Depression in the Workplace: Getting our Patients Back to Work and Productive

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Psychiatrist, Grey Nuns Hospital

The greatest enemy of knowledge is not ignorance, it is the illusion of knowledge

Stephen Hawking

Depression is Nasty


Global patterns of workplace productivity for people with depression

Objectives

• Discuss the impact of depression in the workplace
• Reflect on how to assess and treat the depressed worker, with emphasis on choosing the most appropriate antidepressant
• Present “real world” data from the AtWoRC study addressing the relationship between cognitive symptoms and work productivity
• Embrace a holistic and systemic approach to treating the working depressed patient

DR. CHOKKA HAS RECEIVED RESEARCH SUPPORT, SPOKEN FOR, OR SITS ON ADVISORY BOARDS FOR THE FOLLOWING:

<table>
<thead>
<tr>
<th>Advisory board or similar committee</th>
<th>Astra Zeneca, Biovail, BMS, Eli Lilly, GSK, Janssen Ortho, Lundbeck, Pfizer, Shire</th>
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<td>Clinical trials or studies</td>
<td>AZ, BMS, Cephalon, Eli Lilly, Janssen, Lundbeck, Pfizer, Sanofi-Aventis, Shire</td>
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<td>Honoraria or other fees</td>
<td>AZ, Biovail, BMS, Eli Lilly, GSK, Janssen, Lundbeck, Pfizer</td>
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<tr>
<td>Research grants</td>
<td>AZ, Lundbeck, GN Hospital Foundation</td>
</tr>
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</table>

Extent to Which Depressed Canadians Are Able to Function at Work

More than 1 million employed Canadians worked during a depressive episode in the past year (2012)

- 222,200 Canadians with depression are fully functioning at work (23%)
- 310,000 Canadians unable to work due to their depression (40%)
- 266,100 Canadians work part-time because their depression prevents them from working full-time (23%)
- 532,200 Canadians with depression are able to work full-time, but with reduced functioning (17%)

Depression Can Affect One’s Performance and Functioning at Work

Absenteism
- Absence from work (due to depression)
- About 205 hours or 25 days lost in a given year

Presenteeism
- Better treatment of depression to improve functioning could potentially boost the Canadian economy by about $32 billion a year
- Coming to work while depressed and performing with reduced productivity or reduced functioning
- About 487 hours or 60 days lost in a given year

MANAGEMENT OF WORKPLACE DEPRESSION: SHIFTING TO FUNCTIONAL RECOVERY

Treatment Triad: Essentials of Return to Work

Employee/Patient

Employer

Disability World

Iceberg Understanding of Patients and Organizations

EVENTS/SYMPTOMS/BEHAVIOR

PATTERNS

STRUCTURES

MENTAL MODELS

Adapted from Bevin, 2018
Return to Work Principles: The Core

Principle One:
RTW requires coordination, structure, plan, and close communication with main stakeholders

Principle Two:
Employ practices that activate the worker and help person engaged and focused on RTW

Principle Three:
Work accommodations should be seen as an integral part of the RTW

Sylvain et al., BMC Fam Pract, 2016

Treating the Depressed Worker

Effective Return to Work Strategies

• Contact with the employee during sick leave
• Evaluate and plan RTW without worsening condition
• Training for managers and colleagues regarding mental health in the workplace
• Consultation between key RTW stakeholders
• Progressive RTW with accommodations
• Health and work followup with employee

Corbiere M et al., Sante Ment Que, 2017

Factors Promoting RTW: Patient Perspective

• Experiencing hope and power
• Professional’s positive attitudes, beliefs, and behaviour
• Employing a holistic, integrative health and vocational service

Porter et al., Work, 2018
The sick note is an intervention

- Set clear goals with the patient
  - Consider what support the patient needs to return to full function (pharmacotherapy, psychotherapy, etc.)
  - Recognize what the patient can do, rather than not do
- If you decide the depressed patient requires time off work, make an endpoint – time should be limited
  - Manage patient expectations with respect to duration of time off work
  - They should begin to see symptom improvement within 2 weeks off work (as with medication)
- Patient must remain active
  - E.g., exercise, therapy, etc.
  - Can’t stay in bed all day
- Importance of regular monitoring and follow-up (as needed) for symptoms and function
- Work closely with Employee Assistance Program, disability case manager, etc. for safe return to work

Sick notes and disability forms

- Provides opportunity for physician to advise patient on strategies to remain in or return to work, which is a measure of treatment success
- An ill person should not automatically be advised time off work
- Some individuals who are prescribed sickness absence are at risk of losing work habits, motivation, and work relationships
- Length of absence is a risk for physical and mental deterioration, psychological distress, social exclusion, loss of income, etc.
- The longer a patient is off work the lower the chances of returning:
  - 3 to 6 months off – less than 50%
  - ≥12 months off – less than 20%

Remaining in work or returning as soon as possible is therapeutic:
- Helps to promote recovery, full participation in society, independence, reduces poverty, and improves quality of life and well-being

2016 Canadian MDD guidelines: Treat to full functional recovery

**Short-term goals**  
Acute phase of treatment
- Remission of symptoms
- Restoring function

<table>
<thead>
<tr>
<th>Remission of symptoms</th>
<th>Restoring function</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-12 WEEKS</td>
<td></td>
</tr>
</tbody>
</table>

**Long-term goals**  
Maintenance phase of treatment
- Return to full function and quality of life
- Prevention of recurrence

<table>
<thead>
<tr>
<th>Return to full function and quality of life</th>
<th>Prevention of recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-24 MONTHS or longer</td>
<td></td>
</tr>
</tbody>
</table>

Treatments that address all symptoms (emotional, physical and cognitive) lead (ideally) to FULL FUNCTION
How are we documenting functional outcomes in the Depressed Worker

Validated Outcome Measures

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Clinician-Rated</th>
<th>Patient-Rated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>• Hamilton Depression Rating Scale (HAM-D, HAM-7)</td>
<td>• Personal Health Questionnaire (PHQ-9)</td>
</tr>
<tr>
<td></td>
<td>• Montgomery Asberg Depression Rating Scale (MADRS)</td>
<td>• Quick Inventory for Depressive Symptomatology, Self-Rated (QIDS-SR)</td>
</tr>
<tr>
<td></td>
<td>• Inventory for Depressive Symptomatology (IDS)</td>
<td>• Clinically Useful Depression Outcome Scale (CUDOS)</td>
</tr>
<tr>
<td>Functioning</td>
<td>• Multidimensional Scale of Independent Functioning (MSIF)</td>
<td>• Sheehan Disability Scale (SDS)</td>
</tr>
<tr>
<td></td>
<td>• WHO Disability Assessment Scale (WHO-DAS)</td>
<td>• WHO-DAS, self-rated</td>
</tr>
<tr>
<td></td>
<td>• Social and Occupational Functioning Assessment Scale (SOFAS)</td>
<td>• Lam Employment Absence and Productivity Scale (LEAPS)</td>
</tr>
<tr>
<td></td>
<td>• Ways of Coping Scale (WOC)</td>
<td>• Workplace Health and Psychological Survey</td>
</tr>
</tbody>
</table>

Choosing the right ADM: What is your method?

• Guideline Based
• Research Based
• Clinical Experience
• Patient/Medication Factors
• Symptom Based
• Expert Based
• Coverage
• Mood and Day Dependant

CANMAT Pharmacotherapy Recommendations

1st LINE
- Bupropion (NDRI)
- Citalopram (SSRI)
- Desvenlafaxine (SNRI)
- Duloxetine (SNRI)
- Escitalopram (SSRI)
- Fluoxetine (SSRI)
- Fluvoxamine (SSRI)
- Mirtazapine (2-adrenergic agonist; 5-HT2 antagonist)
- Paroxetine (SSRI)
- Sertraline (SSRI)
- Vortioxetine (Multimodal)

2nd LINE
- Amitriptyline, clomipramine, others (TCAs)
- Levomilnacipran (SNRI)
- Nortriptyline (reversible inhibitor MAO-A)
- Quetiapine (AAP)
- Quetiapine (AAP)
- Selegiline transdermal (irreversible inhibitor MAO-B)
- Tranylcypromine
- Reboxetine (NRI)

3rd LINE
- Phenelzine (irreversible inhibitor MAO)
- Trazodone (SRI; 5-HT2 antagonist)
- Vilazodone (SRI, 5-HT1A partial agonist)
Effects of antidepressants on occupational impairment

- Systematic review of randomised clinical trials with newer antidepressants and any validated measure of occupational functioning or impairment
- 42 randomised clinical trials found
- 28 trials had work functioning data available
- Only 1 trial in employed population

Available evidence suggests antidepressant treatment improves workplace outcomes in MDD

- 13 placebo-controlled and 4 active comparator clinical trials reported on the efficacy of:
  - agomelatine
  - bupropion
  - desvenlafaxine
  - duloxetine
  - fluoxetine
  - levomilnacipran
  - sertraline
  - venlafaxine
  - vortioxetine

Systematic review: Efficacy of antidepressants on workplace functioning in MDD

- Only 1 trial in employed population
- Studies reported standardized measures of workplace functioning (e.g., Sheehan Disability Scale-work item).
- Limitations: Included trials evaluated work-related disability as a secondary outcome using subjective rating scales.

Factors in Selecting an Antidepressant

Patient Factors
- Clinical features and dimensions
- Comorbid conditions
- Response and side effects during previous use of antidepressants
- Patient preference

Medication Factors
- Comparative efficacy
- Comparative tolerability (potential side effects)
- Potential interactions with other medications
- Simplicity of use
- Cost and availability

Evidence Based: Choosing the Optimal ADM

1. Primary:
   - Efficacy – response rate at 8 weeks (or as close as possible within the range of 4-12 weeks), i.e. patients with a ≥50% reduction in the total score of a validated observer rating scale for depression (HAM-D17 or MADRS)
   - Acceptability – treatment discontinuation for any reason at 8 weeks

2. Secondary:
   - Endpoint depression score
   - Remission rate
   - Proportion of patients who dropped out early due to adverse events
Combined efficacy and acceptability: all trials

- Antidepressants are closely clustered
- All are better than placebo (22)


Combined efficacy + acceptability based on head-to-head trials

- 3 antidepressants had the most favourable profile for efficacy and acceptability:
  1. Vortioxetine (21) had the greatest net clinical benefit
  2. Escitalopram (8)
  3. Agomelatine (1)

Cipriani, A. et al., Lancet, 2018

Relative Importance of Depressive symptoms and Function

- Emotional
- Cognitive
- Physical

Antidepressant Selection: Clinical Dimensions

<table>
<thead>
<tr>
<th>Levels of Evidence</th>
<th>LEVEL 1</th>
<th>LEVEL 2</th>
<th>LEVEL 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive Dysfunction</td>
<td>Vortioxetine• Bupropion • Duloxetine • SSRIs*</td>
<td>Moclobemide</td>
<td></td>
</tr>
<tr>
<td>Sleep Disturbances</td>
<td>Agomelatine• Mirtazapine • Quetiapine • Trazodone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic Symptoms</td>
<td>Duloxetine (pain) • Bupropion (fatigue) • Other SNRIs (pain) • SSRIs (fatigue)* • Duloxetine (energy)*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Comparisons only with placebo

SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin noradrenaline reuptake inhibitor


Cognitive symptoms of MDD predict workplace productivity and performance


Cognitive symptoms account for more variability in workplace functioning than total depression severity

ASRS, ADHD Symptom Rating Scale; EWPS, Endicott Workplace Productivity Scale; HAM-D17, Hamilton Depression Rating Scale.

Post-hoc analysis of 260 participants from the International Mood Disorders Collaborative Project

Predictors of workplace performance by EWPS (N=260)

Cognitive symptoms and Depression severity

** p<0.001

Cognitive symptoms account for more variability in workplace functioning than total depression severity

Clinical Trials from the Lab to the Clinic: Translational Research

All types of studies have their relative strengths and weaknesses

<table>
<thead>
<tr>
<th>Strength of evidence</th>
<th>Type of study</th>
<th>Purpose</th>
<th>Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stronger</td>
<td>RCT (explanatory)</td>
<td>Efficacy</td>
<td>Internal</td>
</tr>
<tr>
<td>Weaker</td>
<td>RCT (pragmatic)</td>
<td>Effectiveness</td>
<td>External</td>
</tr>
<tr>
<td></td>
<td>Observational</td>
<td>Can it work?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Administrative database</td>
<td>Does it work in the real world?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chart review</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Registry decision model</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Strength of evidence

Type of study

Purpose

Validity

AtWoRC Study: Key Questions

is an interventional, open-label, Canadian study

Q1 Does improvement in cognitive function result in increased work-related productivity in patients with depression receiving vortioxetine in a real-life setting?

Q2 How does vortioxetine impact on cognitive function in patients

- Receiving 1st treatment for current MDE?
- With inadequate response to previous antidepressant treatment ("switch")?
  - Patients with MDD who had inadequate response to treatment with 1 antidepressant at labelled doses for ≥ 6 weeks
  - The opinion of the investigator is that treatment with another antidepressant is warranted

Primary objective

To describe the association / correlation between change from baseline to Week 12 in

- Patient-reported cognitive symptoms (PDQ-D20)
- Work productivity loss (WLQ)

in gainfully employed adult patients receiving vortioxetine for an MDE

AtWoRC Study: Key Questions

Primary objective

AtWoRC, At Work, On Research, Canadian Cooperative Depression Research Network; MDE, major depressive episode

Chokka PR et al. CNS Spectrums, 2018;

PDQ-D20, Perceived Deficits Questionnaire for Depression 20 items; WLQ, Work Limitations Questionnaire; MDD, major depressive disorder

Chokka PR et al. CNS Spectrums, 2018;

PDQ-D20, Perceived Deficits Questionnaire for Depression 20 items; WLQ, Work Limitations Questionnaire; MDD, major depressive disorder

Chokka PR et al. CNS Spectrums, 2018;
**Study design**

Vortioxetine: flexible dose (10–20 mg/day)
- 1st treatment of MDE
- Switch
- 2nd treatment of MDE

**Baseline clinical characteristics**

<table>
<thead>
<tr>
<th>Mean scores at baseline (Week 0)</th>
<th>1st treatment (n=97)</th>
<th>Switch (n=99)</th>
<th>Total (n=196)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDQ-D20</td>
<td>49.7 (12.1)</td>
<td>49.5 (12.1)</td>
<td>49.6 (12.0)</td>
</tr>
<tr>
<td>QIDS-SR</td>
<td>18.7 (2.6)</td>
<td>18.1 (2.8)</td>
<td>18.4 (2.7)</td>
</tr>
<tr>
<td>GAD-7</td>
<td>15.5 (4.7)*</td>
<td>14.0 (4.8)</td>
<td>14.8 (4.8)</td>
</tr>
<tr>
<td>CGI-S</td>
<td>4.1 (0.6)</td>
<td>4.1 (0.5)</td>
<td>4.1 (0.5)</td>
</tr>
<tr>
<td>WLQ, % productivity loss</td>
<td>15.9 (11.4)</td>
<td>17.7 (11.1)</td>
<td>16.8 (11.1)</td>
</tr>
<tr>
<td>WPAI, % overall impairment</td>
<td>66.0 (23.7)</td>
<td>69.1 (22.7)</td>
<td>67.6 (23.2)</td>
</tr>
<tr>
<td>SDS</td>
<td>21.0 (4.8)</td>
<td>21.0 (5.5)</td>
<td>21.0 (5.1)</td>
</tr>
<tr>
<td>WHODAS</td>
<td>21.1 (6.8)</td>
<td>21.0 (7.9)</td>
<td>21.0 (7.4)</td>
</tr>
<tr>
<td>DSST</td>
<td>47.5 (11.2)</td>
<td>45.0 (12.1)</td>
<td>46.2 (11.7)</td>
</tr>
</tbody>
</table>

**Patients who had improved cognitive function following treatment with vortioxetine also had improved workplace productivity**

Partial correlation between change in PDQ-D20 and change in WLQ productivity loss from baseline to Week 12 (OC)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>r</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAS*</td>
<td>151</td>
<td>0.634</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1st treatment</td>
<td>79</td>
<td>0.679</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Switch</td>
<td>72</td>
<td>0.577</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Adjusted for age, sex, baseline PDQ-D20, baseline WLQ productivity loss, disease duration and disease severity (baseline QIDS-SR, baseline CGI-S)
Change in work productivity: WLQ

Mean change in WLQ subscales and productivity loss from baseline to Week 12 (OC)

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Baseline</th>
<th>Week 12</th>
<th>Mean Change</th>
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</thead>
<tbody>
<tr>
<td>Time management</td>
<td>-24.7</td>
<td>-9.4</td>
<td>-15.3</td>
</tr>
<tr>
<td>Physical limitations</td>
<td>-30.4</td>
<td>-9.4</td>
<td>-21.0</td>
</tr>
<tr>
<td>Role limitations</td>
<td>-24.4</td>
<td>-4.5</td>
<td>-19.9</td>
</tr>
<tr>
<td>Cognitive limitations</td>
<td>-26.4</td>
<td>-6.6</td>
<td>-19.8</td>
</tr>
</tbody>
</table>

Decrease by Week 4

Mean change in WLQ subscales and productivity loss from baseline to Week 12 (OC)

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Baseline</th>
<th>Week 12</th>
<th>Mean Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time management</td>
<td>-29.7</td>
<td>-9.0</td>
<td>-20.7</td>
</tr>
<tr>
<td>Physical limitations</td>
<td>-30.7</td>
<td>-9.4</td>
<td>-21.3</td>
</tr>
<tr>
<td>Role limitations</td>
<td>-24.4</td>
<td>-4.5</td>
<td>-19.9</td>
</tr>
<tr>
<td>Cognitive limitations</td>
<td>-26.4</td>
<td>-6.6</td>
<td>-19.8</td>
</tr>
</tbody>
</table>

QIDS Response and Remission at Week 12

<table>
<thead>
<tr>
<th>1st Treatment (n=89)</th>
<th>Switch (n=84)</th>
<th>Total FAS (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response</td>
<td>64%</td>
<td>35%</td>
</tr>
<tr>
<td>Remission</td>
<td>62%</td>
<td>33%</td>
</tr>
</tbody>
</table>

Change in cognitive symptoms and performance

Mean change in PDQ-D20 from baseline to Week 12 (OC)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 12</th>
<th>Mean Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st treatment (n=97)</td>
<td>49.2</td>
<td>26.3</td>
</tr>
<tr>
<td>1st treatment (n=97)</td>
<td>49.3</td>
<td>26.5</td>
</tr>
</tbody>
</table>

Mean change in DSST from baseline to Week 12 (OC)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 12</th>
<th>Mean Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st treatment (n=97)</td>
<td>55.0</td>
<td>11.0</td>
</tr>
<tr>
<td>1st treatment (n=97)</td>
<td>55.2</td>
<td>11.0</td>
</tr>
</tbody>
</table>

Change in function and disability

Mean change in SDS from baseline to Week 12 (OC)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 12</th>
<th>Mean Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st treatment (n=97)</td>
<td>21.0</td>
<td>14.0</td>
</tr>
<tr>
<td>1st treatment (n=97)</td>
<td>21.1</td>
<td>14.3</td>
</tr>
</tbody>
</table>

Mean change in WHODAS from baseline to Week 12 (OC)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 12</th>
<th>Mean Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st treatment (n=97)</td>
<td>21.0</td>
<td>12.0</td>
</tr>
<tr>
<td>1st treatment (n=97)</td>
<td>21.1</td>
<td>12.1</td>
</tr>
</tbody>
</table>
Association between GAD-7 and WLQ

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Pearson Correlation</th>
<th>p value</th>
<th>Strength</th>
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<tbody>
<tr>
<td>FAS</td>
<td>196</td>
<td>0.599</td>
<td>&lt;0.001</td>
<td>Moderate</td>
</tr>
<tr>
<td>1st treatment</td>
<td>97</td>
<td>0.638</td>
<td>&lt;0.001</td>
<td>Strong</td>
</tr>
<tr>
<td>Switch</td>
<td>99</td>
<td>0.565</td>
<td>&lt;0.001</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

- As anxiety symptoms improve, workplace productivity also improves
- Exploratory endpoint but signal detected

Missed work days related to depression

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Days (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st treatment</td>
<td>61</td>
</tr>
<tr>
<td>Switch</td>
<td>23</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
</tr>
<tr>
<td>1st treatment</td>
<td>14</td>
</tr>
<tr>
<td>Switch</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
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</table>

Health care related to depression

<table>
<thead>
<tr>
<th>Group</th>
<th>Yes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>61</td>
</tr>
<tr>
<td>Week 12</td>
<td>23</td>
</tr>
</tbody>
</table>

Most common adverse events at Week 12

<table>
<thead>
<tr>
<th>Event</th>
<th>Patients, % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>27.8 (60)</td>
</tr>
<tr>
<td>Headache</td>
<td>12.5 (27)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>9.7 (21)</td>
</tr>
<tr>
<td>Drug ineffective</td>
<td>7.4 (16)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>6.9 (15)</td>
</tr>
</tbody>
</table>

No new safety signals were observed
Discontinuation at Week 12

<table>
<thead>
<tr>
<th>Reason</th>
<th>1st treatment (n=107), % (n)</th>
<th>Switch (n=109), % (n)</th>
<th>Total (n=216), % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withdrew consent</td>
<td>4.7 (5)</td>
<td>8.3 (9)</td>
<td>6.5 (14)</td>
</tr>
<tr>
<td>Adverse drug reaction</td>
<td>4.7 (5)</td>
<td>4.6 (5)</td>
<td>4.6 (10)</td>
</tr>
<tr>
<td>Inadequate drug effect</td>
<td>0.0 (0)</td>
<td>2.8 (3)</td>
<td>1.4 (3)</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>1.9 (2)</td>
<td>0.9 (1)</td>
<td>1.4 (3)</td>
</tr>
<tr>
<td>Other</td>
<td>1.9 (2)</td>
<td>0.9 (1)</td>
<td>1.4 (3)</td>
</tr>
<tr>
<td>Protocol deviation</td>
<td>0.9 (1)</td>
<td>0.9 (1)</td>
<td>0.9 (2)</td>
</tr>
<tr>
<td>Lack of drug effect</td>
<td>0.0 (0)</td>
<td>1.8 (2)</td>
<td>0.9 (2)</td>
</tr>
<tr>
<td>Rate of discontinuation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinued</td>
<td>14.0 (15)</td>
<td>20.2 (22)</td>
<td>17.1 (37)</td>
</tr>
</tbody>
</table>

All patients involved

AtWoRC Conclusions:

- Improvement in Cognitive Symptoms strongly correlated with improvement in Work Productivity
- Improvement in Depressive Symptoms and Severity
- Less missed days at Work
- Improvement in Anxiety led to improved Work Productivity
- Improved Functioning (SDS, WHODAS)
- Mean Dose of Vortioxetine for new starts or switch was 15 mg/day
- Vortioxetine well tolerated, No new safety signals

Other strategies that could help improve overall functioning?

- Psychotherapy (Work CBT)
- Positive psychology
- Behavioral activation
- Lifestyle change (exercise, sleep, diet, etc.)
- Patient involved in their recovery

Summary and key take-home points

- More than 1 million employed Canadians were unable to work or worked below full capacity due to depression symptoms over the course of 1 year (absenteeism and presenteeism)
  - Only 17% were fully functioning at work
- Restoring symptoms and return to full function and quality of life are key goals of treatment in MDD – right from the start
  - This is relevant and important for all patients, especially those in the workforce
- There is emerging evidence that improvement in cognitive symptoms with vortioxetine is strongly correlated with improved work productivity and function
  - To help patients achieve full functional recovery, select a treatment that is effective at improving all symptom dimensions and overall functioning