

Update on the Treatment of Depression: Tailoring an Approach to the “Chinese” Patient

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Disclosure Statement 2007-2008

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Clinical Trials/Grants

- Advanced Neuromodulation Systems, Inc.
- AstraZeneca
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- Canadian Institutes of Health Research
- CANMAT
- H. Lundbeck
- Litebook Company, Inc.
- Mathematics of Information and Advanced Technology Systems
- VGH-UBC Hospital Foundation

Stockholder

- None



Depression

- Title: Depression
- Authors: Dr. Raymond Lam and Dr. Hiram Mok, University of British Columbia
- Oxford University Press, 2008
- Concise pocket book
- Clinically oriented
- Available at www.amazon.ca

Outline

- Differences in treating “Chinese” patients with depression
- Recent developments in depression management
 - Guidelines
 - Measurement-based care
 - Psychotherapies
 - Antidepressant safety and sequencing
- Working with Depression: optimizing work function

Depression in “Chinese” Patients

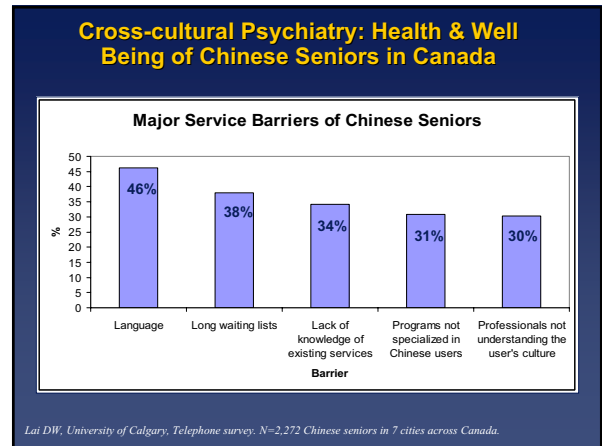
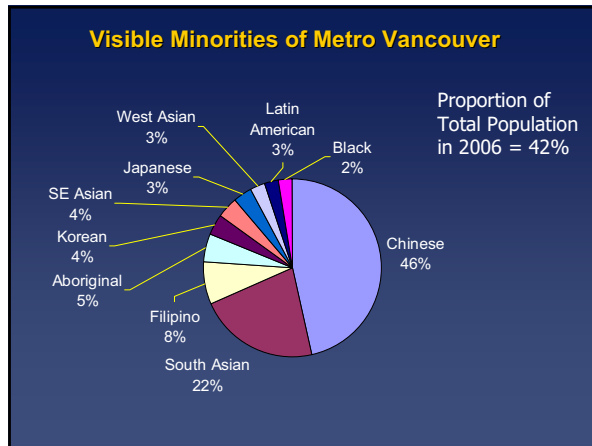
- Prevalence rates in China and other Asian countries are lower than in North America
- Chinese more likely to report somatic features, less likely to report previous depressive episodes
- Chinese are equally likely to report core depressive symptoms
- Chinese are less likely to seek help for psychiatric disorders
- All these features in Chinese are attenuated by acculturation

Parker G et al, 2005, 2006, 2007; Yen S et al, 2000; Ryder AG et al, 2008; Kung WW & Lu PC, 2008;



2010 Olympic Winter Games

VANCOUVER 2010



B.C. Clinical Guidelines for Depression

- Practical recommendations with level of evidence
- Pharmacotherapy and psychotherapy
- Acute and maintenance treatment
- Use of monitoring tools
- Focus on self-management
- Flow sheet

www.UBCmood.ca

The PHQ-9 (Personal Health Questionnaire)

- Self-rated scale is the "HbA1c" of depression.
- Takes 3-5 minutes to complete.
- Is highly sensitive and specific for the diagnosis of depression.
- Can be used to monitor progress (including remission criteria scores).
- Validated in Chinese populations.

TOTAL SCORE	DEPRESSION SEVERITY
0-4	None
5-9	Mild Depression
10-14	Moderate Depression
15-19	Moderate-severe Depression
20-27	Severe MDD

PHQ-9 is adapted from PRIME-MD TODAY, developed by Spitzer RL, Kroenke K, & Williams JBW. ©1999 Pfizer Inc.; Young A et al., 2002

Evidence-based Psychotherapies

Cognitive Behavioural Therapy (CBT)

- Depressed people have negative and distorted thinking patterns (self-critical, hopeless thoughts) and self-defeating behaviours
- CBT helps people to identify and deal constructively with these negative thoughts and behaviours
- Mindfulness-based CBT (MCBT) may be particularly helpful to prevent episodes in recurrent depression

Interpersonal Therapy (IPT)

- Depressed people have problems with key relationship issues (grief, role disputes, role transitions, social isolation)
- IPT helps people to identify and deal constructively with these relationship problems

Antidepressants c.2008

TCA Amitriptyline Imipramine Clomipramine Trimipramine Maprotiline Amoxapine Nortriptyline Desipramine	SSRI Citalopram [Celexa] Escitalopram [Cipralex/Lexapro] Fluoxetine [Prozac] Fluvoxamine [Luvox] Sertraline [Zoloft] Paroxetine [Paxil]	NDRI Bupropion-SR/XL [Wellbutrin]
MAOI Phenelzine Tranylcypromine	SARI Trazodone {Nefazodone}	SNRI Duloxetine [Cymbalta] Venlafaxine-XR [Effexor]
		NaSSA Mirtazapine [Remeron]
		RIMA/B Moclobemide [Manerix] Selegiline patch [EMSAM]

Antidepressants in "Chinese" Patients

- Stigma issues
- Drug metabolism
- Use of alternative/complimentary treatments

Difficulties in Studying Suicidality Associated with Antidepressants

- Suicidality is associated with the underlying disease
- Patients present and start treatment at a time when they are feeling worst
- Suicidality is an uncommon occurrence
- Suicidality can be easily mis-identified
- Other clinical factors may mediate higher risk of suicidality (previous suicidality, comorbid conditions)
- In clinical trials, those at higher risk for suicidality are excluded
- In naturalistic/epidemiologic studies, selection of antidepressants is not random

Lam RW, Kennedy SH, 2004

Suicidality and antidepressants Summary of evidence

Type of Study	Adults	Youth
RCTs and meta-analyses	Safe ✓	Caution indicated
Prescription databases	Safe ✓	Caution indicated
Forensic databases	Safe ✓	Safe ✓
Pharmaco-epidemiology	Safe ✓	Safe ✓

Benefit-Risk Assessment for Antidepressants in Major Depressive Disorder

Group	Medication	Benefit (Efficacy)	Risk (Suicidality)
Adults (18-65 yrs)	All antidepressants	Level 1	Level 2
Elderly (>65 yrs)	All antidepressants	Level 1	Level 3
Children & Adolescents (<18 yrs)	Fluoxetine	Level 1	Level 2
	Other antidepressants	Level 1	Level 2

■ Safe/Effective ■ Probably safe ■ Caution required

Lam RW, Kennedy SH, 2004

Antidepressants in "Chinese" Patients

- Stigma issues
- Drug metabolism
 - Genetic variations in CYP450, especially 2D6 & 2C9
 - 33% Chinese vs. <10% Caucasians have reduced activity
 - May result in higher plasma levels and side effect burden
- Use of alternative/complimentary treatments
 - Survey of 370 Chinese patients seen at VGH Cross-Cultural Psychiatry Clinic
 - 30% were taking Chinese Traditional Medicines

Kim K et al, J Clin Pharmacology 2004; Mok H, Yeh J, BC Medical Journal, 2007

Safety profile of first-line antidepressants

Antidepressant	Safety	Drug Interactions
Citalopram	■	■
Escitalopram	■	■
Duloxetine	■	Avoid inhibitors of CYP 1A2
Paroxetine	■	Avoid inhibitors of CYP 2D6
Sertraline	■	■
Venlafaxine-XR	Caution re comorbidity	■
Bupropion-SR / XL	Caution re comorbidity	Moderate inhibition of CYP 2D6
Mirtazapine	■	■

■ No issues

Sequenced Treatment Alternatives to Relieve Depression (STAR*D)

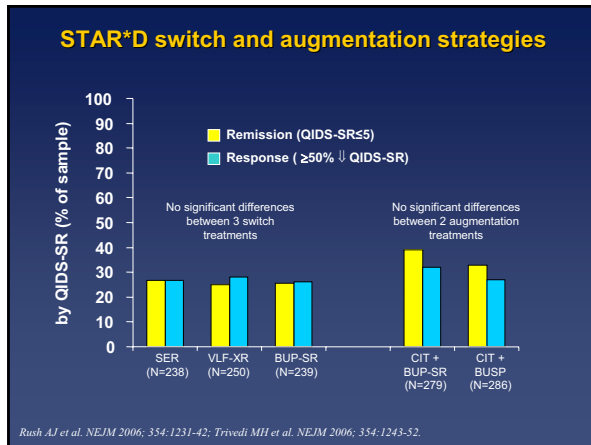
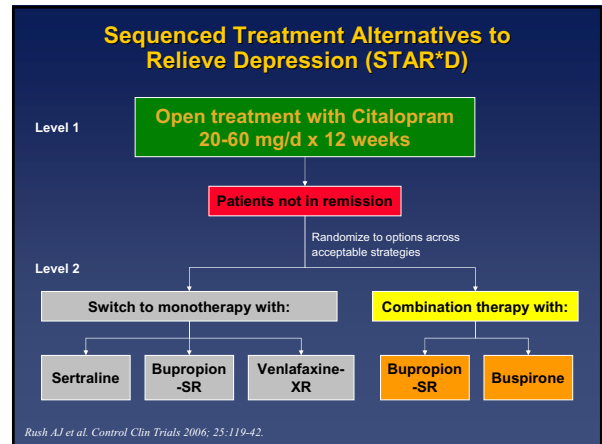
Question:

- "What do you do if the first antidepressant doesn't work?"

State-of-the-Art Features

- Real-world population
- Large sample size
- "Measurement-based" care
- Focus on remission
- Patient preference/clinical equipoise
- Psychotherapy and pharmacotherapy

Rush AJ et al. Control Clin Trials 2006; 25:119-42.



Sequenced Treatment Alternatives to Relieve Depression (STAR*D) – Level 2

Conclusions

- Switch within class or out-of-class is equivalently effective for SSRI-nonresponders.
- Bupropion combination is more effective and better tolerated than buspirone augmentation.
- May want to use combination before switch in partial responders.

Depression & Anxiety Are at Work Every Day in Canada

7 out of 10 patients with Depression are in the workforce

- On average, depressed workers reported 32 days in the past year when they were totally unable to work or carry out normal activities
- Work-related productivity losses due to depression are estimated to be \$4.5 billion

Health Report, Statistics Canada Health Statistics Division, 2006:17(4):1-88. Stephens & Joubert. The Human Face of Mental Health and Mental Illness in Canada. Gov Can. 2006:57-69.

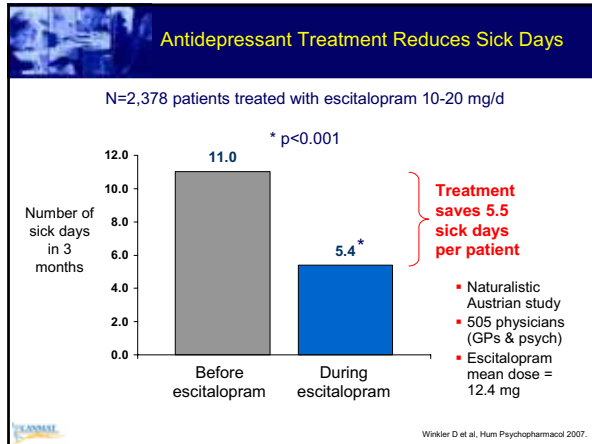
Absenteeism is a Huge Economic Problem

People with depression:

- ▶ are 3x more likely to have sick days in past month
- ▶ have 1.5-3.2 more work-disability days per month
- ▶ have 3-5 times more work-disability days

- Depression leads to the loss of the equivalent of 205,000 people from the Canadian work force each year

Gnam 1997; Parikh et al, 1996; Kessler et al, 1999; Broadhead et al, 1990



The LWAPS® (Lam Work Absence and Productivity Scale)

- Self-rated scale assessing symptoms and function at work.
- Was designed specifically for depressed patients in primary care settings.
- Takes only 5 minutes to complete.
- Can be used to track progress and to help in work/off work decisions.

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Antidepressant Skills at Work: A Self-Care Tool for Employees with Depression

- Self-care manual based on CBT principles.
- Incorporates workplace-specific content.
- Available on internet for free download at www.camha.ca

Should I tell people at work about my depression?

Should I take time off work?

How can I return to work successfully?

What lifestyle changes might be helpful?

Bisker D, Gilbert M, Samra J, CARMMA, 2007; www.camha.ca

Working with Depression CHE Program

- Educational intervention focusing on work function as an important outcome (recovery vs. remission).
- Small groups, GP/Psychiatrist co-facilitators.
- Scales for depression and work outcomes.
- Half-day program.

3 case-based modules:

- Depression tools for physicians.
- Optimizing medications.
- Prevention and management of disability.

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