Is Zero a Must? The Impact of Residual Symptoms in Major Depressive Disorder

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Objectives

• Review the prevalence, burden, and impact of major depressive disorder (MDD)
• Consider the burden of inadequate treatment of MDD, the prevalence of residual symptoms, and their impact on patient functioning and outcomes
• Discuss the urgency to treat residual symptoms
• Review strategies for addressing residual symptoms in patients with MDD
Polling Question

What is the biggest impact that you feel that residual symptoms have on your patients with MDD?

A. Impact on quality of life (home and social)
B. Impact on productivity at work
C. Impact on comorbid illness
D. Impact on suicide risk
THE BASICS OF MAJOR DEPRESSIVE DISORDER

Prevalence, burden, and impact
Background

- Depression is the most common diagnosis among patients seen by psychiatrists in the United States (US)\(^1\)
- MDD is a serious, chronic, disabling illness affecting more than 350 million people worldwide\(^2\)
- MDD results in a substantial burden of disease to both the individual and society\(^3\)
- Residual symptoms are common and cause significant psychosocial and occupational functional impairment\(^4,5\)

The Prevalence of Major Depressive Disorder Is Likely Underestimated and the Diagnosis Is Often Delayed

- Prevalence rates are likely underestimated due to:
  - Underdiagnosis:
    - Significant social stigma may prevent patients from seeking or accepting care for MDD\(^1\)
    - Certain providers may be uncomfortable discussing mental health with patients\(^2\)
  - Misdiagnosis:
    - Nonspecific symptoms\(^1\)
    - Significant heterogeneity and comorbid conditions\(^1\)

- Treatment of MDD is often delayed for years or even decades\(^3\)
  - A nationally representative US sample (N = 9282) found a projected median of 8 years between MDD symptom onset and first contact with a care provider\(^3\)

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Did You Know?

- During an 5-year prospective study of patients with MDD, the suicide incidence rate per 1,000 patient years was 21-fold higher during depressive episodes, and fourfold higher during partial remission, compared with full remission\(^1\)

- Having 1 employee with depression was reported to cost an employer an estimated $20,000 to $35,000 in direct and indirect costs over 2 years (2004–2007 data)\(^2\)

- In the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study (a randomized, controlled treatment trial in outpatients with MDD \([N = 4041]\)), patients who were treatment responders without remission were almost twice as likely as those in remission to suffer a relapse during the first year following successful treatment\(^3,4\)

Impact of Major Depressive Disorder on Patients and Others

- The impact of MDD on patients includes the comorbidity of MDD and other illnesses,¹ the negative impact on the patient’s quality of life (QoL),² and the increased risk of suicide³
- The impact of MDD on caregivers includes the negative impact on the caregiver’s QoL,⁴ concerns about the future,⁵ and interpersonal difficulties with the patient⁵
- The impact of MDD on a patient’s children include an increased risk of mental and physical illnesses⁶,⁷ and higher healthcare expenditures in the children⁸

DISCUSSION
COURSE OF ILLNESS: RESIDUAL SYMPTOMS
Polling Question

Which residual symptom do you most commonly see in patients with MDD in your clinical experience?

A. Sleep disturbances
B. Difficulty concentrating
C. Mood disturbances (eg, loss of interest or enjoyment)
D. Effects on appetite
Remission is the Goal

Remission is also defined as attainment of a virtually asymptomatic status (17-item HAM-D score ≤ 7) for at least 2 consecutive weeks.\(^3\)

HAM-D, Hamilton Depression Rating Scale; MADRS, Montgomery–Åsberg Depression Rating Scale.

Persistent Symptoms\textsuperscript{a} in Major Depressive Disorder Remitters Are Common and Negatively Affect Outcomes

\begin{itemize}
\item Residual symptoms increase the risk for suicide and relapse\textsuperscript{1}
\item Residual symptoms have an adverse impact on psychosocial and occupational functioning\textsuperscript{2, 3}
\end{itemize}

\textsuperscript{a}Persistent symptoms defined as QIDS-SR\textsubscript{16} item score $\geq 1$. QIDS-SR\textsubscript{16}, Quick Inventory of Depressive Symptomatology-Self Report 16 item; STAR*D, Sequenced Treatment Alternatives to Relieve Depression.

Impact of Residual Symptoms on Patient Functioning and Outcomes

- Residual symptoms cause significant and often persistent psychosocial and occupational functional impairment\(^1,2,3\)
- Patients being treated for MDD who have residual symptoms have an increased risk of depressive relapse\(^4,5\)

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Time Followed</th>
<th>Relapsed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paykel(^4)</td>
<td>70</td>
<td>15 months</td>
<td>▪ 76% of patients with residual symptoms&lt;br&gt;▪ 25% of patients with no residual symptoms</td>
</tr>
<tr>
<td>Pintor(^5)</td>
<td>139</td>
<td>4 years</td>
<td>▪ 91% of patients with partial remission&lt;br&gt;▪ 51% of patients with complete remission</td>
</tr>
</tbody>
</table>

- Patients with residual symptoms tend to have poor psychosocial functioning\(^6\)

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Predictors of Relapse and Recurrence in Major Depressive Disorder

Proportion of patients with (●) and without (▲) residual symptoms relapsing after remission (log rank statistic = 17.43, df = 1, $P < 0.001$)

Comparison of STAR*D Participants

Relapse During Follow-up Phase by Number of Acute Treatment Steps for STAR*D Participants Who Entered Follow-up Phase:

In Remission

- **Significant overall difference among steps** ($\chi^2 = 23$, df = 3, $P < 0.0001$)

Not In Remission

- **Significant overall difference among steps** ($\chi^2 = 13$, df = 3, $P < 0.005$)

Remission and Functioning

Note: Normal functioning defined as a Social and Occupational Functioning Assessment Scale score ≥ 80. *P < 0.001.

- Normal functioning at endpoint (Month 6) was significantly associated with a complete response at baseline (ie, after 3 months of acute antidepressant treatment).

DISCUSSION
CONSEQUENCES OF RESIDUAL SYMPTOMS

What can we do to treat them?
Urgency to Treat Residual Symptoms

- Residual depressive symptoms are associated with an increased risk of relapse and poor psychosocial functioning\(^1,2\)

- Adequate pharmacological intervention early in the disease is important to reduce the amount of the time in a depressed state, thereby decreasing the risk of suicide\(^1,2\)

Incidence of Suicide Attempts

Note: Data indicate the incidence rate per 1000 patient-years based on Poisson distribution.

- Over 5 years follow-up, risk of suicide attempts was 21-fold during a major depressive episode compared with full remission (N=332 vs 16 per 1,000 patient-years)

Challenges and Integrated Care Strategies for Major Depressive Disorder

• Patients experience a partial response to antidepressant treatment, yet:
  – Still experience lingering feelings of depressed mood
  – Still experience insomnia or aches and pains
  – Still experiences feelings of hopelessness and dissatisfaction with life

• Patients needing social support don’t have access to, or are not interested in, social group support

• Patients feel that family members are frustrated or angry with them, and don’t understand their struggles
Measurement-based Care

- Among practitioners, clinical treatment of depression is often associated with wide variations in dosage and duration of treatment\(^1\)
- Measurement-based care was developed as a systematic approach to evaluate patient progress and eliminate variability in patient treatment among physicians
  - In STAR*D, measurement-based care included the routine measurement of symptoms and side effects at each treatment visit; a treatment manual was used by treating physicians that detailed precisely when and how to modify medication regimens or doses based on results of assessments\(^2\)
- A wide variety of physician-rated and patient-rated scales are currently available to evaluate patient symptoms, functioning ability, treatment progress, and side effects\(^3\)
  - For more information, please see: http://www.outcometracker.org/scales_library.php

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Resilience Strategies

- With increasing time/depressive episodes, remitted patients may become more vulnerable to depression via increased stress sensitivity
  - Resilience is a dynamic, multidimensional process that may be deficient in people who have a mental illness
  - There are multiple aspects to improving resilience, such as:
    - Improving stress recovery from minor daily stressors
    - Increasing positivity
    - Training flexibility (employing appropriate coping strategies to meet different demands)

- Resilience interventions aim to increase patients’ ability to handle stressors (decreasing stress-sensitivity and increasing stress adaptability)
  - Interventions may focus on:
    - **Positivity training** aimed at increasing well-being, positive emotions and resilience (eg, well-being therapy)
    - **Stress inoculation training**, which posits that moderate amounts of stress can help people become more resilient to future stressors by enlarging their coping repertoire and increasing confidence
    - **Meditation**, which may induce changes in neural processes to support skills that transfer to novel areas in the patient’s life (eg, mindfulness-based therapy)
