REVIEW

Improving Mental Health Outcomes in Patients with Major Depressive Disorder in the Gulf States: A Review of the Role of Electronic Enablers in Monitoring Residual Symptoms

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Abstract: Up to 75% of individuals with major depressive disorder (MDD) may have residual symptoms such as amotivation or anhedonia, which prevent full functional recovery and are associated with relapse. Globally and in the Gulf region, primary care physicians (PCPs) have an important role in alleviating stigma and in identifying and monitoring the residual symptoms of depression, as PCPs are the preliminary interface between patients and specialists in the collaborative care model. Therefore, mental healthcare upskilling programmes for PCPs are needed, as are basic instruments to evaluate residual symptoms swiftly and accurately in primary care. Currently, few if any electronic enablers have been designed to specifically monitor residual symptoms in patients with MDD. The objectives of this review are to highlight how accurate evaluation of residual symptoms with an easy-to-use electronic enabler in primary care may improve functional recovery and overall mental health outcomes, and how such an enabler may guide pharmacotherapy selection and positively impact the patient journey. Here, we show the potential advantages of electronic enablers in primary care, which include the possibility for a deeper "dive" into the patient journey and facilitation of treatment optimisation. At the policy and practice levels, electronic enablers endorsed by government agencies and local psychiatric associations may receive greater PCP attention and backing, improve patient involvement in shared clinical decision-making, and help to reduce the general stigma around mental health disorders. In the Gulf region, an easy-to-use electronic enabler in primary care, incorporating aspects of the Hamilton Depression Rating Scale to monitor amotivation, and aspects of the Montgomery-Åsberg Depression Rating Scale to monitor anhedonia, could markedly improve the patient journey from residual symptoms through to full functional recovery in individuals with MDD.

Keywords: electronic tools, functional recovery, knowledge gaps, major depression, primary care, residual outcomes

Introduction

Globally, and within the Gulf region, many disparities exist in mental healthcare delivery for patients with major depressive disorder (MDD), and there is a paucity of in-depth scientific literature on depression specific to the Gulf region.[1] In the World Health Organization (WHO) Eastern Mediterranean Region, there are more than 50 million cases of depressive disorders, with an estimated mean number of years lived with disability of 685 per 100,000 population.[2]

Importantly, infrastructure-related barriers restrict patient access to appropriate mental healthcare.[3] These barriers include inadequate logistical support for primary care, deficient systematic strategies for patient referral from primary to secondary care, and the extensive workload of primary care physicians (PCPs).[3] Nonetheless, PCPs have a critical role to

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play in identifying, monitoring, and managing depressive symptoms, as approximately 60% of all mental healthcare provision occurs in the primary care environment.[4] The principal clinical aim in patients with MDD is to attain complete remission of depressive symptoms and normalisation of psychosocial functioning to the level before manifestation of depression.[5] However, even after receiving antidepressant therapy or psychotherapy, many individuals with depression continue to experience residual symptoms, which often include fatigue, loss of interest and low energy, together with anxiety, and which prevent complete functional recovery.[6] Furthermore, patients with (rather than without) residual symptoms after treatment of an MDD episode are more likely to experience relapse of depression.[6] Therefore, in some settings, it is recommended to continue antidepressant maintenance therapy for ≥2 years in patients with marked residual symptoms, thus again underscoring the pivotal monitoring responsibility that PCPs have in the management of patients with residual symptoms.[4]

Consequently, this review describes how accurate assessment of residual symptoms, particularly symptoms associated with low affect (eg, amotivation, anhedonia), in people with MDD could facilitate enhanced functional recovery and improved mental health outcomes in the Gulf States. The rationale for introduction of an easy-to-use electronic enabler to assess residual symptoms, especially at the primary care level, and potentially to suggest an appropriate pharmacotherapy to positively impact the patient journey is also discussed.

## Increased Reliance on Primary Care Physicians

A major challenge regarding mental healthcare delivery and optimisation is the patient-perceived stigma of a psychiatric diagnosis.[3,4] This stigma can manifest as patients: being reluctant to seek a referral to a psychiatric centre; having an aversion to treatment options; being poorly adherent to treatment schedules or self-stopping their medications without medical guidance; and, sometimes, lacking trust in PCPs.[7–9] Internationally, it is acknowledged that PCPs have important roles to play in recognising residual symptoms of depression and in understanding the relationships between residual symptoms, stable remission or a risk of relapse, and impaired patient functioning.[10,11] In the Gulf region, there is a growing dependency on PCPs for the appropriate diagnosis and follow-up of people with MDD.[12] In Qatar, for example, community-based care is evolving, and new services are expanding for female populations, migrant workers, and young adults.[13] In the UAE, also, more work is needed to destigmatize mental illness, especially in the area of strongly held, traditional family values, which may prevent some men from seeking medical help.[14]

Clearly, a need exists for mental healthcare upskilling programmes for PCPs in the Gulf region,[3] as these healthcare professionals initiate patient care and conduct follow-up, often based on receipt of information from within the collaborative care model (eg, from obstetricians, gynaecologists, social workers, or care coordinators). Indeed, the potential limitations of some PCPs (eg, inadequate training, extensive workload) in identifying and managing residual symptoms, together with the previously mentioned infrastructure-related barriers that restrict patient access to appropriate levels of mental healthcare, may have a marked, detrimental impact on patients' functional recovery.[3] In addition, potential confounders of the clinical picture are that psychiatric conditions often manifest as somatic complaints, which are generally addressed at primary care centres; however, underlying depression and anxiety are often unrecognised,[15,16] and the healthcare and societal costs of such under-recognition of psychiatric conditions in primary care settings are substantial.[17,18]

Residual Symptoms and Reduced Functional Recovery

During antidepressant pharmacotherapy for patients with MDD, including patients in remission, varied residual symptoms (eg, amotivation, anergia, anhedonia, anxiety, emotional blunting, fatigue, guilt, insomnia, loss of interest, pain, pessimism, reduced cognitive function, reduced libido, weight gain, and work impairment) may occur.[5,6,10,19–23] Indeed, residual symptoms are frequent, and recent cross-sectional studies suggest that these symptoms affect approximately 45–75% of patients with depression, with marked interindividual variability.[5,6,24,25] One multicentre, cross-sectional study evaluated the association of residual symptoms with social functional impairment in 1503 patients with depression who had recovered by ≥50% (by visual analogue-scale evaluation) after antidepressant pharmacotherapy for 8–12 weeks.[5] Among these patients, 39% had marked functional impairment (Sheehan Disability Scale score >6). Factors significantly associated with functional impairment included loss of interest (Quick Inventory of Depressive Symptomatology Self-

Report [QIDS-SR16] item 7; p < 0.0001), mental anxiety (QIDS-SR16 item 9; p = 0.0011), sleep disorders (QIDS-SR16 item 1; p = 0.0232), appetite (QIDS-SR16 item 3; p = 0.0037), energy (QIDS-SR16 item 8; p = 0.0110) and disease course (p = 0.0004) (Figure 1). Moreover, patients with (versus those without) functional impairment were statistically significantly (p < 0.0001) more likely to experience the following residual symptoms: sleep disorder, depressed emotion, inattention, poor self-feeling, being negative, loss of interest, decreased energy, mental anxiety, and residual somatic symptoms (Figure 2).[5]
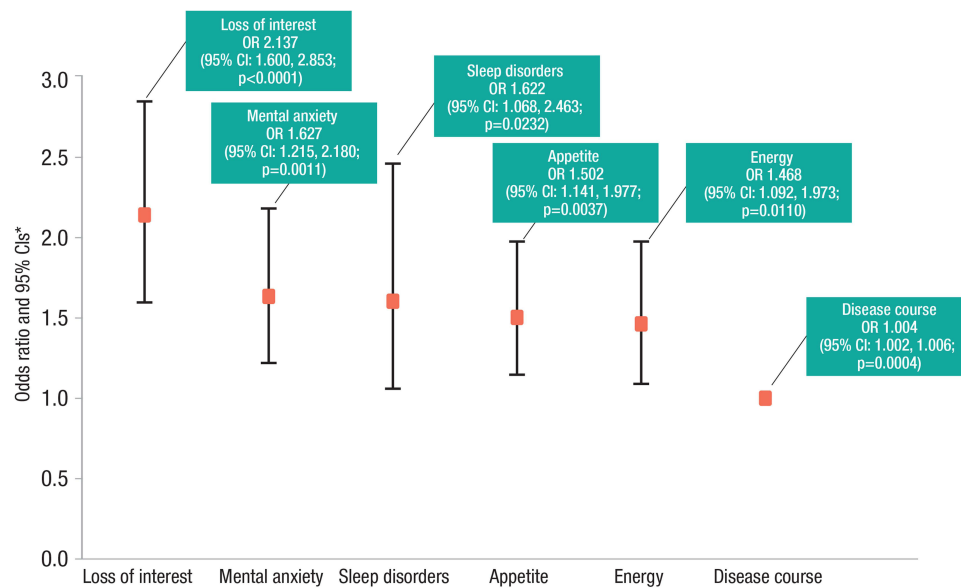
Figure 1 Factors significantly associated with social functional impairment in patients with depression.
Notes: Data from Wang et al[5] *Odds ratio for patients with (SDS score >6) versus those without (SDS score ≤6) social functional impairment.
Abbreviations: CI, confidence interval; OR, odds ratio; SDS, Sheehan Disability Scale.
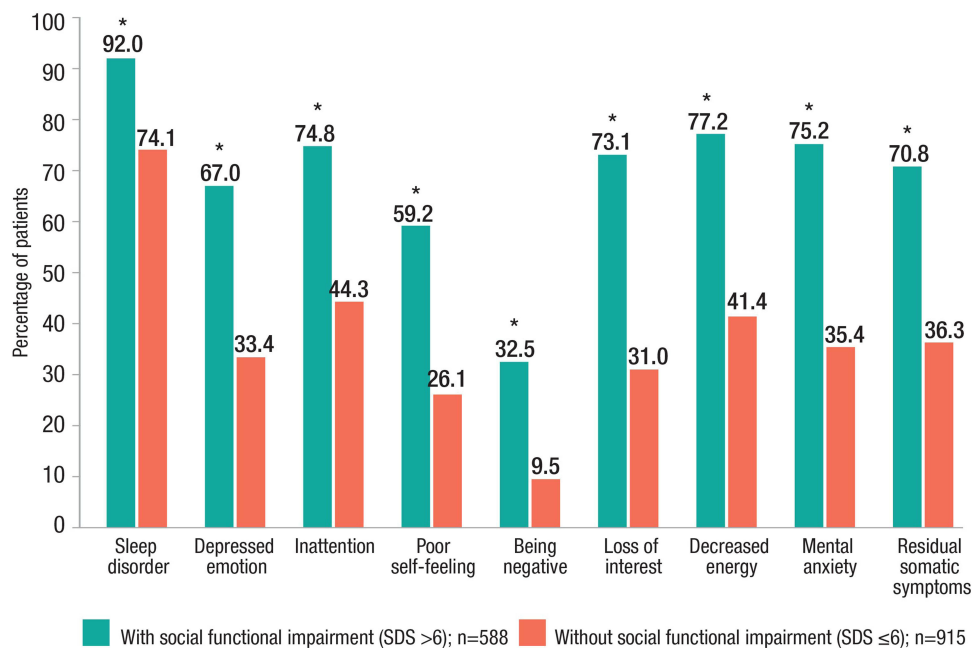
Figure 2 Incidence of residual symptoms in patients with depression, with or without social functional impairment.
Notes: Data from Wang et al[5] *All differences between the two groups were statistically significant (p < 0.0001).
Abbreviation: SDS, Sheehan Disability Scale.

It may often be difficult to clearly differentiate residual symptoms from adverse effects (AEs) of antidepressant pharmacotherapy, such as emotional blunting and sleep disturbances.[10] Moreover, residual symptoms of reduced positive affect, such as amotivation, anhedonia and pessimism, may continue after the resolution of other symptoms, such as distress, irritability and negative mood.[22] Residual symptoms also prevent full functional recovery, and patients with (rather than without) residual symptoms are more likely to relapse.[6] In addition, residual symptoms may contribute to a chronicity of depression, reduced quality of life, reduced social functioning, an increased risk of suicide attempts, and an increased societal burden.[24] Thus, targeting specific residual symptoms associated with functional impairment (eg, amotivation, anhedonia) may increase the likelihood of full functional recovery.

Amotivation

Amotivation is a frequently observed residual symptom of depression that has an important bearing on the selection of appropriate antidepressant pharmacotherapy.[26,27] Indeed, in several settings, serotonin and norepinephrine reuptake inhibitors are often the preferred pharmacotherapy for patients with depression and marked amotivation; for treatment-refractory disease, bupropion may be an appropriate second-choice intervention.[28]

Motivational deficits (ie, a reduced interest and drive to start and maintain goal-directed activities) and amotivation are associated with clusters of residual symptoms.[29–31] Such clusters may include activity and work impairment, general somatic symptoms (eg, anergia), psychomotor retardation, and a negative impact on goal-directed behaviours and goal-related cognition and emotional responses.[29–31] Among 1563 patients with major depression involved in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, motivational deficits persisted in more than 70% of participants after citalopram therapy.[29] Motivational deficits were significantly linked ($p < 0.001$) with worse functional impairment, overall and in each functional domain assessed (ie, home management, private activities, relationships, social activities, and work functioning). Motivational deficits were also significantly linked ($p < 0.001$) with poorer subjective quality of life and overall life satisfaction and had a significant detrimental impact on functional outcomes beyond that attributed to other symptoms of depression.[29]

Anhedonia

Anhedonia, a markedly decreased interest or pleasure in all, or almost all, daily activities on almost every day (as indicated by observation or subjective report), is a core symptom of MDD.[32–34] Moreover, anhedonia comprises several deficits in reward processing, such as in anticipation, consummation and decision-making, and is a major prognostic indicator of disease progression and interventional outcomes in MDD.[33] Anhedonia is also associated with MDD severity, an extended disease course, and in several cases is a negative long-term prognostic factor; indeed, it has been reported that anhedonia increases the risk of worse long-term outcomes by more than three-fold.[32,33] In addition, anhedonia has been linked with an increased risk of suicide.[32,33]

In the primary care setting, identification of anhedonia may often be missed, in part because of time constraints on clinicians; however, care coordinators can play a comprehensive role in identifying, reporting, and managing anhedonia. Furthermore, distinction should be made between anhedonic symptoms (eg, subjective patient reports of loss of interest or enjoyment) and signs (eg, clinically defined pathological behaviours, such as lack of positive emotions, identified during a patient interview).[34] Overall, approximately 70–75% of patients with MDD have clinically significant anhedonic symptoms; thus, it is particularly challenging for patients to attain full functional recovery.[25,35]

The presence of anhedonia in patients with MDD has a major influence on treatment selection: for example, the widely used selective serotonin reuptake inhibitors (SSRIs) appear to have limited efficacy in improving positive emotions and enhancing inadequate reward feedback and motivation, such that SSRIs are unlikely to fully alleviate anhedonic symptoms.[33,36,37] Nevertheless, SSRIs with some activity in the dopaminergic system (eg, fluoxetine, sertraline) may have some efficacy in the setting of anhedonic symptoms, as also does venlafaxine, which acts on both the dopaminergic and noradrenergic system.[25,38] Other drugs with a dopaminergic component of activity (eg, aripiprazole, bupropion) may be appropriate adjunctive therapies in the setting of anhedonic symptoms.[33,39] Importantly, specific evaluation of additional assessment instruments is needed to enhance understanding and identification of anhedonia and to improve outcomes for patients with MDD and anhedonia.[33]

Basic Instruments to Evaluate Residual Symptoms and Functional Recovery

In the United States, PCPs play an important role in identifying and treating depression: it is estimated that approximately 60% of all mental healthcare is delivered by primary care, and approximately 80% of all prescriptions for antidepressants emanate from physicians who are not mental healthcare specialists.[4]

In the Gulf region, there is a growing dependency on PCPs for the identification of residual symptoms in people with MDD.[12] Therefore, appropriate upskilling programmes may be required for PCPs, with a specific focus on residual symptoms and functional recovery, as PCPs need to recognise the relationship between residual symptoms and the risk of relapse and impaired functioning. Basic instruments are required to evaluate residual symptoms swiftly and accurately in the primary care setting. In this regard, elements of the Hamilton Depression Rating Scale (HDRS) and Apathy Evaluation Scale (AES) have been validated for measuring amotivation,[29,30] and elements of the Montgomery-Åsberg Depression Rating Scale (MADRS) have been validated for measuring anhedonia.[40–42] Importantly, improved diagnosis of depression at the primary care level permits more holistic intervention, which may ultimately have a beneficial effect on long-term healthcare costs;[43,44] such holistic treatment can also help to reduce stigma surrounding mental illness and, within an integrated care model, can facilitate patient access to specialty mental healthcare services.[45,46]

Interestingly, a recent systematic literature review from Canada identified 49 validated patient-reported outcome measures (PROMs) that could be used to evaluate features of life engagement in adults regarding general mental health.[47] Under the concept of motivation/reward/energy–apathy, two PROMs were frequently identified: the Behavioral Activation System scale and the AES Self-Report short version. Overall, the three most regularly identified PROMs were under the concept of pleasure–anhedonia: the Revised Chapman Physical and Social Anhedonia Scales; the Snaith–Hamilton Pleasure Scale (SHAPS); and the Temporal Experience of Pleasure Scale (TEPS).[47] Other systematic reviews have reported on suitability of the Patient Health Questionnaire-9 (PHQ-9) for depression screening in the primary care setting,[48,49] and in some regions, government healthcare agencies now advocate the use of the PHQ-9 in comprehensive screening programmes for patients with noncommunicable diseases.

Amotivation

In the Gulf region, the potential use of basic instruments to measure the residual symptom of amotivation may represent a valuable addition to the primary care armamentarium, especially given the growing dependency on PCPs for the appropriate diagnosis and follow-up of people with MDD. User-friendly instruments, such as items 7 (work and activities), 8 (retardation), and 13 (general somatic symptoms) on the HDRS,[29] not only facilitate the identification of amotivation as a residual symptom but can also permit differentiation between sedation as an AE of medication and sedation as a direct consequence of amotivation, thereby directing appropriate treatment selection or switching.

Anhedonia

Some of the most widely used instruments to measure anhedonia include the SHAPS, TEPS and Dimensional Anhedonia Rating Scale (DARS), although these instruments have various limitations.[33,47,50,51] Generally, there are a lack of instruments to specifically evaluate anhedonia in patients with MDD, although DARS is focused on evaluating multidimensional aspects of anhedonia in MDD and can assess pleasure associated with food and natural and social stimuli, in terms of anticipation, consummation and decision-making.[33,50] In various studies, DARS total score demonstrated high internal consistency reliability (0.92–0.96), as also did DARS subscale scores (0.75–0.92).[48] In addition, considerable convergent validity was identified between the DARS and SHAPS, and marked divergent validity was identified between the DARS and depression scores.[48] Nonetheless, before wider adoption and optimisation in clinical settings, DARS requires further research into facets such as scale structure and test reproducibility.[33,50]

A simpler and more appropriate, validated instrument for use by PCPs to assess anhedonia in the Gulf region might be the MADRS anhedonia factor, based on items 1 (apparent sadness), 2 (reported sadness), 6 (concentration difficulties), 7 (lassitude), and 8 (inability to feel) of the MADRS.[40–42]

Electronic Enablers to Evaluate Residual Symptoms and Functional Recovery

A roundtable meeting, supported by Viatris, was held in Dubai, United Arab Emirates (UAE) in May 2023, in which three leading mental health experts from UAE and Qatar and representing different healthcare systems explored the challenges and opportunities associated with managing depression in the region. Other meeting objectives were to recognise areas for improvement and to contribute to the development of more effective strategies for depression management, with a goal of improving mental health and overall well-being of populations in the Gulf region. Thus, the experts reviewed gaps in current mental healthcare delivery, underlined the increasing importance of PCPs for appropriate diagnosis and follow-up, including the identification and monitoring of residual symptoms, and reiterated the emphasis on functional recovery and improved quality of life for patients.

Discussion at the roundtable meeting also highlighted some of the rapid advances being made with artificial intelligence (AI) and machine learning (ML; eg, ChatGPT) in many medical and non-medical fields. Thus, in the Gulf States, it seems prudent to explore the potential of electronic enablers comprising some of the abovementioned, basic instruments,[29,40–42] used together with appropriate decision-making guidance that considers comorbidities and symptom profiles in detail.[52–54] The experts considered that such research and implementation in practice would likely aid in the identification and monitoring of residual symptoms, and possibly also in identification of the most appropriate anti-depressant pharmacotherapy for individual patients with MDD. Overall, the experts maintained that such tailored-treatment strategies will likely facilitate the attainment of full functional recovery by a greater proportion of patients with MDD.

Based on the nine core symptoms of MDD in the Diagnostic and Statistical Manual of Mental Disorders version 5,[32] the STAR*D study revealed a total of 227 unique symptom profiles for MDD.[53] In addition, guidelines for the management of MDD have listed more than 15 different potential first-line interventions for the treatment of MDD.[52] Thus, the experts endorsed that many opportunities now seem to exist to electronically monitor patients for residual symptoms and make treatment decisions in primary care in the Gulf States. The experts re-emphasised that content of these electronic tools could be based on simple instruments for assessing residual symptoms, such as aspects of the HDRS and the MADRS anhedonia factor, together with full consideration of comorbidities and treatment guidance, so that a precision-medicine approach can be adopted and antidepressant pharmacotherapy can be tailored to target the symptoms and needs of individual patients with MDD.

Precision psychiatry using computational approaches to individualise mental healthcare delivery is a developing field, in which increased collaboration is required between mental healthcare professionals and AI researchers to ensure that ML approaches can improve healthcare outcomes.[55] Internationally, numerous AI tools and devices are in active research for the diagnosis and management of anxiety and depression. For example, an AI-enabled chatbot, using aspects of the HDRS and Inventory of Depressive Symptomatology, was evaluated for its potential in the early detection of depression,[56] whereas other investigators questioned the consistency and reliability of ChatGPT in providing mental healthcare support.[57] Other researchers reported 89% accuracy for an AI-based decision support system in diagnosing mental disorders;[58] tree-based ML models effectively predicted changes in PHQ-9 scores in patients with subclinical depression who received stepped care or usual care;[59] and other ML methods were used successfully to predict treatment response.[60,61] Wearable AI devices (eg, wrist watches) were developed to monitor physical activity, sleep, and heart rate, in tandem with additional self-report of MADRS scores, although much further research into wearable AI devices is required.[62–64] An ML approach using smartphone sensors was also used to predict high negative affect in adolescents.[65]

Overall, introducing ML tools into the diagnosis, monitoring and treatment of depression is challenging because of the numerous symptom profiles and current variability in clinical practice.[66] However, ML approaches were associated with significantly better predictions than chance, based on data from the STAR*D study (ML accuracy 65%; p < 0.0001) and Combining Medications to Enhance Depression Outcomes (COMED) study (accuracy 60%; p = 0.043). In addition, an ML strategy based on cognitive test scores attained 72% accuracy in predicting antidepressant treatment response. Although several barriers exist to the implementation of ML in clinical practice, such as accuracy, cost, user acceptability and understanding, and ethical issues, "… it is clear that ML prediction algorithms will be part of depression treatment in

the future and clinicians should be prepared for their arrival".[66] Nevertheless, much research remains to be done before assimilating AI algorithms into mental healthcare, and some physicians remain sceptical and continue to prefer human-derived rather than ML-based clinical support tools.[67]

The experts highlighted that, to date, few if any electronic enablers have been designed to specifically monitor residual symptoms in patients with MDD, thus further endorsing the need for a user-friendly, electronic tool for monitoring residual symptoms. The experts addressed some of the possible pitfalls of introducing such electronic tools in the Gulf region to help PCPs identify, monitor and treat the residual symptoms of depression: a generally high index of suspicion among PCPs regarding these tools; perceived complexity, limited understanding and time-management issues; PCPs becoming "swamped" by too many electronic enablers; tools being more relevant to some residual symptoms than others; or some PCPs over-relying on electronic tools, such that practice flexibility may be reduced.

Conversely, the experts also addressed the potentially major advantages of electronic enablers in the primary care setting for the detection, monitoring and treatment of residual symptoms of depression: by addressing interconnected symptoms and comorbidities, electronic enablers will permit a deeper "dive" into the patient journey through depressive disorders and will likely facilitate appropriate treatment selection or treatment switching if necessary; some enablers may ultimately be endorsed by local psychiatric associations, thus instilling greater PCP confidence in the tools; and use of the enablers may promote patient involvement in shared clinical decision-making, may help to reduce the general stigma surrounding mental health disorders, and may enhance patient confidence in PCPs. Subsequently, with an individualised treatment approach and the potential for reduced AEs of antidepressant pharmacotherapy, patient adherence to treatment and treatment outcomes may improve. The experts concluded that it is likely that a well-validated and accepted, easy-to-use electronic enabler will facilitate the patient journey from the residual symptoms of depression through to the attainment of full functional recovery.

Potential Implications of Electronic Enablers for MDD Management in the Gulf States

Throughout this paper, which provides a narrative review of the potential clinical utility of electronic enablers in the primary care management of residual symptoms in patients with MDD in the Gulf region, three principal themes have been stressed and warrant further emphasis: patients' perspectives of MDD and stigma associated with the condition; the use of measurement-based care (MBC) and electronic enablers to improve mental health outcomes; and some of the policy and practice implications of introducing electronic enablers into mental healthcare programmes. Given the lack of in-depth scientific literature on depression specific to the Gulf region,[1] some extrapolation of data from other regions may be appropriate.

Patients' Perspectives of MDD, and Associated Stigma

Improved awareness of patients' perspectives of MDD and of patients' journeys along treatment and recovery pathways can help to address patients' unmet needs, improve patient involvement in shared clinical decision-making, and enhance holistic mental healthcare outcomes and patients' quality of life.[68] Indeed, healthcare process mapping or mapping the patient journey can more accurately assist decision-making and augment disease management and control.[68] "Expert patients" with good insight into their condition can assume greater involvement in aspects of disease management, with consequent improvements in treatment adherence, symptoms, and quality of life.[68,69] Thus, Mapping the Patient Journey Towards Actionable Beyond the Pill Solutions (MAPS), a project in low- and middle-income countries (LMICs; including the UAE), was designed to improve healthcare outcomes in patients with noncommunicable diseases such as depression.[70,71] MAPS used an evidence-mapping strategy to evaluate several key features of the patient journey: disease awareness; screening for disease and risk factors; diagnosis; treatment; adherence to treatment; and disease control or remission.[70]

A specific and important focus of MAPS in the UAE was to use combined structured and unstructured data-search collation to identify an evidence-gap map.[71] A key finding was marked variability in the prevalence of depression in various settings: for example, 48–82% of participants in community-based settings during the COVID-19 pandemic; 22–

37% in university students; and 2–46% in urban dwellers. Additional variability in MAPS findings was evident, as the estimated rate of depression awareness was low (only 13% of patients were aware of their condition), although at a government university, the screening rate for depression was high (34–91% of participants). The estimated overall rate of adherence to pharmacotherapy and psychotherapy was particularly low (<1%) in some settings, although anecdotal reports indicated a higher, yet still markedly variable adherence rate (15–50%). The evidence gaps identified in MAPS permit the development of a strategic "model of care" for patients with depression in the UAE. The model should focus on mental healthcare collaboration between PCPs, psychiatrists, physicians, care partners and integrated therapists and on social reintegration for patients. Thus, some of the important goals throughout the patient journey are to improve the delivery of disease awareness programmes; the use of targeted screening tools and technological developments such as mobile diagnostic tools; the reduction of stigma around mental illness; the use of patient-centred care, with simplified schedules of antidepressant therapy and enhanced patient–psychiatrist communication; and the funding and investment in future research and technology.[71]

More generally, by collating local, patient-centred data, the principal goals of the MAPS project were to gain a stronger grasp of patients' journeys and to encourage enhanced involvement of patients as shared clinical decision-makers.[70] Attainment of these goals should allow patients to travel along treatment and recovery journeys with greater ease and confidence, and to reach the desired destination of overall improved healthcare outcomes.[70] Additional advantages of adopting patient-centred care are the opportunities to engage patients' families in care settings,[72,73] and to appropriately consider cultural traditions, family values, and socioeconomic factors, thereby potentially improving patient satisfaction and healthcare-professional productivity, and reducing the gamut of healthcare costs.[68]

It is widely recognised that personal and perceived stigma are associated with residual depression;[74] stigma negatively influences quality of life;[75,76] and stigma is a major barrier to patients with MDD seeking treatment.[74,77,78] However, knowledge gaps exist regarding the lived experiences and treatment journeys of patients with MDD,[79,80] and an important aspect of full functional recovery from MDD is how patients manage to liberate themselves from perceived public stigma.[74,79] In a recent, "bottom-up" review of the lived experiences of "expert patients" with depression, individual patient experiences differed according to social and cultural factors (eg, loneliness, poor communication, stigma, stereotypes), and ethnicity, gender, and race.[80] Inter-individual treatment experiences (eg, behavioural therapy, pharmacotherapy, psychotherapy) varied, as also did patients' attitudes towards acknowledgement of vulnerability and the need for help from healthcare professionals, and acknowledgement of the recovery journey.[80] Therefore, on a regional basis, lived-experience findings from expert patients can be particularly pertinent, as such findings can have a marked influence on education, research, and patterns of clinical practice.[80] Indeed, information from expert patients could potentially play a pivotal role in the development and utility of electronic enablers in identifying and monitoring residual symptoms of MDD in patients in primary care.

In a recent, cross-sectional, Thai study in 384 patients with MDD, almost 55% of whom had residual depression, PHQ-9-evaluated depression in the patients with residual depression was negatively associated with total quality-of-life score, as measured by the WHO Quality of Life Brief (WHOQOL-BRIEF) questionnaire ($\rho = -0.58$; $p < 0.001$).[74] Moreover, quality-of-life domain scores were also significantly ($p < 0.001$) negatively correlated with residual depression: physical domain, $\rho = -0.51$; psychological domain, $\rho = -0.67$; and environmental domain, $\rho = -0.34$. Total stigma score (ie, for personal and perceived stigma), as measured by the Mental Health Consumers' Experience of Stigma questionnaire, was significantly and positively linked with depression ($\rho = 0.24$; $p < 0.001$): personal stigma itself was significantly and positively linked with depression ($\rho = 0.38$; $p < 0.001$), whereas perceived stigma alone was not ($\rho = 0.07$; $p \geq 0.05$). Logistic regression analyses revealed that for each 1-point increase in total WHOQOL-BRIEF score, the risk of residual depression decreased (adjusted odds ratio 0.93; 95% confidence interval: 0.91, 0.96). Overall, factors significantly linked with residual symptoms were higher education levels, higher personal stigma, lower median age, lower quality of life, single or divorced status, and student status. Importantly, these results suggest that a necessary strategy, besides appropriate treatment for the residual symptoms of depression, is to try to support self-esteem and reduce personal stigma in an effort to improve patient quality of life.[74] Indeed, supporting self-esteem is a key aspect of trying to reduce the detrimental effect of personal stigma on quality of life.[74,81]

Other important factors to consider when trying to enhance quality of life in patients with residual symptoms of MDD are age and family relationships.[74] Furthermore, if the previously emphasised need for PCP upskilling on residual

symptoms is adequately met, then the direct consequences will likely be a strengthened therapeutic alliance, with greater patient confidence in and communication with PCPs; an increased ability of PCPs to allay patients' concerns and stigma; and an improved quality of care and quality of life for patients.

Measurement-Based Care and the Use of Electronic Enablers

MBC refers to the use of evaluation tools in a systematic fashion to monitor patients and assist with clinical decision-making.[82,83] Response and remission rates in depression are greater when MBC, via the use of well-validated outcome measures, is adopted to direct pharmacotherapy selection or switching, compared with when MBC is not used.[82,84–87] However, MBC remains underutilised in behavioural healthcare settings.[88,89]

As detailed earlier, the upsurge in the use of digital technologies in general medicine has provided opportunities for enhanced patient-centred care and precision medicine to improve patient journeys towards full functional recovery.[68] Some of the important aspects that improved patient-centred care allows are enhancements in the accurate diagnosis of medical conditions; the engagement and involvement of patients in shared clinical decision-making; adherence to treatment; and reducing the stigma of mental illness.[68,90] The WHO produced evidence-based guidelines on the use of digital technologies and MBC to strengthen healthcare systems, with some of the key guidelines focusing on the use of telemedicine between healthcare providers, clinical decision support systems for healthcare professionals, digital monitoring of patients' health status, and e-learning for healthcare professionals.[68,91] In the specific area of mental healthcare in LMICs (eg, the UAE), where the growing disease burden from mental illnesses is a major problem, digital technologies are now being widely investigated to try to improve screening and diagnosis, the appropriate selection of psychotherapy, psychophysiological insights based on environmental and physiological measurements, and patient follow-up.[68,92,93] Furthermore, a recent policy document from the European Psychiatric Association (EPA) suggests that ML algorithms used in predictive psychiatry might ultimately assist in the identification of patients with residual symptoms of MDD who are most likely to relapse; however, much additional research is needed on the full potential of ML in precision and predictive psychiatry.[90,94,95]

Importantly, the use of technology-enhanced MBC may facilitate the greater adoption of MBC by allowing patients with depression to more readily complete outcome measures.[88] In an online survey of clinicians (n = 108) and patients with depression (n = 131), only 40% of clinicians reported that they routinely used MBC; however, 88% of clinicians indicated a greater willingness to adopt MBC if it was accessible electronically. Moreover, 89% of patients reported a willingness to use mobile apps for symptom monitoring.[88]

Almost two decades ago, a web-based system, the Internet-based Self-assessment Program for Depression (ISP-D) was used to accurately identify patients with MDD and subsyndromal depressive symptoms.[96] The ISP-D was administered to a total of 579 study participants, with a mean completion time of 8.9 minutes. Overall, 31.8% of participants completed a retest, and the 2-week test–retest reliability for the ISP-D tool was high (weighted κ=0.801). Validity testing was conducted in a subgroup of 55 study participants: sensitivity, 81.8%; specificity, 72.7%; positive predictive value, 66.7%; negative predictive value, 85.7%; and overall diagnostic accuracy for MDD, 76.4%.[96]

Subsequently, many electronic enablers have been evaluated. For example, the MoodFX patient-centred, e-health tool was assessed in a study in 49 patients with MDD.[97] Mean System Usability Scale score for the MoodFX was 72.7, demonstrating good usability: 78% of patients used the MoodFX ≥3 times during the 6-month study period. Furthermore, the MoodFX versus control group had significantly better PHQ-9 and QIDS-SR scores, and a greater 6-month response rate.[97] Another study reported the user-centred design of Pathway Platform, an electronically enabled care platform for patients with MDD designed to improve patient engagement, MBC, and shared clinical decision-making, and to enhance outcomes and deliver extra support to patients with MDD over their entire treatment and recovery journeys.[98] A deep learning-based natural language processing approach was used to evaluate depressive symptoms in clinical interviews in 329 patients with MDD (387 audio recordings).[99] A multi-granularity and multi-task joint training model had an F1 score (the harmonic mean of recall and precision) of 0.719 for the classification of depression severity and a score of 0.890 for identifying depressive symptoms.[99]

Several other examples of electronic enablers with potential viability for the evaluation of residual symptoms of MDD and functional recovery are detailed earlier in the section on Electronic Enablers to Evaluate Residual Symptoms

and Functional Recovery. Overall, it should be re-emphasised that to ensure the quality of MBC, new diagnostic and monitoring tools should be easy-to-use and efficient to permit their optimal uptake into primary care. Ultimately, some of the electronic enablers outlined earlier may satisfy these primary care criteria while also providing a sensitive means of monitoring responses to pharmacotherapy and psychotherapy. The latter point is particularly pertinent from the standpoints of patient-centred care and patient empowerment, as new, easy-to-use and efficient electronic enablers may allow PCPs and patients to accurately view how symptoms are changing over time, with the likely added benefits of the further endorsement and use of shared clinical decision-making.

Policy and Practice Implications

It was emphasised above that the routine use of MBC facilitates better treatment outcomes and improves the patient journey from the residual symptoms of depression through to functional recovery.[100] In LMICs, individual patient journeys depend on the investments made by national healthcare systems.[68] Frequently, the delivery of healthcare services is disjointed, the quality of care is inconsistent, and a substantial, unofficial healthcare sector supplies long-term healthcare, such that patient journeys are rarely smooth.[68,69] In many LMICs, even access to healthcare services is sub-standard, as noted from a poor ratio of providers to patients and high out-of-pocket healthcare costs.[68,101] Moreover, healthcare expenditure in most LMICs is very low at only about 4% of gross domestic product.[68,102]

Importantly, mental health problems such as depression are often not identified at routine check-ups in primary care, and improved integration of mental healthcare services is needed within community-based and primary care settings.[68,103] For a greater move towards the use of electronic enablers in primary care in LMICs to facilitate improved diagnosis and monitoring, shared clinical decision-making, and truly patient-centred care, policy-level commitments are required to ensure the equitable delivery of affordable, effective, and safe healthcare.[68] However, while digital technology has potential advantages such as reducing disease stigma and improving treatment adherence,[104,105] at national policy-making levels, possible problems such as privacy (ie, maintaining data confidentiality and security) and ethical issues will have to be addressed.[90]

Interestingly, a recent policy paper from the EPA outlined the needs for enhanced primary care awareness of mental illness; reduced stigma around mental illness; greater integration of patients and their families and friends into care networks; the swift introduction of ML to guide diagnosis, monitoring and treatment; and the increased general use of apps and electronic devices in routine disease management.[90] From a policy standpoint, appropriate data protection laws will be required, and ethical electronic health records will have to be established.[90]

Conclusions

Residual symptoms of depression are common and may manifest in up to 75% of patients, with the attendant problems with chronicity of depression, reduced quality of life, reduced social functioning, and failure to attain full functional recovery. Targeting specific residual symptoms such as amotivation and anhedonia may increase the likelihood of full functional recovery. In the Gulf region specifically, there is a growing reliance on PCPs for the diagnosis, monitoring, and treatment of depression. Thus, in the primary care setting in the Gulf region, an easy-to-use electronic enabler incorporating facets of the HDRS to monitor amotivation and facets of the MADRS to monitor anhedonia could markedly improve the patient journey from residual symptoms through to full functional recovery in people with MDD.

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Author Contributions

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represented through the paper. All authors have provided their critical review, feedback, additions, further references, and guidance.

Disclosure

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