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PERSPECTIVES

Optimizing Identification and Management of Depression in Neurological Diseases: A Narrative Review and Expert Perspective

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Abstract: Comprehensive brain health is increasingly being recognized as critically important worldwide and incorporates elements of neurological and psychiatric health. This evolution in the view of cerebral wellbeing considers the many factors that can affect brain health and the interconnectedness of conditions affecting this organ. Such interplay between neurological and depressive diseases is highlighted by observations that these conditions share underlying pathophysiology and frequently co-occur in the same patient. A review of the literature on depression in post-stroke, Parkinson's disease, multiple sclerosis, and migraine, confirmed the high prevalence of depression in patients with neurological diseases, with approximately one third of patients with neurological diseases having depression. The search results also highlighted the importance of early detection of depression, and that appropriate treatment may substantially improve outcomes of both the depression and the neurological disease. However, there was a disparity in the amount of literature on depression in the different neurological diseases, with only three of the 80 retrieved articles discussing migraine and depression. Information on multidisciplinary care was also limited. Unmet needs with respect to management of depression in patients with neurological diseases include effective screening processes that can differentiate between overlapping symptoms. There is also a lack of clear, evidence-based treatment guidelines. Based on our clinical experience, we provide recommendations for best practice management of depression in patients with neurological diseases, including structured patient interviews to aid with diagnosis of depression, involvement of patient families and friends where relevant, multidisciplinary care that incorporates personalized treatment based on the specific symptoms, co-medications and needs of the patient, and continued follow up and monitoring. Antidepressant options are available with different mechanisms of action and adverse event profiles. Overall, evidence indicates that depression in neurological disorders is underdiagnosed and undertreated. We suggest that structured screening and tailored, multidisciplinary care can improve outcomes.

Keywords: major depressive disorder, nervous system disease, brain disease, antidepressant, personalized, mood

Introduction

Neurological diseases (such as stroke, Parkinson's disease [PD], multiple sclerosis, and migraine) and psychiatric diseases (such as depression) affect the brain and consecutively, other related organ systems, are inter-related and share underlying genetic and molecular pathophysiology.[1,2] Therefore, it is important to consider both neurological and psychiatric symptoms when assessing and managing patients. In 2022, the World Health Organization (WHO) in a position paper underscored the importance of ensuring comprehensive brain health, which includes "brain functioning across cognitive, sensory, social–emotional, behavioral and motor domains".[3] The concept of brain health focusses on complete cerebral wellbeing, encompassing both neurological and psychiatric manifestations, transcending these

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traditionally separate disciplines.[4,5] The WHO intersectoral global action plan on epilepsy and other neurological diseases (2022–2031) emphasizes the importance of supporting the "recovery, wellbeing and participation of people living with neurological conditions, while reducing associated mortality, morbidity and disability, promoting human rights, and addressing stigma and discrimination through interdisciplinary and intersectoral approaches."[6] With the high prevalence of neurological and psychiatric conditions,[7] and the substantial impact on the individual and society,[6,8] it is important to ensure timely diagnosis and treatment.

The link between neurological diseases or injury and depression has long been established, with articles from 1945 to 1953 discussing depression in PD,[9] multiple sclerosis,[10] and brain injuries,[11] focusing on how optimal patient management should consider co-occurrence of such conditions. However, neurological and psychiatric diseases have often been viewed and treated separately by neurologists and psychiatrists,[1] and considerable reluctance still exists in viewing psychiatric conditions as brain diseases.[12] The evolution of screening tools and therapeutic strategies has substantially improved clinical management but unmet needs remain.[1,13] Furthermore, considerable challenges exist in treating co-occurring neurological and psychiatric diseases,[14] including diagnostic difficulty due to overlapping symptoms,[15–17] and time constraints when treating patients with these complex disorders.[18] Depression in patients with neurological diseases is considered more difficult to treat than in those without,[15] and understanding, diagnosing, and managing neurological and psychiatric comorbidities in a coordinated way is still complicated by the existence of separate specialties (ie, neurology and psychiatry) Patients also encounter challenges from social stigma,[19] sociocultural considerations, occupational difficulty, disability and poor access to mental health care, which can worsen psychiatric conditions.[20] To date, international and national expert consensus recommendations have been developed to support diagnosis and management of depression in patients with epilepsy[21,22] and neurodegenerative diseases.[23,24] However, additional guidance to assist healthcare professionals (HCPs) is warranted in other neurological conditions.

The aim of this article is to review the latest evidence on depression in major neurological diseases, with a focus on stroke, PD, multiple sclerosis, and migraine, and to provide information to help HCPs manage these conditions. In stroke, PD, multiple sclerosis, and migraine, depression is common but its diagnosis and management might appear complex. Moreover, there is a lack of evidence-based guidelines for these disorders, especially for migraine. We include global studies and those from North America and Europe and provide our expert opinion on best practice management.

Methods

This is a narrative review informed by a targeted search and expert opinion. The methodology for the narrative review complies with the Scale for the Assessment of Narrative Review Articles guidelines. A PubMed search was undertaken on 23 February 2026 to identify articles on depression in people who had suffered a stroke or in those with PD, multiple sclerosis, or migraine. The search was also tailored to identify articles covering the following topics regarding depression: screening methods, epidemiology, impact, clinical unmet needs, pharmacological treatment options, and multidisciplinary care. The search strategy and string are provided in Table 1. The results were screened for articles that met our inclusion criteria (see Table 1 for details), were focused on adults, and that were research articles, systematic reviews or meta-analyses, international or larger studies, or studies in North America and Europe. Exclusion criteria included: biomarker or mechanistic studies, articles focused on treatment of the associated neurological disease rather than depression, studies including only one or two specific pharmacological treatments, and editorial, Delphi or narrative review articles (except guidelines). To focus on the articles with the highest scientific rigor, where multiple results were retrieved on the same topic, those considered to be large (N≥500) or the articles with the highest number of patients were selected. The search results are provided in Figure 1.

Results: Literature-Derived Findings

Of the 80 articles from the literature search selected for inclusion, 43 were focused on post-stroke depression, 19 and 15 were focused on depression in PD and multiple sclerosis, respectively, and only three discussed depression in people with

Table 1 Search Strategy and PubMed Search String

Category	Information
Database	PubMed
Date	23 February 2026
Filters	October 2014 to present, English language
Search	**Title**: Depression AND (parkinson* OR "PD" OR "multiple sclerosis" OR "MS" OR (stroke OR poststroke) OR migraine) **AND** Title/Abstract: (management OR treatment OR Epidemi* OR qol OR "quality of life" OR multidisciplinary OR unmet) OR Title: (screen* OR diagnosis OR care) OR All fields: ("neuro* impact" AND "biopsychosocial impact" AND "psychosocial impact") **AND** Text Word: (human OR man OR patient* OR subject* OR person OR people OR individual OR individuals) **NOT** (acupuncture OR music OR virus OR ectopic OR covid* OR rat OR rats OR mouse OR mice OR preclinical OR phototherapy OR homeop* OR magnet* OR "traditional chinese medicine" OR "estrogen replacement" OR "hormone replacement" OR malnutrition OR diet OR telehealth OR natal OR prenatal OR perinatal OR menopaus* OR RNA OR DNA OR mir OR MicroRNA* OR genetic OR SNP OR polymorphism OR innate OR HbA1c OR Aromatherapy OR vitamin OR mindfulness OR exercise OR electric* OR validity OR pilot OR Microbiota Oxidati* OR plant* OR serum[title] OR smok* OR game* OR correction[title])
String	Depression[Title] AND (parkinson*[Title] OR "PD"[Title] OR "multiple sclerosis"[Title] OR "MS"[title] OR (stroke[Title] OR poststroke[Title]) OR migraine[Title]) AND (management[Title/Abstract] OR treatment[Title/Abstract] OR Epidemi*[Title/Abstract] OR qol[Title/Abstract] OR "quality of life"[Title/Abstract] OR multidisciplinary[Title/Abstract] OR unmet[Title/Abstract] OR screen*[Title] OR ("neuro* impact" AND "biopsychosocial impact" AND "psychosocial impact") OR diagnosis[Title] OR care[Title]) AND (human[Text Word] OR man[Text Word] OR patient*[Text Word] OR subject*[Text Word] OR person[Text Word] OR people[Text Word] OR individual[Text Word] OR individuals[Text Word]) NOT (acupuncture OR music OR virus OR ectopic OR covid* OR rat OR rats OR mouse OR mice OR preclinical OR phototherapy OR homeop* OR magnet* OR "traditional chinese medicine" OR "estrogen replacement" OR "hormone replacement" OR malnutrition OR diet OR telehealth OR natal OR prenatal OR perinatal OR menopaus* OR RNA OR DNA OR mir OR MicroRNA* OR genetic OR SNP OR polymorphism OR innate OR HbA1c OR Aromatherapy OR vitamin OR mindfulness OR exercise OR electric* OR validity OR pilot OR Microbiota Oxidati* OR plant* OR serum[title] OR smok* OR game* OR correction[title])

Note: *Denotes truncation to retrieve all words that share the same root in a database search.

migraine. Of the migraine articles, all three described the impact of depression. Information on multidisciplinary care was limited.

Epidemiology and Prevalence

The literature analysis found that patients with neurological diseases had an increased risk of suffering from depression versus those without, with approximately one third of patients with neurological diseases screening positive for depression (Table 2). A meta-analysis of 245 articles and 493,681 patients who suffered a prior stroke found an almost 3-fold risk of developing depression compared with the control population.[25] Studies have also investigated whether certain socio-demographic characteristics are associated with prevalence of depression in people with neurological diseases, and further research is needed in this area. In terms of socio-demographic characteristics related to post-stroke depression, three studies found that depression risk was slightly higher in females than males following a stroke.[26–28] Regarding race, an analysis of 831,471 privately insured post-stroke patients in the US found that diagnosis rates were lower in Asian, Black and Hispanic vs White patients (Asian HR=0.63, 95% CI: 0.60–0.66; Black HR=0.76, 95% CI: 0.74–0.78; Hispanic HR=0.88, 95% CI: 0.86–0.90).[26] Another study of 586 patients with a first-ever stroke found that some ethnic differences can result from socio-demographic and health factors, especially low educational attainment.[29] Age was also associated with risk of post-stroke depression. Of 274 patients with stroke or transient ischemic attack,

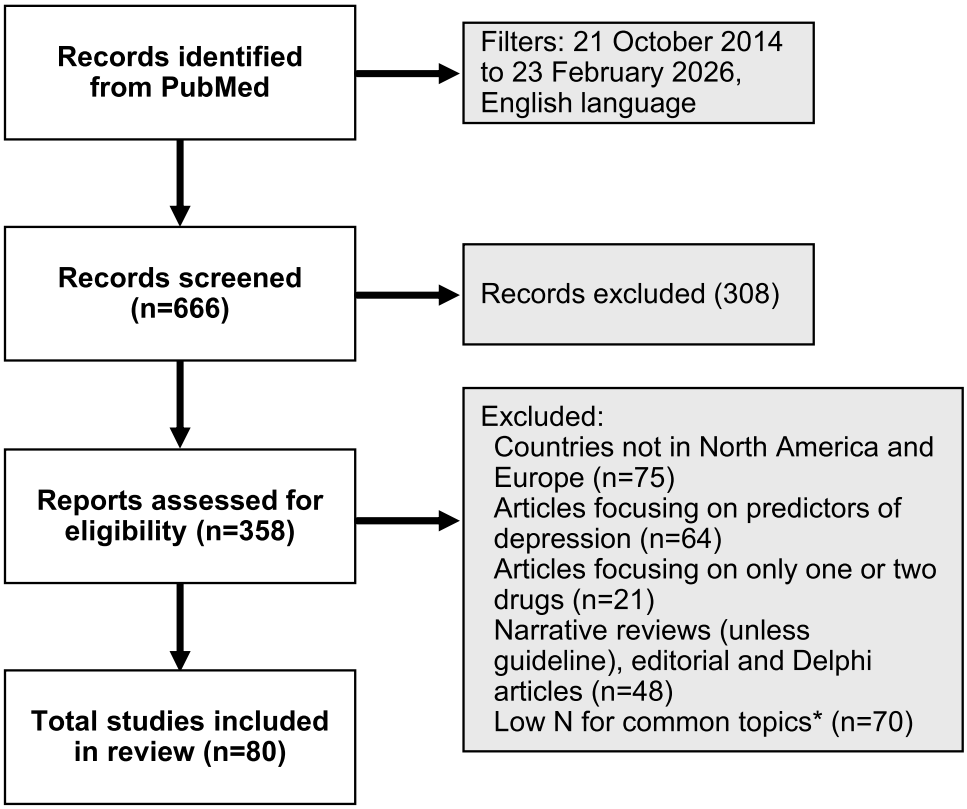

Figure 1 Search results flow diagram.
Note: *Where multiple articles existed on the same topic (ie, for "prevalence" and "impact" with regard to stroke, Parkinson's disease and multiple sclerosis), those with N ≥500 or the three articles with the highest number of patients were selected.

those who were younger reported greater depression symptoms and less executive dysfunction than older patients, emphasizing the need for screening across ages.[30] In concordance with this, a database analysis from a US neurological institute including 7946 outpatients with epilepsy, stroke, or multiple sclerosis found that increasing age was associated with reduced odds for depression in people with post-stroke or multiple sclerosis.[31] Similarly, a decline in post-stroke depression was observed in adults aged over 64 in a US survey of 10,889 participants with stroke or transient ischemic attack of whom 60% were ≥65 years of age.[32] Medical history and post-stroke symptoms can also be associated with risk of depression, which was found to be as likely or slightly more likely in patients with post-stroke dysphagia versus those without (12.0% vs 9.5%; p=0.003; N=9163) in a retrospective, cross-sectional study.[33] The AHA/ASA scientific statement listed the most consistent predictors of post-stroke depression to include physical disability, stroke severity, depression before stroke, and cognitive impairment.[34]

Six studies in the search results provided prevalence data demonstrating the association between PD and depression (Table 2). Moreover, an analysis of US National Health and Nutrition Examination Survey (NHANES) 2005–2016 data, found that patients with PD were 3.3-fold more likely to be diagnosed with depression than people without PD.[41] Diagnoses of PD and depression can occur within a short timeframe, as evidenced by a Canadian primary care electronic medical record study with a 2-year snapshot, which found that 58% of patients with PD and depression received the depression diagnosis within 1 year of their PD diagnosis.[39] Interestingly, the remaining 42% of patients with PD and depression in this study were diagnosed with depression before PD.[39] In a retrospective case-control analysis of 17,711 patients with PD or Lewy body dementia (LBD) from Danish registers, depression rates were higher than matched controls (patients with rheumatoid arthritis, chronic kidney disease and osteoporosis) from 8 years prior to PD or LBD diagnosis though to up to 5 years after diagnosis.[46] Regarding socio-demographics, an analysis of 62,783 inpatients with PD from the USA found the prevalence of comorbid depression to be higher in White vs Black patients.[43]

Table 2 Prevalence of Depression in People with Neurological Disorders

Patient Population/Source	Location	Prevalence of Depression	Reference
Stroke			
US NHANES 1982–1992 data (121/9919 individuals with prior stroke)	US	Point prevalence: 37.1% (vs 17.3% among individuals without stroke)	Razmara et al 2017[35]
Meta-analysis of 245 studies comprising 493,681 patients	Global	Point prevalence: 34.5%	Naghedi et al 2025[25]
≥533 patients with mild to moderate ischemic stroke or intracerebral hemorrhage from the Brain Attack Surveillance in Corpus Christi project (2014–2016)	Texas, US	Period prevalence: 35% at 3 months 25% at 6 months 26% at 12 months	Dong et al 2021[36]
586 patients with a first stroke between 2011 and 2015	Texas, US	Period prevalence at 90 days poststroke: 30.4% for Mexican Americans 20.7% for non-Hispanic Whites	Dong et al 2018[29]
US neurological institute database of 7946 outpatients with epilepsy, stroke, or multiple sclerosis	US	Point prevalence: 23%	Viguera et al 2018[31]
US claims data on 8089 patients with acute ischemic stroke admitted July 2016–July 2017	US	Cumulative risk of poststroke depression: 13.4% at 1 year 15.3% at 1.5 years	Stein et al 2023[37]
Acute ischemic stroke hospitalizations in the US National Inpatient Sample (2003–2017)	US	Point prevalence: 2.7% with diagnosis of major depressive disorder using ICD-9 and ICD-10 codes	Patel et al 2023[27]
Parkinson's disease			
Meta-analysis of 129 studies	Global (28 countries)	Point prevalence: 38%	Cong et al 2022[38]
Canadian primary care electronic medical records	Canada	Point prevalence: 38%	Singian et al 2016[39]
Secondary claims data of German adults aged ≥65 years	Germany	Point prevalence: 33%	Riedel et al 2016[40]
NHANES 2005–2016 data	US	Point prevalence: 26% on day of screening exam	DeMarco et al 2021[41]
513 patients in the UK	UK	Period prevalence: 21% Year 1 24% Year 2	Landau et al 2016[42]
US inpatients	US	Point prevalence: 18%	Imran et al 2019[43]
Multiple sclerosis			
13,821 people with multiple sclerosis	US and Europe	Point prevalence: 36%	Chan et al 2021[44]
US neurological institute database of 7946 outpatients with epilepsy, stroke, or multiple sclerosis	US	Point prevalence: 29%	Viguera et al 2018[31]
Migraine			
2400 people with migraine	US	Point prevalence: 34%	Wu et al 2016[45]

Abbreviations: ICD-9 and ICD-10, 9th and 10th revisions of the International Classification of Diseases; NHANES, US National Health and Nutrition Examination Survey.

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Adding to the evidence of the close link between depression and neurological diseases, electronic medical databases studies found that people living with multiple sclerosis were two- to three-times more likely to have new, treated depression[47] and had an annual prevalence ratio of 1.8[48] versus people without multiple sclerosis. In terms of socio-demographics, a study of 13,821 people with multiple sclerosis found that reporting of depressive symptoms was more common in Black vs White people, whereas age and sex had little impact.[44] Conversely, among 2400 people with migraine, depression was more likely to be reported in White versus Black people and in females versus males.[45]

Screening and Diagnosis

Results from the literature search confirmed the importance of early screening and diagnosis of depression in patients with neurological diseases, although data were lacking for migraine. A meta-analysis of six studies reported that early screening for post-stroke depression enhances functional recovery, improves quality of life, and reduces mortality rates in stroke survivors, suggesting that routine screening for post-stroke depression could improve long-term patient outcomes.[49] In a recent study of patients matched on demographics and stroke characteristics (N=115), routine depression screening and intervention resulted in significantly lower odds of poor outcomes (odds ratio, 0.37 [95% CI, 0.203–0.654], $p<0.001$).[50] Continued screening for depression during follow-up is also important. A study found that depression symptoms were present in more than one third of 201 post-stroke patients and it worsened between hospitalization and follow-up.[51] Similarly, over a 4-year study of 513 people with PD, the rate of observed depression increased from 21% to 24%, highlighting the need for ongoing assessment.[42] A descriptive study of 1214 patients found that increasing Geriatric Depression Scale (GDS) scores were associated with motor symptoms, non-motor symptoms, cognition, sleepiness, and quality of life (all $p<0.001$), and that depression should be regularly assessed in patients with PD, especially in those with deteriorating symptoms.[52] It is important to carefully choose which screening tool to use for depression. In a study of 329 people with multiple sclerosis, the Beck Depression Inventory (BDI) Fast Screen detected fewer cases of mild to moderate depression than the BDI-II in a head-to-head comparison.[53] In a study of 345 people with multiple sclerosis, fatigue, anxiety and depression correlated with self-reported cognitive function more reliably than objective measures of cognitive function, suggesting that screening for fatigue, anxiety and depression is important for accurate clinical interpretation of subjective cognitive measures.[54] Similarly, in a prospective cohort study of 828 people with multiple sclerosis, increased self-reported psychosocial fatigue, cognitive fatigue and number of comorbidities were predictive of anxiety and depression.[55]

Despite the recognized importance of depression screening, it is not always performed consistently in clinical practice. In a small study based in Berlin, Germany (N=57), only 36% of post-stroke patients recalled being previously screened for depression, and only 43% of those also recalled out-patient screening, suggesting that systematic screening for depression is lacking.[56] The study further suggested that there is an unmet need for sufficient care in the out-patient setting for patients with depression.[56] Rates of screening for depression may be improved by using a standardized form, including for post-stroke.[57,58] A study at five movement disorder clinics found that depression screening of patients with PD can be achieved at much higher levels using a formal tool than is currently practiced, but there are barriers to implementation, including lack of time.[59] Of the 378 patients screened with the 15-item GDS, 45% had depression, which improved over a 12-month follow-up period.[59] To combat lack of time, it may be possible to streamline screening by selecting questionnaire items that tend to predict depression well, without using the entire questionnaire.[60] Short questionnaires also exist that can be effective for screening. For example, the Whooley questions, a 2-item yes/no questionnaire, was found to efficiently and sensitively detect depression among 148 ambulatory older adults with coronary heart disease and prior stroke.[61] However, caution must be exercised when using short versions, as the 2-item Patient Health Questionnaire was not found to be effective in identifying depression during hospital admission for 337 acute stroke.[62]

Some research groups have developed tools to support early identification of depression in neurological diseases, for example the Post-stroke Depression Prediction Scale, which was developed to predict the risk of depression in the second month after stroke following an assessment in the first week.[63] Similarly, a rapid visual analogue screening tool, the Emotional Thermometer 7 tool, was found to perform comparably to the Hospital Anxiety and Depression Scale (HADS) - Depression Subscale (HADS-D) in patients with multiple sclerosis and

could enable rapid screening for depression.[64] In clinical practice, patient- and caregiver-reported symptoms are an important indicator of depression. It is also important for clinicians to look for cues in follow-up that could suggest depression, for example, a study of stroke survivors found that reporting lack of access to rehabilitation, or concerns about adequacy of care received, might be cues for the presence of depressive symptoms.[65]

Impact

Depression was found to have a substantial impact on patients with neurological diseases. Multiple studies have reported an association between stroke, depression and all-cause mortality,[35,66,67] and post-stroke depression was associated with poor functioning and quality of life using datasets from large numbers (>2500) of patients.[33,68] In an Italian post-stroke rehabilitation unit, patients with depression (N=280) showed greater disability, reduced effectiveness of rehabilitative treatment, and longer length of stay than those without depression (N=280).[69] The authors note from their clinical experience that post-stroke depression can cause feelings of apathy, social withdrawal, and difficulty with thinking, which can slow recovery and rehabilitation. In the literature, non-responders to antidepressants were reported to exhibit worse rehabilitation outcomes than responders.[69] Another study found that hospitalized patients with stroke and major depressive disorder (MDD; n ~16,000) had a 40% higher chance of severe disability, morbidity, and not being discharged to home than stroke patients without MDD.[27] The authors suggested that prompt screening and management of depression could mitigate inferior outcomes.[27]

In PD, data from individuals using the Parkinson's Progression Markers Initiative (PPMI) dataset showed that worsening depression, as assessed by the GDS-15, was significantly associated with a subsequent decline in self-reported physical function (N=1128)[70] and with activities of daily living (N=892) and vice versa.[71] Similarly, in another study, BDI scores were associated with a decline in multiple measures of disease severity, and had the strongest association with quality of life rather than motor or cognitive measures.[72] Another study concurred that quality of life among 300 patients with PD was strongly related to depression.[73] Similarly, comorbid depression in people living with multiple sclerosis significantly increased the risk of worsening disability (N=1791),[74] and was found to be a potent mediator between fatigue and mental health quality of life in a cross-sectional analysis of data from an international cohort of 2104 people with multiple sclerosis.[75] The three studies on patients with migraine from the literature analysis (N=2400, N=531 and N=567, respectively) suggested that depression increased healthcare costs,[45] independently decreased quality of life,[76] and impacted career success.[77]

Treatment

In a small 6-month prospective observational cohort study in patients with stroke (N=73), temporal analyses indicated that depressive symptoms and self-efficacy correlated with physical activity the following month.[78] Depressive symptoms had a dominant effect, whereby if they were high, physical activity was low regardless of self-efficacy. This led the authors to suggest that targeted intervention for depressive symptoms could improve future self-efficacy and physical activity.[78] A systematic review examining a range of non-pharmaceutical approaches for treatment of depression in patients with stroke found that few studies showed substantial improvement of symptoms, and suggested interdisciplinary collaboration is needed for optimal outcomes.[79] Multiple meta-analyses and systematic reviews have evaluated antidepressant treatment for post-stroke depression. A Cochrane systematic review found that while the evidence is of very low quality, pharmacological interventions and psychological therapy may prevent depression and improve mood after stroke.[80,81] By comparison, non-invasive brain stimulation had little to no effect on the prevalence of depression.[80] Several reports found that antidepressants improved depression, stroke health, and quality of life, suggesting the importance of early therapy initiation to reduce morbidity, with consideration of possible adverse events in some individual patients.[82–85] There are differences in opinion as to whether sufficient evidence exists to be able to select a preferred antidepressant for post-stroke depression.[84,86–88] In a meta-analysis of 12 randomized controlled trials covering ten antidepressants with a total of 707 participants with post-stroke depression, paroxetine (selective serotonin reuptake inhibitor; SSRI), trazodone (serotonin antagonist and reuptake inhibitor), and nortriptyline (tricyclic antidepressant; TCA) were among those found to have reasonable efficacy and acceptability profiles.[87] However, the conclusions were based on single studies for paroxetine and trazodone.[87] In another meta-analysis reviewing 13 agents from 15

randomized controlled trials with a total of 876 participants with post-stroke depression, paroxetine (treated patients: N=30), duloxetine (serotonin and norepinephrine reuptake inhibitor; SNRI; N=20), trazodone (N=6), and fluoxetine (SSRI; N=192) were among those discussed regarding adequate efficacy and safety, although the number of patients treated with each agent varied considerably.[86] A systematic review examining data from five randomized controlled trials comprising 247 patients with post-stroke depression treated with one of seven different SSRIs or serotonin and/or norepinephrine reuptake inhibitors (SNRIs) suggested both drug classes exerted clinical benefit.[88] All these studies were limited by small sample sizes of the clinical trials and lack of head-to-head comparisons, and the authors highlighted that pharmacologic strategies should be individualized based on patient characteristics, symptoms and vulnerability to certain adverse events.[84,86–88]

Analyses on the frequency of treatment have also been undertaken. Data on 759 post-stroke individuals from the US Medical Expenditure Panel Surveys, for the years 2011, 2013 and 2015, found that 51.2% were prescribed only antidepressants, 12.6% utilized both antidepressants and psychotherapy, and 31.7% recorded no treatment.[89] SSRIs were the most frequently used antidepressants, and adherence to treatment was higher for those prescribed combination therapy versus antidepressants only.[89] The highest proportions of untreated stroke survivors were males (p=0.04), those aged 40–64 years (p<0.001), and those with Black race (p=0.02).[89] Separately, two US claims datasets found that 69% of patients with post-stroke depression were prescribed antidepressants,[26,37] with SSRIs being the most common.[37] In contrast, a systematic review found only 24% of 2280 people with depression across 29 stroke cohorts were using antidepressant medication.[90] Among privately insured patients, rates of treatment were higher in women versus men (risk ratio (RR) 1.19, 95% CI: 1.17–1.21), lower in Asian, Black and Hispanic vs White patients (Asian RR=0.85, 95% CI: 0.80–0.90; Black RR=0.92, 95% CI: 0.89–0.94; Hispanic 0.96, 95% CI: 0.93–0.99), and higher among older patients.[26] Therefore, potential inequities exist in treatment of post-stroke depression by sex, race/ethnicity, and age, which may reflect barriers other than healthcare access.[26]

Regarding other neurological diseases, a 2024 study of 7 years of PPMI data reported an association between anxiety and depression at onset of PD (N=490) with multiple negative longitudinal trajectories, and suggested that treatment of anxiety and depression may improve motor and non-motor outcomes.[91] However, two US studies concluded that depression is underrecognized and undertreated in PD, with only half of patients with mild or moderate–severe depression taking antidepressants in one study,[52] and 58% of patients with PD and depression receiving antidepressant treatment in another study.[92] Using the US NHANES 2005–2016 data, 62% of patients with PD were found to use antidepressants.[41] By contrast, in a Canadian primary care study, 86% of patients diagnosed with depression concurrent with PD were prescribed antidepressants.[39] Meta-analyses assessing agents such as SSRIs and TCAs found that treatment improved depressive symptoms in patients with PD, with side effects varying between the different options.[93–95] The most common antidepressants prescribed for PD were SSRIs.[39,92] In multiple sclerosis, studies from 2014 and 2015 found that a large proportion of patients with depression were recommended some form of antidepressant treatment (be it pharmacological or not), but that outcomes were not necessarily improved by the treatment, suggesting a need for management optimization.[96,97] In a later study, of 21% of people with multiple sclerosis diagnosed with depression, 57% were recommended treatment for their depression and 55% were prescribed antidepressants, of which SSRIs were the most common, followed by SNRIs.[98] In one study in patients with migraine, 65% of those with co-occurring depression used antidepressants.[45] While the evidence on migraine is limited, studies suggested that management of comorbid depression could improve patient functioning[77] and treatment outcomes and reduce health costs.[45]

Guidelines and Unmet Needs

Several studies from the search results highlighted the need for more evidence-based guidelines for the management of depression in neurological diseases.[99] A Canadian study of 33 HCPs, seven patients with co-existing depression/anxiety along with PD, and their caregivers, found that patients struggled with communicating symptoms and accessing services, and HCPs experienced difficulty in implementing guideline recommendations due to lack of evidence regarding efficacy.[100] A review of guidelines for management of depression and anxiety in PD and dementia also suggested that while management recommendations exist, there remain gaps in the evidence.[101] A review of multiple sclerosis

guidelines highlighted the need for high-quality, comprehensive clinical practice guidelines for depression with clear recommendations that can be globally implemented by HCPs.[102]

Discussion and Expert Clinical Recommendations

The literature search herein identified multiple unmet needs for screening and management of patients with neurological diseases and depression, including standardized screening pathways with optimal screening tools and comprehensive guidelines founded on solid evidence. The literature analysis also revealed a lack of studies of depression in people with migraine with the search criteria used here. The few results in patients with migraine seem clinically very relevant, given the strong link between depression and migraine that has been reported.[103] The European Group for the Study of Resistant Depression found that 13.5% of females and 6.2% of males with MDD had co-occurring migraine.[104] In this group of patients with MDD, those with co-existing migraine had significantly higher functional disability and were more likely to be younger, of non-Caucasian origin, outpatients, and suffering from comorbid asthma.[104]

Discussion of multidisciplinary treatment was also notably absent from the search results. Multidisciplinary approaches individualized to the specific needs of each patient are increasingly important to ensure comprehensive brain health, and thus more guidance is required in this regard. Considering the literature review results and our own experience, we further discuss multidisciplinary care and key elements of the patient journey below.

From our perspective, stepwise clinical pathways for depression in populations with neurological diseases include: 1. identification/screening; 2. triage and risk assessment; 3. diagnostic clarification (including symptom overlap and differential diagnosis); 4. first-line management, and 5. follow-up/monitoring. Escalation and referral criteria should also be checked at each stage. In our view, multidisciplinary care enhances best management, and primary care plays an important role within a collaborative or stepped-care model, including: early detection and repeated assessment; initial management in uncomplicated cases; longitudinal monitoring of treatment response and tolerability; coordination across neurology, psychiatry, psychotherapy, and rehabilitation services; and checking referral thresholds for specialist psychiatric care. A proposal for best practice identification and management of depression in people with neurological diseases is presented in Table 3.

Screening and Diagnosis

The literature analysis supported the importance of detecting symptoms of depression in patients with neurological diseases early so they can be treated early and adequately In our experience, diagnosing and treating depression improves neurological symptoms, and facilitates adherence to the treatment of both brain diseases and their further comorbidities However, diagnosis of depression in patients with neurological diseases can be challenging due to heterogeneous and overlapping symptoms.[15–17]

In PD, overlapping symptoms can include fatigue, lack of energy, appetite loss, psychomotor slowing, cognitive impairment (including communication difficulties and lack of concentration for example), and insomnia.[105] In addition, patients with PD more frequently experience anhedonia than depressed mood because of their impaired dopaminergic system.[105] In our experience, a correlation between motor and mental symptoms of PD is commonly seen, where fluctuations in depressed mood as well as physical symptoms can be correlated with periods of low dopamine levels. Therefore, observing how mood symptoms change during the day may help to distinguish depression from PD-related non-motor symptoms, especially if they follow motor fluctuations.

The strong link between fatigue and depression makes use of depression scales challenging in patients living with multiple sclerosis.[105] In our clinical experience, anxiety may occur prior to depression in patients with multiple sclerosis. Symptoms of fatigue can be particularly challenging to differentiate between multiple sclerosis and depression. Moreover, risk of depression can be higher among pregnant women with multiple sclerosis than for other patients with multiple sclerosis. Depression in patients with migraine often occurs with anxiety, can be more severe in chronic cases, can result in sleep dysfunction, and has a significant impact on daily life.[106] Fatigue, appetite loss and insomnia are the most common overlapping symptoms in patients with migraine.[17]

When assessing depression in patients with neurological diseases, each symptom needs to be considered in detail to determine whether it is accounted by the neurological disease. Given that fatigue can be a symptom related to

Table 3 Proposed Best Practice for Identification and Management of Depression in Neurological Disorders Throughout the Patient Journey

Proposed Best Practice	Disease-Specific Considerations	Confounding Factors
Screening and diagnosis		
• Routinely screen all patients with neurological diseases for depression • Use validated screening tools (eg, PHQ-9, HADS, BDI-II) • Consider perspectives from families and caregivers (eg, type of symptoms, time of onset) • Assess for atypical presentations, especially in cognitive impairment	**Post-stroke**: • Screen for depression, anxiety, and sleep problems • Use scales validated in stroke populations (eg, PHQ-9 with cognitive adaptation) • High risk in first 3–6 months post-event **Multiple sclerosis**: • Screen regularly for depression and anxiety, especially during relapses or treatment changes • Use scales to determine if depression is occurring along with fatigue **Parkinson's disease**: • Symptoms may overlap with motor features; consider apathy, fatigue, and slowed thinking as depressive equivalents **Migraine** • Depression is almost twice as frequent in those with migraine compared to those without[103] • Screen for depression in those experiencing episodic migraine	• Overlapping symptoms with neurological disorders • Limited consultation time
Referral and management		
• Take time to differentiate between primary depression and neurodegenerative apathy or fatigue • Conduct cognitive and neuropsychological assessments if needed • Educate patients and families on the interaction between neurological illness and depression Advise patients about educational websites and patient associations • Spend time with the patient for deeper exploration of management options • Perform neuro-psychological testing to uncover dysfunction that could be a cause of depression • Ensure multidisciplinary involvement Consult a psychiatrist for resistant and severe depression • Refer to a psychiatrist for depression with psychotic or suicidal symptoms • Urgently refer to specialist mental health services if patient presents a considerable immediate risk to themselves or others	**Post-stroke**: • Involve psychologist support early as part of the rehabilitation **Multiple sclerosis**: • Refer to psychologists for patient support, especially in the first phases of the disease • Involve a psychology/psychiatry team for progressive multiple sclerosis support **Parkinson's disease**: • Apathy vs depression distinction is key **Migraine** • Psychiatric input advised in patients with chronic migraine and high disability	• Stigma and under-recognition of psychiatric symptoms can delay diagnosis across all neurological conditions

(*Continued*)

Table 3 (Continued).

Proposed Best Practice	Disease-Specific Considerations	Confounding Factors
Treatment		
• Use a personalized approach based on symptoms • In elderly patients, use monotherapy where possible • Choose formulations of treatment (eg, intravenous, drops, slow or quick release) based on symptoms and patient functionality • Suggest non-pharmacological treatment, including psychotherapy, diet and physical exercise; involve family and friends for motivational factors • Use appropriate communication tailored to the patient's needs	**Post-stroke**: • Consider intravenous formulations for patients who cannot swallow • SSRIs may aid recovery, but risk of bleeding and hyponatremia should be assessed **Multiple sclerosis**: • Screen for sexual dysfunction prior to treatment initiation to differentiate symptoms related to the disease • Use maintenance treatment after the acute phase of treatment • Consider side effects that could impact on QoL, and consider side effects of multiple sclerosis treatments • Avoid benzodiazepines **Parkinson's disease**: • Trazodone is frequently used in patients with Parkinson's disease • SSRIs can be combined with trazodone, but monotherapy may be preferred **Migraine** • Preventive treatment can include antidepressants with additional effects on pain (eg, duloxetine) or antidepressants that help relieve headache symptoms • Amitriptyline is commonly used for migraine prevention, but is not an antidepressant at lower doses • Drugs with frequent adverse events and effects on body weight should be avoided	• Effective treatment may not be timely (eg, because of delayed presentation or diagnosis), impacting on both patients' quality of life and with clinical consequences for their neurological disorder • Cognitive impairment and psychological complexity can limit therapy adherence • Polypharmacy increases risk of adverse effects • Fatigue and executive dysfunction affect therapy uptake
Follow up		
• Monitor functional impairment and QoL over time • Monitor treatment compliance • Assess treatment strategies and modify if needed • Maintain good communication between experts and comprehensive documentation for continuity of care across different settings • Refer for occupational rehabilitation where relevant	**Post-stroke**: • Provide a follow-up schedule to aid follow up across different clinical settings • Depression may reoccur, therefore long-term monitoring is essential **Multiple sclerosis**: • Frequently monitor functional impairment and QoL (eg, with SF-36) • Depression often fluctuates with disease course **Parkinson's disease**: • QoL assessments (particularly self-rated scales) are important over time **Migraine**: • Depression may worsen with increased headache frequency or medication overuse	• Progression of underlying neurological disease complicates mood management • Caregiver burnout impacts patient outcomes • There is limited access to psychiatric care in some settings • Limited time and patient complexity can make thorough evaluation of depressive symptoms and personalization of care challenging

Abbreviations: BDI-II, Beck Depression Inventory-II; HADS, Hospital Anxiety and Depression Scale; PHQ-9, Patient Health Questionnaire-9; QoL, quality of life; SF-36, 36-Item Short Form Survey; SSRI, selective serotonin reuptake inhibitor.

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neuroinflammation,[107] it should always be thoroughly assessed and considered. Depression diagnosis can also be assisted by using structured patient interviews, simple tools including self-rating scales (eg, Patient Health Questionnaire-9 [PHQ-9], Generalized Anxiety Disorder-7 questionnaire, or BDI), and asking the views of the patients' families Potential tools for rapid screening are also available[64] In some centers, structured assessments are used. For example, at University Hospital Bern an informal internal interview structure developed by the Department of Movement Disorders is used that asks about motor and non-motor symptoms systematically for every patient at every visit to the outpatient clinic. For non-motor symptoms, patients and their families/caregivers are asked about cognitive deficits, hallucinations, apathy, hypodopaminergic symptoms, depression, fear, insomnia, REM disturbances, sleep apnea, restless legs, pain, hyposmia, obstipation, orthostatic dysregulation, and incontinence. Medication and therapeutic interventions are also assessed. However, depression and further frequent psychiatric manifestations, including anxiety, sleep disturbances and various psychosomatic phenomena, are not consistently assessed in every center across neurological diseases. Moreover, a lack of staff time or the inability to provide a tool to the patient ahead of a visit can be barriers to implementation.[59] Thus, site-specific processes are needed to optimize screening rates.[59]

In our experience, it is also important to consider neurological diseases in patients whose initial diagnosis is depression, because neurological conditions can be uncovered during an initial presentation of depression.[15,108,109] For example, depression is a common non-motor symptom of PD.[38] Indeed, one study from the literature revealed a high incidence of depression preceding a PD diagnosis.[39] A bidirectional association between major depression and migraine has also been suggested,[103] and the presence of either disease can increase the risk of onset for the other.[110] In cases where depression is reported after diagnosis of a neurological disease, it can be unclear whether the depressive symptoms first presented after the neurological diagnosis, or if the depression was uncovered during additional assessments following the neurological diagnosis. Caution should also be taken when screening for PD in patients with depression, because some psychiatric medications can interfere with diagnostic approaches.[111] Ideally, movement disorder specialists should be consulted prior to investigative approaches such as dopamine transporter imaging.[111]

Digital screening and monitoring tools can be useful for remote administration of validated symptom measures, longitudinal symptom and functional tracking, and telehealth-supported follow-up. Digital tools can support continuity of care and timely identification of clinical deterioration. The tools available vary by country and include applications like edupression (edupression.com).

Management Strategies

The substantial impact of depression in neurological diseases highlights the need for early recognition and appropriate treatment.[74,75] Management strategies depend on the severity of the depression and whether it is acute or chronic. In our experience, typical features of acute depression include a clear worsening of symptoms over days to months, which may be linked to a trigger, eg, brain trauma, neurological disease diagnosis, functional decline, sleep disruption, medication changes, or personal stressor In these cases, a risk assessment should be prioritized along with rapid stabilization of symptoms with therapy and a short-interval follow-up Per the UK National Institute for Health and Care Excellence (NICE) guidance, cases should be referred to psychiatry or specialist mental health services where psychotic symptoms or a risk of harm presents.[112] Chronic depression is typically characterized by: longstanding (≥2 years)[112] low mood, anhedonia, or hopelessness; normalized suffering ("this is just how I am now"); persistent functional erosion, social withdrawal, and/or treatment fatigue; and more complex comorbidity (eg, anxiety, insomnia, pain, substance use, personality traits, cognitive issues, or psychosocial stressors) Management for chronic depression usually needs a longer-term treatment plan, stepped care, and attention to contributing factors (such as sleep, pain, isolation, disability, caregiving burden, medication burden, or other personal stressors) Per NICE guidance, patients with neurological disease and chronic depression symptoms or severe depression should be referred to specialist mental health services for coordinated multidisciplinary care if their personal and social functioning is significantly impaired from depression and previous treatments have not improved symptoms.[112] Depression severity is a combination of symptoms, duration, and functional impact, not only symptom count.[112] Considerations regarding whether to apply standard outpatient care, crisis-level psychiatric care and home treatment teams, or inpatient care include both the severity of the depression and the supportability of the patient (Table 4). Crisis and home treatment teams should be used where there is a risk of harm

Table 4 Criteria for Outpatient versus Inpatient or Urgent Crisis-Level Psychiatric Care

Outpatient Care	Inpatient or Urgent Crisis-Level Psychiatric Care
• Depression is mild to moderate (or severe but stable) • No immediate danger to self/others • The patient can maintain basic self-care (food, fluids, medications, hygiene) • Reliable follow-up is possible • Social support exists (or can be mobilized) • Cognition/communication is sufficient for collaborative treatment • Neurological disease is medically stable enough for ambulatory psychiatric management • Risk is manageable and function is preserved enough	• Immediate suicide risk or high-risk self-harm • Severe depression with rapid deterioration and no safe support structure • Depression with psychotic symptoms (delusions/hallucinations) • Severe self-neglect or inability to eat or drink • Catatonia, severe agitation, or dangerous behavioral dyscontrol • Diagnostic uncertainty requiring intensive observation (eg, bipolar depression, delirium versus depression, steroid-related mood disorder, psychogenic nonepileptic seizures or functional symptoms with acute risk) • Failure of outpatient treatment with escalating risk • Outpatient monitoring unsafe due to neurological disease or other medical condition

or where the neurological disease impacts access to outpatient care. Inpatient treatment may be required for severe depression that cannot be supported by crisis and home treatment teams. In all cases, a multidisciplinary approach is ideal for optimal management and outcomes.

Patients not responding to initial antidepressant treatment should be identified early to determine additional or alternative treatments[69] Numerous studies in patients with neurological diseases have demonstrated that appropriate management of depression improves patient functioning and quality of life.[45,77,82,83,93–95,113–115] The literature analysis also revealed that SSRIs and SNRIs are the most commonly prescribed antidepressants. Of interest, a study found that patients taking SSRIs were more likely to have a favorable socio-demographic profile and a lower severity of depressive symptoms compared with patients taking other types of antidepressants.[116] The authors of this article speculated that experience with SSRIs in patient populations with favorable socio-demographic and clinical profiles may have influenced treatment choice, rather than relevant pharmacological differences in mechanisms of action between antidepressants.[116] In comparison, use of first-line SNRIs has been associated with patients with more severe MDD, although the SNRIs do not necessarily result in superior treatment outcomes compared with alternative antidepressants.[117] While SSRIs and SNRIs are commonly prescribed, it is important to assess which antidepressant may be the most relevant treatment for each patient on an individual basis, particularly given the complexity of the needs of many patients with neurological diseases and depression. Key considerations for treatment include the individual nature of the symptoms, efficacy and safety, co-occurring conditions, and managing comedications, especially in elderly patients.[118] In older people, both untreated depression and antidepressant use can increase fall risk.[119] Antidepressant side effects that can contribute to fall risk include orthostatic hypotension, sedation, and electrolyte changes.[119] For patients with co-existing migraine, higher rates of inferior treatment outcomes have been reported so caution should be taken to avoid insufficient treatment.[104] Insufficient treatment is unfortunately still frequent, potentially due to a fear of the serotonergic syndrome, which is very rare, since it can be elegantly avoided by selection of appropriate augmentation and combination treatments avoiding polypharmacy including SSRIs, SNRIs and tranylcypromine.[120,121] While patient numbers were low and varied, the literature analysis highlighted the potentially beneficial effect of a range of antidepressant drug classes for treatment of post-stroke depression and PD, including SSRIs (paroxetine and fluoxetine), SNRIs (duloxetine), SARIs (trazodone), TCAs (nortriptyline).[84,86–88,93–95] Therefore, antidepressant options can be tailored based on the drug properties, disease characteristics and patient needs. In our view, trazodone in particular is a safe and effective first-line choice for depression in patients with neurological diseases, particularly those with co-occurring anxiety, agitation or sleep disorders.[122] Trazodone has better tolerability than other treatment options in terms of body weight, cognitive disturbances, and sexual dysfunction,[123] and has few drug–drug interactions.[122] As with all drug classes, adverse events must be carefully monitored, especially in vulnerable elderly patients. Slowly up-titrating the drug and administering drugs with sedative effects before bedtime can improve tolerability.[122]

In our experience, electroconvulsive therapy (ECT) can be useful in selected cases of depression in patients with neurological diseases, for example in patients not responding to conventional antidepressants or esketamine,

those with severe depression and psychotic symptoms, or organic catatonia. It has been reported that ECT can improve motor symptoms in patients with PD beyond impact on psychiatric symptoms.[124] It should be noted that ECT is often contraindicated after stroke, in patients with acute vascular events or who have structural changes in the brain. In practice, there are important country-specific differences in use of ECT – this approach is more commonly used in Northern Europe, particularly in Scandinavia as well as in Egypt, but rarely used in other countries such as Italy. Exercise can also be a valuable intervention that often results in improvements in both depression and the neurological condition. It is also important to proactively manage sleep dysfunction when it occurs as part of the symptomology of depression or a neurological disease.

We note that loss of patients to follow-up is common in post-stroke, especially once patients are discharged from rehabilitation care. Given that depression commonly reoccurs and relapses, ongoing follow-up and monitoring over time is important, especially in the context of chronic progressive neurological conditions.

Multidisciplinary Care

The literature search identified no articles focused on multidisciplinary care for patients with neurological diseases and depression. In our opinion, multidisciplinary care, including neurologists, psychiatrists, primary care physicians, specialist nurses, physiotherapists, psychotherapists, and patient associations and social services where appropriate, can optimize patient management.[115] However, such care is often impractical due to limited resources. Management flows involving different specialties should be optimized at individual centers based on practicalities and costs, with a view to multidisciplinary care wherever possible. It is of benefit for neurologists and psychiatrists to work together in partnership, both from a clinical point of view, and in sharing ideas and suggestions for management in scientific meetings and discussions. In order to enable early improvement and optimal treatment outcomes of the individual clinical manifestations, the multidisciplinary approach should be employed during the entire diagnostic/treatment process to avoid disease progression, treatment resistance and chronicity. Psychiatric consultation is especially critical in cases of resistant or severe depression.

Future Considerations

Implementation of screening protocols is needed to optimize the identification of patients with neurological diseases and depression. The current PHQ-9, HADS, or BDI questionnaires can be recommended since they are easy to implement in routine clinical practice. Development and provision of structured interview scripts and simple screening tools would additionally be helpful in this regard. Further development of screening tools that account for the overlapping symptoms of depression and neurological diseases is also needed.[125] In the future, devices combined with artificial intelligence could further help monitor symptoms and functionality, and provide useful information to patients.

Our literature analysis confirmed that the evidence base is currently uneven across neurological conditions, with more extensive data for depression in patients with stroke and PD than multiple sclerosis and migraine. We have observed that depression is common in multiple sclerosis and highly clinically relevant, but study designs and outcomes are heterogeneous, and many patients remain undertreated or symptomatic despite treatment in real-world care. For migraine, psychiatric comorbidity is frequent[45] and clinically meaningful, but condition-specific depression treatment pathways and interventional evidence remain comparatively limited, and the literature is often focused on association rather than integrated management. Further high-quality evidence is required on managing depression in multiple sclerosis and migraine and in a range of other neurological disorders currently underrepresented in the literature, such as myelitis, neuropathy, myopathy, and functional neurological disorder. There is a need for: additional condition-specific prospective and interventional studies on various treatment options for depression in different neurological disorders; harmonized outcome measures, including on functional outcomes and quality of life; studies that better address symptom overlap (eg, fatigue, sleep disturbance, cognitive symptoms, and apathy) to inform differential diagnosis; and implementation research testing integrated neurology–psychiatry/primary care pathways in real-world settings Filling these knowledge and evidence gaps is important for avoiding overgeneralization while preserving the clinical usefulness of a transdiagnostic framework. Our recommendations are partly generalizable across conditions at the level of clinical care principles (ie, routine screening or case identification, risk assessment, attention to symptom overlap, stepped care, collaborative management, and longitudinal follow-up), but clinical

implementation must be adapted to disease-specific characteristics (eg, symptom phenomenology, cognitive burden, disability, disease course, and treatment context).

Limitations

As with any research based on a literature search, other pertinent articles may not have been retrieved using the selected search string The exclusion of non-global studies outside of North America and Europe is also a limitation of the study, and additional guidelines accounting for region-specific environments are needed. Depression can present differently in different world regions and in low-resource settings, and family roles, stigma, and access to care shape outcomes. Moreover, multidisciplinary care is not practical in most clinics in low-resource settings. The focus on stroke, Parkinson's disease, multiple sclerosis, and migraine, and the absence of other neurological disorders from the article is an additional limitation. The few studies found on depression in patients with migraine also limits the evidence-based information for this condition.

Conclusion

In this article we focus on depression in stroke, PD, multiple sclerosis, and migraine as models of neurological diseases. While information on migraine and some other neurological diseases is limited, overall, we believe that neurological diseases and depression should be viewed together and the interplay between them should be considered when deciding upon the most appropriate treatment. Collaboration between neurologists and psychiatrists is important during the entire diagnostic and treatment process to avoid disease progression and the development of chronicity and treatment resistance. Considering overall brain health and individual needs for each patient seems to be crucial to optimize outcomes. Treatments need assessing for the benefit-risk ratio based on individual disease and patient characteristics. The suggestions provided in this article work best in well-resourced settings, and local adaptation is needed for low-resource or culturally different contexts.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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