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## Protocol for Psychopharmacologic Management of Behavioral Health Comorbidity in Adult Patients with Diabetes and Soft Tissue Infections in a Tertiary Care Hospital Setting



2.0 Contact Hours



2.0 Pharmacology Contact Hours

**Aaron Pinkhasov, MD, FAPA** • Clinical Associate • Professor of Medicine and Psychiatry • Stony Brook University School of Medicine • Stony Brook, New York • Chairman • Department of Behavioral Health • Winthrop University Hospital • Mineola, New York

**Deepan Singh, MD, FAPA** • Clinical Assistant Professor • Psychiatry • Stony Brook University School of Medicine • Stony Brook, New York • Child, Adolescent and Adult Psychiatrist • Winthrop University Hospital • Mineola, New York

**Benjamin Kashan, MD** • Clinical Research Fellow • Division of Wound Healing and Regenerative Medicine, Department of Surgery • Winthrop University Hospital • Mineola, New York

**Julie DiGregorio, CCRP** • Supervisor • Research and Clinical Trials • Division of Wound Healing and Regenerative Medicine, Department of Surgery • Winthrop University Hospital • Mineola, New York

**Theresa M. Criscitelli, EdD, RN, CNOR** • Assistant Vice President • Perioperative Services, Division of Wound Healing and Regenerative Medicine, Department of Surgery • Winthrop University Hospital • Mineola, New York

**Scott Gorenstein, MD, FACEP** • Clinical Assistant Professor • Surgery • Stony Brook University School of Medicine • Stony Brook, New York • Clinical Director • Division of Wound Healing and Regenerative Medicine, Department of Surgery • Winthrop University Hospital • Mineola, New York

**Harold Brem, MD, FACS** • Professor • Surgery • Stony Brook University School of Medicine • Stony Brook, New York • Chief • Division of Wound Healing and Regenerative Medicine, Department of Surgery • Winthrop University Hospital • Mineola, New York

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### **GENERAL PURPOSE:**

**To provide information about the effect of psychiatric comorbidities on wound healing in patients with diabetes mellitus (DM).**

### **TARGET AUDIENCE:**

**This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and nurses with an interest in skin and wound care.**

### **LEARNING OBJECTIVES/OUTCOMES:**

**After participating in this educational activity, the participant should be better able to:**

- 1. Discuss the connection between DM and the development of psychiatric comorbidities.**
- 2. Identify the drugs recommended in the treatment of these psychiatric comorbidities.**
- 3. List cautions and contraindications related to the drugs discussed.**

### **ABSTRACT**

In patients with diabetes mellitus type 2, psychiatric comorbidities such as depressive and anxiety disorders are 60% or more prevalent than in the general population. The severity of mental illness and the duration of diabetes have been shown to correlate with worsening glycemic control, thus impeding wound healing. A retrospective chart review was conducted in all patients with diabetes mellitus admitted to the wound service with prior or current psychiatric symptoms of anxiety, depression, or cognitive impairment. A psychopharmacologic protocol was developed based on the clinical data collected and treatment parameters used by the behavioral health consultation liaison service.

**KEYWORDS:** behavioral health, comorbidity, psychiatry, type 2 diabetes, soft tissue infection

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Diabetes-related soft tissue infections and associated complications, such as loss of a limb, add to the burden of emotional stress and decrease quality of life in the affected population.<sup>4,8</sup> Aside from depression and anxiety, patients with DM have a 60% greater risk of developing dementia.<sup>9</sup> Patients with DM and coexisting depression have higher rates of vascular dementia<sup>10</sup> and Alzheimer disease.<sup>11,12</sup> The aforementioned comorbidities coupled with out-of-range blood glucose concentrations and fluctuations impact the brain and cognition<sup>12</sup> and further predispose patients to the development of delirium.

It is also well recognized that patients with inadequately treated psychiatric symptoms are more likely to have maladaptive behaviors, such as smoking<sup>13</sup> and poor dietary habits,<sup>14</sup> consequently delaying wound healing in patients with DM.<sup>6,7</sup> Moreover, various meta-analyses of the literature report that mental illness, especially depression, in patients with DM reduces adherence to treatment regimens.<sup>15</sup>

The authors have developed a protocol to address the lack of practical clinical guidelines and scarcity of professional resources for the management of psychiatric comorbidity in patients with diabetes and soft tissue infections. Their protocol is based on clinical data gathered and the treatment parameters used by the psychiatric consultation liaison (CL) service in a tertiary care hospital with a dedicated diabetes limb salvage program.

### **METHODS**

A retrospective chart review was conducted on all patients with DM admitted to the wound care service in a tertiary care hospital in the New York metropolitan area over a 6-month period. The authors analyzed the patients receiving psychiatric CL services, which were ordered because of prior or current psychiatric

### **INTRODUCTION**

In patients with diabetes mellitus (DM) type 2, behavioral health (BH) comorbidities such as depressive and anxiety disorders are 60% or more prevalent than in the general population.<sup>1</sup> Multiple, prospective studies have demonstrated that depression is an independent risk factor for the development of DM type 2.<sup>2</sup> A diagnosis of diabetes, in turn, doubles the risk of depression.<sup>3</sup>

For patients with an established diagnosis of DM, depression can increase the risks of microvascular and macrovascular disease complications, such as ischemic heart disease, diabetes-related retinopathy, and peripheral vascular disease.<sup>4</sup> The severity of depression and the duration of diabetes have been shown to correlate with worsening glycemic control,<sup>5</sup> thus impeding wound healing.<sup>6–8</sup>

symptoms of anxiety, depression, or cognitive impairment. Using these inclusion criteria, 24 consecutive patients were selected. Data were collected on the patients' psychiatric diagnoses and treatment recommendations as documented in the psychiatry consultation reports. The authors' hospital's CL service is composed of American Board of Psychiatry and Neurology board-certified psychiatrists who use semistructured psychiatric diagnostic interviews based on the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* to establish diagnoses.<sup>16</sup> As part of the assessment, personal and family histories of nicotine dependence and other substance use disorders among these patients were evaluated. Treatment decisions used by the CL service were then critically analyzed to develop a practical protocol for the management of psychiatric presentations in these patients.

## RESULTS

Based on the data collected on the most frequently recommended medications for the commonly observed diagnoses mentioned previously, a protocol was developed (Figure). This protocol includes the frequently occurring clinical variables that determine treatment decisions. In addition, the recommendations consider the cautions and contraindications for medications and reflect current knowledge of psychopharmacology as applied to this population.

The authors recommend using selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and bupropion as a first line of treatment for depression in this population. In patients with depression and neuropathic pain, tricyclic antidepressants or SNRIs are recommended. Both classes of medications are thought to exert their effect via serotonin and norepinephrine reuptake inhibition.<sup>17</sup> Although tricyclic antidepressants are more effective in the treatment of neuropathic pain,<sup>18,19</sup> their significant anticholinergic adverse effect profile warrants caution in older adult patients, because of the risk of delirium.<sup>20</sup>

Most antidepressants have the potential to cause weight gain.<sup>21</sup> In patients with obesity concerns, the authors recommend use of bupropion or fluoxetine, as these agents have not been associated with weight gain.<sup>22,23</sup> In patients motivated to overcome nicotine dependence, bupropion is effective<sup>23</sup>; however, properties of bupropion may worsen anxiety and insomnia.<sup>23</sup>

In depressed patients with insomnia and poor appetite, the authors recommend the use of mirtazapine.<sup>24</sup> Trazodone is preferred, however, in patients with insomnia who are overweight and/or have hyperlipidemia. In patients with multiple comorbidities and resultant polypharmacy, escitalopram is an optimal antidepressant because of its few drug-drug interactions.<sup>25</sup>

Patients with claustrophobia should be given lorazepam before exposure to anxiety-provoking situations,<sup>26</sup> such as hyperbaric oxygen treatment or magnetic resonance imaging. The half-life of lorazepam is longer in older adult patients and in patients with

hepatic impairment; however, it is preferred over other benzodiazepines because of its lower potential for serum accumulation and lack of active metabolites.<sup>27</sup> In patients with generalized anxiety disorder, SSRIs, SNRIs, or buspirone may be used.<sup>28</sup> Of note, both SSRIs and SNRIs may initially exacerbate anxiety if not titrated gradually. Clonazepam may be added to the treatment regimen until SSRIs or SNRIs take full anxiolytic effect. Once a patient is on an adequate dose of SSRIs or SNRIs and symptoms subside, clonazepam should be gradually tapered. The relatively long-acting effect of clonazepam is more useful in the treatment of panic attacks,<sup>29</sup> compared with shorter-acting benzodiazepines, such as alprazolam. Benzodiazepines may cause delirium in vulnerable patient populations.<sup>30</sup>

The authors suggest that gabapentin, pregabalin, and/or SNRIs are effective treatments for neuropathic pain in patients with anxiety.<sup>31</sup> In patients with documented substance use disorders and anxiety, the authors prefer to use medications with low abuse potential, such as gabapentin, pregabalin, or hydroxyzine. Hydroxyzine has a strong anticholinergic effect<sup>32</sup> and should be avoided in patients at risk of delirium.

Healthcare providers should be aware of the prevalence of delirium in the postsurgical and other frail patients. The potential etiology of delirium should be addressed, and nonpharmacological interventions should be initiated before use of antipsychotic medications. Low-dose quetiapine is recommended for hyperactive delirium in patients at risk of developing extrapyramidal adverse effects.<sup>33</sup> Alternatively, low-dose oral haloperidol may be used when orthostatic hypotension, sedation, or QTc prolongation is of concern.<sup>34</sup>

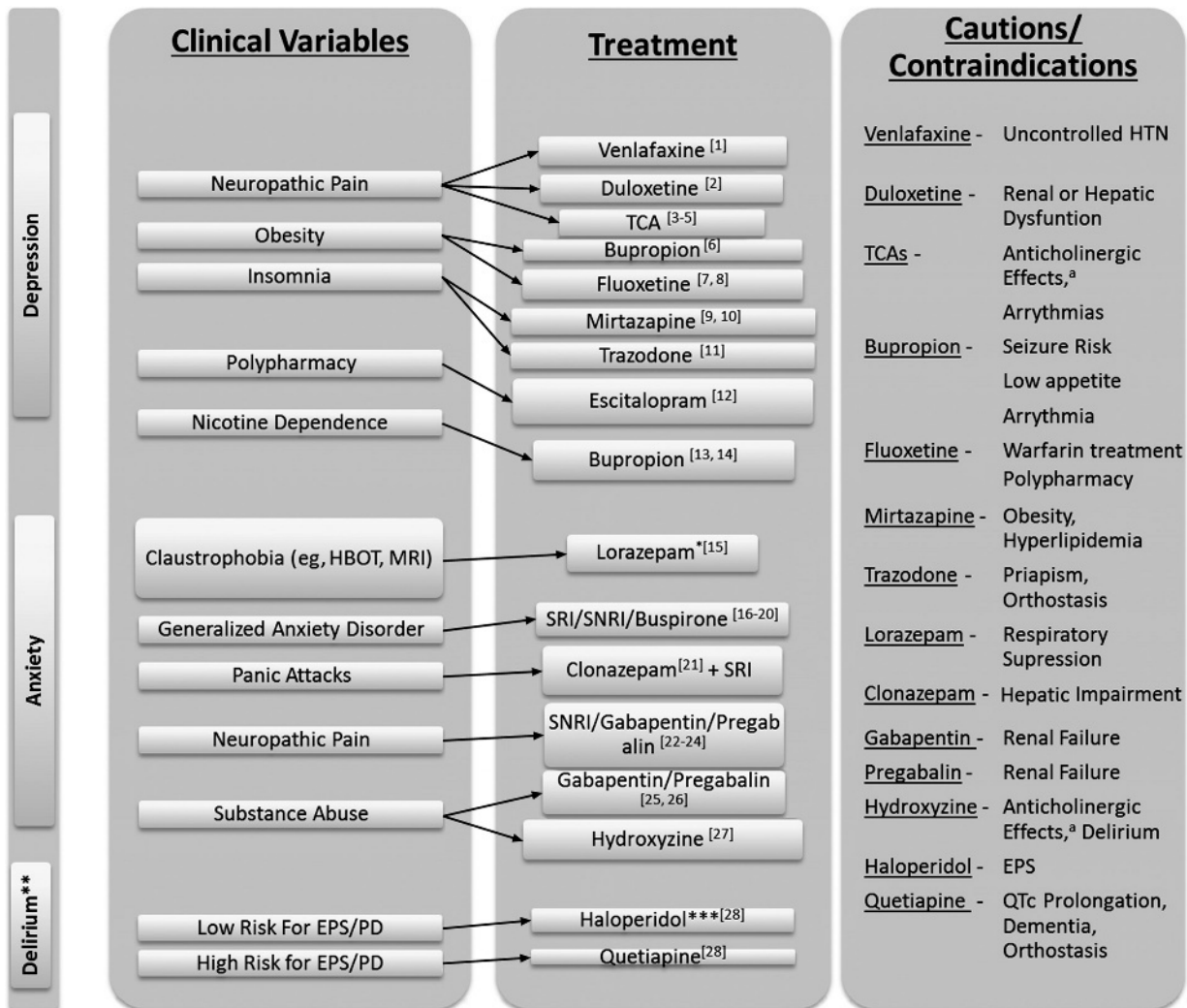
## DISCUSSION

The authors' institution has a diabetes limb salvage program specifically dedicated to soft tissue infections secondary to DM. Years of interdisciplinary care has demonstrated that issues of mental health impeded recovery and need to be adequately addressed. This became possible with the involvement of a dedicated psychiatric CL service.

Although there is no literature describing diabetes-related soft tissue infections and depression as a variable affecting clinical outcomes, a plethora of literature describes the interplay between DM and depression.<sup>5,15</sup> Stress has been shown to delay wound healing in a murine model.<sup>35</sup> In patients with DM types 1 and 2, feelings of anxiety and depression correlate with an increase in proinflammatory cytokines.<sup>36</sup> Negative emotions impacting physiologic processes, such as glucocorticoid up-regulation, increased cortisol levels, increased production of proinflammatory cytokines,<sup>37-40</sup> and/or maladaptive behaviors, have also been described.<sup>41</sup> The exact pathophysiology by which impaired mental health in patients with DM affects wound healing is not well

**Figure.**

**ALGORITHM FOR THE MEDICATION MANAGEMENT OF COMMON PSYCHIATRIC COMORBIDITIES IN PATIENTS WITH DIABETES AND SOFT TISSUE INFECTIONS**



Abbreviations: HTN, hypertension; TCA, tricyclic antidepressants; SSRI, selective serotonin receptor inhibitor; SNRI, serotonin norepinephrine reuptake inhibitor; EPS, extra-pyramidal symptoms; PD, Parkinson's Disease; QTc, QT interval (corrected); HBOT, hyperbaric oxygen therapy; MRI, magnetic resonance imaging

- \* Lorazepam given prior to procedure/HBOT/MRI testing
- \*\* Environmental changes already in place prior to/along with medication management.
- \*\*\* Low dose haloperidol standing and/or as needed.
- <sup>a</sup> Anticholinergic Effects: eg, constipation, urinary retention, dry mouth, blurred vision

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## Figure.

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#### Case Study

A 41-year-old African American woman with a history of diabetes mellitus was admitted to the hospital for the management of a poorly healing sacral wound. The patient developed a pilonidal cyst 6 months prior to presentation, which gradually progressed and needed multiple debridements and regular hyperbaric treatments. She was a smoker and nonadherent to cessation. The wound care team noticed that the patient was very irritable, tearful, and anxious during her stay. In addition, she would leave the floor frequently to smoke cigarettes. Noticing the patient's mood instability, a psychiatry consultation was requested. Although initially hesitant, once educated about the high prevalence of depression and associated poor prognosis with wound healing, the patient agreed to the consult. On evaluation, the patient revealed a depressed mood, hopelessness, helplessness, fatigue, insomnia, poor appetite, and low self-esteem. She also reported a generalized sense of anxiety and an overwhelming

fear that she would never be able to return to normal functioning. She reported not wanting to quit smoking because that was the only thing she could still control. She denied any other medical conditions.

Based on her presentation, the patient was diagnosed with depression and anxiety. Her treatment plan included motivational interviewing to help with smoking cessation and venlafaxine extended release, gradually titrated up to 150 mg, to address both the pain and psychiatric complaints. For her anxiety, she was prescribed clonazepam 0.25 mg/3 times a day. In addition, she was provided with supportive psychotherapy. Before discharge, the patient's symptoms of depression and anxiety significantly decreased, and she accepted nicotine replacement therapy. Her subjective sense of wellbeing was much improved at discharge. She was provided with outpatient psychiatric follow-up for continuity of care.

understood. Proposed mechanisms include the hypothalamic-pituitary-adrenal and the sympathetic-adrenal medullary axes signaling biochemical pathways.<sup>42</sup> This complex interplay further emphasizes the need for a multidisciplinary approach to screen for

mental illness in patients with DM who present with wounds and soft tissue infections. As demonstrated in the case example, early psychoeducation and focused psychopharmacological intervention promote optimal health outcomes.



In highlighting the limitations of this study, it should be noted that the assessed data were limited to a retrospective chart review and that the authors did not assess the outcomes of the treatment longitudinally. The goal of this study was to provide healthcare professionals with a practical psychopharmacology algorithm to address commonly encountered psychiatric comorbidity in patients with diabetes-related wounds. Although the authors recognize the value of behavioral interventions other than medication and strongly recommend approaches such as supportive and cognitive behavioral therapy, these were not the focus of this study.

The authors emphasize that each institution must develop its own mechanism to address common psychiatric comorbidities in this vulnerable population. Given the shortage of mental health providers,<sup>43</sup> access to timely and appropriate psychiatric services remains a challenge. Consequently, some institutions may have limited access to psychiatry CL services to evaluate and treat wound care patients with diabetes. Resources such as the Patient Health Questionnaire 9 (Table 1), Mini-Mental Status Examination,<sup>44</sup> and Generalized Anxiety Disorder 7-item scale<sup>45</sup>

may be used by the surgical wound care team for psychiatric screening. In addition, it is important to screen patients for substance abuse and, when appropriate, use existing institutional treatment protocols such as the Clinical Institute Withdrawal Assessment of Alcohol Scale-Revised (Table 2) and the Clinical Institute Narcotic Assessment Scale.<sup>46</sup>

It is well known that mentally ill patients account for high readmission rates to the general hospital—as much as 38% within 6 months of discharge.<sup>47</sup> Diabetes mellitus and its complications independently account for increased healthcare spending and readmission rates in the United States.<sup>48</sup> To the authors' knowledge, no studies to date have evaluated healthcare costs and clinical outcomes of patients with diabetes-related soft tissue infections and comorbid mental illness.

## CONCLUSIONS

Mental health issues are common in patients with diabetes-related soft tissue infection and if left unaddressed can significantly worsen healing and overall prognosis. Integration of mental

**Table 1.**  
**PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)**

Over the last <b>2 weeks</b> , how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
FOR OFFICE CODING _____ 0 _____ + _____ + _____ + _____ =Total Score: _____				
If you checked off <u>any</u> problems, how <u>difficult</u> have these problems made it for you to do your work, take care of things at home, or get along with other people?				
Not difficult at all <input type="checkbox"/>	Somewhat difficult <input type="checkbox"/>	Very difficult <input type="checkbox"/>	Extremely difficult <input type="checkbox"/>	

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an education grant from Pfizer Inc. No permission is required to reproduce, translate, display, or distribute this questionnaire.

**Table 2.**

**CLINICAL INSTITUTE WITHDRAWAL ASSESSMENT OF ALCOHOL SCALE, REVISED (CIWA-Ar)**

Patient: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_ (24 hour clock, midnight = 00:00)

Pulse or heart rate, taken for one minute: \_\_\_\_\_ Blood pressure: \_\_\_\_\_

**NAUSEA AND VOMITING** – Ask “Do you feel sick to your stomach? Have you vomited?” Observation.

- 0 no nausea and no vomiting
- 1 mild nausea with no vomiting
- 2
- 3
- 4 intermittent nausea with dry heaves
- 5
- 6
- 7 constant nausea, frequent dry heaves and vomiting

**TREMOR** – Arms extended and fingers spread apart. Observation.

- 0 no tremor
- 1 not visible, but can be felt fingertip to fingertip
- 2
- 3
- 4 moderate. with patient’s arms extended
- 5
- 6
- 7 severe, even with arms not extended

**PAROXYSMAL SWEATS** – Observation.

- 0 no sweat visible
- 1 barely perceptible sweating, palms moist
- 2
- 3
- 4 beads of sweat obvious on forehead
- 5
- 6
- 7 drenching sweats

**TACTILE DISTURBANCES** – Ask “Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?” Observation.

- 0 none
- 1 very mild itching, pins and needles, burning, or numbness
- 2 mild itching, pins and needles, burning, or numbness
- 3 moderate itching, pins and needles, burning, or numbness
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

**AUDITORY DISTURBANCES** – Ask “Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?” Observation.

- 0 not present
- 1 very mild harshness or ability to frighten
- 2 mild harshness or ability to frighten
- 3 moderate harshness or ability to frighten
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

**VISUAL DISTURBANCES** – Ask “Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?” Observation.

- 0 not present
- 1 very mild sensitivity
- 2 mild sensitivity
- 3 moderate sensitivity
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

*(continues)*

**Table 2.**

**CLINICAL INSTITUTE WITHDRAWAL ASSESSMENT OF ALCOHOL SCALE, REVISED (CIWA-Ar), CONTINUED**

**ANXIETY** – Ask “Do you feel nervous?” Observation.

- 0 no anxiety, at ease
- 1 mild anxious
- 2
- 3
- 4 moderately anxious, or guarded, so anxiety is inferred
- 5
- 6
- 7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

**AGITATION** – Observation.

- 0 normal activity
- 1 somewhat more than normal activity
- 2
- 3
- 4 moderately fidgety and restless
- 5
- 6
- 7 paces back and forth during most of the interview, or constantly thrashes about

**HEADACHE, FULLNESS IN HEAD** – Ask “Does your head feel different?

Does it feel like there is a band around your head?” Do not rate for dizziness or lightheadedness. Otherwise, rate severity.

- 0 not present
- 1 very mild
- 2 mild
- 3 moderate
- 4 moderately severe
- 5 severe
- 6 very severe
- 7 extremely severe

**ORIENTATION AND CLOUDING OF SENSORIUM** – Ask “What day is this? where are you? Who am I?”

- 0 oriented and can do serial additions
- 1 cannot do serial additions or is uncertain about date
- 2 disoriented for date by no more than 2 calendar days
- 3 disoriented for date by more than 2 calendar days
- 4 disoriented for place/or person

Total CIWA-Ar Score \_\_\_\_\_

Rater's Initials \_\_\_\_\_

Maximum Possible Score 67

The *CIWA-Ar* is not copyrighted and may be reproduced freely. This assessment for monitoring withdrawal symptoms requires approximately 5 minutes to administer. The maximum score is 67 (see instrument). Patients scoring less than 10 do not usually need additional medication for withdrawal.

Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *British Journal of Addiction* 1989;84:1353-7.

health and diabetes-related wound healing services is essential to optimize adherence to treatment recommendations and improve clinical outcomes. Given the prevalence of BH comorbidities in patients affected by DM and the shortage of BH providers in the field, the authors present a practical, current, and evidence-based psychopharmacological protocol designed to manage common mental health problems in this vulnerable population. Future research is needed to elucidate the pathophysiological mechanisms of mental health effects on DM control and the effects of comprehensive BH management on the healing of diabetes-related wounds, treatment adherence, hospital readmission rates, and overall morbidity and mortality. ●

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