Management of Depression and Insomnia

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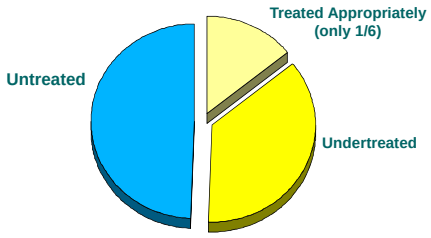
Mental health problems in the world & in Singapore

- 450 million suffer from mental disorders
- 1 in 4 persons will develop a mental or behavioural disorder in their lifetime
- **Anxiety & Depression**: 6.5% of population
- **Minor Psychiatric Illness**: 15.7% of population

Mental disorders in primary care

- 25% of patients have a mental disorder
- 88% of patients with mental disorder seek primary care first
- Diagnosis missed half the time for depression, more for eating disorders and alcoholism

Depression usually untreated or undertreated in Primary Care

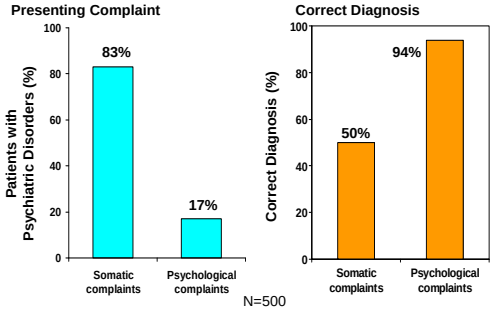


Hirschfeld et al. *JAMA.* 1997;277:333-340.

Obstacles to diagnosis

- Insufficient time
- Presentation with somatic symptoms
- Competing problems
- Stigmatization
- Minimization

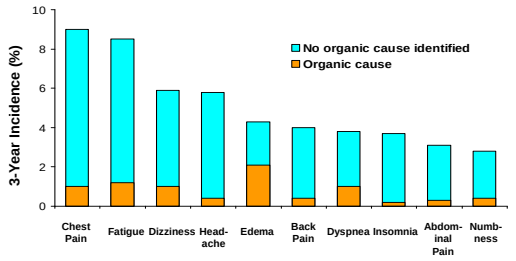
Presentation influences psychiatric diagnosis in primary care



N=500

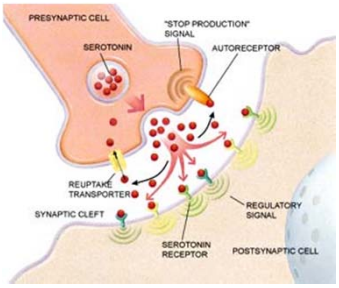
Bridges KW, Goldberg DP. *J Psychosom Res*. 1985;29:563-569.

Physical complaints are rarely organic



Kroenke K, Mangelsdorff AD. *Am J Med*. 1989;86:262-266.

The Medical Model of Depression



Hollister LE. Antidepressant agents. In: Katzung BG, ed. *Basic & Clinical Pharmacology*. New York, NY: McGraw-Hill; 1997.

Neurobiology of Depression

Serotonin-related symptoms

Impulse • Appetite Aggression

Norepinephrine-related symptoms

Motivation • Zest Energy • Social drive

Stahl. J Clin Psychiatry 1999; 60: 213-214.
Healy et al. J Psychopharmacol 1997; 11 (Suppl): S25-S31.

Diagnostic Criteria for Major Depressive Disorder

- Five or more of the following for at least 2 weeks
  - Depressed mood*
  - Loss of interest or pleasure*
  - Appetite/weight change
  - Sleep disturbance
  - Psychomotor disturbance
  - Fatigue or low energy
  - Feelings of worthlessness or inappropriate guilt
  - Impaired ability to think or concentrate
  - Recurrent thoughts of death or suicide

*At least one of these symptoms must be present.

Adapted from *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. (*DSM-IV*™). 1994:327, 339.

Depression and Comorbidity

Prevalence of Depression as a Concomitant Condition

Cancer:	25%
Diabetes:	32.5%
Postpartum:	10%–20%
Poststroke:	32%
Post-myocardial infarction:	16%

Massie, Holland. *J Clin Psychiatry*, 1990. Lustman et al. *Diabetes Care*, 1988.
Dobie and Walker. *J Am Board Fam Pract*, 1992. Morris et al. *Int J Psychiatry Med*, 1990.
Frasure-Smith et al. *Circulation*, 1995.

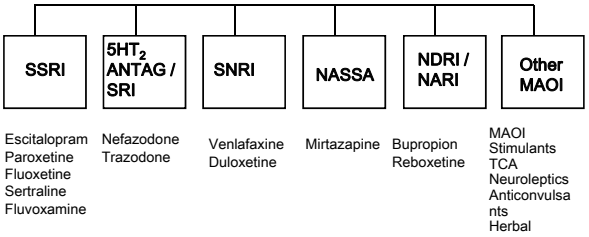
Non-Pharmacologic Therapies

- Psychological Interventions
- Social Intervention
- Electroconvulsive Therapy (ECT)

Antidepressants

- Used in both anxiety and depression
- Effective in mild, moderate or severe depression
- 60 -70% response rate in depression
- Effectiveness comparable between and within classes
- Improvements seen in 2 weeks; sometimes up to 4-8 weeks

Pharmacologic Classes



Antidepressants: TCAs

- Older and time-tested, cheap
- Problems of anticholinergic side-effects, postural hypotension and sedation
- Toxic in overdose; cardiac effects
- Imipramine, amitriptyline, clomipramine and dothiepin (prothiaden)
- Dose 10 – 150 mg/day
- Usual effective dose 25-100 mg/day
- Once daily at night; titrate up 25 mg/day

Antidepressants: SSRIs

Generic name	*Trade name(s)*	*Dose (mg/day)*
Fluoxetine	Prozac, Magrilan	20-60
Fluvoxamine	Faverin, Luvox	50-300
Lexapro	Escitalopram	10-20
Sertraline	Zoloft	50-200
Paroxetine	Seroxat, Paxil	20-60

Antidepressants: SSRIs

- Newer, costlier
- Safer in overdose
- Less problematic side-effects
- Broad spectrum of activity
  - Depression
  - Anxiety
  - OCD
  - PTSD
- Side effects
  - Overstimulation, insomnia (early)
  - Sexual – erectile dysfunction
  - GI effects

Antidepressant Classes

Class	*Examples*	*Action*	*Precautions*
Tricyclic antidepressants	Amitriptyline,Imipramin, Clomipramine, Nortryptyline, Dothiepin	Inhibit serotonin & NE uptake; anticholinergic-antimuscuranic; alpha1-adrenergic antagonist; anithistamine	Anticholinergic effects, postural hypotension, confusion, weight gain, CVS effects, toxicity in overdose
MAOIs	Phenelzine, Tranylcypromine	MAO inhibition causes NE accumulation	Postural hypotension, dietary restrictions, drug interactions, sexual dysfunction
SSRIs	Fluoxetine, Fluvoxamine, Paroxetine, Escitalopram, Sertraline	Selectively inhibits 5HT reuptake	Agitation, akathisia, anxiety, insomnia, sexual dysfunction, GI effects, withdrawal effects

Class	*Examples*	*Action*	*Precautions*
SNRI	Venlafaxine Duloxetine	Inhibits 5HT and NE reuptake	Same as SSRIs (low doses), hypertension, insomnia, agitation, headache (high doses)
SARI	Nefazadone	Serotonin antagonist & reuptake inhibitor	Somnolence, asthenia
NaSSA	Mirtazapine	Alpha2, 5HT1, 5HT2, H1 antagonism → Enhances NE & 5HT neurotransmission	H1 antagonism – sedation, weight gain
NDRI	Bupropion	NE and Dopamine reuptake inhibitor	Stimulation, agitation, nausea, insomnia, seizures (4/1000)
	Trazodone	5HT antagonist	Sedation, postural hypotension, nausea

SNRI (Serotonin Norepinephrine Re-uptake)

- Dual Mechanism of action
- Useful as second line drug
- Also useful in painful somatic symptoms
- Examples Duloxetine, Venlaflexine
- Side effects similar to SSRIs
- Need to monitor BP for Venlaflexine
- Duloxetine has approval for diabetic neuropathy

NaSSA (Noradrenergic and Specific Serotonergic)

- Mirtazepine (Remeron)
- Alpha-2 adrenergic receptors that normally inhibit the release of the neurotransmitters norepinephrine (noradrenaline) and serotonin, thereby increasing active levels in the synapse
- Mirtazapine is a potent antagonist of 5-HT2 and 5-HT3 receptors. Reducing side effects of sexual dysfunction and GI effects
- Prominent anti-histamine effect. Weight gain and sedation prominent

Choosing An Antidepressant

- Cost
- Symptom profile
  - E.g. Sleep disturbance, risk of overdose, obsessive symptoms, prominent anxiety
- Side effect profile
  - E.g. Anticholinergic effects, cardiotoxicity, sexual effects, weight gain
- Previous history of response/non response (patient/family)
- Dosing schedule

Dosages and Treatment

- Dosages typically similar for adult primary care and psychiatric patients
- Acute treatment: 8 to 12 weeks
- Maintenance treatment: 6-12 months symptom-free
- *"The dose that makes them well is the dose that keeps them well"*

Management Guidelines

- Adequate dose of antidepressant therapy
- Adequate duration: 8-12 months
- Prophylaxis at full dose for recurrent depression
  - 2 or more episodes
  - Prominent family history
  - Significant suicide risk

Initiating therapy

- May start with *full* dose or *half*-dose
- May need to cover with *short-term* BZPs to manage anxiety and insomnia initially
- Response takes 10 to 21 days, sometimes longer
- Side effects usually settle within a week
- Beware the "one-dose" patient

Suboptimal response?

- Increase to maximum tolerable dose
- Maintain for adequate duration
  - 4-8 weeks
- Deal with psychosocial stressors
- Manage anxiety
  - Relaxation techniques
    - Progressive muscle relaxation and imagery
  - Short-term benzodiazepines
    - Xanax, Ativan

Suboptimal response?

- Consider switch *within* class first
- Then consider switch *outside* class
- Augmentation
  - Lithium, Thyroxine, Antipsychotics
- ECT
- ***Avoid combining antidepressants***

SSRIs: Commonly reported side effects

- Nausea, GI discomfort
- Anxiety, restlessness during initiation
- Drowsiness, lethargy
- Insomnia
- Sexual / erectile dysfunction

Monitoring

- No specific blood monitoring required for anti-depressants
- Venlaflexine requires BP monitoring
- Continuous monitoring of disease symptoms

Prognosis

10-yr relapse rate
(1st-time major depressives)

50%!!

Generalists Give Good Care for Mood Disorders

- 85-95% depressed patients treated by PCP successfully without referral
- Prognosis of patients treated by PCP's better than that of patients treated by psychiatrists

What is insomnia ?

- One or more of the following symptoms:
  - Difficulty falling asleep
  - Waking up frequently during the night with difficulty returning to sleep
  - Waking up too early in the morning
  - Unrefreshing sleep
  - Perception of poor quality sleep even if true sleep was obtained

The International Classification of Sleep Disorders Diagnostic & Coding Manual, 2nd ed. American Academy of Sleep Med

Client: Sanofi-Synthelabo Singapore Pte Ltd
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Frequency: Daily

Sleepless in S'pore? Most say 'no' to pills

Insomnia is on the rise with 17 million sleeping-pill prescriptions given in 1998. But due to addiction worries, many prefer soup to over-the-counter pills

Not a problem for only the elderly

YOUNGER patients are coming forward for treatment, a sign that insomnia is no longer the problem of just the elderly, said consultant psychiatrist Tan Chee Tin. Stress and anxiety are the most common reasons affecting insomniacs. Try writing down thoughts to relieve anxiety, and do not bring work worries home, recommends Mr Adrian Lau, a counsellor at Mount Elizabeth Charter Behavioural Health Services.

SLEEPLESS Singaporeans who want help nodding off may be taking sleeping pills because they are worried about becoming addicted to the drugs.

In a survey of 200 people who took pills, 17 per cent of five said they feared addiction to sleeping pills and so avoided taking them.

Only 12 per cent of respondents who took prescription or medication for insomnia, compared with nearly 60 per cent who took herbal preparations such as soup and tea.

The survey was carried out in January and last month by a research company for Sanofi-Synthelabo, a drug company that makes sleeping tablets. The results were released at a press conference on Thursday.

The 200 people with sleeping problems were recruited when the research firm surveyed 600 randomly-selected people age 20 and above to discover incidence of insomnia.

They were classed as insomniacs because they said they experienced at least one sleeping problem three or more times a week.

These problems included being unable to fall asleep within 30 minutes of going to bed, waking up in the middle of the night and having difficulty falling asleep again.

Consultant psychiatrist Tan Chee Tin described the survey as "very significant".

Said Dr Tan: "It reflects the situation and has reaffirmed our concerns that insomnia is on the rise.

In 1998, 17 million prescriptions for sleeping preparations in the US were approved to 19 million in 1998, he said, adding that these were

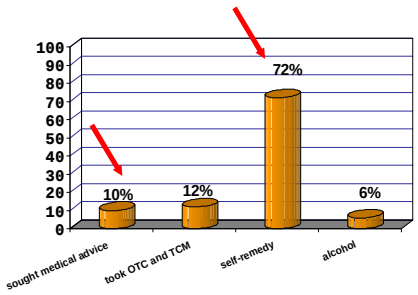
The latest available figures from the Ministry of Health, Singapore, show a trend similar to hospital or attendance clinics with sleep problems, Dr Tan said. He could not give any figures but said younger people, like the problem of just the elderly as younger patients are coming forward for treatment.

Stress and anxiety were the most common reasons why respondents gave for their sleep troubles.

Mr Adrian Lau, a counsellor at Mount Elizabeth Charter Behavioural Health Services, said writing down thoughts can help relieve anxiety and people should try not to bring their work worries home.

His advice to those who have continuous problems sleeping more than a week is to seek help from their family doctor or a specialist.

What do you do to manage your sleep disorder?



Treatment of Insomnia

- Sleep hygiene
- Refer to a sleep specialist
  - Drug treatment
  - Non-drug treatment

Sleep Hygiene

- Temperature:
  - Optimal temperature for sleep is quite cool, around 15.6 to 20 degrees Celsius
  - Temperatures in this range help to facilitate the decrease in core body temperature that in turns initiates sleepiness

- Bed: Should only be used only for sleep, with activities such as work, reading and even worrying kept outside the bedroom
- Sharing a bed often leads to poor quality sleep because people are regularly disturbed by their loved ones during the night
- On average, couples suffered up to 50% more disturbances when sleeping with their partners than they did on their own

- Keeping regular hours and habits
  - If you can't fall asleep within 15 to 20 minutes, leave the bedroom and do something relaxing such as reading or listening to soft music
  - Your sleep-wake patterns are regulated by an internal 'clock' that dictates when you feel sleepy; only return to bed when you feel sleepy again
  - Avoid long afternoon naps

- Avoidance of stimulants and stimulation activities close to bedtime (vigorous exercise, intense work and exciting TV programmes)
- Avoid heavy meals or spicy foods 2 to 3 hours before bedtime
- Avoid using alcohol as a sleep aid
- Stress management and relaxation
- Exercise regularly

Drug treatment

Drug Treatment

- Benzodiazepines
- Newer short acting hypnotics:
  - Zopiclone
  - Zolpidem
- Antihistamines
- Psychiatric drugs e.g. anti-depressants, anti-psychotics

Benzodiazepines (BZP)

- Anti-anxiety
- Hypnotic/sedative
- Anticonvulsant
- Muscle relaxant effect
- Effect can be short acting or long acting

- Sedation:
  - Anxiolytic properties
  - Behavioral disinhibitory effects:
    - Euphoria, Impaired judgment, Loss of self-control
  - Exert such effects at dosages that cause minor CNS depression
  - Anterograde Amnesia

- Hypnosis
  - ↓ Latency of sleep onset
  - ↑ Stage 2 NREM Sleep i.e. light sleep
  - ↓ REM sleep duration:
    - may cause anxiety, irritability, rebound ↑ REM sleep
  - However, usage > 2 week:
    - tolerance of effects on sleep

Dependence

- Psychologic & Physiologic
  - Psychological Reliance
  - Physiological dependence: Withdrawal syndrome upon abstinence
  - Affected by $T_{½}$
- Less likely if:
  - taken once a day
  - long acting drug taken
  - taken for short periods
  - if taken only when necessary

Short-acting BZP

- More likely to produce withdrawal symptoms in long term use, especially if taken several times a day or patients with personality problems
- Examples:
  - Midazolam- Dormicum
  - Lorazepam- Ativan
  - Alprazolam –Xanax
  - Bromazepam-Lexotan

Long-acting BZP

- Examples:
  - Diazepam-Valium
  - Nitrazepam-Mogadon
  - Chlordiazepoxide-Librium
  - Chlorazepate-Tranxene
  - Flurazepam-Dalmadorm

The Newer short acting hypnotics

- Zolpidem (Stilnox®) and Zopiclone
  - Mechanisms of actions differ
  - Speed on Onset: Approx 30 minutes
  - Medium Acting: Approx 8 hours
  - No hangover effect
  - Preserves sleep architecture
  - Minimal rebound nightmares
  - Minimal addictive potential

The Newer short acting hypnotics

- Zolpidem (Stilnox®)
  - The absence of active metabolites, and the rapid elimination prevents any drug accumulation
  - Short duration of action and absence of next-day residual effects
  - Generally well tolerated and effective in elderly patients

- Side effects (Australian Adverse Drug Reactions Bulletin, Vol 26, No 1, Feb 2007)
  - Visual hallucinations
  - Amnesia
  - Sleep walking
  - Automatic behaviour 'while asleep' e.g. binge eating and house painting

HOME

Docs too free with giving out pills? It's like trafficking

Those who traffick in depressant drugs risk jail and caning but rogue doctors are, at most, fined and banned from practising medicine for life

No matter how much a doctor supplies to patients, the Central Narcotics Bureau cannot act against him as doctors are legally allowed to give patients drugs.

By FAIMA KHALIK

- With the update on prescribing benzodiazepines guidelines on September 2008, it is important for you to be familiar with our local MOH guidelines

Important points before starting any benzodiazepines.

- Take a complete history including alcohol, legal and illegal drug history. *Caution when starting benzodiazepines on patients with history of drug and alcohol abuse*
- Limited to 2 to 4 weeks; use the lowest effective dose
- Inform patient at the start of treatment of limited duration

Important points before starting any benzodiazepines.

- Inform patient of side effects and potential problems like dependence
- When in doubt, issue small quantities at a time
- Encourage all patients with dependency to withdraw and consider referring to the IMH Addiction Medicine Department/CAMP
- Treat any underlying causes like depression, panic disorder, etc
- Consider alternatives like psychological intervention and a referral to psychologist

Non-drug option

- Cognitive behavioural therapy (CBT)
  - Help patients change the behaviours and thoughts that can get in the way of a good night's sleep
  - Cognitive part: teaches you to change the anxiety-producing thoughts that interfere with your ability to sleep
  - Behavioural part: aims at actions that impair your ability to sleep, such as spending too much time in bed