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This ACADEMIC HIGHLIGHTS section of *The Journal of Clinical Psychiatry* presents the highlights of the virtual roundtable “Patient Functioning and Life Engagement: Unmet Needs in MDD and Schizophrenia,” which was held May 10, 2022.

The roundtable was chaired by **Christoph U. Correll, MD**, Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, and Charité Universitätsmedizin, Berlin, Germany. The faculty were **Zahinoor Ismail, MD**, Department of Psychiatry, Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; **Roger S. McIntyre, MD**, Mood Disorder Psychopharmacology Unit, University Health Network, Department of Psychiatry, University of Toronto; Institute of Medical Science, University of Toronto; and Departments of Psychiatry and Pharmacology, University of Toronto, Toronto, Ontario, Canada; **Roueen Rafeyan, MD**, Department of Psychiatry, Feinberg School of Medicine, Northwestern University, Chicago, Illinois; and **Michael E. Thase, MD**, Department of Psychiatry, Perelman School of Medicine of the University of Pennsylvania, and the Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, Pennsylvania.

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# Patient Functioning and Life Engagement: Unmet Needs in Major Depressive Disorder and Schizophrenia

Christoph U. Correll, MD; Zahinoor Ismail, MD; Roger S. McIntyre, MD; Roueen Rafeyan, MD; and Michael E. Thase, MD

Definitions of treatment success used in clinical trials of medications for serious mental illness have generally focused on reduction in symptoms assessed via observer-rated instruments such as the Montgomery-Asberg Depression Rating Scale and the Hamilton Depression Rating Scale in MDD and the Positive and Negative Syndrome Scale (PANSS) and Brief Psychiatric Rating Scale in schizophrenia. In recent years, there has been a shift toward incorporating outcomes into clinical research that are patient-reported and reflect outcomes and goals that are meaningful to the patient.<sup>1,2</sup> These outcomes include aspects of functioning (eg, activities of daily living and role fulfillment),<sup>3</sup> as well as life engagement, which interacts with symptomatic and functional outcomes and encompasses aspects such as motivation and vitality.

In a recent roundtable meeting, a panel of 5 experts discussed life engagement and its relationship to symptoms and functioning in patients with major depressive disorder (MDD) and schizophrenia. This ACADEMIC HIGHLIGHTS summarizes their discussion.

## LIFE ENGAGEMENT

In the context of mental health, patient life engagement consists of positive health aspects relating to cognition (including “hot” cognition, ie, cognition colored by emotion), vitality, motivation, and reward, and the ability to feel pleasure.<sup>4</sup> Research has demonstrated associations between life engagement and increased well-being and decreased psychological distress.<sup>5</sup> Functional outcomes associated with life engagement include a sense of perceived significance and fulfillment of one’s life and participation in valued and meaningful activities.<sup>6</sup> Dr Correll characterized life engagement as involving the entire person and having behavioral, emotional, and cognitive aspects, as well as a higher level of meaning and purpose. He explained that the essence of engagement is to *connect* with the world and others and to regain a sense of self that often becomes eroded by mental illness and its symptoms.

## Life Engagement in Patients With MDD

Life engagement as a treatment goal addresses MDD symptomatology: among patients with inadequate response to antidepressants, lack of motivation, a key aspect of life engagement, is the most common non-core symptom,<sup>7</sup> and anhedonia scores are especially elevated in patients with unremitted MDD compared with other illnesses.<sup>8</sup> Further, as demonstrated in a survey by the Depression and Bipolar Support Alliance, patients indicate that aspects of life engagement reflect outcomes that are important to them.<sup>9</sup> Another survey comparing the outcomes that physicians and patients consider important in remission from depression showed that the items ranked most important by physicians mostly reflected absence

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Figure 1. Four-Domain Conceptual Model of Life Engagement<sup>a</sup>

Domain	Low	High
Emotional (affect/mood)	Negative affect/mood, flat, depressed	Positive affect/mood, happy, hopeful
Physical (energy)	Low energy, fatigued, tired	High energy, energized, motivated, productive
Social (interest)	Low involvement, disengaged, anhedonia, disinterested	Involved, engaged, interested
Cognitive (alertness/thinking)	Low arousal, brain fog, slowed thinking	High arousal, alert, clarity, attentive, aware

<sup>a</sup>Adapted from Weiss et al.<sup>4</sup>

of depressive symptoms, while those highly ranked by patients tended to reflect positive affect.<sup>10</sup>

To capture the essential elements of life engagement, exit interview data were pooled from 3 open-label studies<sup>11-13</sup> of adjunctive brexpiprazole in MDD patients with inadequate response to antidepressants. The interviews assessed patients' experiences with MDD prior to the trials and their perception of treatment benefits after finishing the trials. Vocabulary used in the 105 transcripts was reviewed, and, in consultation with a panel of expert psychiatrists, a model of life engagement was developed.<sup>4</sup> The model consists of 4 domains: emotional (affect/mood), physical (energy), social (interest), and cognitive (alertness/thinking). Figure 1 shows this conceptual framework for life engagement. Based on the roundtable discussion, Dr Correll proposed expanding the model to include a fifth domain: Identity (meaning/purpose/belonging), with low levels characterized by a sense of isolation, fragmentation,

lack of purpose, and disconnectedness and high levels characterized by a sense of belonging, meaning, self-efficacy, and connectedness.

**Clinical picture.** Regarding the clinical profile of a patient who is disengaged, Dr McIntyre acknowledged that there is not a singular phenotype for disengagement in depression. However, in his experience, lassitude, or apathy, is a defining feature of the commonly encountered patient who presents with disengagement at his clinic. When thinking about the future, he said, these patients often feel that they do not have much to look forward to. They might request treatment with psychostimulants or noradrenergic medications. He also observed that these patients often attempt to remedy feelings of disengagement in maladaptive ways, such as by using drugs or alcohol. Although these behaviors are not by definition associated only with disengagement, they could be acting as a harmful proxy for a sense of vitality, a sense of lived experience, and a positive valence that the patient is missing.

As to the profile of an MDD patient who is engaged with life, positive valence was cited by Dr Thase as an important component: "Positive affect; the sense that one can feel something that is joyful to experience, close to a peak experience; and the ability to engage in a warm and well-related fashion. The feelings go beyond being functionally back to one's better self. In describing life engagement, I think of terms like 'lit up,' meaning alive and full of life."

**Life Engagement in Patients With Schizophrenia**

Life engagement encompasses outcomes that are important to patients with schizophrenia as well.<sup>14</sup> A study of 105 schizophrenia outpatients revealed that their most valued goals for treatment included improved cognition, satisfaction, and independence.<sup>4,15</sup>

To investigate whether the 4-domain model of life engagement developed from MDD exit interview data would also resonate with patients with schizophrenia, qualitative interviews were conducted with adults with

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schizophrenia who were receiving maintenance treatment with an antipsychotic.<sup>16</sup> Patients spontaneously described their understanding of life engagement and then evaluated the relevance of the 4-domain conceptual model of life engagement. A majority of the patients, 64%, provided a definition of life engagement that aligned with the study definition. When presented with the 4-domain model of life engagement previously identified from exit interviews with MDD patients, 96% of the patients felt that all 4 domains were important to life engagement.<sup>16</sup>

**Clinical picture.** In describing the clinical picture of a patient engaged with life, Dr Rafeyan mentioned a patient of his with schizophrenia for whom the journey to find appropriate medications has been difficult. Although the patient's symptoms are stabilized, he still experiences residual symptoms including auditory hallucinations. However, he regularly attends a day program, and when he comes for office visits, he has a bright, neat outfit on, his eyes are "smiling," and he has excitement about his life and what he is doing. Dr Rafeyan stated that, as a clinician, this is a major turning point for him in terms of the patient's treatment journey. As a point of contrast, he said that he often sees patients for whom symptoms are fairly well controlled, but their interaction with their surroundings, their family, and their peers and colleagues is minimal, and there is no excitement; those patients are disengaged with life.

## SYMPTOMATIC IMPROVEMENT AND LIFE ENGAGEMENT

Symptom control plays a critical role in determining patients' quality of life, and recent longitudinal data demonstrated the influence of symptoms on subjective satisfaction and interest in life.<sup>17</sup> However, symptom control has been shown to be only one factor affecting quality of life. Data based on patient-reported outcomes from the Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) study indicated that after treatment, > 50% of MDD patients continued to experience severely impaired quality of life, and, even among patients in remission, 32% continued to experience reduced quality of life.<sup>18</sup> A systematic review<sup>19</sup> identifying domains important to people with serious mental illness found that although symptoms, or "ill-being," were an intrinsic aspect of quality of life, others included feeling in control and having autonomy, a positive self-image, a sense of belonging, engagement in meaningful and enjoyable activities, and hope and optimism.

The roundtable participants agreed that, in terms of chronology, symptom improvement must happen first or at least concurrently with the improvement of functioning and life engagement. For both MDD<sup>20</sup> and schizophrenia,<sup>21</sup> "time is brain," and the longer symptoms go untreated, the harder it is to improve to a point where one can engage. As Dr Ismail explained, focusing on symptoms is important in the acute phase, and they are what help in making a

diagnosis. At the time of admission to the hospital, for example, symptoms are necessarily the primary target of treatment, but later in the treatment journey, they become less important. Other factors emerge as impactful because they contribute to how people are doing overall, including how the patient is tolerating their medications, whether they are getting out of bed, how they are engaging with the people they love, and whether they are getting back to doing the things that they want to do. He noted that, over time, those factors are much more important to patients than simply reducing symptom burden according to a rating scale.

Although the relationship between symptomatic outcomes and life engagement outcomes is fluid, Dr Correll stated,

For patients with schizophrenia, if one is really disrupted by thought disorder or positive symptoms or, later, by negative symptoms, it's hard to engage with yourself, with the outer world, with goals, especially when the hedonic and the reward value is missing. For patients with depression, everything is 'down.' The future is not seen as something that's even accessible. Rumination and guilt might be present as well. So, these symptoms must be tackled first. We most likely have to engage the patient both pharmacologically and psychosocially and also involve the environment for improvement to occur.

**Clinical picture.** Dr Ismail provided a profile of a patient with schizophrenia who, despite symptom reduction, has incomplete functional improvement and a lack of life engagement:

The patient has symptom improvement such that they are essentially symptom free, but they are sedated, have gained some weight, have parkinsonism, and none of this is fun for them. So, they're no longer hallucinating, and they no longer believe that the neighbors are spying on them through the wall and through the faucets, but life is not very pleasurable. There's a kind of weight on them that prevents them from going to the next level and going outside and speaking to the neighbors, who they now trust, and making friends, and trying to go back to school. And without those things, the person has symptom improvement, perhaps some degree of functional improvement, but is missing a real sense of being back in the world.

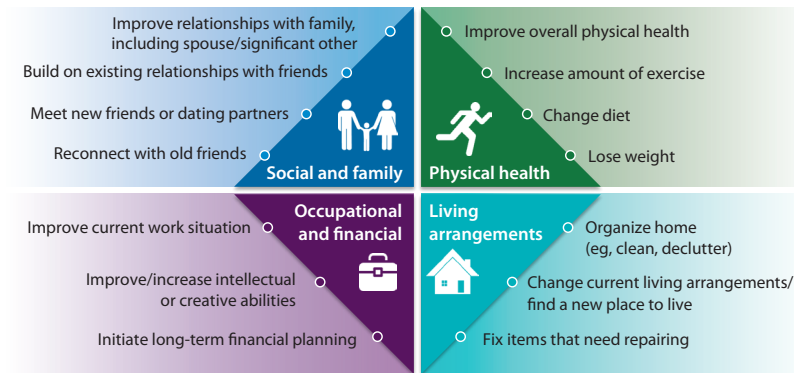
## FUNCTIONING AND LIFE ENGAGEMENT

### Functional Improvement

For both schizophrenia and MDD, life engagement is intertwined with patient functioning, since it reflects the functional outcomes of life fulfillment, well-being, and participation in activities that are meaningful to the individual.<sup>4,6</sup> Although related, functioning and life engagement differ; *functioning* is a broader term centered on role fulfillment and performance of activities in a social context,<sup>22</sup> while *life engagement* is more closely related to quality of life and grounded in a subjective sense of connection with others, as well as the ability to experience pleasure.

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**Figure 2. Goals That Are Meaningful to Patients With Major Depressive Disorder<sup>a</sup>**



<sup>a</sup>Based on Battle et al.<sup>23</sup>

**Figure 3. Goals That Are Meaningful to Patients With Schizophrenia<sup>a</sup>**



<sup>a</sup>Based on Ramsay et al.<sup>24</sup>

Goals for functional improvement differ for patients with MDD vs schizophrenia (Figures 2 and 3),<sup>23,24</sup> but for both disorders, it is intuitively clear that achievement of these functional goals would be affected by aspects of life engagement such as motivation and energy. As shown in a network analysis, motivation and pleasure have pivotal roles in determining social functioning and are intervention targets for improving functional outcomes.<sup>25</sup> The roundtable participants also cited cognition as an area of overlap affecting both life engagement and functional (eg, psychosocial, occupational) outcomes.<sup>26</sup>

The relationship between life engagement and functional improvement was summarized as being bidirectional in nature: the more a patient engages—is alert, has energy, has interest in social activities—the more functional they become, and the more functional the patient becomes, the more opportunities they have to engage.

**Functional Recovery**

Functional recovery can be thought of in the simplest terms as a return to the patient’s highest pre-disease level of functioning in domains such as those listed in Figures 2 and 3 (eg, work and domestic responsibilities, self-care, independent living, family and social relationships, participation in community activities). Alternately, for some patients, recovery may mean achievement of functioning in these areas for the first time.

Both functioning and aspects of life engagement play important roles in patients’ definitions of recovery. According to a study by Zimmerman et al,<sup>27</sup>

the 3 items most often judged by MDD patients to be important in determining remission were, first, the presence of positive mental health features such as optimism and self-confidence; second, feeling like one’s usual, normal self; and third, a return to usual level of functioning. Along these lines, Dr McIntyre commented that the elements important for full recovery are resolution of symptoms and return of function, but *also* a regain of the full repertoire of well-being that patients recall prior to their illness onset.

Recovery is also a personal journey that is unique to the patient,<sup>28</sup> and an area of commonality between functional recovery and life engagement is that both are influenced by the patient’s own life context. This personalization was highlighted by Dr Rafeyan: “I usually approach the goal of recovery as trying to help my patients have meaningful lives—whatever that means to the patient. That might mean taking pride in helping around the house, or working part-time, or feeling happy and looking forward to attending their day program, or being able to socialize with their colleagues.”

Dr Ismail again pointed to a bidirectional relationship between functioning and life engagement, this time in the context of recovery. Without life engagement, he stated, there may be some functional improvement, but it is modest, or skin deep. A throughline between life engagement and functional recovery is the patient’s sense of *agency*, or “CEO status” over their own life and relationships. As one recovers fully and regains functioning, one also gains the ability to manage their interface with the world and control their engagement with the world in a way that is suitable for them.

**Clinical picture.** Dr Thase described what a patient might look like if they were functionally recovered but not engaged with life. A patient of his was the managing partner of a large firm. She worked 60 hours a week and earned a high salary, and she made decisions that influenced the lives and well-being of many people. But she wasn’t happy; life had no joy or “spark.” She also did not desire sex and mentioned that she and her partner had not been sexually

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active for months. This patient's functional recovery, in the professional domain, would be at perhaps the 95th or 99th percentile. On a multidimensional functional recovery scale that includes intimate relationships and friendships, she might have been at the 75th percentile across domains. She was not truly well, though, and what was missing for her was the capacity to engage with life. Therefore, despite having a clear response to treatment for a long period of time, without relapses, she lacked the dimension that would make her truly well even though she was *functionally* recovered.

## COLLABORATING WITH PATIENTS TO INCORPORATE LIFE ENGAGEMENT AS A GOAL

Treatment guidelines for both MDD<sup>29-31</sup> and schizophrenia<sup>32-34</sup> state that patients' preferences and goals should be discussed with the patient in the context of adequate background information, and the patient's personal goals should then be part of treatment planning. In fact, discordance between patient and clinician treatment goals that goes unaddressed can lead to reduced adherence and influence treatment outcomes.<sup>15</sup> Patients value the reestablishment of a sense of engagement as a high-priority therapeutic objective,<sup>10,16</sup> relayed Dr McIntyre, and that alone serves as the clarion call for action with respect to discussing life engagement with patients and assessing it.

Dr Ismail observed that collaborating with patients on life engagement as an outcome is also significant because it reflects a paradigm shift from the traditional treatment goals. Previously, the motivation for schizophrenia treatment was to bring a patient's symptoms to a level at which the patient is not bothering anyone, whereas in the current and future approach, the goal is for the patient to have a productive life that is meaningful to them and those who are close to them. He explained that in the past, the bar had been set low in "industrial psychiatry": sedate the patient, reduce their positive symptom burden, and move on. This approach takes away the patient's agency, their individual wishes and desires, and their *voice*. Every person with schizophrenia is an individual who wants to live a meaningful and enjoyable life, so looking ahead to improvement beyond simple symptom control is essential.

The panelists acknowledged that physicians might be reluctant to initiate a potentially long conversation about life engagement, since visit time is short. However, Dr McIntyre argued, using a framework to set objectives, such as SMART (Specific, Measurable, Attainable, Relevant, and Time-bound), "actually saves you time. And in addition to producing concrete objectives, for me it has also provided fertile ground to understand what engagement would mean for that particular patient."

### Benefits for Patients

In considering the question of what assessment of life engagement would mean for patients, it was agreed that the

importance of shared goal-setting lies partly in the patient's being able to see what is possible. Dr Correll emphasized, "It's important for patients to focus on goals that are formulated, and having higher aims for patients can actually lead them down that path." Dr Rafeyan observed that if clinicians do not assess life engagement and make sure patients are engaged with life, many patients will do the minimum: they will stay by themselves and isolate, which can exacerbate symptoms; he added that, post-pandemic, we are all familiar with the effects of isolation.

Dr Rafeyan further explained that, importantly, discussions about life engagement can even help put patients at ease about psychiatric treatment in general. "Many patients are very appreciative of the discussions about life engagement and find them helpful, especially initially. Often, patients come to our offices for the first time and have never seen a psychiatrist or mental health provider before, and they're very uneasy about our interventions and medications; they're concerned about the effects medication will have on them. Especially in schizophrenia, we often hear patients express, 'I don't want to be a zombie': that's the mental image they have about psychiatric treatment. So when they hear from us that our goal for them is in fact the opposite—for them to be functioning to their best ability and go back to doing things that they did before, or maybe weren't able to do because of the disease—it helps them understand that our goal is different. Discussing functional goals and life engagement early helps dispel the myth many hold about psychiatric treatment, which is very important." The importance of functional goals and life engagement invites the need for measurement of these outcomes in clinical and research settings.<sup>35</sup>

### Goal-Setting for Patients With MDD vs Schizophrenia

Dr Correll posited that patients with MDD might be more engaged than those with schizophrenia to begin with. Clinicians could draw on previous engagement and essentially reconnect the patient to existing goals rather than having to create new goals, because people with mood disorders tend to be more connected to life in general than people with schizophrenia. Dr Thase agreed that more collaboration in the development of a patient-centric plan could be expected in a subset of the population with mood disorders. However, he also made the point that the effects of early onset, chronic depression that begins in adolescence can be as defining and debilitating as those seen in schizophrenia in terms of impairment and one's perception of what is possible:

There are differences in activity between these illnesses. If you are tall by nature, you will always be tall. Likewise, if you have an illness-related deficit in the ability to engage or express affect, of course that changes what might be possible. But it's our job as clinicians to recognize what might and might not be treatable with negative signs and symptoms, and what we can do in a reparative sense to help people who have illness characteristics that may not be specifically treatable.

## Timing

Dr Ismail emphasized that the road to life engagement starts with the initial clinical interaction and never stops. He advises his trainees to keep both relapse prevention and full recovery of functioning and engagement in mind from the patient's first visit, in the clinic, or even in first-episode patients in the emergency department (ED). The idea is to treat with longer-term outcomes in mind: simply sedating patients and having them become less psychotic and less agitated in the ED is insufficient. He also pointed to the role of early treatment of schizophrenia in preserving the patient's ability to engage.



## A "Quadruple Aim" for Clinicians

Dr Correll issued the following challenge to clinicians:

1. Be engaged with the goal of helping patients achieve life engagement by discussing it with them and implementing a concrete treatment plan (eg, using the SMART framework).
2. Be engaged with the patient and use interpersonal skills to create an effective treatment alliance, because without it, there could be difficulty with adherence or with pursuing goals. For that, interpersonal skills are needed.
3. Be engaged with the treatment team and the patient's significant others: Connect with the multiprofessional treatment team and nonprofessional care partners in the patient's life to make achievement of life engagement for patients more likely and sustainable.
4. Be engaged with their own lives: If clinicians just "function" and are not engaged in things that give them resources so they can pass on the "spark" of engagement, they will fall short of helping patients achieve it.

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