Study or Subgroup	Weight	Odds Ratio IV, Random, 95% CI
Alves 1999	3.8%	1.47 [0.63, 3.45]
Ballus 2000	3.5%	2.65 [1.09, 6.43]
Bielsky 2004	7.2%	0.71 [0.40, 1.24]
Costa e Sliva 1998	10.7%	1.00 [0.66, 1.51]
Detke 2004	6.8%	1.15 [0.64, 2.07]
Goldstein 2002	3.6%	1.53 [0.63, 3.71]
Goldstein 2004	6.2%	2.05 [1.10, 3.82]
Mehtonen 2000	5.7%	1.90 [0.99, 3.68]
Montgomery 2004	8.4%	0.99 [0.60, 1.64]
Nirenberg 2007	12.7%	1.36 [0.96, 1.93]
Perahia 2006	7.1%	1.04 [0.59, 1.84]
Rudolph 1999	6.2%	2.03 [1.09, 3.79]
Schatzberg 2006	5.8%	1.47 [0.77, 2.83]
Shelton 2006	6.1%	1.48 [0.79, 2.79]
Sir 2005	6.3%	0.71 [0.38, 1.33]
Total (95% CI)	100.0%	1.27 [1.06, 1.52]

Total events
Heterogeneity: Tau² = 0.03; Chi² = 19.63, df = 14 (*P* = 0.14): *P* = 29%
Test for overall effect: Z = 2.62 (*P* = 0.009)

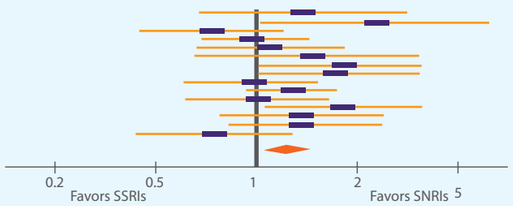
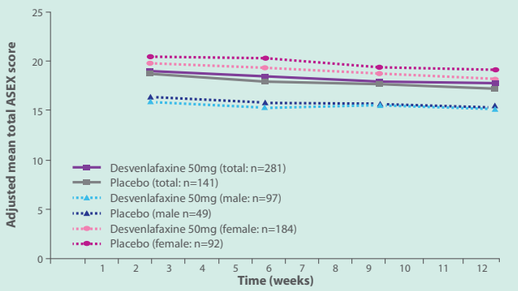


Figure 5. Comparison of efficacy of SSRIs and SNRIs (Machado M et al. 2010)

Efficacy of desvenlafazine for MDD

Meta-analysis of the data from five fixed-dose studies showed that desvenlafaxine significantly improved the symptoms of depression relative to placebo as indicated by the significantly greater decreases in HAM-D17 scores for desvenlafaxine at 50 mg/d and 100 mg/d doses. Desvenlafaxine at a dose of 50 mg/day was effective in treating both moderate and severe MDD. Using the same dose, desvenlafaxine significantly improves different SDS Domains after 8 weeks of treatment. Desvenlafaxine not only improved function as indicated by the SDS, but appeared to have tolerable side-effects and did not differ from placebo in the areas of weight gain and sexual function. (Figure 6).



ASEX, the Arizona Sexual Experience Scale. The ASEX is a 5-item assessment of sexual functioning, uses gender-specific language to measure the patient's level of sex drive, psychological and physiological arousal, and ease of and satisfaction with orgasm. Possible scores range from 5 to 30, with a higher score indicating more sexual dysfunction.

Figure 6. Arizona Sexual Experience Scale in patients with treatment of desvenlafaxine

WFSBP Guideline for GAD

In addition to its indication on depression, desvenlafaxine also improves anxiety symptoms associated with depression (Tourian et al. 2010). SNRIs, together with pregabalin and SSRIs, are first line recommended treatment for general anxiety disorders, according to the WFSBP Guideline 2012.

Psychiatric Disorders Guideline
World Federation of Societies of Biological Psychiatry (WFSBP) 2012 - Generalized Anxiety Disorder

1st line recommendations
Pregabalin, escitalopram, paroxetine, sertraline, venlafaxine, duloxetine, quetiapine

2nd line recommendations
Imipramine, diazepam, lorazepam, hydroxyzine

Figure 7. WFSBP guideline for GAD

Adjuvant treatment for depression

In addition to the pharmacological treatment, physicians can also consider adjuvant treatment that could be beneficial and additive to the response to treatment. Remission is achieved by integrating evidence based antidepressants, psychotherapy and other emerging nonpharmacologic approaches. These include psychotherapy, light therapy, use of herbal products such as St. John's wort and OMEGA 3, and exercise. A mindfulness based cognitive therapy, in addition to antidepressant treatment, can increase the prefrontal cortex functioning and decrease the reactivity of amygdala. These help to restore brain health and increases the chances of remission.

Refereces:
Kendler et al. Am J Psychiatry 2000;157:1243–51.
Machado and Einarson. J Clin Pharm Ther. 2010;35:177-88.
Mitchell et al. Lancet 2009;374:609-19.
Tourian et al. CNS Spectr. 2010;15:187-93.
Trivedi MH, et al. Arch Gen Psychiatry 2004;61:669-80.

Organised by:

E-Motion Alliance
情緒動力聯盟

The E-Motion Alliance was founded in 2010 aimed at promoting early diagnosis and screening mood disorders to prevent further complications in the primary care sector and the local community.

A Contemporary and Evidence Based Understanding and Approach to the Assessment and Treatment of Depression

Highlights of Symposium by Professor Pratap R.Chokka

The seminar covered various topics including the neurobiology of depression and an objective based approach to diagnosing and screening for depression. It also reviewed the potential advantages of multi-receptor acting medications with a focus on desvenlafaxine in the treatment of depression. Finally, a patient focused, integrative and evidence based approach to management of depression was discussed.

Professor Pratap R.Chokka MD, FRCPC
Clinical Professor, University of Alberta
Psychiatrist, Grey Nuns Hospital

Etiology of Depression

Decades ago, most researchers believed that neurotransmitter dysregulation (e.g. level of serotonin or other monoamines) caused depression. Contemporary views support that depression is a syndrome that can be associated and affected by the impact of early life adverse events with changes in cognitive and affective behaviors. It is also associated with impairment in connection between certain regions of the brain, and the decline of the level of brain-derived neurotrophic factor (BDNF). The presence of depression, anxiety or stress is found to be neurotoxic and many severely and chronically depressed patients are found to have brain atrophy.

What are the risk factors for developing depression? Both genetic factors and stress play important roles in depression. There is evidence suggesting that if someone carries a short allele for the serotonin transporter gene, and in combination with stress, they are more likely to express depressive symptoms. A study by Kendler (2000) reveals that the susceptibilities to develop depression in response to stress are different at different stages of the depression episodes. For those patients with zero to nine previous depressive episodes, the depressogenic effect of stressful life events declined substantially with increasing episode number. In other words, a major stress event is needed to trigger the early episodes of depression, while on the other hand, the brain becomes more susceptible to minor stress events at the later stage of depression episodes.

Depression is also considered to be a failure to self regulate in response to emotional difficulties. It is normal that everyone gets experience of sadness, failure and anxiety everyday and most people can come through and cope with the difficulties. However, depressed patients seem to lack this ability as they fail to cope with these adverse events. They are easily provoked by stress and saddened by adversities.

What happens in the brain of a depressed patient?

The above phenomenon may be partly explained by the fact that there is miscommunication between certain regions of the brain in depressed patients. The front part of the brain known as the cortex, and specifically the prefrontal region acts as the executive control center analysing, interpreting and enabling appropriate reactions to information ascending from subcortical regions including the thalamus, amgydala, and hippocampus, which function as the brain's alarm system, and store memories associated with life events. Depressed patients seem to have altered processing of neural pathways connecting cortical and subcortical pathways.

Evidence to support this altered neural pathways come from functional MRI which indicate hypoactivity (blue) in the dorsolateral prefrontal cortical regions

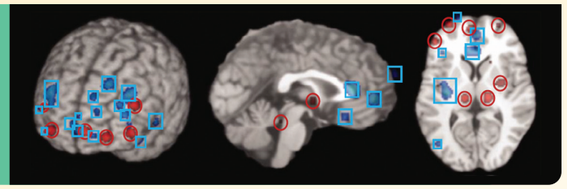


Figure 1. Dorsolateral PFC and dorsal ACC activity in patients with MDD (Fitzgerald et al. 2008)

and hyperactivity (red) in subcortical structures. In the future treatments for depression will target enhancing neural communication between different brain areas and restore appropriate functioning of effected regions.

Depression is a disease of the whole body

Depression is not only a brain disease but also a disease of our body. There is a paradoxical relationship between somatic symptoms and mental disorders. Evidence has shown that patients with multiple unexplained symptoms are more prone to suffer from depression and other mental disorders. Dysregulation of the HPA axis in depression leads to alterations in cortisol and norepinephrine and has been associated with increased visceral fat, insulin resistance, hypertension, diabetes, and atherosclerosis. Patients with myocardial infarct (MI), who developed post MI depression, may have a higher risk of sudden death within the first 6 months after the MI, which is four times higher than those patients without depression. Depression in these studies was an independent risk factor for the second MI.

Diagnosis and monitoring of depression with useful tools

All of the above evidence suggests that early intervention and diagnosis for depression is important. This is especially applicable for family physicians as they are usually among the first tier of medical professionals who make contact with depressed patients. It is important for them to screen early and make a correct diagnosis for depression. A study by Mitchell (2009) indicated that general physicians correctly identified 47.5% of depression cases. For every 100 unselected patients seen in primary care, there will be 10 correctly diagnosed cases of MDD, 15 false positive cases and 10 missed cases (false negative).

There are many tools to aid in the diagnosis and monitoring of patients with MDD. Patient Health Questionnaire-9 (PHQ-9) (Figure 2) is one of the useful tools that can be used for diagnosis and monitoring of the severity of the symptoms of the depressed patients.

病人健康狀況問卷 - 9 (PHQ -9)

在過去兩個星期，你有多經常受以下問題困擾？(請用✓勾選你的答案)	完全沒有	幾天	一半以上的天數	近乎每天
1. 做任何事都覺得沉悶或者根本不想做任何事	0	1	2	3
2. 情緒低落、抑鬱或絕望	0	1	2	3
3. 難於入睡；半夜會醒或相反地睡覺時間過多	0	1	2	3
4. 覺得疲倦或活力不足	0	1	2	3
5. 胃口極差或進食過量	0	1	2	3
6. 不喜歡自己— 覺得自己做得不好、對自己失望或有負家人期望	0	1	2	3
7. 難於集中精神做事，例如看報紙或看電視	0	1	2	3
8. 其他人反映你行動或說話遲緩；或者相反地，你比平常活動更多 — 坐立不安、停不下來	0	1	2	3
9. 想到自己最好去死或者自殘	0	1	2	3

FOR OFFICE CODING 0 + ____ + ____ + ____

= Total Score: ____

如果你剔選出以上任何問題，這些問題對你的工作、處理家中事務或與人相處時來說有多少困難？

○完全沒有困難　○有一些困難　○非常困難　○極度困難

本問卷由Robert L. Spitzer博士、Janet B.W. Williams博士、Kurt Kroenke博士和同事用Pfizer Inc.提供的教育基金設計無需准許即可複製、翻譯、展示或分發。

Total Score	Depression Severity
0 - 4	Not Depressed
5 - 9	Mild
10 - 4	Moderate
15 - 19	Moderate-Severe
20 - 27	Severe MDD

Figure 2. Patient Health Questionnaire-9

The patients were asked, in 9 questions, for their mood and feeling over the last two weeks. Each question is scored from 0 to 3, indicating the frequency of the patients being bothered by the particular problem. A total score of 20-27 will clearly indicate severe MDD while a low score of 5-9 will indicate a mild MDD case. Physicians can ask the patient to fill in the form while waiting for the consultation, as they can probably finish the form in 5-10 minutes. This helps the patients to engage in the treatment process. Physicians can also make use of this form for regular monitoring the effectiveness of treatment during the course of treatment process.

Specific emphasis is now being placed on the need to expand our focus from current symptom-based outcomes of remission and response to measures that can also capture positive emotional recovery, well-being, and functional status, and to integrate these measures into everyday primary care practice.

Sheehan Disability Scale is a patient-rated, measure of disability and impairment on their family, work/school and social life. It is important for the physician to know about not only the symptom but also the functioning impairment in depressed patients.

Sheehan Disability Scale

A brief, patient rated, measure of disability and impairment.

Please mark ONE circle for each scale.

WORK* / SCHOOL

The symptoms have disrupted your work / school work:

Not at all (0) — Mildly (1–3) — Moderately (4–6) — Markedly (7–9) — Extremely (10)

☐ I have not worked / studied at all during the past week for reasons unrealted to the disorder.
*Work includes paid, unpaid volunteer work or training

SOCIAL LIFE

The symptoms have disrupted your social life / leisure activities:

Not at all (0) — Mildly (1–3) — Moderately (4–6) — Markedly (7–9) — Extremely (10)

FAMILY LIFE / HOME RESPONSIBILITIES

The symptoms have disrupted your family life / home responsibilities:

Not at all (0) — Mildly (1–3) — Moderately (4–6) — Markedly (7–9) — Extremely (10)

Days Lost
On how many days in the last week did your symptoms cause you to miss school or work or leave you unable to carry out your normal daily responsibilities? ____

Days Unproductive
On how many days in the last week did you feel so impaired by your symptoms, that even though you went to school or work, your productivity was reduced? ____

Figure 3. Sheehan Disability Scale.
Available at http://www.cqaimh.org/pdf/tool_lof_sds.pdf

There are studies indicating that the use of self assessment tools could deliver better treatment outcome. The Texas Medication Algorithm Project by Trivedi et al. (2004) evaluated algorithm-guided treatment versus treatment as usual in patients (n=350) with MDD. Algorithm-guided therapy included regular assessment of treatment response and critical decision points when revisions in treatment strategies should be undertaken (based on validated rating scales and side effect burden).

Results indicated that patients receiving algorithm-guided therapy had significantly greater symptom reduction compared with those who received treatment as usual.

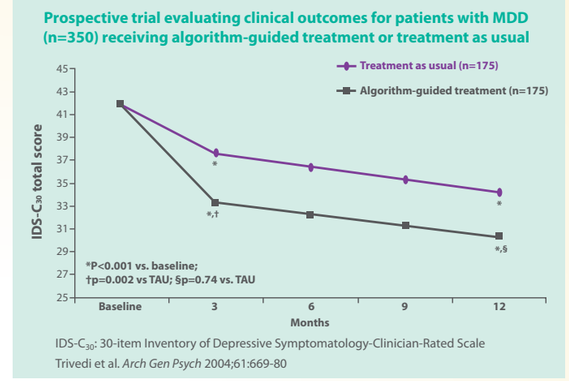


Figure 4. Measurement-based care leads to better outcomes vs. usual care (Trivedi et al. 2004)

SSRIs vs SNRIs

The development of antidepressants have evolved over time. Historically, Tricyclic antidepressants (TCAs) were developed and were used extensively from the 1950's to the late 1980's. The 1990's heralded the introduction of the Selective Serotonin Receptor Inhibitors (SSRI) and recently the introduction of agents that target serotonin and norepinephrine (SNRI) including venlafaxine and its metabolite desvenlafaxine (Pristiq®).

SNRIs are recommended as the first line treatment for depression in Canadian and USA clinical guidelines.

Although there is some debate as to which class of antidepressants are more effective in achieving remission, a recently published meta-analysis of head-to-head randomized clinical trials compare the efficacy of SSRIs and SNRIs (Machado et al., 2010). **The odds ratio was 1.27, favouring SNRIs (Figure 5).** Meta-analytic remission rates were 48.5 ± 3.2% and 41.9 ± 4.2% for SNRIs and SSRIs, respectively.