Acta Psychologica 241 (2023) 104078

Contents lists available at ScienceDirect

Acta Psychologica

journal homepage: www.elsevier.com/locate/actpsy

Longitudinal interactions between residual symptoms and physiological stress in the remitted symptom network structure of depression

Aoife Whiston[a,*], Eric R. Igou[a], Dònal G. Fortune[a], Analog Devices Team[b], Maria Semkovska[c]

[a] Department of Psychology, University of Limerick, Co., Limerick, Ireland
[b] Michael Collins, Integrated Precision, and Daniel Audesse, Digital Healthcare Systems at Analog Devices Inc., United States of America
[c] DeFREE Research Unit, Department of Psychology, University of Southern Denmark, Denmark

ARTICLE INFO

Keywords:
Depression
Relapse
Remission
Stress
Network models
Electrodermal activity
Wearable sensing

ABSTRACT

Residual symptoms and stress are amongst the most reliable predictors of relapse in remitted depression. Standard methodologies often preclude continuous stress sampling or the evaluation of complex symptom interactions. This limits knowledge acquisition relative to the day-to-day interactions between residual symptoms and stress. The study aims to explore the interactions between physiological stress and residual symptoms network structure in remitted depression. Twenty-two individuals remitted from depression completed baseline, daily diary (DD), and post-DD assessments. Self-reported stress and residual symptoms were measured at baseline and post-DD. Daily diaries required participants to use a wearable electrodermal activity (EDA) device during waking hours and complete residual symptom measures twice daily for 3-weeks. Two-step multilevel vector autoregression models were used to estimate contemporaneous and dynamic networks. Depressed mood and concentration problems were central across networks. Skin conductance responses (SCRs), suicide, appetite, and sleep problems were central in the temporal and energy loss in the contemporaneous network. Increased SCRs predicted decreased energy loss. Residual symptoms and stress showed bi-directional interactions. Overall, depressed mood and concentration problems were consistently central, thus potentially important intervention targets. Non-obtrusive bio-signal measures should be used to provide the clinical evidence-base for modelling the interactions between depressive residual symptoms and stress. Practical implications are discussed throughout related to focusing on symptom-specific interactions in clinical practice, simultaneously reducing residual symptom and stress occurrences, EDA as pioneering signal for stress detection, and the central role of specific residual symptoms in remitted depression.

1. Introduction

Depression is the leading cause of disability worldwide (WHO, 2018). Much of depression's disease burden is linked to the disorder's refractory nature (Greden, 2001). Depression relapse refers to the return of depressive symptoms after remission - not meeting major depressive disorder (MDD) syndrome criteria for 2–3 weeks (De Zwart et al., 2019; Frank et al., 1991; Monroe & Harkness, 2011). Current relapse estimates show those experiencing a first episode of depression have 50–60 % risk of experiencing a second episode. For subsequent episodes, relapse risk reaches 70–90 % (Burcusa & Iacono, 2007; Monroe & Harkness, 2012; Solomon et al., 2001). Whilst figures suggest a “relapse-remitting” course is the norm for depression, some cases are acute/time-limited (Buckman et al., 2018; Monroe & Harkness, 2012; Mueller et al., 1999). It is therefore important to address what factors contribute to a relapse-remitting course of depression. This study aims to explore interactions between two robust predictors of depression relapse – residual symptoms and stress, using a wearable technology and longitudinal network models over a three-week period.

Although predictors of depression relapse vary, research shows residual depression symptoms are a consistently robust relapse predictor (Faravelli et al., 1986; Paykel et al., 1995; Pintor et al., 2004; Simons et al., 1986; Teasdale et al., 2001; Van Londen et al., 1998). Residual depression symptoms are those that may persist, in milder forms, in remitted individuals following acute phase treatment (Judd et al., 1998; Paykel, 2007). Approximately 70–90 % of patients experience at least one residual symptom, potentially lasting one year after the index episode (Mojtabai & Olfson, 2004; Nierenberg et al., 2010; Wade et al.,

* Corresponding author.
E-mail address: aoife.whiston@ul.ie (A. Whiston).

https://doi.org/10.1016/j.actpsy.2023.104078
Received 28 March 2023; Received in revised form 16 October 2023; Accepted 4 November 2023
Available online 8 November 2023
0001-6918/

2009). These symptoms increase future relapse risk and impair psychological functioning (Mojtabai, 2001; Nierenberg et al., 2010). So far, research has identified fatigue, guilt, depressed mood, anxiety, cognitive, and sleep problems as common residual symptoms post-treatment (Fava et al., 2014; Nil et al., 2016; Sakurai et al., 2017; Wade et al., 2009). Although identifying post-treatment symptoms is important, research must now understand the complex relationships between residual symptoms and mechanisms linking symptoms to relapse (Rasmussen & Young, 2018).

Relating to mechanisms linking residual symptoms to depression relapse, research shows stress may play a central role (Harkness et al., 2014; Morris et al., 2012). Stress is the body's non-specific response to any demand for change (Selye, 1985). It is a complex response mechanism promoted by the sympathetic nervous system, hypothalamic pituitary adrenal axis (HPA), and the release of stress hormones- cortisol, adrenaline, and noradrenaline. These hormonal changes have been used in investigating stress, depression relapse, and residual symptoms (Bos, 2005; Gradl et al., 2019). For example, in remitted depression, Morris et al. (2012) identified greater residual symptoms at 35-weeks in those exhibiting higher cortisol reactivity to low stressors. Moreover, HPA axis dysfunction in response to stress consistently shows to be a risk for future relapse (Admon et al., 2015; Ahrens et al., 2008; Bockting et al., 2012; Chopra et al., 2008; Holsen et al., 2013; Morris et al., 2014). Much like earlier research, Morris et al. (2012) used saliva samples to measure stress. Saliva, blood, and urine samples, although gold standard stress observations, can be obtrusive and do not efficiently enable continuous sampling (Gradl et al., 2019). Thus, furthering understanding of the complex relationships between physiological stress and residual symptoms, requires time-intensive, complex modelling (Hammen, 2005), which is now possible due to longitudinal network models and wearable healthcare technologies.

Psychometric network modelling is a data-driven approach representing psychological constructs as systems of autonomous, interacting components (Borsboom & Cramer, 2013; McNally, 2016). Networks comprise nodes (e.g., residual symptoms) and edges– relationships between nodes (Robinaugh et al., 2020). In longitudinal networks, edges can be *temporal* whereby nodes predict measured components from one time point to the next, or *contemporaneous* referring to relationship between nodes within a timeframe (Epskamp et al., 2018). Network models of residual depression symptoms predominantly focus on identifying central symptoms- those with the most connections to others. These include loss of interest, loss of effort, feeling disliked, and concentration difficulties (Groen et al., 2019; Santos Jr et al., 2018). Network models have also made advancements in understanding interactions between depression and stress. For example, Aalbers et al. (2019) show that self-reported stress, mood, and concentration problems interact over time.

No study has explored longitudinal networks of physiological stress and residual symptoms in remitted depression. This may be due to the highly parsimonious data collection techniques required for longitudinal physiological stress measures (Gjoreski et al., 2017; Wichers et al., 2019). For example, although hormone tracking through blood, urine, or saliva is the gold standard for stress detection, in daily life, these could be considered obtrusive and impractical. However, bio-signals - physiological changes within the body induced by stress hormones, may prove a more feasible alternative (Gradl et al., 2019). Electrodermal activity (EDA) – a measurement of the change in electrical properties of the skin resulting from stress, is one of the most widely used bio-signals for stress detection (Can et al., 2019). EDA signals consist of two components: the skin conductance level (SCL)- slow-changing, underlying signal, and the skin conductance response (SCR)- faster signal changes in response to stressors (Hemmelmann, 2018). Wearable research-grade devices (e.g., ADI Study Watch) have now been developed, enabling continuous and unobtrusive EDA measures (Broeders, 2017; Yoshimoto & Izumi, 2019). These devices have been applied to various non-restricted daily-life studies, yielding stress detection accuracy ranges between 75 and 95 % (Gjoreski et al., 2016; Muaremi et al., 2014; Sano & Picard, 2013).

To date, only three studies have applied wearable EDA devices to depression research in daily life. Two studies show SCRs are more frequent, stronger, and predictive of depression severity in current depression (Ghandeharioun et al., 2017; Pedrelli et al., 2020). The third piloted the ADI Study Watch over seven days and showed greater SCRs on one day predicted an increase in residual symptoms on the next day in remitted depression (Anonymous, 2022). Conducted in preparation for the present study, this pilot provided preliminary results on stress and residual symptom interactions, suggesting that ADI Study Watch procedures can be successfully implemented. Due to the pilot's smaller sample, longitudinal network models could not be estimated. Thus, this study aims to explore interactions between stress and the residual symptom network structure of remitted depression using a wearable EDA device. Specifically, the research question aims to examine how specific residual symptom and stress interact over time in remitted depression?

2. Methods

This study was approved by the Faculty of Education and Health Science Ethics Committee, University of Limerick. Informed consent was obtained from all participants.

2.1. Design

This study was a prospective cohort design. Questionnaire data were captured at baseline and the three-week post-daily diary (post-DD) assessment. The prospective aspect involved daily assessments and physiological stress monitoring from baseline to post-DD. Daily diaries required participants to self-report depressive symptoms on their smartphones twice daily for three weeks. Physiological stress was also continuously measured by EDA using the ADI Study Watch.

2.2. Sample

The sample comprised 22 individuals, who met the following inclusion criteria: age $\geq$ 18 years; in remission from a primary MDD diagnosis (DSM-IV; APA, 2000) as confirmed with the Structured Clinical Interview for Depression (SCID; APA, 2000) conducted by author AW supervised by a clinical psychologist (DF); scored $<$20 on the Beck's Depression Inventory-II (BDI-II; Beck et al., 1961); received psychological (e.g., cognitive behavioural therapy; CBT), pharmacological (antidepressants; ADMs) or combined treatment (e.g., CBT + ADMs) for their last depressive episode(s). ADMs were permitted provided no recent (within 3 months) changes to dosage, or medication type; were proficient in English; smartphone owner; capability of providing informed consent and following research procedures. Exclusion criteria were: current diagnosis of MDD (APA, 2000), history of or current psychotic episode – due to elevated suicide risk (APA, 2000; Castelein et al., 2015), significant visual problems – due to mobile phone survey readability, and currently pregnant - due to associated changes in fluid distribution potentially confounding EDA signals (Kushner et al., 1996).

2.3. Procedure

2.3.1. Recruitment

This study started in June 2021. Due to COVID-19, recruitment posters were distributed via snowball sampling utilising the University of Limerick student population, personal and social networks. Interested individuals contacted the researcher via email to receive a study information pack that included a detailed information letter, research privacy notice, informed consent form, and a link to an online screening questionnaire.

2.3.2. Screening

Participants had the opportunity to ask questions before completing the online screening questionnaire. The participants signed an informed consent form that included consent to conduct daily diaries and consent to wear the ADI Study Watch for three weeks should eligibility be confirmed. The online screening tool included questions on participant demographics, previous depressive episode(s), and general health (e.g., comorbidities). Individuals returning consent forms, the screening questionnaire, and meeting inclusion criteria (2)–(7) were invited forward for SCID assessment to confirm no current MDD episode. Due to COVID-19, SCID's were conducted via telephone or Microsoft Teams.

2.3.3. Baseline and daily diaries

For individuals eligible to enter the study based on informed consent, screening questionnaire, BDI-II score, and SCID, their BDI-II (Cronbachs alpha; $a = 0.71$) assessment was used as a baseline assessment. The Patient Health Questionnaire-9 ($a = 0.63$; PHQ-9; Spitzer, 1999) and the stress subscale of the Depression Anxiety and Stress Scale-21 ($a = 0.72$; DASS-21-S; Lovibond & Lovibond, 1995) were also administered to measure self-reported stress and residual symptoms at baseline. Eligible participants then began the daily diaries for three weeks. As well as wearing the ADI Study Watch during waking hours for continuous EDA measures every morning (8:00 AM) and evening (8:00 PM), participants received an email directing them to a web-based diary questionnaire in a secure environment. Self-report daily diaries measured residual depression symptoms using the PHQ-9 presented in a random order to avoid practice effects. Diaries took approximately 5 min to complete. Participants had a three-hour window to fill in with a reminder delivered every hour. Evening diaries also asked participants to report any medication changes or procedural problems.

2.3.4. Post-daily diary (post-DD)

Upon completion of the three-week diary period, participants completed their post-DD assessment via email. Here, participants completed the BDI-II (a = 0.85), PHQ-9 (a = 0.77), and the DASS-21-S (a = 0.89). Then, participants were thanked, debriefed, and provided the opportunity to ask questions. Participants received the following financial compensation: €5 for week-one completion, an additional €10 for week two completion, and an additional €15 for week-three completion, resulting in a maximum potential payment of €30. See Fig. 1 for an overview of the study procedure and timeline.

2.4. Instruments

2.4.1. Daily diary self-report

Residual depression symptoms were measured using the PHQ-9 (Spitzer, 1999). This 9-item measure required participants to self-report depression symptom severity on a scale of 0–3. The PHQ-9 incorporates DSM-IV-TR (APA, 2000) MDD diagnostic criteria and captures the following residual depression symptoms: anhedonia, depressed mood, sleep problems, energy problems, appetite problems, guilt, concentration difficulties, psychomotor agitation/retardation, and suicidal ideation. The PHQ-9 was altered by asking participants to '*Indicate how much each statement applies to you RIGHT NOW?*' compared to the original time frame of the '*past-two weeks*'. This alteration was required to eliminate retrospective recall, which may be biased in the context of depression symptoms and offer real-time/real-world assessments of residual symptoms - reflective of ecological momentary assessment approaches (Torous et al., 2015).

2.4.2. ADI Study Watch

The ADI Study Watch is a battery-operated wrist-worn vital-signs monitor that includes technology simultaneously supporting motion tracking, biopotential, optical heart rate, bio-impedance, and temperature measurements (Broeders, 2018). Here, bio-impedance, specifically EDA, was the signal of interest. ADI's Study Watch EDA sensors detect minute changes in conductivity by using an alternating current (AC) applied over two dry electrodes (Broeders, 2017). ADI Study Watch EDA sensors work on a low power consumption rate (<80uA at an output rate of 4 Hz) and are specifically designed for a continuous (36–48 h) measurement of stress per charge (Broeders, 2018).

2.5. Data analysis

2.5.1. Comparison of baseline and post-DD assessments

Paired sample *t*-tests and Cohen's *d* were used to investigate whether BDI-II, PHQ-9, and DASS-42-S scores changed in the three weeks between baseline and post-DD.

2.5.2. EDA data cleaning and pre-processing

EDA data from the ADI Study Watch was transferred via USB to ADI's Vital Signs Monitoring program. Raw data logs were downloaded to a secure computer. The real part of admittance (conductance), provided in the unit of micro Siemens (μS) sampled at 4 Hz, was the signal measure used. This was necessary for use in artifact and skin conductance response (SCR) detection algorithms outlined below. EDA data were then sorted into separate csv files representing daily intervals for each participant. Each participant's daily interval EDA files were then analysed using 'EDA Explorer' Python scripts (Taylor et al., 2015). First, signals were run through EDA Explorers' artifact detection algorithm. Here, machine learning binary classifiers detect noise within EDA signals, labelling every 5 s of a signal as either 'containing artifact' (−1) or

Fig. 1. Overview of study timeline and procedures.

'containing no artifact' (1). Second, EDA signals were processed to detect SCRs and associated features, including 'EDA'– amplitude at the apex in μS, 'Amp'– amplitude of SCR, that is [amp = (EDA at apex)-(EDA at start of the SCR)] in μS, and 'Max_deriv'– maximum derivative of SCR in μS per second. As SCRs were the measure of interest, to ensure no artifacts were counted as SCRs, initially, only SCRs in 'containing no artifact' data were kept. However, as EDA Explorers' artifact detection method classifies entire 5-second intervals as 'containing artifact', it is possible clean SCRs could have occurred in this timeframe. Thus, SCRs within 'containing artifact' intervals were retained if they fell within two standard deviations of the 'EDA', 'Amp', and 'Max_deriv' of all 'clean' SCRs for each participant.

SCRs were then incorporated into daily diary AM and PM measures by calculating the average number of SCRs per hour within a +/− four-hour window of the participants' AM and PM survey completion time. This was necessary to maximise the use of EDA data obtained.

2.5.3. Network estimation

Network models were estimated for residual depression symptoms and SCRs using two-step multilevel vector auto-regression models (mlVAR; Bringmann et al., 2013; Epskamp et al., 2018). The mlVAR is a combination of both a vector auto-regression model, allowing for the repeated measures of variables within participants, with a multilevel model, allowing for the VAR coefficients to differ across participants (Bringmann et al., 2013). First, temporal networks estimated lag-one associations between residual symptoms and SCRs after controlling for all other lagged associations across individuals. Here, how well one variable predicts other variables (including itself) at the next time point accounting for all other variables is estimated– Granger causality (Granger, 1969). Second, contemporaneous networks estimated variable associations within the same timeframe controlling for all other variables and temporal associations. Here, associations between residual symptoms and SCRs that may occur at a faster pace than the temporal model time lag are estimated (Jordan et al., 2020). To make models computationally tractable, random effects were orthogonal; random slopes and intercepts were uncorrelated (Aalbers et al., 2019).

All networks were graphed using '*qgraph*', consisting of nodes- residual symptoms and SCRs, and edges- the statistical relationship between nodes (Epskamp et al., 2012). For temporal networks, edges were directed, indicated by arrows. Contemporaneous networks had undirected edges. Upon estimating networks, centrality indices- how influential a node is within the network, were investigated (Opsahl et al., 2010). For contemporaneous networks, *strength centrality* was obtained by calculating the sum of all edge weights. For temporal networks, the sum of edge weights of connections going out from a node, and *in-strength*, the sum of edge weights of incoming connections to a node, were calculated.

Importantly, mlVAR requires stationarity- stability of means and variances of variables over time. However, self-reports rarely meet this assumption (Bringmann et al., 2018; de Vos et al., 2017). Therefore, using '*tseries*' (Trapletti & Hornik, 2020), both the Kwiatkowski-Phillips-Schmidt-Shin test (KPSS; 1992) and augmented Dickey-Fuller (ADF; Dickey & Fuller, 1979) tests were used to examine diary stationarity (Jordan et al., 2020; Schlitzer, 1995). Combining tests was important as these tests show a greater likelihood of Type 1 errors (Cochrane, 1991). Upon conducting stationarity tests, it was decided not to detrend data due to only 16 % (KPSS; 32/200 trends) and 18 % (ADF; 36/200 trends) of data showing non-stationarity, very little overlap in results across tests– 8/68 trends common, and the exploratory nature of these analyses- detrending has potentially problematic consequences, limiting exploratory power of studies (Isvoranu et al., 2022).

Missing data for diaries were imputed using predictive mean matching (PMM)- estimates the likely values of missing data by matching to the observed data (Little, 1988). Self-report diaries were considered missing if they were: not answered, answered during or after the next survey's timeframe, or conducted within 4 h before the next diary. ADI Study watches diaries were considered missing if there was no watch data ±4 h around each participant's survey completion time. Prior to PMM, as missingness >10 % may lead to bias, participant diaries with >10 % missingness were compared to those with <10 % missingness using independent *t*-tests and x^2 tests on all baseline variables to investigate if data were missing at random (Bennett, 2001).

Finally, as the mlVAR model is considered relatively '*new*' formal power analyses have not been worked out based on intensive longitudinal data (Rosen et al., 2022). Thus, this study was required to follow the '*rules of thumb*' and '*normative reporting suggestions*' put forward across the network literature. This involved having between 20 and 50 timepoints per-participant to uncover directed edges whilst reducing the potential for Nickell's (1981) bias – presence of negative autoregressive effects (Jordan et al., 2020).

3. Results

3.1. Demographics

Twenty-two participants (15 Female, 7 Male) were recruited (Mage = 26.45, SD = 8.28, range 18–43). Seven participants were actively taking antidepressant medication(s) (ADMs; Agomelatine, $n = 1$; Bupropion, $n = 1$; Duloxetine, $n = 1$; Escitalopram, $n = 1$; Mirtazapine $n = 1$, Sertraline, $n = 3$). Five participants reported one or more past or current comorbid disorder(s) (Anxiety, $n = 4$; Eating, $n = 2$, Personality, $n = 1$; Post-Traumatic Stress, $n = 1$). Six participants were in full-time employment, three in part-time employment, and thirteen unemployed. See Table 1 for a participant-level breakdown.

3.2. Baseline to post-daily diary

Paired samples *t*-tests showed no significant differences in BDI-II, PHQ-9, and DASS-42-S scores from baseline to post-DD. Independent samples *t*-tests also showed no significant differences in baseline BDI-II and PHQ-9 scores across ADM, comorbidity, and gender categories, nor in baseline DASS-42-S scores across ADM and gender categories. However, participants with past or current comorbidities reported significantly higher stress on the DASS-42-S relative to those without comorbidities ($d = 1.62$). See Table 2.

3.3. Daily diaries

Two participants were excluded from daily diary analyses due to having 50 % of diaries missing and terminating the diary phase early. For the remaining diaries, the total self-report measure missingness was 4.88 % (range 0 %–23.81 %). Two participants had self-report missingness >10 %, and these data were assumed to be missing at random (see Table 1 for a participant-level breakdown).

3.3.1. ADI Study Watch data

The following describes the group-level averages for ADI Study Watch data (see Table 1 for a participant-level): 12 % ($N = 101/840$, range = 0 %–26 %) of dairies were missing at random across the sample, often due to user technical issues (e.g., letting the battery run out and forgetting to wear). Ten participants had ADI Study Watch missingness >10 %. Average numbers of SCRs was 16.15 per hour ($SD = 13.677$, range 0–118.87), SCRs had an average EDA level of 0.181 ($SD = 0.171$, range 0.0005–1.846). Average wear time ±4 h around diaries was 5.13 h ($SD = 0.86$). Although only clean SCRs were kept for analysis, the average percentage of artifacts varied considerably across the sample and was 20.02 % ($SD = 12.90$ %, range 1.69 %–52.02 %).

3.3.2. Residual symptoms and SCR's networks

Fig. 2 displays the temporal network - lag-one relations from one 8-hour window to the next. Table 3 shows a breakdown of network node names to PHQ-9 residual symptoms and stress. Significant ($p < 0.05$)

Table 1
Participant level descriptive statistics.

Participant number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Gender	Female	Female	Female	Female	Female	Male	Male	Male	Female	Female	Female	Female	Female	Female	Male	Female	Female	Female	Male	Male	Male	Female
ADM	No	No	No	No	Yes	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	No	No	No	No	No	No	Yes
Comorbidities	No	No	Yes	No	No	No	No	Yes	Yes	No	No	Yes	No	No	No	No	No	No	Yes	No	No	No
BDI-II																						
Baseline	2	19	17	8	19	17	9	5	19	9	12	11	15	7	8	17	1	12	18	13	7	10
Post-DD	2	6	13	11	11	22	15	22	27	14	20	9	15	4	7	14	1	17	5	9	8	4
DASS-42-S																						
Baseline	0	8	8	7	3	6	8	12	12	5	4	5	2	1	3	9	3	3	7	3	6	0
Post-DD	4	4	7	15	2	7	7	9	11	12	8	4	1	0	0	10	0	4	1	3	3	0
PHQ-9																						
Baseline	NA	7	8	11	13	8	6	3	13	4	5	10	5	2	4	11	0	3	8	5	3	3
Post-DD	1	1	8	5	9	8	10	8	13	9	12	5	6	4	3	16	1	10	3	5	6	2
Daily complete	41	41	42	NA	41	41	42	38	38	40	42	40	32	41	42	42	NA	39	33	41	42	41
Daily M	0.75	0.65	8.93	NA	8.37	10.15	9.11	2.55	10.39	4.98	8.38	3.53	3.19	0.71	1.36	15.74	NA	7.61	2.61	1.80	3.69	0.32
(SD)	(1.24)	(1.73)	(2.69)	NA	(3.15)	(1.85)	(0.50)	(3.03)	(4.81)	(2.90)	(3.28)	(2.23)	(1.57)	(0.90)	(1.97)	(3.38)	NA	(2.95)	(2.94)	(1.57)	(2.63)	(1.08)
ADI Study Watch																						
SCR M (SD)	14.22	16.38	20.31	NA	19.42	10.33	17.12	23.99	9.15	19.47	2.30	30.84	11.53	14.24	1.44	13.33	NA	29.99	16.34	17.19	7.34	35.03
	(5.20)	(10.55)	(11.99)	NA	(10.78)	(9.79)	(7.42)	(6.76)	(8.60)	(10.20)	(5.16)	(23.24)	(8.47)	(8.77)	(1.50)	(7.29)	NA	(10.87)	(11.56)	(8.20)	(6.67)	(17.12)
Artifact %	27.27	9.98	18.15	NA	35.47	6.31	20.71	26.18	9.11	8.21	52.02	18.52	12.07	33.89	5.11	23.32	NA	25.29	12.00	16.92	1.69	38.24
Hours	5.68	5.90	7.57	NA	5.17	5.42	3.58	4.15	4.48	5.17	4.83	5.07	5.61	4.90	3.89	4.61	NA	5.81	4.64	5.06	5.14	5.85
Daily Complete	38	42	33	NA	39	36	31	38	36	35	40	33	40	37	35	42	NA	28	40	40	41	34

Note: ADM = antidepressant medications; SCR = skin conductance responses, hours = average number of hours of ADI Study Watch wear time ±4 h around each diary measure; Post-DD = post-daily diary assessment.

Table 2
Descriptives and results of *t*-tests.

Scale	Mean	SD	Range	p
Baseline to post-DD descriptives				
BDI-II				
Baseline	11.59	5.52	1–19	
Post-DD	11.64	7.01	1–27	0.976
PHQ-9				
Baseline	6.29	3.70	0–13	
Post-DD	6.59	4.11	0–16	0.531
DASS-42-S				
Baseline	5.23	3.42	0–12	
Post-DD	5.09	4.36	0–15	0.853
Baseline comparisons				
Antidepressant medication				
BDI-II				
Yes	13.57	5.16		
No	10.67	5.60		0.260
PHQ-9				
Yes	6.86	4.60		
No	6.00	3.33		0.629
DASS-42-S				
Yes	3.86	4.06		
No	5.87	3.02		0.207
Comorbidities				
BDI-II				
Yes	14.00	5.92		
No	10.88	5.37		0.278
PHQ-9				
Yes	8.40	3.65		
No	5.63	3.58		0.148
DASS-42-S				
Yes	8.80	3.11		
No	4.18	2.79		0.004
Gender				
BDI-II				
Male	11.00	5.07		
Female	11.87	5.87		0.741
PHQ-9				
Male	5.29	2.14		
Female	6.79	4.26		0.548
DASS-42-S				
Male	6.43	3.10		
Female	4.67	3.52		0.271

Note: SD = standard deviation; Post-DD = post-daily diary assessments.

positive auto-regressive coefficients with the strongest edges were identified for *anhedonia* (edge weight; *ew* = 0.14), *guilt* (*ew* = 0.19), *sleep* (*ew* = 0.14), and *appetite* (*ew* = 0.23) problems. A positive auto-regressive coefficient was also identified for *SCRs* (*ew* = 0.10), although this did not reach significance. Significant, positive edges with the strongest edge weights were also observed from *anhedonia*- > depressed *mood* (*ew* = 0.15), *energy* loss- > depressed *mood* (*ew* = 0.12), and *concentrate* difficulty- > depressed *mood* (*ew* = 0.13). A negative edge was observed from *SCR*- > *energy* loss (*ew* = −0.06). Other positive edges with relatively strong edge weights not reaching significance included problems with *sleep*- > *suicide* (*ew* = 0.14) and *concentrate* difficulty- > *energy* loss (*ew* = 0.12). Regarding centrality, depressed *mood*, followed by *SCRs* and *suicide* showed the highest in-strength – greatest sum of edge weights of significant incoming connections. *Concentrate*, *appetite*, and *sleep* problems showed the highest - greatest sum of edge weights of significant connections going out from a node(s) (Fig. 3).

Fig. 2 also displays the contemporaneous network- relations amongst residual symptoms within the same timeframe controlling for all other variables and temporal associations. Positive edges with the strongest edge-weights reaching significance ($p < 0.05$) included *anhedonia*-depressed *mood* (*ew* = 0.28), *psychomotor-concentrate* difficulty (*ew* = 0.23), *energy* loss-psycho*motor* (*ew* = 0.20), and *energy* loss-*sleep* problems (*ew* = 0.14; Fig. 3). Residual symptoms with the highest strength centrality were depressed *mood*, *concentrate* difficulty, and *energy* loss.

4. Discussion

This is the first examination of the residual symptom network structure in remitted depression and its interactions with physiological stress using a wearable EDA device. For residual symptoms, *anhedonia*, *guilt*, *sleep*, and *appetite* problems showed positive autoregressive effects in the temporal network. Strongest edges were observed from *anhedonia*, *energy* loss, and *concentration* problems to depressed *mood* in the temporal network. In the contemporaneous network strongest edges were between *anhedonia*-depressed *mood*, *psychomotor-concentration* problems, and *energy* loss-*psychomotor*. Depressed *mood* and *concentration* problems were central across both temporal and contemporaneous networks. *SCRs*, *suicide*, *appetite*, and *sleep* problems were central in the temporal network. *Energy* loss was also central in the contemporaneous network. Regarding relationships between physiological stress and residual symptoms, increased *SCRs* predicted a decrease in *energy* loss and showed high in-strength centrality in the temporal network.

4.1. Residual symptoms

Across residual symptom networks, depressed *mood* and *anhedonia* were some of the most strongly connected and central residual symptoms, confirming previous post-treatment network models (Bos et al., 2018; Lorimer et al., 2020; Whiston et al., 2022). Regarding *anhedonia*, positive autoregressive coefficients in the temporal network show this symptom is self-sustaining. Thus, reporting *anhedonia* in one diary is associated with greater reporting of it in the next diary. Possible explanations for residual *anhedonia* may relate to research showing this symptom is resistant to certain pharmacotherapies. Alternatively, CBT may neglect this symptom with the primary aim of repairing negative cognitions (Cao et al., 2019; Dunn et al., 2019). Identifying residual *anhedonia* is important as this symptom appears chronic due to its' auto-regressive effects and its associations with increased feelings of depressed *mood* in the contemporaneous and temporal networks.

Further related to depressed *mood*, this symptom was central in the contemporaneous network and showed high in strength in the temporal network. Thus, depressed *mood* is reactive to other symptoms. For example, deterioration of depressed *mood* is likely to occur after other symptoms deteriorate. This result expands on previous temporal network models, whereby experiencing *anhedonia*, *energy* loss, or *concentration* problems in one diary all predicted greater depressed *mood* in the next (Bos et al., 2018; Savelieva et al., 2021). Identifying residual symptoms with high in-strength is important, as these are often end points of the spread of network activation, potentially indicating relapse risk. However, research does show targeting improvements in depressed *mood* is likely to trigger other symptom improvements (Savelieva et al., 2021). Strategies developed to specifically target these core MDD residual symptoms, such as augmented depression therapy (ADepT), could be considered as part of a stepped-care residual symptom intervention (Dunn et al., 2019).

Sleep and *appetite* problems were also prevailing residual symptoms, particularly in the temporal network, showing auto-regressive effects, high, and strong inter-connections. Thus, reporting *sleep* problems in one diary predicts an increase in both *sleep* and *appetite* problems in the next diary, with *appetite* problems becoming self-sustaining. Going beyond previous research showing prevalence rates of residual sleep and appetite problems reach 70 %, we show they are not only prevalent but complexly interact (Nierenberg et al., 2010). Explanations for this may relate to sleep problems' role in altering appetite-regulating hormones. Research shows *sleep* problems are chronic stressors activating the HPA axis– further observed here from the directed, although non-significant edge from *sleep*- > *SCR* (Yap et al., 2020). This HPA axis activation increases energy expenditure and metabolic rates, altering appetite (Lin et al., 2020; Vgontzas et al., 2014). Although the PHQ-9 does not enable speculation on whether insomnia (vs. hypersomnia) increases (vs. decreases) appetite, research consistently shows insomnia leads to

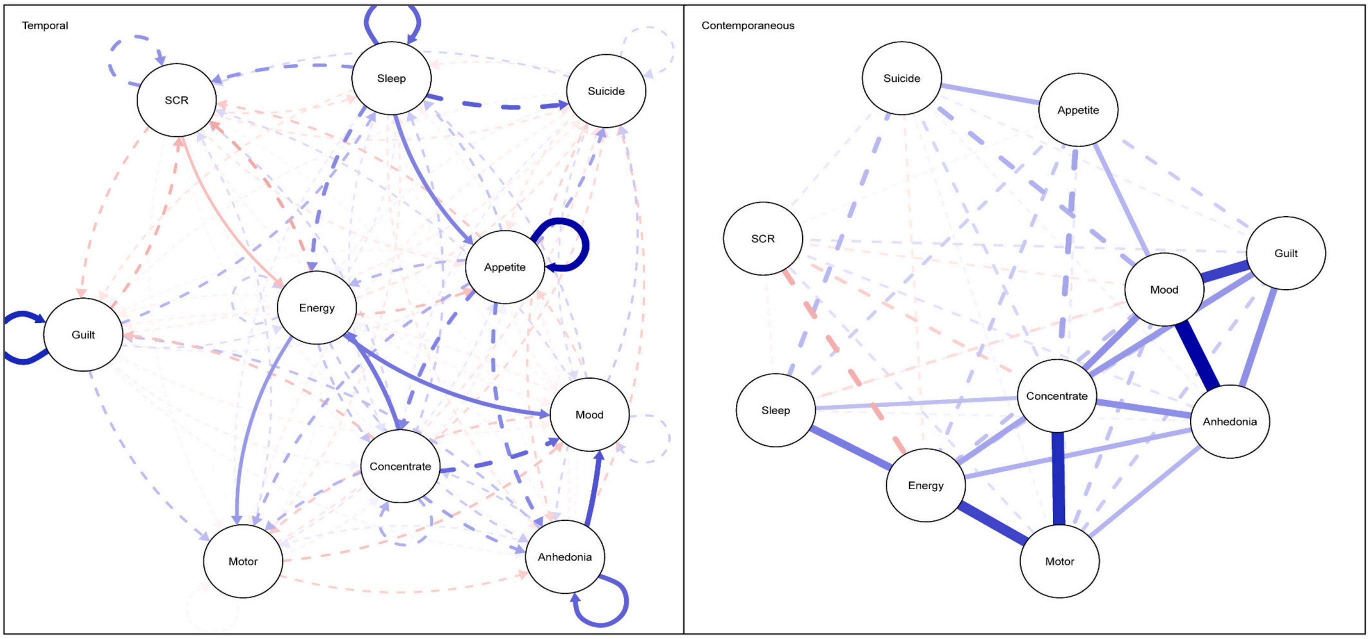

Fig. 2. Networks of residual symptom and skin conductance responses.
Note: Solid edges indicate significant edge-weights, and dashed edges indicate non-significant edge-weights. Blue edges indicate node activation, and red edges indicate node inhibition.

Table 3
Network node names to PHQ-9 symptoms and stress.

Node name	Symptom
Anhedonia	Anhedonia
Appetite	Appetite problems (poor appetite or overeating)
Concentrate	Trouble concentrating
Energy	Energy loss
Guilt	Guilty feelings, self-failure
Mood	Depressed mood
Motor	Psychomotor problems (agitation or retardation)
SCR	Skin conductance response (stress)
Sleep	Sleep problems (insomnia or hypersomnia)
Suicide	Suicidal thoughts

increased appetite (López-Gil et al., 2021). Nevertheless, identifying residual *sleep* and *appetite* problems is important, as both are sensitive biological rhythms often constituting prodromal relapse symptoms–evident by their high out-strength in the temporal network (Germain & Kupfer, 2008). Sleep-focused treatments alongside usual clinical management of residual symptoms may be required to target *sleep* problems and reduce the spread of network activation to depressed *mood* and *appetite* problems (Li et al., 2012).

Concentration problems were another prominent residual symptom, showing strong interconnectedness and high centrality across temporal and contemporaneous networks. This aligns with previous research showing depression remission is associated with persistent cognitive dysfunction, especially concerning selective attention (Semkovska et al., 2019), with the prevalence of residual *concentration* problems reaching 44 % (Conradi et al., 2011). Centrality and interconnectedness of residual *concentration* problems may relate to this symptom being less likely to respond to common depression treatments (Kaser et al., 2017). Alternatively, this symptom could also arise as an ADM side effect (Zajecka et al., 2013). However, ADM side effect explanations are unlikely for current results, with only seven participants taking ADMs. Even so, identifying residual *concentration* problems is important, high out-strength of this symptom means its' activation has stronger exacerbating effects on other symptoms, leaving networks potentially vulnerable to relapse (Lorimer et al., 2020). Our findings also align with recent meta-analytical evidence suggesting that attentional biases slow down psychomotor processing in depression remitters (Semkovska, 2021). This is shown here, whereby *concentration* problems predicted *energy* loss in the temporal network and showed strong co-occurrences with psycho*motor* problems, *anhedonia*, and depressed *mood* in the contemporaneous network.

4.2. Physiological stress and residual symptoms

Physiological stress, operationalized as *SCRs*, shows significant associations with residual *energy* loss. That is, increased *SCRs* at one diary predicted a decrease in *energy* loss at the next. This finding is consistent with research showing depression may result from inefficient energy regulation in response to stress (Arnaldo et al., 2022). Specifically, when faced with stressors, the sympathetic nervous system and HPA axis are activated, providing additional energy resources for the collection of new information. In adaptive stress responses, once this stressor is no longer threatening, the HPA axis should inhibit itself via a negative feedback loop (Heim et al., 2008). This is not observed here with a positive, although non-significant feedback loop from *SCRs*, consistent with research showing potential HPA axis dysfunction in remitted depression (Admon et al., 2015; Ahrens et al., 2008; Bockting et al., 2012; Chopra et al., 2008; Holsen et al., 2013; Morris et al., 2014). This repeated engagement of stress reactions overrules adaptive values of stress leading to the perseverance of energy, which may result in pervasive negative affect, anhedonia, and depression risk (Arnaldo et al., 2022). Identifying this link between *SCRs* and *energy* loss is important as it gives insight into one possible path from depression remission to potential relapse, and the perseverance of energy resources may also lead to immunosuppressant effects having further health consequences (Coutinho & Chapman, 2011).

Surprisingly, *SCRs* also show high in-strength in the temporal network, suggesting that deterioration of *SCRs* is likely to occur following the deterioration of other symptoms. This may relate to the stress generation hypothesis (Hammen, 2005): depression symptoms, behavioural tendencies, and cognitive characteristics are not just products of stress but are also likely to lead to greater stress (Liu, 2013). Research shows that stress generation is not specific to current

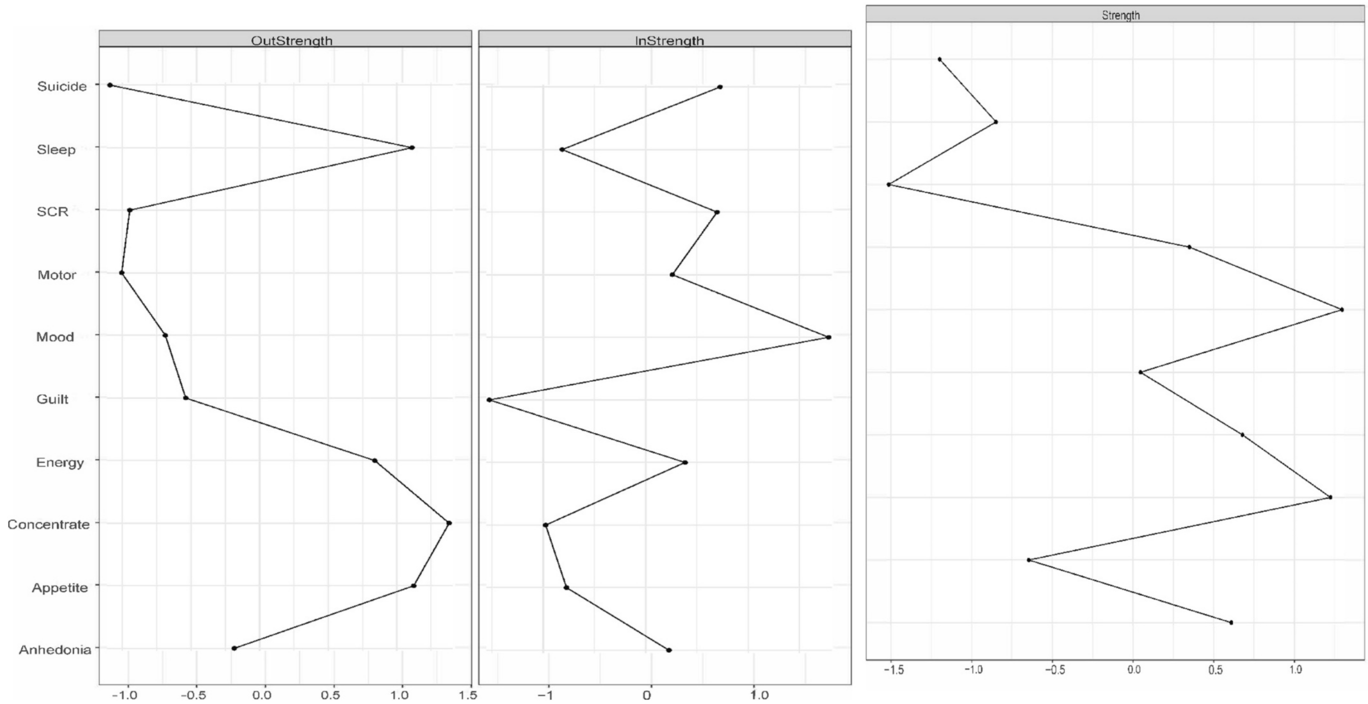

Fig. 3. Centrality plots of residual symptoms and skin conductance responses.
Note: "OutStrength" and "InStrength" represent centrality indices for the temporal network. "Strength" represents centrality for the contemporaneous network.

depression but also persists in remission, acting as a potential explanatory mechanism underlying relapse (Hammen, 2005; Wen et al., 2021). However, all residual symptoms predicting *SCRs* at the next time-point despite showing moderately strong edge weights do not reach significance. Identifying *SCRs*' high in-strength is important as it provides support for the stress generation and, taken together with *SCRs* predicting *energy* loss, supports research showing relationships between stress and residual symptoms are bi-directional (Hammen, 2005; Liu, 2013).

4.3. *Clinical implications*

Clinical implications of the current study are fourfold. First, results suggest complex causal interactions between depressive symptoms and the environment in remission. This highlights the importance of focusing on symptom-specific interactions in clinical practice. For example, using cognitive behavioural interventions to reduce occurrences amongst fatigue related symptoms (*sleep* problems - > *energy* loss). Second, results provide strong support for bi-directional residual symptom and stress interactions. For remitted depression, simultaneously reducing residual symptoms and stress occurrences may have greater impact on reducing relapse risk – e.g., via mindfulness-based stress reduction or cognitive therapy techniques (Querstret et al., 2020). Third, EDA quantified reliably physiological stress as it is exclusively produced by the sympathetic autonomic nervous system (Tronstad et al., 2022). Potential exists for the integration of EDA stress classification systems into commercial sensing technologies for real-time early detection and preventative measures related to stress and depression. Finally, a recurring aspect across results was the central role of specific residual symptoms - *depressed mood, anhedonia, sleep, appetite*, and *concentration*. Drawing on the centrality hypothesis – the most central nodes are the best intervention targets; it may be advisable to focus first-line depression treatments or relapse prevention strategies on these central symptoms (Lunansky et al., 2022). Subsequent research is required to further explore the validity of the centrality hypothesis and identify which clinical interventions may be most impactful on key network elements.

4.4. *Research contributions*

This study is the first to examine links between residual symptoms and stress in remitted depression using wearable technology designed specifically for continuous EDA measures and network models developed specifically for uncovering complex associations between multivariate data. It builds on previous research by showing specific residual symptoms– *depressed mood, anhedonia, sleep, appetite*, and *concentration* problems remain central and strongly connected during remission. Moreover, the study goes beyond existing research by showing elevated *SCRs* in daily life may be a biomarker for residual symptomology due to their high in-strength and bi-directional symptom interrelations. Future research should first extend SCRs monitoring to make claims on depression relapse, and second, confirm current *SCR* findings utilising either the same or a combination of other bio-signals (e.g., heart-rate variability). Nevertheless, we hope current results provide the first steps towards disentangling the role of residual symptomology and physiological stress in remitted depression.

4.5. *Limitations*

Although the PHQ-9 is designed to cover DSM-IV depression symptom criterion, it does not contain detailed information on three bidirectional symptoms- *sleep*, *appetite*, and psycho*motor* problems. Therefore, when participants report *sleep* problems, one cannot distinguish insomnia from hypersomnia (Fried et al., 2014). As it is plausible bi-directional symptoms arise from different aetiologies, future studies should seek more information on bi-directional symptoms.

Participants were predominantly students, thus limiting generalizations. Moreover, almost a quarter of participants reported comorbid disorders, potentially influencing results. Whilst excluding comorbidities is common in controlled trials, it does not reflect real-world depression (Westen et al., 2004). Subsequent studies with other samples should continue allowing comorbidities- reflecting depression reality- to enable comprehensive explorations of residual symptoms and stress.

Monitoring EDA in "real life" conditions as opposed to a laboratory setting meant physiological signals were potentially more sensitive to specific environmental events and conditions – e.g., temperature changes and pressure or movement artifacts (Zahmat Doost & Zhang, 2023). Whilst ambulatory EDA data is inherently noisy, the current study applied EDA Explorers' peak and artifact detection algorithms which shows to accurately detect SCRs in the presence of artifacts and the absence of temperature or accelerometer data.

The EDA Explorers' artifact algorithm detected noise within the data, labelling every 5 s as 'containing artifact' or 'containing no artifact' (Taylor et al., 2015). Although EDA Explorers' peak detection algorithm proves accurate in artifact-rich datasets, the same has not been shown for the artifact detection algorithm. Often, artifacts are overestimated. Resultantly, clean SCRs occurring within five second intervals 'containing artifacts' could potentially be missed (Hemmelmann, 2018). However, the current study employed a manual inspection technique whereby SCRs within 'containing artifact' intervals were kept provided they fell within two standard deviations of the 'EDA', 'Amp', and 'Max_deriv' of all 'clean' SCRs for each participant. Thus, it is unlikely the potential over-estimation of artifacts impacted current SCRs results presented.

The ADI Study Watch includes technology simultaneously supporting motion tracking, biopotential, optical heart rate, bio-impedance, and temperature measurement (Broeders, 2018). Here, EDA was the only signal measured. This was a trade-off between collecting more signals or reducing (a) study burden for participants and (b) technological demands placed on the device. Only measuring EDA required participants to charge the ADI Study Watch once every 48 h, with the flash memory lasting beyond 3 weeks. Nevertheless, subsequent studies should explore these findings using different bio-signals alone or in combination.

Although the number of measurement points per-person was satisfactory and did not lead to Nickell's (1981) bias, a limitation of the study is sample size. To date, neither formal power analyses nor R packages to estimate the stability and accuracy of group-level network models based on intensive longitudinal data exist (Rosen et al., 2022; Schumacher et al., 2022). Thus, this study followed the '*rules of thumb*' heuristic currently used across the literature to determine the minimum acceptable data availability for the conduct of longitudinal network analyses, namely disposing with at least 20–50 timepoints per participant (Jordan et al., 2020). Moreover, due to the exploratory nature of this study and the potential of not uncovering all significant edges a larger sample might do, current results graphed both significant and non-significant edge weights. Replication of current results is encouraged using a larger sample size.

Finally, temporal networks represent Granger causality (Granger, 1969). Temporal relationships should not be interpreted as direct causality. For example, were variables measured at the correct timeframe, or did we capture residual symptoms and stress with valid measures (Fried, 2020)? Thus, whilst this study is exploratory, its value lies in generating hypotheses on interactions between residual symptoms and stress.

4.6. Conclusion

Our results have important clinical and research implications. Specifically, residual symptoms not only persist in remitted depression but are dynamic in their centrality and co-occurrences. Stress - *SCRs*, shows high in-strength and predicts reduced *loss of energy* at the next time point. These bi-directional residual symptom and stress relations both show to be associated with future relapse risk. *Depressed mood* and *concentration* problems also show high centrality across networks. These symptoms may be associated with the start – *concentration* problems, and end – *depressed mood* of network activation, leaving networks further vulnerable to relapse. Thus, relapse prevention strategies or first-line treatments targeting these central residual symptoms and reducing stress may impact reducing relapse risk. Moreover, due to the availability of wearable devices and free algorithms, greater analyses of bio-signals are an important step for psychological research. Overall, we hope this study gives further insight and provides hypotheses-generating work on interactions between physiological stress and the residual symptom network structure of remitted depression using a wearable EDA device.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Aoife Whiston reports financial support was provided by Irish Research Council and Analog Devices Inc. through the IRC Enterprise Partnership Scheme (EPSPG/2020/487).

Data availability

Data will be made available on request.

References

Aalbers, G., McNally, R. J., Heeren, A., De Wit, S., & Fried, E. I. (2019). Social media and depression symptoms: A network perspective. *Journal of Experimental Psychology: General, 148*(8), 1454 (LINK).
Admon, R., Holsen, L. M., Aizley, H., Remington, A., Whitfield-Gabrieli, S., Goldstein, J. M., & Pizzagalli, D. A. (2015). Striatal hypersensitivity during stress in remitted individuals with recurrent depression. *Biological Psychiatry, 78*(1), 67–76. https://doi.org/10.1016/j.biopsych.2014.09.019
Ahrens, T., Deuschle, M., Krumm, B., van der Pompe, G., den Boer, J. A., & Lederbogen, F. (2008). Pituitary-adrenal and sympathetic nervous system responses to stress in women remitted from recurrent major depression. *Psychosomatic Medicine, 70*(4), 461–467. https://doi.org/10.1097/PSY.0b013e31816b1aaa
American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR*.
[Anonymous 2022] Details omitted for double-anonymized reviewing.
Arnaldo, I., Corcoran, A. W., Friston, K. J., & Ramstead, M. J. (2022). Stress and its sequelae: An active inference account of the etiological pathway from allostatic overload to depression. *Neuroscience & Biobehavioral Reviews, 104590*. https://doi.org/10.1016/j.neubiorev.2022.104590
Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4*(6), 561–571. https://doi.org/10.1001/archpsyc.1961.01710120031004
Bennett, D. A. (2001). How can I deal with missing data in my study? *Australian and New Zealand Journal of Public Health, 25*(5), 464–469. https://doi.org/10.1111/j.1467-842X.2001.tb00294.x
Bockting, C. L., Lok, A., Visser, I., Assies, J., Koeter, M. W., Schene, A. H., & DELTA Study Group. (2012). Lower cortisol levels predict recurrence in remitted patients with recurrent depression: A 5.5 year prospective study. *Psychiatry Research, 200*(2–3), 281–287. https://doi.org/10.1016/j.psychres.2012.03.044
Borsboom, D., & Cramer, A. O. (2013). Network analysis: An integrative approach to the structure of psychopathology. *Annual Review of Clinical Psychology, 9*, 91–121. https://doi.org/10.1146/annurev-clinpsy-050212-185608
Bos, E. H. (2005). Interpersonal mechanisms in recurrence of depression. University Library Groningen[Host]. https://pure.rug.nl/ws/portalfiles/portal/2899430/c1.pdf.
Bos, F. M., Fried, E. I., Hollon, S. D., Bringmann, L. F., Dimidjian, S., DeRubeis, R. J., & Bockting, C. L. (2018). Cross-sectional networks of depressive symptoms before and after antidepressant medication treatment. *Social Psychiatry and Psychiatric Epidemiology, 53*(6), 617–627. https://doi.org/10.1007/s00127-018-1506-1
Bringmann, L. F., Ferrer, E., Hamaker, E. L., Borsboom, D., & Tuerlinckx, F. (2018). Modeling nonstationary emotion dynamics in dyads using a time-varying vector-autoregressive model. *Multivariate Behavioral Research, 53*(3), 293–314. https://doi.org/10.1080/00273171.2018.1439722
Bringmann, L. F., Vissers, N., Wichers, M., Geschwind, N., Kuppens, P., Peeters, F., … Tuerlinckx, F. (2013). A network approach to psychopathology: New insights into clinical longitudinal data. *Plos One, 8*(4), Article e60188. https://doi.org/10.1371/journal.pone.0060188
Broeders, J. (2017). The sensors behind the GEN II wearable device. Retrieved from Analog Devices International website: https://www.analog.com/en/technical-articles/the-sensors-behind-the-gen-ii-wearable-device.html.
Broeders, J. (2018). Jack of all trades in impedance measurement. Retrieved from Analog Devices International website: https://www.analog.com/en/technical-articles/jack-of-all-trades-in-impedance-measurement.html.
Buckman, J. E. J., Underwood, A., Clarke, K., Saunders, R., Hollon, S. D., Fearon, P., & Pilling, S. (2018). Risk factors for relapse and recurrence of depression in adults and how they operate: A four-phase systematic review and meta-synthesis. *Clinical Psychology Review*. https://doi.org/10.1016/j.cpr.2018.07.005
Burcusa, S. L., & Iacono, W. G. (2007). Risk for recurrence in depression. *Clinical Psychology Review, 27*(8), 959–985. https://doi.org/10.1016/j.cpr.2007.02.005

Can, Y. S., Arnrich, B., & Ersoy, C. (2019). Stress detection in daily life scenarios using smart phones and wearable sensors: A survey. *Journal of Biomedical Informatics, 103139*. https://doi.org/10.1016/j.jbi.2019.103139

Cao, B., Zhu, J., Zuckerman, H., Rosenblat, J. D., Brietzke, E., Pan, Z., … McIntyre, R. S. (2019). Pharmacological interventions targeting anhedonia in patients with major depressive disorder: A systematic review. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 92*, 109–117. https://doi.org/10.1016/j.pnpbp.2019.01.002

Castelein, S., Liemburg, E. J., De Lange, J. S., Van Es, F. D., Visser, E., Aleman, A., … Knegtering, H. (2015). Suicide revisited: Significant reduction of suicide rate over the last two decades—A replication study of a Dutch incidence cohort with recent onset psychosis. *European Psychiatry, 30*(S1), 1. https://doi.org/10.1016/S0924-9338(15)30760-4

Chopra, K. K., Segal, Z. V., Buis, T., Kennedy, S. H., & Levitan, R. D. (2008). Investigating associations between cortisol and cognitive reactivity to sad mood provocation and the prediction of relapse in remitted major depression. *Asian Journal of Psychiatry, 1* (2), 33–36. https://doi.org/10.1016/j.ajp.2008.09.006

Cochrane, J. H. (1991). A critique of the application of unit root tests. *Journal of Economic Dynamics and Control, 15*, 275–284. https://doi.org/10.1016/0165-1889(91)90013-q

Conradi, H. J., Ormel, J., & De Jonge, P. (2011). Presence of individual (residual) symptoms during depressive episodes and periods of remission: A 3-year prospective study. *Psychological Medicine, 41*(6), 1165–1174. https://doi.org/10.1017/S0033291710001911

Coutinho, A. E., & Chapman, K. E. (2011). The anti-inflammatory and immunosuppressive effects of glucocorticoids, recent developments and mechanistic insights. *Molecular and Cellular Endocrinology, 335*(1), 2–13. https://doi.org/10.1016/j.mce.2010.04.005

de Vos, S., Wardenaar, K. J., Bos, E. H., Wit, E. C., Bouwmans, M. E. J., de Jonge, P., & Waldorp, L. J. (2017). An investigation of emotion dynamics in major depressive disorder patients and healthy persons using sparse longitudinal networks. *Plos One, 12*(6). https://doi.org/10.1371/journal.pone.0178586 (Artic).

de Zwart, P. L., Jeronimus, B. F., & de Jonge, P. (2019). Empirical evidence for definitions of episode, remission, recovery, relapse and recurrence in depression: A systematic review. *Epidemiology and Psychiatric Sciences, 28*(5), 544–562. https://doi.org/10.1017/S2045796018000227

Dickey, D. A., & Fuller, W. A. (1979). Distribution of the estimators for autoregressive time series with a unit root. *Journal of the American Statistical Association, 74*, 427–431. https://doi.org/10.1080/01621459.1979.10482531

Dunn, B. D., Widnall, E., Reed, N., Owens, C., Campbell, J., & Kuyken, W. (2019). Bringing light into darkness: A multiple baseline mixed methods case series evaluation of Augmented Depression Therapy (ADepT). *Behaviour Research and Therapy, 120*, Article 103418. https://doi.org/10.1016/j.brat.2019.103418

Epskamp, S., Cramer, A. O., Waldorp, L. J., Schmittmann, V. D., & Borsboom, D. (2012). qgraph: Network visualizations of relationships in psychometric data. *Journal of Statistical Software, 48*(4), 1–18. https://doi.org/10.18637/jss.v048.i04

Epskamp, S., Waldorp, L. J., Mõttus, R., & Borsboom, D. (2018). The Gaussian graphical model in cross-sectional and time-series data. *Multivariate Behavioral Research, 53*(4), 453–480. https://doi.org/10.1080/00273171.2018.1454823

Faravelli, C., Ambonetti, A., Pallanti, S., & Pazzagli, A. (1986). Depressive relapses and incomplete recovery from index episode. *The American Journal of Psychiatry, 143*(7), 888–891. https://doi.org/10.1176/ajp.143.7.888

Fava, M., Ball, S., Nelson, J. C., Sparks, J., Konechnik, T., Classi, P., … Thase, M. E. (2014). Clinical relevance of fatigue as a residual symptom in major depressive disorder. *Depression and Anxiety, 31*(3), 250–257. https://doi.org/10.1002/da.22199

Frank, E., Prien, R. F., Jarrett, R. B., Keller, M. B., Kupfer, D. J., Lavori, P. W., … Weissman, M. M. (1991). Conceptualization and rationale for consensus definitions of terms in major depressive disorder: Remission, recovery, relapse, and recurrence. *Archives of General Psychiatry, 48*(9), 851–855. https://doi.org/10.1001/archpsyc.1991.01810330075011

Fried, E. I. (2020). Theories and models: What they are, what they are for, and what they are about. *Psychological Inquiry, 31*(4), 336–344. https://doi.org/10.1080/1047840X.2020.1854011

Fried, E. I., Nesse, R. M., Zivin, K., Guille, C., & Sen, S. (2014). Depression is more than the sum score of its parts: Individual DSM symptoms have different risk factors. *Psychological Medicine, 44*(10), 2067–2076. https://doi.org/10.1017/S0033291713002900

Germain, A., & Kupfer, D. J. (2008). Circadian rhythm disturbances in depression. *Human Psychopharmacology: Clinical and Experimental, 23*(7), 571–585. https://doi.org/10.1002/hup.964

Ghandeharioun, A., Fedor, S., Sangermano, L., Ionescu, D., Alpert, J., Dale, C., … Picard, R. (2017, October). Objective assessment of depressive symptoms with machine learning and wearable sensors data. In *2017 seventh international conference on affective computing and intelligent interaction (ACII)* (pp. 325–332). IEEE. https://doi.org/10.1109/ACII.2017.8273620.

Gjoreski, M., Gjoreski, H., Luštrek, M., & Gams, M. (2016, September). Continuous stress detection using a wrist device: In laboratory and real life. In *Proceedings of the 2016 ACM International Joint Conference on Pervasive and Ubiquitous Computing: Adjunct* (pp. 1185–1193). ACM. https://doi.org/10.1145/2968219.2968306.

Gjoreski, M., Luštrek, M., Gams, M., & Gjoreski, H. (2017). Monitoring stress with a wrist device using context. *Journal of Biomedical Informatics, 73*, 159–170. https://doi.org/10.1016/j.jbi.2017.08.006

Gradl, S., Wirth, M., Richer, R., Rohleder, N., & Eskofier, B. M. (2019, May). An overview of the feasibility of permanent, real-time, unobtrusive stress measurement with current wearables. In *Proceedings of the 13th EAI International Conference on Pervasive Computing Technologies for Healthcare* (pp. 360–365). ACM. https://doi.org/10.1145/3329189.3329233.

Granger, C. W. (1969). Investigating causal relations by econometric models and cross-spectral methods. *Econometrica: Journal of the Econometric Society*, 424–438. https://doi.org/10.2307/1912791

Greden, J. F. (2001). The burden of recurrent depression: Causes, consequences, and future prospects. *Journal of Clinical Psychiatry, 62*, 5–9.

Groen, R. N., Snippe, E., Bringmann, L. F., Simons, C. J., Hartmann, J. A., Bos, E. H., & Wichers, M. (2019). Capturing the risk of persisting depressive symptoms: A dynamic network investigation of patients' daily symptom experiences. *Psychiatry Research, 271*, 640–648. https://doi.org/10.1016/j.psychres.2018.12.054

Hammen, C. (2005). Stress and depression. *Annual Review of Clinical Psychology, 1*, 293–319. https://doi.org/10.1146/annurev.clinpsy.1.102803.143938

Harkness, K. L., Theriault, J. E., Stewart, J. G., & Bagby, R. M. (2014). Acute and chronic stress exposure predicts 1-year recurrence in adult outpatients with residual depression symptoms following response to treatment. *Depression and Anxiety, 31*(1), 1. https://doi.org/10.1002/da.22177

Heim, C., Newport, D. J., Mletzko, T., Miller, A. H., & Nemeroff, C. B. (2008). The link between childhood trauma and depression: Insights from HPA axis studies in humans. *Psychoneuroendocrinology, 33*(6), 693–710. https://doi.org/10.1016/j.psyneuen.2008.03.008

Hemmelmann, J. H. (2018). Validity of the EDA-Explorer as a means for artifact rejection and peak detection in electro dermal activity data-analysis (Master's thesis). University of Twente. https://essay.utwente.nl/76114/.

Holsen, L. M., Lancaster, K., Klibanski, A., Whitfield-Gabrieli, S., Cherkerzian, S., Buka, S., & Goldstein, J. M. (2013). HPA-axis hormone modulation of stress response circuitry activity in women with remitted major depression. *Neuroscience, 250*, 733–742. https://doi.org/10.1016/j.neuroscience.2013.07.042

Isvoranu, A.-M., Epskamp, S., Waldorp, L. J., & Borsboom, D. (2022). *Network psychometrics with R: A guide for behavioral and social scientists*. New York: Routledge.

Jordan, D. G., Winer, E. S., & Salem, T. (2020). The current status of temporal network analysis for clinical science: Considerations as the paradigm shifts? *Journal of Clinical Psychology, 76*(9), 1591–1612. https://doi.org/10.1002/jclp.22957

Judd, L. L., Akiskal, H. S., Maser, J. D., Zeller, P. J., Endicott, J., Coryell, W., … Rice, J. A. (1998). Major depressive disorder: A prospective study of residual subthreshold depressive symptoms as predictor of rapid relapse. *Journal of Affective Disorders, 50* (2–3), 97–108. https://doi.org/10.1016/S0165-0327(98)00138-4

Kaser, M., Zaman, R., & Sahakian, B. J. (2017). Cognition as a treatment target in depression. *Psychological Medicine, 47*(6), 987–989. https://doi.org/10.1017/S0033291716003123

Kushner, R. F., Gudivaka, R., & Schoeller, D. A. (1996). Clinical characteristics influencing bioelectrical impedance analysis measurements. *The American Journal of Clinical Nutrition, 64*(3), 423S–427S. https://doi.org/10.1093/ajcn/64.3.423S

Li, S. X., Lam, S. P., Chan, J. W., Yu, M. W., & Wing, Y. K. (2012). Residual sleep disturbances in patients remitted from major depressive disorder: A 4-year naturalistic follow-up study. *Sleep, 35*(8), 1153–1161. https://doi.org/10.5665/sleep.2008

Lin, J., Jiang, Y., Wang, G., Meng, M., Zhu, Q., Mei, H., … Jiang, F. (2020). Associations of short sleep duration with appetite-regulating hormones and adipokines: A systematic review and meta-analysis. *Obesity Reviews, 21*(11), Article e13051. https://doi.org/10.1111/obr.13051

Little, R. J. (1988). Missing-data adjustments in large surveys. *Journal of Business & Economic Statistics, 6*(3), 287–296. https://doi.org/10.1080/07350015.1988.10509663

Liu, R. T. (2013). Stress generation: Future directions and clinical implications. *Clinical Psychology Review, 33*(3), 406–416. https://doi.org/10.1016/j.cpr.2013.01.005

López-Gil, J. F., Gaya, A. R., Reuter, C. P., Caetano, C. I., Sentone, R. G., Caetano, H. B. S., & Brazo-Sayavera, J. (2021). Sleep-related problems and eating habits during COVID-19 lockdown in a southern Brazilian youth sample. *Sleep Medicine, 85*, 150–156. https://doi.org/10.1016/j.sleep.2021.07.003

Lorimer, B., Delgadillo, J., Kellett, S., & Brown, G. (2020). Exploring relapse through a network analysis of residual depression and anxiety symptoms after cognitive behavioural therapy: A proof-of-concept study. *Psychotherapy Research, 30*(5), 650–661. https://doi.org/10.1080/10503307.2019.1650980

Lovibond, P. F., & Lovibond, S. H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy, 33*(3), 335–343. https://doi.org/10.1016/0005-7967(94)00075-U

Lunansky, G., Naberman, J., van Borkulo, C. D., Chen, C., Wang, L., & Borsboom, D. (2022). Intervening on psychopathology networks: Evaluating intervention targets through simulations. *Methods, 204*, 29–37. https://doi.org/10.1016/j.ymeth.2021.11.006

McNally, R. J. (2016). Can network analysis transform psychopathology? *Behaviour Research and Therapy, 86*, 95–104. https://doi.org/10.1016/j.brat.2016.06.006

Mojtabai, R. (2001). Residual symptoms and impairment in major depression in the community. *American Journal of Psychiatry, 158*(10), 1645–1651. https://doi.org/10.1176/appi.ajp.158.10.1645

Mojtabai, R., & Olfson, M. (2004). Major depression in community-dwelling middle-aged and older adults: Prevalence and 2-and 4-year follow-up symptoms. *Psychological Medicine, 34*(4), 623–634. https://doi.org/10.1017/S0033291703001764

Monroe, S. M., & Harkness, K. L. (2011). Recurrence in major depression: A conceptual analysis. *Psychological Review, 118*(4), 655. https://doi.org/10.1037/a0025190

Monroe, S. M., & Harkness, K. L. (2012). Is depression a chronic mental illness? *Psychological Medicine, 42*(5), 899–902. https://doi.org/10.1017/S0033291711002066

Morris, M. C., Kouros, C. D., Hellman, N., Rao, U., & Garber, J. (2014). Two prospective studies of changes in stress generation across depressive episodes in adolescents and

emerging adults. *Development and Psychopathology, 26*(4pt2), 1385–1400. https://doi.org/10.1017/S0954579414001096
Morris, M. C., Rao, U., & Garber, J. (2012). Cortisol responses to psychosocial stress predict depression trajectories: Social-evaluative threat and prior depressive episodes as moderators. *Journal of Affective Disorders, 143*(1–3), 223–230. https://doi.org/10.1016/j.jad.2012.05.059
Muaremi, A., Bexheti, A., Gravenhorst, F., Arnrich, B., & Tröster, G. (2014, June). Monitoring the impact of stress on the sleep patterns of pilgrims using wearable sensors. In *IEEE-EMBS international conference on biomedical and health informatics (BHI)* (pp. 185–188). IEEE. https://doi.org/10.1109/BHI.2014.6864335.
Mueller, T. I., Leon, A. C., Keller, M. B., Solomon, D. A., Endicott, J., Coryell, W., … Maser, J. D. (1999). Recurrence after recovery from major depressive disorder during 15 years of observational follow-up. *American Journal of Psychiatry, 156*(7), 1000–1006. https://doi.org/10.1176/ajp.156.7.1000
Nickell, S. (1981). Biases in dynamic models with fixed effects. *Econometrica: Journal of the Econometric Society*, 1417–1426. https://doi.org/10.2307/1911408
Nierenberg, A. A., Husain, M. M., Trivedi, M. H., Fava, M., Warden, D., Wisniewski, S. R., … Rush, A. J. (2010). Residual symptoms after remission of major depressive disorder with citalopram and risk of relapse: A STAR* D report. *Psychological Medicine, 40*(1), 41–50. https://doi.org/10.1017/S0033291709006011
Nil, R., Lütolf, S., & Seifritz, E. (2016). Residual symptoms and functionality in depressed outpatients: A one-year observational study in Switzerland with escitalopram. *Journal of Affective Disorders, 197*. https://doi.org/10.1016/j.jad.2016.02.062 (245-25).
Opsahl, T., Agneessens, F., & Skvoretz, J. (2010). Node centrality in weighted networks: Generalizing degree and shortest paths. *Social Networks, 32*(3), 245–251. https://doi.org/10.1016/j.socnet.2010.03.006
Paykel, E. S. (2007). Cognitive therapy in relapse prevention in depression. *International Journal of Neuropsychopharmacology, 10*(1), 131–136. https://doi.org/10.1017/S1461145706006912
Paykel, E. S., Ramana, R., Cooper, Z., Hayhurst, H., Kerr, J., & Barocka, A. (1995). Residual symptoms after partial remission: An important outcome in depression. *Psychological Medicine, 25*(6), 1171–1180. https://doi.org/10.1017/S0033291700033146
Pedrelli, P., Fedor, S., Ghandeharioun, A., Howe, E., Ionescu, D. F., Bhathena, D., … Picard, R. W. (2020). Monitoring changes in depression severity using wearable and mobile sensors. *Frontiers in Psychiatry, 1413*. https://doi.org/10.3389/fpsyt.2020.584711
Pintor, L., Torres, X., Navarro, V., Matrai, S., & Gastó, C. (2004). Is the type of remission after a major depressive episode an important risk factor to relapses in a 4-year follow up? *Journal of Affective Disorders, 82*(2), 291–296. https://doi.org/10.1016/j.jad.2003.11.008
Querstret, D., Morison, L., Dickinson, S., Cropley, M., & John, M. (2020). Mindfulness-based stress reduction and mindfulness-based cognitive therapy for psychological health and well-being in nonclinical samples: A systematic review and meta-analysis. *International Journal of Stress Management, 27*(4), 394. https://doi.org/10.1037/str0000165
Rasmussen, J., & Young, A. H. (2018). Challenges of residual symptoms and functioning in management of MDD. *Progress in Neurology and Psychiatry, 22*(3), 6–8. https://doi.org/10.1002/pnp.505
Robinaugh, D. J., Hoekstra, R. H., Toner, E. R., & Borsboom, D. (2020). The network approach to psychopathology: A review of the literature 2008–2018 and an agenda for future research. *Psychological Medicine, 50*(3), 353–366. https://doi.org/10.1017/S0033291719003404
Rosen, M., Betz, L. T., Montag, C., Kannen, C., & Kambeitz, J. (2022). Transdiagnostic psychopathology in a help-seeking population of an early recognition center for mental disorders: Protocol for an experience sampling study. *JMIR Research Protocols, 11*(8), Article e35206. https://doi.org/10.2196/35206
Sakurai, H., Suzuki, T., Yoshimura, K., Mimura, M., & Uchida, H. (2017). Predicting relapse with individual residual symptoms in major depressive disorder: A reanalysis of the STAR* D data. *Psychopharmacology, 234*(16), 2453–2461. https://doi.org/10.1007/s00213-017-4634-5
Sano, A., & Picard, R. W. (2013, September). Stress recognition using wearable sensors and mobile phones. In *2013 Humaine Association Conference on Affective Computing and Intelligent Interaction* (pp. 671–676). IEEE. https://doi.org/10.1109/ACII.2013.117.
Santos, H. P., Jr., Kossakowski, J. J., Schwartz, T. A., Beeber, L., & Fried, E. I. (2018). Longitudinal network structure of depression symptoms and self-efficacy in low-income mothers. *Plos One, 13*(1), Article e0191675. https://doi.org/10.1371/journal.pone.0191675
Savelieva, K., Komulainen, K., Elovainio, M., & Jokela, M. (2021). Longitudinal associations between specific symptoms of depression: Network analysis in a prospective cohort study. *Journal of Affective Disorders, 278*, 99–106. https://doi.org/10.1016/j.jad.2020.09.024
Schlitzer, G. (1995). Testing the stationarity of economic time series: Further Monte Carlo evidence. *Ricerche Economiche, 49*, 125–144. https://doi.org/10.1016/0035-5054(95)90019-5
Schumacher, L., Burger, J., Echterhoff, J., & Kriston, L. (2022). *Methodological and statistical practices of using symptom networks to evaluate mental health interventions: A systematic review*. https://doi.org/10.31234/osf.io/ea7fu
Selye, H. (1985). The nature of stress. *Basal Facts, 7*(1), 3–11.
Semkovska, M. (2021). Cognitive function and neurocognitive deficits in depression. Chapter 33. In C. Martin, L. Hunter, V. Patel, V. Preedy, & R. Rajendram (Eds.), *Vol. I. Neuroscience of depression* (pp. 361–371).
Semkovska, M., Quinlivan, L., O'Grady, T., Johnson, R., Collins, A., O'Connor, J., … Gload, T. (2019). Cognitive function following a major depressive episode: A systematic review and meta-analysis. *The Lancet Psychiatry, 6*(10), 851–861. https://doi.org/10.1016/S2215-0366(19)30291-3
Simons, A. D., Murphy, G. E., Levine, J. L., & Wetzel, R. D. (1986). Cognitive therapy and pharmacotherapy for depression: Sustained improvement over one year. *Archives of General Psychiatry, 43*(1), 43–48. https://doi.org/10.1001/archpsyc.1986.01800010045006
Solomon, D. A., Keller, M. B., & Leon, A. C. (2001). Multiple recurrences of major depressive disorder. In *, 2001(1). Year book of psychiatry and applied mental health* (pp. 257–258).
Spitzer, R. L. (1999). *Patient health questionnaire: PHQ*. New York: New York State Psychiatric Institute.
Taylor, S., Jaques, N., Chen, W., Fedor, S., Sano, A., & Picard, R. (2015, August). Automatic identification of artifacts in electrodermal activity data. In *2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* (pp. 1934–1937). IEEE. https://doi.org/10.1109/EMBC.2015.7318.
Teasdale, J. D., Scott, J., Moore, R. G., Hayhurst, H., Pope, M., & Paykel, E. S. (2001). How does cognitive therapy prevent relapse in residual depression? Evidence from a controlled trial. *Journal of Consulting and Clinical Psychology, 69*(3), 347. https://doi.org/10.1037/0022-006X.69.3.347
Torous, J., Staples, P., Shanahan, M., Lin, C., Peck, P., Keshavan, M., & Onnela, J. P. (2015). Utilizing a personal smartphone custom app to assess the patient health questionnaire-9 (PHQ-9) depressive symptoms in patients with major depressive disorder. *JMIR Mental Health, 2*(1), Article e3889. https://doi.org/10.2196/mental.3889
Trapletti, A., & Hornik, K. (2020). tseries: Time series analysis and computational finance (R package). https://cran.r-project.org/web/packages/tseries/tseries.pdf.
Tronstad, C., Amini, M., Bach, D. R., & Martinsen, Ø. G. (2022). Current trends and opportunities in the methodology of electrodermal activity measurement. *Physiological Measurement, 43*(2), 02TR01. https://doi.org/10.1088/1361-6579/ac5007
Van Londen, L., Molenaar, R. P. G., Goekoop, J. G., Zwinderman, A. H., & Rooijmans, H. G. M. (1998). Three-to 5-year prospective follow-up of outcome in major depression. *Psychological Medicine, 28*(3), 731–735. https://doi.org/10.1017/S0033291797006466
Vgontzas, A. N., Fernandez-Mendoza, J., Miksiewicz, T., Kritikou, I., Shaffer, M. L., Liao, D., … Bixler, E. O. (2014). Unveiling the longitudinal association between short sleep duration and the incidence of obesity: The Penn State Cohort. *International Journal of Obesity, 38*(6), 825–832. https://doi.org/10.1038/ijo.2013.172
Wade, A. G., Schlaepfer, T. E., Andersen, H. F., & Kilts, C. D. (2009). Clinical milestones predict symptom remission over 6-month and choice of treatment of patients with major depressive disorder (MDD). *Journal of Psychiatric Research, 43*(5), 568–575. https://doi.org/10.1016/j.jpsychires.2008.09.008
Wen, A., Quigley, L., Yoon, K. L., & Dobson, K. S. (2021). Emotion regulation diversity in current and remitted depression. *Clinical Psychological Science, 9*(4), 563–578. https://doi.org/10.1177/2167702620978616
Westen, D., Novotny, C. M., & Thompson-Brenner, H. (2004). The empirical status of empirically supported psychotherapies: Assumptions, findings, and reporting in controlled clinical trials. *Psychological Bulletin, 130*(4), 631. https://doi.org/10.1037/0033-2909.130.4.631
Whiston, A., Lennon, A., Brown, C., Looney, C., Larkin, E., O'Sullivan, L., … Semkovska, M. (2022). A systematic review and individual patient data network analysis of the residual symptom structure following cognitive-behavioral therapy and escitalopram, mirtazapine and venlafaxine for depression. *Frontiers in Psychiatry, 13*. https://doi.org/10.3389/fpsyt.2022.746678
WHO. (2018). Depression in Europe: Facts and figures. Retrieved from http://www.euro.who.int/en/health-topics/noncommunicable-diseases/mental-health/news/news/2012/10/depression-in-europe/depression-in-europe-facts-and-figures.
Wichers, M., Schreuder, M. J., Goekoop, R., & Groen, R. N. (2019). Can we predict the direction of sudden shifts in symptoms? Transdiagnostic implications from a complex systems perspective on psychopathology. *Psychological Medicine, 49*(3), 380–387. https://doi.org/10.1017/S0033291718002064
Yap, Y., Slavish, D. C., Taylor, D. J., Bei, B., & Wiley, J. F. (2020). Bi-directional relations between stress and self-reported and actigraphy-assessed sleep: A daily intensive longitudinal study. *Sleep, 43*(3), Article zsz250. https://doi.org/10.1093/sleep/zsz250
Yoshimoto, M., & Izumi, S. (2019). Recent progress of biomedical processor SoC for wearable healthcare application: A review. *IEICE Transactions on Electronics, 102*(4), 245–259. https://doi.org/10.1587/transele.2018CDI0001
Zahmat Doost, E., & Zhang, W. (2023). Mental workload variations during different cognitive office tasks with social media interruptions. *Ergonomics, 66*(5), 592–608. https://doi.org/10.1080/00140139.2022.2104381
Zajecka, J., Kornstein, S. G., & Blier, P. (2013). Residual symptoms in major depressive disorder: Prevalence, effects, and management. *The Journal of Clinical Psychiatry, 74*(4), 18127 (doi:10.488/JCP.12059ah1).