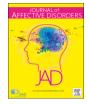
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Review article Assessment of perimenopausal depression: A review

Jasmine Willi^{a,b}, Ulrike Ehlert^{a,b,*}

^a Clinical Psychology and Psychotherapy, University of Zurich, Binzmühlestrasse 14, Zurich 8050, Switzerland
^b URPP Dynamics of Healthy Aging Research Priority Program, University of Zurich, Zurich, Switzerland

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ABSTRACT

Keywords: Background: Within the female life cycle, the perimenopause is considered as a critical period for the devel-Perimenopausal depression opment of depression. Prevalence rates are particularly high during this phase. Perimenopausal depression is Female depression characterized by affective symptoms as well as menopause-specific somatic complaints. Currently, a variety of Assessment questionnaires are used to assess mood during the perimenopause. The aim of this review is to determine the Depression scale instruments employed to assess perimenopausal depression. Methods: We searched the databases PubMed, Cochrane Library and PsycINFO for human studies investigating perimenopausal depression, and subsequently screened for the assessment instruments used to measure mood and menopause. A total of 37 articles were included. Results: Altogether, 14 different instruments were applied to assess mood during menopause. The CES-D was by far the most frequently used depression scale, appearing in 16 out of the 37 studies. The methods used to identify perimenopausal status and symptoms were inconsistent. Limitations: Due to lacking information about data and methodology, a selection bias is conceivable. Additionally, a publication bias is possible. Finally, there is inevitable subjectivity in the screening process of a systematic search. Conclusions: The assessment of depression in the menopausal transition is highly heterogeneous, reducing the overall comparability of study results. Furthermore, menopausal complaints are not sufficiently taken into account. Accordingly, the use of a menopause-specific depression scale is highly recommended in order to account for physical and mood-related symptoms in the menopausal transition.

1. Background

Depression has become the leading cause of disease-related disability among women in the world today (Kessler, 2003; Lopez and Murray, 1998). The prevalence of depression is at least twice as high in women as in men (Kessler, 2003; Seedat et al., 2009; Weissman et al., 1993), and it has been demonstrated that a variety of well-known risk factors for depression are strongly associated with female gender (Kühner, 2001; Nolen-Hoeksema, 1990; Riecher-Rössler, 2010). As a consequence, the World Health Organization (WHO) has called for a reinforced endeavor to reduce this prevalence through gender-specific research and interventions (Lopez and Murray, 1998; Üstün et al., 2014).

Onset rates of depression among women appear to be particularly high during the reproductive transition phases (Cohen et al., 2006; Soares and Zitek, 2008) such as the late phase of the menstrual cycle (Hantsoo and Epperson, 2015; Reid, 2017), postpartum (Schiller et al., 2015; Steiner et al., 2003), and the menopausal transition (Becker et al.,

2007; Judd et al., 2012; Soares and Zitek, 2008).

The menopausal transition represents the passage from reproductive to non-reproductive life. Methods for defining the inception of perimenopause were presented over two decades ago by Brambilla and colleagues (Brambilla et al., 1994) and were further developed towards a distinct set of criteria by the Stages of Reproductive Aging Workshop (STRAW) (Soules et al., 2001). In accordance with the STRAW criteria, the perimenopause is defined as the time span between the first major variations in menstrual cycle length (i.e. variations greater than seven days different from the individual's normal cycle length) and the completion of 12 consecutive months without any menses (Soules et al., 2001). The anchor point of menopause is defined retrospectively after this 12 months of amenorrhea following the final menstrual period, and is itself followed by the postmenopausal phase (Soules et al., 2001). The menopausal transition is known to be a highly complex phase due to dynamic changes in sex hormones and reproductive function (Burger, 2002; Freeman et al., 2004a; Soares, 2010; Soares and Cohen, 2001). Furthermore, this period is characterized by a range of menopause-

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^{*} Corresponding author at: Clinical Psychology and Psychotherapy, University of Zurich, Binzmühlestrasse 14, Zurich 8050, Switzerland. *E-mail address*: u.ehlert@psychologie.uzh.ch (U. Ehlert).

specific complaints (Maki et al., 2018; Soares and Zitek, 2008; Woods and Mitchell, 1997) such as vasomotor symptoms (Joffe et al., 2002; Santoro, 2008; Seritan et al., 2010), sleep disturbances (Greenblum et al., 2013; Prairie et al., 2015; Shaver and Woods, 2015), vaginal dryness (Freeman et al., 2006; O'Neill and Eden, 2017), breast pain (Payne, 2003), joint pains (Bacon, 2017; Buckler, 2005), change in cognitive function and performance (Greendale and Derby, 2011; Weber et al., 2013), significant life stressors, or psychosocial challenges (Bromberger et al., 2011; Maartens et al., 2002; Woods et al., 2008). The variety of menopausal complaints co-occur and overlap with the presentation of mood disturbances during this stage (Maartens et al., 2002; Maki et al., 2018), leading to an increased risk of new or recurrent onset of depression (Bromberger et al., 2011; Cohen et al., 2006; Woods et al., 2008). Women with a history of depression, especially during prior reproduction-related phases of hormonal changes, exhibit an elevated risk of depression during the perimenopause (Bromberger et al., 2015; Gyllstrom et al., 2007; Soares and Cohen, 2001). Despite these findings, however, the notion of a menopauseassociated depression has been at the center of clinical and scientific debate for many years (Bromberger and Kravitz, 2011; Freeman et al., 2004b), resulting in a lack of clarity regarding the assessment and treatment of perimenopausal depression. To assess overall menopausal complaints, the Menopausal Rating Scale (MRS) has proven to be a reliable and repeatedly used instrument (Chedraui et al., 2007; Hauser et al., 1999). To assess perimenopausal depression, by contrast, various different screening measures are currently applied in the research (Maki et al., 2018; Zöllner et al., 2005). The purpose of this review is to identify and evaluate depression scales (i.e. self-report and externalrating questionnaires) used to assess perimenopausal depression.

2. Methods

2.1. Search strategy

A systematic literature search was conducted in the PubMed, Cochrane Library and PsycINFO databases to identify relevant records until September 2018. Keywords and subject headings were combined corresponding to the respective database thesaurus. The search string comprised the components (a) "perimenopause" and related terms, and (b) "depression" and synonyms. All searches were restricted to studies conducted in humans.

2.2. Screening and selection procedure

The following inclusion criteria were applied to the identified records: (a) women in the stage of menopausal transition, (b) assessment of mood-specific symptoms (i.e., depression or depressiveness). Exclusion criteria included comorbidities, pharmacological or hormonal treatment studies, investigation of women within the pre- or postmenopausal phase only, records reporting on the same sample, and missing or inconclusive information about strategies employed to assess mood. For the final selection, full-text reading of all remaining records was conducted to evaluate their eligibility. Finally, a subsequent search for additional articles within the reference section of the included records ensued. The screening and selection procedure is shown in Fig. 1.

2.3. Data extraction

Included articles were inspected for information about the first author, year of publication, country of study implementation, study design and duration, sample size, age and menopausal status of the study participants, and instruments used to assess perimenopausal mood disorder.

3. Results

3.1. Search results

Our search yielded 3041 records. Nine duplicates were excluded immediately. Therefore, a total of 3032 records were screened, of which 2966 were excluded because they did not present original research (e.g. reviews) or were considered irrelevant based on their title or abstract. Full-text assessment for eligibility of the remaining 66 records followed. Of these, 29 were excluded because participants had comorbid diagnoses, the studies were pharmacological or hormonal treatment studies, or the studies only assessed women in the pre- or postmenopausal phase. In total, 37 articles were considered eligible for inclusion in this review. Table 1 shows the characteristics of these studies.

3.2. General data

Eight longitudinal studies with a duration of 1 to 20 years as well as 29 cross-sectional studies were included, resulting altogether in 62'478 participants, aged 35–70 years. Two studies focused on perimenopausal women only, two on pre- and perimenopausal women, and six on periand postmenopausal women. A total of 26 studies investigated the pre-, peri- and postmenopause.

3.3. Menopausal characteristics

In 19 studies, the determination of the women's menopausal status was based on menstrual bleeding patterns; three studies conducted hormonal analyses to identify the perimenopausal status; eight research papers stated compliance with the STRAW criteria; and three records provided no information about the determination of menopausal stages.

3.4. Prevalence and risk factors of perimenopausal depression

The studies consistently reported a high prevalence of depression in the menopausal transition. Although some of the studies found no differences between the three stages of menopausal transition regarding depressive symptoms (Almeida et al., 2016; Anniverno et al., 2017; Bosworth et al., 2001; Zang et al., 2016), most reported a particularly high prevalence of depressive symptoms in the peri- or postmenopause (Bromberger et al., 2007; Campbell et al., 2017; Gonçalves et al., 2013; Jafari et al., 2014; Joffe et al., 2002; Juang et al., 2005; Lin et al., 2013; Maartens et al., 2002; Pimenta et al., 2016; Tangen and Mykletun, 2008; Terauchi et al., 2013; Yen et al., 2009; Zainal, 2008). Seven studies reported a prevalence peak during the perimenopause (Campbell et al., 2017; Gonçalves et al., 2013; Joffe et al., 2002; Lin et al., 2013; Tangen and Mykletun, 2008; Yen et al., 2009; Zainal, 2008). An association between climacteric symptoms and depression was found in 11 records (Bosworth et al., 2001; Chedraui et al., 2009; Gibbs et al., 2013; Hu et al., 2016; Juang et al., 2005; Kumari et al., 2005; Reed et al., 2009; Strauss, 2011; Terauchi et al., 2013; Wang et al., 2013; Zang et al., 2016). Two studies reported an association between sleep disturbances and depressive symptoms (Terauchi et al., 2013; Zang et al., 2016). Additionally, one study reported a positive correlation between depressed mood and the frequency of vasomotor and somatic symptoms (Borkoles et al., 2015). More specifically, one study found that severe vasomotor symptoms worsened depressive symptoms (Reed et al., 2009).

Lower educational and economic status were reported to be risk factors for perimenopausal depression in one study (Choi et al., 2004), while another found that negative life events increased the risk of depression (Gibbs et al., 2013). Two studies demonstrated a history of depression as a risk factor for the development of depression in the menopausal transition (Almeida et al., 2016; Gibbs et al., 2013). While one study found an association between premenstrual dysphoric disorder (PMDD) and perimenopausal depression (Richards et al., 2006),

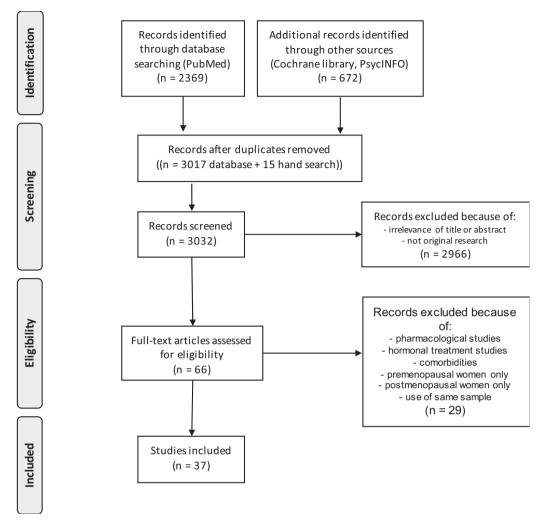


Fig. 1. PRISMA flow diagram.

another study did not reveal any relation between postpartum depression (PPD) or PMDD and perimenopausal depression (Steinberg et al., 2008).

3.5. Assessment of perimenopausal depression

Overall, a total of 14 different scales were used to assess mood across the implemented studies, although only six of them were repeatedly employed: Center of Epidemiological Studies Depression Scale (CES-D), Beck Depression Inventory (BDI), Greene Climacteric Scale (GCS), Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire (PHQ), and Hamilton Rating Scale for Depression (HAMD). Two studies used the Structured Clinical Interview for DSM-IV (SCID-I) as a pre-screening measurement (Cohen et al., 2006; Steinberg et al., 2008).

The CES-D was by far the most frequently used questionnaire, appearing in 16 out of the 37 studies. All of these studies, except for three (Choi et al., 2004; Gonçalves et al., 2013; Hickey et al., 2016), applied the suggested cut-off score of 16 (Radloff, 1977). The BDI was used in six studies, although no details were provided regarding the cut-off scores and the respective classification of severity of depressive symptoms. According to the NICE guidelines and the German S3-guidelines, a total score of 14 to 19 is considered as a mild depressive episode, 20 to 28 as moderate, and 29 to 63 as severe (DGPPN, BÄK, et al., 2009; NICE, 2009). While the suggested cut-off score for the GCS is set at 10 (Barentsen et al., 2001), there was no such information available from the three studies included in this review. Of the four studies using the

HADS, two implemented the recognized cut-off score of 8 (Juang et al., 2005; Tangen and Mykletun, 2008), while the other two provided no respective information (Almeida et al., 2016; Terauchi et al., 2013). Likewise, no respective data were reported for the three studies using the PHQ, for which a cut-off range of 8–11 is accepted (Manea et al., 2012). The HAMD was used in two studies, although only one of these assessed mood solely using this external rating questionnaire (Chedraui et al., 2009). The other study complemented the HAMD with the BDI and the GCS, which resulted in higher scores for self-reported depressive symptoms than for external rating (Anniverno et al., 2017). Fig. 2 shows the frequencies of the applied questionnaires to assess mood in the menopausal transition within the included records.

4. Discussion

Our findings substantiate the high prevalence of depressive symptoms in women during the transition to menopause. Especially within the peri- and the postmenopausal stage, symptoms of depression were frequently reported. However, the results were not consistent regarding the exact onset of depressive symptoms within the menopausal transition. This might be due to differing study designs, including different definitions of the three stages of menopausal transition, or deficient monitoring of physical and mood symptoms over a sufficient time period. Only a small number of studies applied the STRAW criteria, generally leading to a reduced comparability of study findings. Nevertheless, when viewing the results overall, there is substantial evidence of a prevalence peak of depressive symptoms in the

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Author	Country	Study design	Ν	Age	Menopausal status	Instrument menopause	Instrument depression
Almeida et al., 2016	USA	cross-sectional	1612	45–55	pre, peri, post	Bleeding pattern	PHQ-9, HADS
Anniverno et al., 2017	Italy	cross-sectional	156	45–65	peri, post	Bleeding pattern, GCS	BDI, HAMD, GCS
Arachna et al., 2017	India	cross-sectional	594	40-60	peri, post	Bleeding pattern	PHQ-9
Becht et al., 2001	Netherlands	cross-sectional	951	47–56	pre, peri	Bleeding pattern	EDS, RDC
Borkoles et al., 2015	Australia	cross-sectional	213	Ø 52	peri, post	Bleeding pattern	CES-D, WHQ
Bosworth et al., 2001	USA	cross-sectional	581	45–54	pre, peri, post	Bleeding pattern, hormonal analyses	CES-D
Chedraui et al., 2009	Ecuador	cross-sectional	404	40–59	pre, peri, post	Bleeding pattern	HAMD
Choi et al., 2004	Korea	cross-sectional	305	45–55	pre, peri, post	unknown	CES-D
Gibbs et al., 2013	Australia	cross-sectional	76	Ø 50	peri, post	Bleeding pattern, GCS	BDI, GCS
Gonçalves et al., 2013	Portugal	cross-sectional	728	45-64	pre, peri, post	Bleeding pattern, 13-item checklist	CES-D
Jafari et al., 2014	Iran	cross-sectional	218	35–55	pre, peri, post	unknown	BDI, SF-36
Joffe et al., 2002	USA	cross-sectional	584	40-60	pre, peri, post	Bleeding pattern	CES-D
Juang et al., 2005	Taiwan	cross-sectional	1273	40–54	pre, peri, post	Bleeding pattern	HADS
Kumari et al., 2005	England	cross-sectional	2489	39–64	pre, peri, post	Bleeding pattern	SF-36, GHQ
Li et al., 2006	China	cross-sectional	1062	40-60	peri	STRAW criteria, KI	KI, SDS
Li et al., 2008	China	cross-sectional	1280	45–59	pre, peri, post	Bleeding pattern	SDS
Lin et al., 2002	Taiwan	cross-sectional	3359	40–55	pre, peri, post	Bleeding pattern	TDQ
Maartens et al., 2002	Netherlands	cross-sectional	2103	Ø 50	pre, peri, post	Bleeding pattern	EDS
Mauas et al., 2014	Canada	cross-sectional	376	35-60	pre, peri, post	22-item questionnaire	BDI, DEQ
Pimenta et al., 2016	Portugal	cross-sectional	1003	42-60	pre, peri, post	STRAW criteria	DASS
Reed et al., 2009	USA	cross-sectional	1358	45–70	pre, peri, post	Wiklund Menopause Symptom Checklist	PHQ-8
Richards et al., 2006	USA	cross-sectional	105	40–55	peri	STRAW criteria	BDI
Steinberg et al., 2008	USA	cross-sectional	116	40–55	pre, peri, post	STRAW criteria	BDI, CES-D, SCID-D, PRIME-MD
Tangen et al., 2008	Norway	cross-sectional	16,080	35-60	pre, peri, post	Bleeding pattern	HADS
Terauchi et al., 2012	Japan	cross-sectional	237	40-64	peri, post	Bleeding pattern	HADS
Wang et al., 2013	Taiwan	cross-sectional	566	45-60	peri, post	WHI Symptom Scale	CES-D
Yen et al., 2009	Taiwan	cross-sectional	672	40-60	pre, peri, post	Bleeding pattern, GCS	CES-D, GCS
Zainal, 2016	China	cross-sectional	3934	45-60	pre, peri, post	Bleeding pattern	CES-D
Zang et al., 2008	Malaysia	cross-sectional	743	40-60	pre, peri, post	Bleeding pattern	SDS
Bromberger et al., 2007	USA	longitudinal, 5y	10,374	42–52	pre, peri, post	Bleeding pattern	CES-D
Campbell et al., 2017	Australia	longitudinal, 20y	438	45–55	pre, peri, post	STRAW criteria	Affectometer 2, CES-D
Cohen et al., 2006	USA	longitudinal, 7v	460	36 - 45	pre, peri, post	Bleeding pattern	SCID-1, CES-D
Freeman et al., 2006	USA	longitudinal, 8y	436	35-47	pre, peri	Bleeding pattern, hormonal analyses	CES-D, PRIME-MD
Gordon et al., 2016	USA	longitudinal, 1y	52	45-60	pre, peri, post	STRAW criteria	CES-D
Hickey et al., 2016	Australia	longitudinal, 3y	5895	45-50	pre, peri, post	STRAW criteria	CES-D
Strauss, 2011	USA	longitudinal, 9y	986	25-74	pre, peri, post	unknown	Free items about depression
Woods et al., 2006	USA	longitudinal, 15v	508	35-55	pre, peri, post	STRAW criteria, hormonal analyses	CES-D

BDI = Beck Depression Inventory, CES-D = Center of Epidemiological Studies Depression Scale, DASS = Depression Anxiety Stress Scales, DEQ = Depressive Experiences Questionnaire, EDS = Edinburgh Depression Scale, GCS = Greene Climacteric Scale, HADS = Hospital Anxiety and Depression Scale, HAMD = Hamilton Rating Scale for Depression, KI = Kupperman index, MADRS = Montgomery-Asberg Depression Rating Scale, PHQ = Patient Health Questionnaire, PRIME-MD = Primary Care Evaluation of Mental Disorders, RDC = Research Diagnostic Criteria, SCID-D = Structured Clinical Interview for DSM-IV, SDS = Zung Self-Rating Depression Scale, STRAW = Stages of Reproductive Aging Workshop, TDQ = Taiwanese Depression Questionnaire, WHI = Women's Health Initiative.

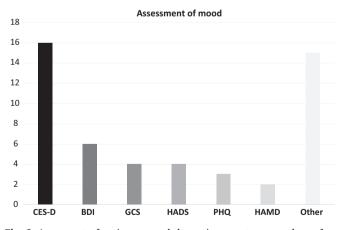


Fig. 2. Assessment of perimenopausal depressive symptoms: numbers of applied questionnaires.

perimenopausal phase. This finding suggests an increased risk of developing depression in the perimenopause and hence supports the hypothesis of perimenopausal depression as a distinct condition and a specific subtype of female depression.

A relationship between physiological climacteric symptoms and

depressive mood was demonstrated by the majority of studies included in this review. This finding appears to be crucial in terms of understanding the nature of perimenopausal depression. Studies have taken first steps towards exploring the interaction between somatic climacteric complaints and mood. Vasomotor complaints seem to have a major impact on the development and maintenance of depressive symptoms (Cohen et al., 2006; Freeman et al., 2004a; Woods et al., 2008). Furthermore, severe vasomotor symptoms appear to have an impact on depressive mood during the menopausal transition. The relationship between menopausal complaints and mood, however, seems to be complex in nature and is not yet fully understood. For instance, so far, research on the effect of depressive mood on the perception of menopausal complaints and vice versa has been sparse. Further insights into the relationship between the perception of climacteric symptoms and poor mood might provide important information about the development and maintenance of perimenopausal depression. While hormonal changes are known to have a strong influence on mood (Fiacco et al., 2018; Fischer et al., 2018; Girdler and Klatzkin, 2007; La Marca-Ghaemmaghami and Ehlert, 2015), the fluctuations in sex steroids in particular were shown to be related to the onset of depressed mood during the menopausal transition (Cohen et al., 2006; de Kruif et al., 2016; Freeman et al., 2006; Gordon et al., 2016). To gain a better understanding of this condition, research on potential risk factors of perimenopausal depression is of utmost interest. Previous

investigations predominantly focused on the history of depression, sleep disturbances, and negative life events (Almeida et al., 2016; Freeman et al., 2004b; Gibbs et al., 2013; Schmidt et al., 2004; Shaver et al., 2015; Studd and Nappi, 2012; Woods et al., 2008). Undoubtedly, however, there are still gaps in the knowledge regarding the underlying etiological factors of perimenopausal depression. The process of filling these gaps might not only contribute to a more profound understanding of this disorder, but should also serve to identify the symptom clusters which shape it.

A key finding of this work is that a variety of different depression scales are currently used to assess mood during the transition to menopause. The majority of studies investigating perimenopausal depression applied the standard depression scales used for the assessment of major depression symptoms. This might give an understanding of a certain range of symptoms and their individual severity (Bromberger & Epperson, 2018). However, it is doubtful whether these instruments meet the challenges of capturing and portraying the complex symptoms of women suffering from perimenopausal depression. Indeed, it appears to be essential to take into account all of the disorder-specific symptoms, including the highly prevalent somatic complaints. Until recently, a menopause-specific mood disorder scale did not exist (Maki et al., 2018). Kulkarni et al. (2018) succeeded to address this shortcoming by developing a precisely tailored assessment tool for perimenopausal depression: the Meno-D. This questionnaire, consisting of 12 items and five subscales, is suggested to be a valuable tool for clinicians and researchers to measure the presence and severity of depression in the perimenopause (Kulkarni et al., 2018). While there is fundamental agreement regarding the range of clinical symptoms of perimenopausal depression (Maki et al., 2018), a corresponding diagnosis is still lacking up to date.

4.1. Limitations

Several limitations should be considered when interpreting our findings. First, our search only yielded a restricted number of suitable records. As a consequence, a publication bias is probable. Second, as some of the records did not provide a full overview regarding data and methodology, a selection bias is conceivable. Third, the purpose of this study was to provide an overview of the assessment tools used to measure perimenopausal depression. Although a systematic approach was used for the literature search, there is inevitable subjectivity regarding the screening process and selection of eligible studies.

4.2. Implications and directions for future research

As a final conclusion, our findings demonstrate the need for further research regarding the development and the profile of perimenopausal depression. The previous lack of a menopause-specific questionnaire for the assessment of the complex symptoms of perimenopausal depression was demonstrated. This deficiency could recently be rectified by the development of the Meno-D. The implementation of such an assessment tool, measuring both the typical physical complaints and the depressive symptoms, is of utmost importance and highly recommended for future investigations. Furthermore, the reevaluation of the different symptom clusters as well as the establishment of a distinct diagnosis appear to be essential and should be addressed in further research. The combination of a precise diagnosis and the use of a corresponding assessment tool are of key importance with respect to the acknowledgement, identification and treatment of perimenopausal depression.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contributions

Conception: JW, UE Acquisition of data: JW Interpretation of data: JW, UE Drafting the manuscript: JW Critical revision: UE The authors declare no competing interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2019.02.029.

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