's even begun* ➢ **Overestimating costs** - If they think I don't know anything, I'm not a great doctor OR the patient will die and I could have prevented ➢ **Underestimating to cope** - . I couldn't bear it if this happened. I don't know that I could bring myself to have another exam

	Social anxiety disorder (aka. Social Phobia)	Generalized Anxiety Disorder	PTSD – post-traumatic stress disorder	Agoraphobia
Define	1. **Marked Fear, anxiety of being judged/ scrutinised - persistent for > 6/12** 2. **Performance/job related (almost always social situation related)** 3. **Social situations avoided** 4. **NO substance abuse** 5. Anxiety feels similar in quality since 1st experience & performance related : **DDx** ➢ 78% of anxiety disorders are CO-MORBID ➢ Depressive disorders ➢ Body dysmorphic disorders ➢ Avoidant personality disorder ➢ Psychotic disorders o Schizophrenia and related o Delusional disorder	Uncontrolled XS worry on **most days for 6 /12 months** with **≥ 3 out of 6 symptoms** **I** rritability **C** oncentration poor (mind going blank) **A** nxiety, nervousness, worry on most days **N** o control overy worry **T** ime > 6/12 **R** estlessness **E** nergy decrease (fatigue) **S** leep impaired (cannot fall asleep or restless unsatisfying) **T** ension in muscles	**Exposure to traumatic event** more than 1/12 ago **either:** ➢ directly or indirectly involved ➢ witnessed or hearing ➢ learning ***At least one month of:*** A. **Intrusive thoughts/dreams / dissociative flashbacks** assoc. w/ traumatic event B. **Persistent avoidance of stimuli /situations** assoc. w/ event **C. Negative alterations in cognition and mood** - e.g. *dissociative amnesia, negative self-criticism, anhedonia* **D. Marked arousal and reactivity – hypervigilance, insomnia, irritable, self-destructive**	OUT OF PROPORTION fear of having anxiety or losing control for at **least 6/12 months** in at **least 2 out of the 5 situations:** 1. *Using Public transport* 2. *Being in open spaces* 3. *Being in enclosed spaces* 4. *Standing in line or in crowd)* 5. *Being outside home alone* Agoraphobic situations **MUST** ➢ Provoke fear ➢ Are actively avoided ➢ NOT due to medical condition (e.g. IBD, PD) ➢ NOT due to judgement from others
Emotional Sx	• Fear **OUT of proportion** to social context • *Anticipatory* anxiety • *Retrospective* anxiety • *Episodic anxiety* (panic attacks)	• Fluctuating anxiety • Worry about worry • Justify their anxiety (e.g. no one will marry me)	1. Anhedonia 2. Persistent negative emotions (fear, horror, anger, guilt or shame)	• Anticipatory anxiety • Intermittent panic > scared of unable to get out > scared no one can come and help
Somatic Sx	• Tremor • **Blushing (DDx: avoidant personality)** • Tachycardia	• Muscle tension • Restlessness • Feeling on edge	• **Insomnia** • **Poor concentration** • **Reckless**	• Tachycardia, tachypnoea • Chest pain • Dizziness
Behaviour Sx	• **Avoidance or enduring social situations with intense fear of anxiety** • **Drinking before meeting up** • **Letting calls go to voicemail** • Limited eye contact	• XS planning • Reassurance seeking	1) **Irritable / angry outbursts (with no obvious trigger)** 2) **Hypervigilance -** constantly on guard) 3) **Avoidance** environment & situations	➢ **Active Avoidance of situation** - avoids peak hours, buses etc. ➢ **Require companion** ➢ **Endured with intense fear or anxiety**
Cognitive Sx	• **Fear of negative evaluation from actions**– *people will notice I'm anxious* • ***Overestimate of being noticed by others*** • ***Overestimate their level of anxiety*** • ***Underestimate ability to cope***	"I'll make a mistake and be sued for medical negligence"	4) **Involuntary Re-live** or re-experience (nightmare, flashbacks, intrusive thoughts), dreams) 5) **Distorted memory or thought about event**	"If I get stuck in traffic, I may panic and have to pull over"
Non-pharm	1) **Psycho-Education** - *provide factsheets* 2) **Self-monitor with diary** (ID anxiety inducing thoughts and situations) 3) **Muscle relaxation techniques** (breathing control and isometric relaxation) **4) CBT → Graded exposure** – repeated exposure to hierarchical fear situations	1) **Psycho-Education** - *provide factsheets* 2) **Muscle relaxation techniques** (breathing control and isometric relaxation) **3) CBT**	• **CBT** • **High risk of drug addiction** – hence avoid addictive meds • Assoc. major depression	
Pharm	**Educate 4-6 wk trial for effect and continue At least 6 month once mood stabilised:** **1) 1st line = anti-depressants** (SSRI – paroxetine, SNRI – venlafaxine) **2) 2nd line** = phenelzine > moclobemide (MAOi) **3) 3rd line = BZD or mirtazapine (poor evidence)** **AVOID BB, TCA and anti-psychotics**		• **1st line = SSRI** (e.g. paroxetine), sertraline) → avoid paroxetine in pregnancy • **2nd line = SNRI** – venlafaxine **DDx: Acute stress disorder – PTSD symptoms < 1/12 in duration** • **trauma focused behavioural therapy + mobilise social support**	

Demographic RF	• Single / non-married • Females • Low SES • Anglo-saxons • Unexmployred	**Clinical RF**	• FHx of anxiety or mood disorder • Presence of physical disorder (E.g. IBD, Parkinson's) • Current or former smoker • Traumatic event (PTSD)

General Investigations & DDx for anxiety

Non-invasive

- **Primary Care PTSD Screen for DSM-5**
- **4-item scale, the SPAN** (*Startle, Physiological Arousal, Anxiety, and Numbness*)

Bedside

- ECG
- Urine drug screen

Bloods

- **FBC**
- EUC / CMP / PTH / Vit D
- LFT
- Fasting BSL, HbA1C
- TFT +/- AM cortisol, urinary metanephrines
- +/- CRP, Non-contrast CTB

ANXIETY is NOT a DIAGNOSIS → CONSIDER DDx

Psych (NOT just anxiety)	• **OCD, mood disorders, MDD,** • **personality disorders,** • **psychotic disorders (1st or early stage – auditory H/L)**
CNS	Migraines, early cognitive impairment, delirium, dementia, temporal lobe epilepsy
Cardiovascular	Arrythmia, MVP, IHD, CCF
Respiratory	Asthma, chronic airflow limitation, LRTi
GIT	IBS, PUD, GORD
Endocrine	Thyroid, hypoBSL, DM, adrenal insufficiency, pheo, menopause, hypercalcemia (HPTH)
Haematological	Anaemia, B12 def.
Genitourinary	UTI in elderly

	Panic Disorder	Specific Phobia	Separation Anxiety Disorder	Adjustment Disorder
Define	Recurrent **unexpected** [**NO TRIGGER**] **abrupt** surge of fear or intense discomfort where there is **At least one of the attacks are followed by 1/12 month of:** **1. Persistent concern/worry about additional panic attacks (**(*fear of death, losing control, going crazy*)) **2. Maladaptive Behaviours to avoid panic attacks (e.***g. avoid exercise*) 3. NOT due to substance abuse 4. NOT due to another MH issue	Marked persistent anxiety or fear about **(1) specific object** or situation for **more than 6 months** ➢ *E.g. Height, Flying, Animals, Seeing blood, Receiving injection (needles)* ➢ NOT due to PTSD, OCD, agoraphobia	**Inappropriate and XS fear or anxiety concerning s**eparation form home OR attachment figures for **> 4 weeks (child) or > 6 months (adult)** **At least 3** of the following below:	Development of emotional and behavioural symptoms in response to known stressor which has occurred **within 3/12 months of Sx** A. OUT-OF-PROPORTION distress B. Impaired ADL C. NOT due to MH D. NOT bereavement **E.** Sx resolve once stressor eliminated
Emotional Sx	**"Overwhelming panic"** • Persistent concern of worry about additional panic attacks (e.g. losing control, having heart attack)	• **(2) Immediate fear or anxiety provoked** by specific object or situation • **(3)** OUT OF PROPORTION fear • **(4) PERSISTENT** fear	Recurrent **distress/worry from** 1. **Thinking about separation** 2. **Losing attachment figure** 3. **Event that could cause separation (**e.g. being lost)	Mimics depression / anxiety
Somatic Sx	**At least 4:** • **CVS** = Palpitations, chest pain, SOB • **ANS –** trembling, diaphoresis • **CNS/GI –** Nausea, light-headed • **Fear of dying or losing control** • *Also other anxiety sx e.g. depersonalisation, derealisation*	• Tension • Restlessness • sweating	**(4) Repeated complaints of any one:** ➢ **headache** ➢ **stomach aches** ➢ **nausea or vomiting**	Mimics depression / anxiety
Behaviour Sx	• **Avoidance behaviours** – stops exercise, drinking water or exposure to unfamiliar situations	**Active (5) avoidance** - Marked urge to flee/run away from specific object or situation	**(5,6) Active reluctance to:** 1. Be **alone** without attachment 2. **Sleep away** from attachment	OUT-OF-PROPORTION distress
Cognitive Sx	**"I'm about to collapse and die"** • Overestimate somatic Sx • Overestimate that panic attack • *Underestimate* ability to recover – e.g. belief will panic or endure forever	➢ Impaired ADL (social/occupational) "I can't stand the sight of blood"	➢ (7) Impaired ADL (social/occupational) ➢ (8) Repeated nightmares with **theme of separation**	Impaired ADL
Non-pharm	*1)* **Psycho-Education** - *provide factsheets* 2) **Self-monitor with diary** (record situation, what they were thinking) 3) **Muscle relaxation techniques** (breathing control and isometric relaxation) 4) **Abdominal breathing (e.g. box breathing)** **5) Breath counting** **6) CBT → Graded exposure** & minimise avoidance – repeated exposure to hierarchical fear situations			**1) CBT with positive reinforcement**
Pharm	**At least 6-12 month trial of the following** ➢ **1st line = anti-depressants** (SSRI – paroxetine, SNRI – venlafaxine) ➢ **2nd line** = phenelzine, moclobemide (MAOi)			Nil

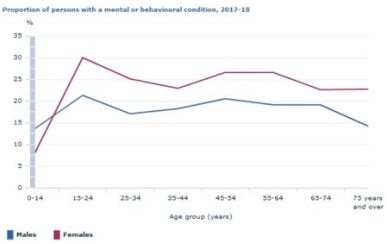
Other – does not fall into anxiety category

- **Selective Mutism** - Consistent failure to speak in specific situations where there is expectation to speak (e.g. school speech) for **at least 1 month ➔ specific to social situation BUT normal cognition**
- **Panic attack [known trigger]**
- **Obsessive compulsive trait = *normal fxn,***
- **OCD = intrusive obsessions, compulsions and good insight**
  Rx: 1) CBT → 2) SSRI or increase dosage if non-responsive after 4-6 wks
- **Substance / Medication-induced** Anxiety Disorder (cocaine, withdrawal)
- Anxiety Disorder due to **Another Medical Condition**
- **Other Specified Anxiety Disorder**
- **Unspecified** Anxiety Disorder (aka **Anxiety Disorder NOS**)

Table A: Prevalence and Age of Onset in Anxiety Disorders (NSMHWB, 2007)

Disorder	12-month prevalence rate	Median age of onset (years)
Panic Disorder	2.6%	30
Agoraphobia	2.8%	22
Social Phobia	4.7%	13
Generalised Anxiety Disorder	2.7%	33
Obsessive Compulsive Disorder	1.9%	19
Posttraumatic Stress Disorder	6.4%	26

Psychological Medicine: Anti-depressants



What is the clear difference of mental disorders to other chronic conditions?

- Affects the young. Higher prevalence at early age then plateaus
- Successful antidepressant Rx → maintained for 6-12 months → then withdrawn
- *Chronically depressed patient may need life-long treatment* (major gap in evidence!)

Risk factors for anxiety and depression

- 1 in 5 [20.1%] **Australians have mental or behavioural conditions** (F>M) → MAINLY due to increase in depression & anxiety related conditions
- Female
- Older age
- Disability / chronic disease

Mx of Depression

1st line: lifestyle	➢ Stop smoking (more effective than any drug) for reducing depression ➢ Regular exercise, sleep hygiene (melatonin), better diet, work/life balance
2nd line: social support	➢ GP support – mental health care plan (organised referral for about 10 Medicare rebatable visits for calendar year) ➢ Referral to psychologists (CBT)
3rd line: meds	➢ Antidepressant effects are delayed (over 2 weeks)= **Therapeutic Lag"** due to increased time for neurons to respond ➢ Check adherence, compliance + co-morbidities ➢ Do we need to switch? Augment? OR increase dose (if tolerating well) **Discontinuous syndrome** [esp. on short-half life meds]– going "cold turkey" **creates Sx of withdrawal** (Flu-like symptoms, Insomnia, Nausea, Imbalance, Sensory disturbances, and Hyperarousal) **and encourages pts to return back to meds**
4th line (augmentation)	If **semi-responsive** to medications consider: ➢ Lithium or T3 augmentation OR 2nd generation anti-psychotics (quetiapine)

What to discuss when starting new meds?

- ➢ Benefits
- ➢ ADR
- ➢ Risk of discontinuation
- ➢ Likely time to respond
- ➢ suggest Mirtazapine or SSRI
- ➢ Titrate accordingly

Class	Selective Serotonin Reuptake Inhibitors (SSRIs) 1st line	Serotonin & NA Reuptake Inhibitors (SNRIs) 1st or 2nd line	Tricyclic antidepressants (TCAs) 2nd line	Monoamine Oxidase inhibitors (MAOi) 3rd line	Serotonin Receptor Antagonist 1st line
E.g.	• ***Escitalopram*** *(lexipro)* • ***Fluoxetine*** *(PRO**ZAC**)* ***young teen taken AM ➔ (longest half life up to 72 hrs*** • ***Paroxetine*** *(NOT for pregnancy)* • ***Sertraline*** *(safe for pregnancy)*	• ***Venlafaxine*** *(Effexor)* • *Desvenlafaxine &* • ***Duloxetine***	• ***Amitriptyline***, • ***Nortriptyline*** *– best tolerated (can monitor TI)* • ***Mianserin*** *– new – fewer CV and anti-chol effects* • ***Imipramine***,	• ***Phenelzine*** *(irreversible) – not available in Aus.* • ***Moclobemide*** (reversible) = Dizziness, GI effect, insomnia	*Mirtazapine (15-60mg nocte)* ➢ *If sedation required*
MoA	SSRIs **BLOCK serotonin transporter (SERT)** in presynaptic terminal → ++++ prolonged 5-HT stimulation ➢ **10 days – 2 weeks** ➢ ***Take AM w/ food*** *(against GI effects)* ➢ Begin w/ **½ therapeutic dose** for 5 days before full dose (to minimise side effects)	SNRIs **block 5HT and NA transporters**→ ++++ prolonged 5-HT + NA stimulation ➢ **more potent** ➢ BUT **more A/E** ➢ Hepatic metabolism	• Block **SERT and NET** in presynaptic terminal → ++++ prolonged 5-HT, NA, stimulation • Need baseline ECG before starting .	• **Inhibits monoamines** (A, NA, serotonin, dopamine) degradation by MAO, increasing their synaptic concentration. • Phenelzine **irreversibly** inhibit MAO-A & MAO-B • Moclobemide **more selective** to MAO-A	1. a2 presynaptic blockade 2. Loss of inhibition 3. Increased NE release 4. Potent H1 antagonist (sedation)
Ind.	• **Major depression (MDD)** • **GAD or social anxiety** • Bulimia nervosa • PMS • OCD or PTSD **GOOD SAFETY PROFILE (** ➢ **Tolerable - Less potent** ➢ **Less risk of OD and A/E**	• **Major depression** • **GAD (*D* and V)** • Diabetic peripheral neuropathic pain (***Duloxetine***) • Panic disorder and social phobia (***Venlafaxine***)	• **Major depression** • **OCD** • **Nocturnal** enuresis (bedwet) (***Imipramine***) • Neuropathic pain (***Amitriptyline***) • Migraine prophylaxis (***Amitriptyline***) • post ECT maintenance (**Nortriptyline + Li**)	Not 1st line • Major depression • Some anxiety disorders • Parkinson's **Needs to be on low tyrosine diet** to prevent HTN crisis (e.g. ➢ aged cheese, ➢ cured meet, ➢ soybeans, ➢ EtOH or any fermented foods	• Major depression
AE	**5 S's** • **Sodium - hypoNa (SIADH)** • **Sleep issue (insomnia , agitation)** • **Size = wt gain** • **Stomach = n/v + C/D** (*5-HT3 trigger zone*) • **Sexual dysfunction** • **Long QTc (citalopram)**	**SSRI A/E plus SNS** Sx • tremor, • diaphoresis, • palpitations, • DRY MOUTH • **HTN** (venlafaxine)	• **Anti-chol DELIRIUM (anti-sludge →** *can't pee, can't spit, can't see -mydriasis*) • **Low Na** • **Cardiotoxic ➔ LONG QTc→ . VT (esp. *Amitriptyline*)** • **H1 – wt gain + sedation** • **A1 - Postural HypoTN, dizzy**	**Tyramine accumulation in gut** →severe SNS reaction esp. after eating cheese! • **Hypertensive crisis** 1) diplopia and agitation 2) fever, restlessness 3) confusion, seizures, coma • **3H's = Hepatocellular jaundice + HTN + Hyperthermia**	**Mirtazapine** • **Hyperphagia** • **Wt gain** • **Sedation (H1) →** best to use at night time • **Anti-chol** (anti-sludge) • **Orthostatic hypoTN**
	Elevated serotonin = +++ energy 1st before +++ mood → increased energy to enact upon suicide ideation		Higher risk of OD Neutropenia (mianserin) Cardiotoxicity = **main cause of death**	Avoid = SSRI, SNRI, TCA, St John's CI = pregnancy (teratogenic)	• Wt gain + hyperphagia

Serotonin syndrome [FEVER – MAN]	Drug interactions – tramadol and ST John's wort ➢ **Mental state** → agitation, hypomania, anxiety, altered LOC ➢ **ANS** → febrile, tachycardia, flushing, sweats, mydriasis ➢ **NEUROMUSCULAR** → clonus, hyperreflexia, tremor, hypertonia	➢ Sedate ➔ IV 0..1mg/kg midazolam ➢ Cool ➢ Intubate ➢ Paralyse ➔ PO cyproheptadine 8mg
St. John's wort (hyperforin)	Weak monoamine reuptake inhibitor **BUT** many interactions → AEs with liver CYP enzymes + SSRIs ➢ Unregulated → different formulations from different suppliers	
Tramadol	Opioid for chronic pain w/ 5-HT effect – amplified reuptake effect	
(Es)Ketamine	NMDA receptor antagonist → **IMMEDIATE EFFECT!**	
Bupropion	NA/Dopamine reuptake inhibitor → less A/E than SSRI ➔ **PBS for nicotine addiction or depression**	

Psychological Medicine: Anxiolytics

Class	Benzodiazepines
MoA	• **Positive allosteric modulator** of the **$GABA_A$** (ligand-gated Cl^- channel) potentiating inhibitory GABA effects ➔ CNS depression ○ **does NOT bind to receptor (hence safe against OD)** • **Metabolised by liver (cyp3A4)**

Sx	• **CNS depression = Sedation (stupor), slurred speech, Muscle relaxation, Anterograde amnesia (memory blackouts), ataxia**
	• **Resp depression = reduced RR** → Cautious in **OSA/COPD** (resp acidosis causes loss of hypoxic drive)
	• Addiction via positive OR negative reinforcement
	  ○ Positive = BDZ potentiates GABA release
	  ○ Negative = tolerance quickly developed wit hin 6 weeks of usage
	• **Withdrawal sx (as early as 6 weeks) ➔**
	  ○ **Somatic =** increased muscle tetany and twitches → [rare] nightmares, panic attacks
	  ○ **Psych =** tremor/sweats, insomnia, agitated, irritable poor memory, depression → [rare] seizures, tinnitus, confusion
	  ○ **Risk factors = High dose (≥50mg/day), prolonged use, short halfolife**

Indication	**Stepwise lowering of dose to minimise withdrawal effects** • **Anxiolytic → should be restricted to short-term treatment** • **Agitation** • **Anti-convulsant** – Rx seizures acutely • **Alcohol withdrawal (DDx: BZD withdrawal)** • **Insomnia (hypnotic effects) –** SA BDZ (e.g. temazepam) → beware of rebound insomnia • **Muscle relaxant** • Potential for misuse → if combined with alcohol and opiates should have a long t1/2 (short-term use recommended)
Examples (equivalent doses)	**Shorter the half life ➔ the worse the withdrawal** • **Midozalam → < 6 hours [short-term]** → anaesthesia OR status epileptic ≥2x seizures within 30mins) • **0.5mg Alprazolam (Xanax)** → 6-12 hrs • **15mg Clobazam (Frisium)** → > 24 hrs → alcohol withdrawal against chronic liver disease • **5mg Diazepam (Valium)** → > 24 hrs (used for alcohol detox and status epilepticus)
AE	**HIGH MORTALITY RATE** • **Common**: Drowsiness, light-headedness, **slurred speech**, dependence, effects on vision, miosis • **Infrequent (0.1-1%)**: Confusion, aggression, anxiety, decrease libido, amnesia, respiratory depression • **Rare (<0.1%):** Allergic reactions, blood disorders (incl. leukopenia and leucocytosis) In elderly, increased risk of: ➢ **50% ↑ Falls** (dose-dependent) – increased reaction time, sedation, ataxic gait ➢ **Fractures (esp, hip)** ➢ **Sedated + Cognitive impairment** - Confusion, memory impairment, inattention ➢ **Poor quality sleep (REM)**

Case Study 1:

Female, 30-year-old, was admitted to detoxication unit (opioid use). She was recently diagnosed with major depression and long-term history of insomnia was reported. Which anti- depressant is she likely to have been prescribed?

* During intake she did not report taking any antidepressant. She stopped taking her medication due to fear of weight gain after reading CMI.

- **Risk factors**: weight gain, insomnia
- **Drugs used**: Mirtazapine

Case Study 2:

Male, 34-year-old, presented to his GP with tremor which started 6-7 days ago. On further investigation, the GP noted he was restless, had an increased muscle tone, and BP was high (158/98 mmHg). Medication history:

- Long-term use: fluoxetine (Major depression), pantoprazole (GORD)
- 2 weeks ago, where he was prescribed paracetamol and tramadol (low back pain). What is the possible cause for this patient tremor? =
- **Cause of tremor:** Serotonin toxicity due to tramadol being added to amplify the reuptake inhibitory effect

Sedatives abused	MoA	Symptoms

Gabapentins / pregabalins	**GABA analogues** (reduce CNS excitability)
	➢ **Pregabalin** = quicker onset of action (! Hr compared to 3 hrs) ➔ same BA despite
		➢ **Neuropathic pain**
		➢ **Misuse (high dose 3-20x)** = addictive effects of :
		  ○ Euphoria, Relaxation, Dissociative effects, craving
		  ○ Combined w/ methadone to enhance **high**
		➢ **Withdrawal** = insomnia, nausea, headache, diarrhoea

GHB (gamma hydroxybutyrate)	*Preferentially activates presynaptic **$GABA_B$ receptors** → **Inhibiting** GABA release **disinhibits** VTA DA cells* (addiction) ➢ Sold in small containers (e.g. vials, fish-shaped soy bottles) ➢ *Aka. Liquid B, fantasy*	**High addiction potential (much quicker)** ➢ CNS = Euphoria, increased libido, agitation, Drowsy, ➢ N/V, , dizziness, Incoordination ➢ **Withdrawal OD =** resp. OD, blackouts, delirium, seizures, death ➢ **Rx: BZD and baclofen**
Opiates (for acute pain ONLY)	***Selectively targets μ-opioid GPCR*** *→ open K+ channel & close Ca channel* ➢ Abused by **older** population ➢ Codeine (highest) → oxycodone → tramadol → morphine → fentanyl' ➢ **Reduced misuse** (but still highest) since now requires Dr prescriptoin	**Chronic** pain dependence (poorly managed) ➢ Drug seeking behaviour ➢ Tolerance and withdrawal ➢ **Reduced ADL**

***Withdrawal Rx ➔ Call drugs and alcohol services ➔ high dose benzodiazepines (acute)**

Anti-Psychotics / Tranquiliser / Neuroleptics

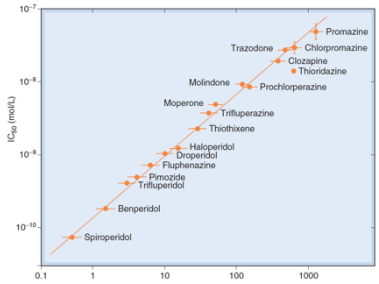
- ***Psychosis*** = disordered thoughts - person loses capacity to distinguish fiction from reality
- ***S+S*** = hallucinations, delusions, disordered thought, disordered behaviour
- ***Onset*** = abrupt, slowly developing, unremitting or relapsing

Classification of antipsychotic drugs

- Main categories are:
  - first-generation ('typical', 'classical' or 'conventional') antipsychotics (e.g. **chlorpromazine**, **haloperidol**, **fluphenazine**, **flupentixol**, **zuclopenthixol**);
  - second-generation ('atypical') antipsychotics (e.g. **clozapine**, **risperidone**, **quetiapine**, **amisulpride**, **aripiprazole**, **ziprasidone**).
- Distinction between first- and second-generation drugs is not clearly defined but rests on:
  - receptor profile;
  - incidence of extrapyramidal side effects (less in second-generation group);
  - efficacy (specifically of **clozapine**) in 'treatment-resistant' group of patients;
  - efficacy against negative symptoms.

Main indications for anti-psychotics

- **Organic disorders** → delirium, DT, dementia
- **Functional disorders** → Schizophrenia, schizoaffective disorder
- **Mood disorders** → **Rx resistant mania** , major depression with psychosis
- **Others** Insomnia, Behavioural disturbances (mood, thinking), Tics

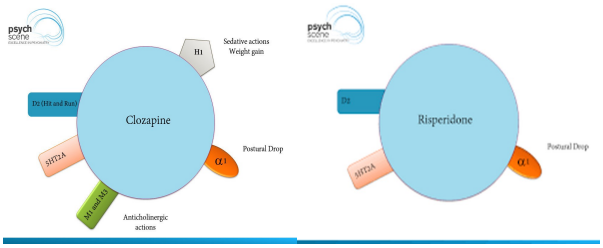


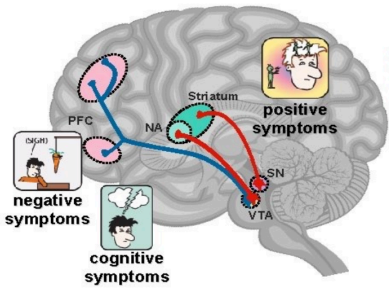
*Most are not specific and non-selective → also bind to **a1, D1/D3, 5-HT, H_1 receptors etc.**

Drugs aim to treat Symptoms (NOT cure)

Outcomes of long-term anti-psychotic drug therapy

- *Live longer, but often with tardive dyskinesia and no ultimate resolution of underlying condition*
- *Any use of antipsychotics **sig. reduces** mortality in schizophrenic populations*





Blocking D2 (found in motor regions, HT)

1. +++ increases DA release → +++ D1 activity
2. increases glutamate release from VTA (not SN) neurons
3. *Nigra-striatal pathway (dorsal striatum*

	Pharmacology	Adverse Side Effects
Conventional Antipsychotics	▸Dopamine D_2 Receptor Antagonists	▸Extrapyramidal symptoms ▸Hyperprolactinemia
Atypical Antipsychotics	▸Dopamine D_2 Receptor Antagonists ▸Serotonin 5-HT_{2A} Receptor Antagonists	▸Metabolic side effects (weight gain, glucose dysregulation, dyslipidemia)

INDICATIONS

1ST GEN = Old antipsychotics

➢ Haloperidol (greater EPSE) → 0.25-0.5mg PO/IM → wait 30 mins b/w doses

2ND GEN = New antipsychotics

Drug	Clozapine	Quetiapine
MoA	Dopamine (D2) receptors antagonists	
Ind	Most effective for: • Rx resistant Schizophrenia • Mania • Psychosis • Suicidal ideation • Behavioural disturbance (Aggression)	• Schizophrenia, • **Bipolar affective disorder** • Psychosis in **Parkinson's patient**
ADV.	• **Most effective drug** • *Pts recover if immediately withdrawn* • *Less EPSE than typicals* • **Start low – titrate up** • **70% of patients benefit**	• *New drug w/ good efficacy* • *Lower incidence* of EPSE motor Sx **(best for Parkinson's)**
A/E	• **Agranulocytosis** → neutropenic sepsis flu-like Sx, fever and sore throat **Rx: GCSF + sx treatment** → prevent with Li, CSF and mitigate RF → need weekly CRP and WCC for 4/12 then monthly for 18/12 (can rechallenge clozapine later) • **Elevated PrL** • **Seizures** • **Myocarditis** (+++ Trop, CRP) → *due to RECENT increased dosage or concurrent Na valproate usage → ICU admission + do not ever restart clozapine*	• **Weight gain** + CV effect • **High misuse** w/ illicit drugs • **Prescribed "off-label"** for anxiety, anorexia, OCD, PTSD, substance use disorder, agitation in dementia

* ***From chlorpromazine on, all antipsychotic drugs are dopamine D2 antagonists (or low efficacy agonists)***

Typical and Atypical (2nd gen) Anti-psychotics

- **➔ do NOT improve dementia ➔ increased falls, VTE, strokes**
- **➔ ONLY target the positive symptoms of schizophrenia**
- **AVOID – EtoH, smoking, caffeine (reduces clozapine levels)**

3rd gen anti-psychotics *(E.g. aripiprazole, cariprazine)*

Cariprazine (only drug able to treat BOTH positive and negative Sx)

➢ Partial dopamine D2/3 agonist and 5HT1A and blocks 5HT2A
➢ Less EPSE, less hyperPRL and less weight gain
➢ A/E = agitation and restlessness

General A/E

Typical anti-psychotics A/E → EPSE + HyperPrl

EPSE	Solution
Acute dystonia (blocked nigrostriatal pathway) "sustained increased and painful tone"- ***laryngospasm (most serious - risk of hypoxia)**, upward eye movement (oculogyric crisis), trismus, lordosis, scoliosis, opisthotonos crisis (hypertext body)*	**RF:** male, young, 1st gen anti-psych, stimulant use, previous dystonic reaction • **1st: Discontinue** anti-psychotic – change anti-psychotic (E.g. clozapine) • **2nd: IV/IM Benztropine (anti-chol)** e.g. 2-8mg Benztropine → esp. for acute oculogyric crisis or dystonia * *Vitamin K, Gingko (low evidence)*
Parkinsonian side effects- Tremors, Bradykinesia, Rigidity, reduced arm swing, shuffling gait → "Simpson Angus side effect"	
Tardive dyskinesia (TD) → irreversible if chronic (Involuntary movements – lip smacking, automatisms)	
Akathisia (10-15%) (inner feeling of restlessness) acute motor agitation, reversible) – *restless leg, rocking, pacing*	
XS PrL (galactorrhea, amenorrhoea, sexual dysfunction)	• **Discontinue** • **Dopamine agonists (e.g. aripiprazole)**

Atypical (2nd gen) anti-psychotics A/E ➔ metabolic side effects

Main side effect	Rx
• **Weight gain** (all anti-psychotics)	Diet, exercise, metformin
• **Glucose dysregulation + Peripheral neuropathy**	Diet, exercise, OHA, **PN, GASTROPARESIS, SBO**
• **Dyslipidaemia**	Statins or cholesterol lowering agents
• *****Seizures*****	Anti-convulsant?
• *****Cardiac issues***** (↑HR, prolonged QT, hypoTN → postural drops)	Preventative measures ➢ Correct dose or use BB

DO NOT MISS

MAJOR COMPLICATIONS	Solution
Neuroleptic malignant syndrome (due to D1/D2 receptor blockade – antipsych or abrupt stoppage of PD) • **Confusion + rigidity + hyperthermia + ANS dysfn** • **CK > 4x ULN**	• **SUPPORTIVE** → IVF → aggressive cooling • **BZD for muscle rigidity** + STOP dopamine antag or give dop agonists (e.g. bromocriptine) • **5-20% mortality rate**
Serotoninergic syndrome ➢ Agitation, restless, delirium, ➢ Clonus, hyper-reflexia, , akathisia, HTN, Hyperthermia	• **Cool** • **Sedate** - *BZD* • **Intubate** • **Paralyse** – *Induction agents*

****Monitoring bloods (weekly for 18 weeks)***
- **FBC (WCC), EUC, LFT, Fasting BSL, Lipids, PrL, ECG + BMI**