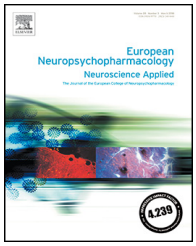
European Neuropsychopharmacology (2019) 29, 349–355

www.elsevier.com/locate/euroneuro



High occupational level is associated with poor response to the treatment of depression: A replication study

Laura Mandelli[a], **Alessandro Serretti**[a,*], **Daniel Souery**[b], **Julien Mendlewicz**[c], **Siegfried Kasper**[d], **Stuart Montgomery**[e], **Joseph Zohar**[f]

[a] *Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy*
[b] *Laboratoire de Psychologie Médicale, Université Libre de Bruxelles and PsyPluriel, Brussels, Belgium*
[c] *Université Libre de Bruxelles, Brussels, Belgium*
[d] *Department of Psychiatry and Psychotherapy, Medical University of Vienna, Vienna, Austria*
[e] *Imperial College, University of London, London, United Kingdom*
[f] *Expert Platform on Mental Health, Focus on Depression, Tel-Aviv University, Tel Aviv, Israel*

Received 1 June 2018; received in revised form 25 September 2018; accepted 7 January 2019

KEYWORDS
Occupation;
Depression;
Treatment;
Treatment resistant depression

Abstract
Major depressive disorder (MDD) is a leading cause of disability and inability to work. There is evidence that occupational factors may precipitate a MDD episode and interfere with the recovery process. In a previous investigation, we found that those employed in high occupational levels had a worse outcome after treatment for depression (Mandelli et al., 2016). The aim of the present study was to further investigate response to treatments for depression according to occupational status on an independent sample of MDD patients.
Six hundred and forty-seven (647) subjects with a stable working occupation were taken from a larger independent sample of MDD patients evaluated for response and resistance to treatment for depression, after at least one adequate treatment trial. Three broad occupational categories were considered: 'manager', 'white-collar', 'blue-collar' and 'self-employed'.
Managers had the highest rate of non-response and resistance to treatments. White-collar workers also had high non-response and resistance rates. At the opposite, Blue-collar workers had significantly lower rates of non-response and resistance. Self-employed were in between White- and Blue-collar workers and did not significantly differ from the other occupational categories.

* Corresponding author.
E-mail address: alessandro.serretti@unibo.it (A. Serretti).

https://doi.org/10.1016/j.euroneuro.2019.01.107

The findings of this replication study substantially support our previous observations. MDD patients employed in high-middle occupations may have a less favorable outcome after standard treatments of depression. Working stressful condition and other psychosocial factors at work should be investigated more closely in relation to treatment outcomes in MDD.

1. Introduction

Major depressive disorder (MDD) is a common and highly disabling disease with a worldwide prevalence of 4.4% according to a recent report of the World Health Organization (2017). The same report ranks MDD as the single largest contributor to non-fatal health loss (7.5% of all years lived with disability). MDD is indeed a major cause of disability (Global Burden of Disease Study 2013 Collaborators, 2017) and its socio-economic impact is substantial and constantly growing (Lepine and Briley, 2011 307; Mathers and Loncar, 2006).

The economic burden of depression is importantly driven by major impairments in productivity at work (Ekman et al., 2013). Besides the negative consequences for the personal life of the affected individuals, MDD strongly limits their ability to work and it represents one of the major causes of workplace absenteeism and presenteeism. In many cases, working ability can be so compromised as to require prolonged and repeated sick leave, till permanent retirement.

For these reasons, the problem of mental illness and MDD in the workplace has gained increasing interest in the recent years (Harvey et al., 2017). It is well recognized that the workplace can represent a source of relevant stress for several workers, which might precipitate the onset of an MDD episode in the predisposed individuals. A large field of investigation, to which we refer the reader for more detailed information, focus on the risk factors in the workplace (Bonde, 2008; Harvey et al., 2017; Theorell et al., 2015) and on the interventions helpful to prevent and adjust such risks (Joyce et al., 2016; Wan Mohd Yunus et al., 2018). The prompt identification and the treatment of MDD can be effective (Lee et al., 2018; Wan Mohd Yunus et al., 2018) and cost-effective from the business perspective (Evans-Lacko et al., 2016).

The knowledge of the psychosocial factors, in the workplace, that may influence the recovery of an individual who has already developed a depressive condition is instead substantially lacking. Some evidence comes from investigations on return to work facilitators in people with mental disease. According to a few studies, a slower return to work in depressed patients may be associated with enduring stressful working conditions (high stain), poor worker control on job organization (low job control/decision latitude), poor social support and poor work motivation in the workplace (Ervasti et al., 2017; Hees et al., 2012; Vemer et al., 2013).

Given the paucity of data, we focused on this issue and in a previous analysis on a sample of workers suffering from MDD (Mandelli et al., 2016) we found that being employed in high occupational positions was associated with a worse response to treatment of depression. In that study, we employed a common scale to graduate occupational categories (Hollingshead, 1975) and derived three levels (high, middle and low). The high occupational level included higher executives, business managers, major-minor professionals, owners of large, medium or small-independent businesses and administrative personnel. These workers showed lower rates of improvement with treatment (response), lower rates of remission, and more failed treatment trials (treatment resistance). Formerly, a study by (Cheng et al., 2007) reported a similar data: subjects in the high-middle occupational level had lower rates of remission compared to those in low occupational levels.

Given the absence of a more detailed characterization of employment factors associated with the outcome of the treatment for MDD, those findings are difficult to explain. A complex interplay of influences is likely to occur, including workplace risk factors (pressure, high demand and responsibility, poor social support from the supervisors and the peers), work/personal life imbalance, as well as lifestyle features of the people in high occupational positions, which may all interfere with the course of illness and the recovery processes. To date, it is not possible to provide clear explanations, but it is important to verify the strength of that finding, though consistent with a previous study.

For this reason, in this investigation we analyzed an independent sample of subjects affected by MDD and evaluated for treatment outcome as done in the previous study, though not similarly evaluated for occupation (here four categories different were considered: “manager”, “white-collar”, “blue-collar” and “self-employed”). As in the previous study (Mandelli et al., 2016), we tested a potential association between employment type and outcome of treatments of depression, hypothesizing a worse outcome in Managers as compared mainly to White- and Blue-collar workers.

2. Experimental procedures

2.1. Sample

The sample was recruited within the context of an international, multicenter, cross-sectional study conducted by the European ‘Group for the Study of Resistant Depression (GSRD)’. The GSRD project has progressed through a series of similar but independent samples and methods of data collection, starting from January 2000 up to February 2004 (Schosser et al., 2012; Souery et al., 2007), then from January 2005 to December 2011 (Souery et al., 2015) and from November 2011 to February 2016 (Dold et al., 2017). Our previous investigation (Mandelli et al., 2016) was carried out on the first large sample (Souery et al., 2007). In this study, we analyzed a new sample, from the last wave of recruitment (Dold et al., 2017).

Recruitment details were described previously (Dold et al., 2017). Briefly, patients were included if they meet Diagnostic and Statistical Manual of Mental Disorders (DSM) IV-TR (APA, 2000) criteria for MDD and received at least one adequate treatment for depression trial for their present depressive episode. Adequacy of treatment was based on (1) duration of at least 4 weeks and (2)

Table 1 Occupational categories stratified for socio-demographic and clinical variables.

		Manager N = 46		White collar N = 476		Blue-collar N = 74		Self-employed N = 51		
		N,	*%*	*N,*	*%*	*N,*	*%*	*N,*	*%*	*p-value*
Females		18,	39.1%	338	71.0%	42	56.8%	23	45.1%	<0.001
		Mean,	*SD*	*Mean,*	*SD*	*Mean,*	*SD*	*Mean,*	*SD*	
Age	*(years)*	50.1,	9.4	46.8	10.7	50.5	10.8	50.7	12.0	.001
			N, %		*N, %*		*N, %*		*N, %*	
Marital status	Single	10,	21.7%	123	25.8%	16	21.6%	13	25.5%	n.s.
	Married/Live with	25,	54.3%	242	50.7%	46	62.2%	28	54.9%	
	Divorced	4,	8.7%	54	11.3%	4	5.4%	5	9.8%	
	Separated	6,	13.0%	50	10.5%	6	8.1%	4	7.8%	
	Widowed	1,	2.2%	8	1.7%	2	2.7%	1	2.0%	
Education	Elementary school	0,	-	8	1.7%	5	6.8%	2	4.1%	.001
	Secondary/ Technical	18,	39.1%	300	63.3%	55	75.3%	23	46.9%	
	High Education	7,	15.2%	81	17.1%	4	5.5%	4	8.2%	
	University	21,	45.7%	85	17.9%	9	12.3%	20	40.8%	
Caucasian		44,	95.7%	454	95.2%	70	94.6%	49	96.1%	n.s.
Family history	*(positive)*	28,	60.9%	297	62.3%	40	54.1%	29	56.9%	n.s.
Suicidal risk	*(present)*	18,	39.1%	211	44.3%	33	44.6%	25	49.0%	n.s.
Antidepressants	SSRI	30,	65.2%	274	54.4%	53	53.5%	33	51.6%	n.s.
	SNRI/NaSSA	8,	17.4%	108	21.4%	21	21.2%	15	23.4%	
	TCA/TeCA	3,	6.5%	25	5%	6	6.1%	1	1.6%	
	Others	5,	10.9%	97	19.2%	19	19.2%	15	23.4%	
Psychotherapy	(yes)	20,	44.4%	159	36.4%	22	31.9%	21	44.7%	n.s.
		Mean,	*SD*	*Mean,*	*SD*	*Mean,*	*SD*	*Mean,*	*SD*	
Severity	*(current MADRS)*	24.9,	8.2	24.3	10.6	23.0	11.6	23.1	12.2	n.s.
Outcome		*N,*	*%*	*N,*	*%*	*N,*	*%*	*N,*	*%*	
	Response	9,	19.6%	142	29.8%	31	41.9%	16	31.4%	.010
	Resistance	21,	70%	192	57.5%	25	44.6%	19	54.3%	0.029

Abbreviations: MDD, Major depressive disorder; AD, treatment for depression; SSRI, Selective serotonin reuptake inhibitors; SNRI, Selective noradrenaline reuptake inhibitors; NaSSA, Noradrenergic and specific serotoninergic drugs; TCA, tricyclic drugs; TeCA, tetratricyclic drugs; MADRS, Montgomery-Asberg depression rating scale

dosage equal or higher than that defined as effective. Exclusion criteria were represented by: (i) any current primary psychiatric disorder other than MDD, (ii) a current or recent substance use disorder, or (iii) a severe or unstable medical/neurological condition potentially impairing the evaluations. The study protocol was approved by the local ethical committees of the participating centers. Patients were included after signing an informed consent.

For the purpose of the present study, we considered only patients aged 18 or more, and in employment at the time of the evaluations. Being unemployed, retired, without occupation, student, stakeholder, invalid, infirm were then supplementary exclusion criteria. The final sample was composed by 46 Managers (7.1%), 476 White-collars (73.6%), 74 Blue-collars (11.4%) and 51 Self-employed (7.9%), for a total of 647 MDD patients (421 females and 226 males, mean age 48.06 ±10.43, range: 21–76 years).

2.2. Evaluations

Socio-demographic and clinical information were collected by trained psychiatrists through a clinical interview specifically accomplished for this study (cross-sectional data collection process). Psychiatric diagnosis and suicidal risk were validated by the Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998).

In the recruitment phase, occupational status was encoded as follows: “with-collar worker”, “manager”, “self-employed”, “blue-collar worker”, “other/unknown”, “retired”, “student” and “unemployed”. According to our supplementary inclusion criterion (in employment at the time of the evaluations), only “manager”, “white-collar worker”, “blue-collar worker” and “self-employed” categories, independently from the employment sector, were considered.

Depressive severity was evaluated by the Montgomery and Åsberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) at the cross-sectional time evaluation (‘current MADRS’, i.e. after at least one adequate treatment trial) and at the retrospective episode onset (‘retrospective MADRS’). This retrospective MADRS rating was based on the patients‘ information during the clinical interview and based on the review of medical records when possible. Response to the last treatment was defined by a ≥ 50% MADRS total score reduction from episode onset; treatment resistance was defined as non-response to ≥2 adequate treatment trials (Kautzky et al., 2018).

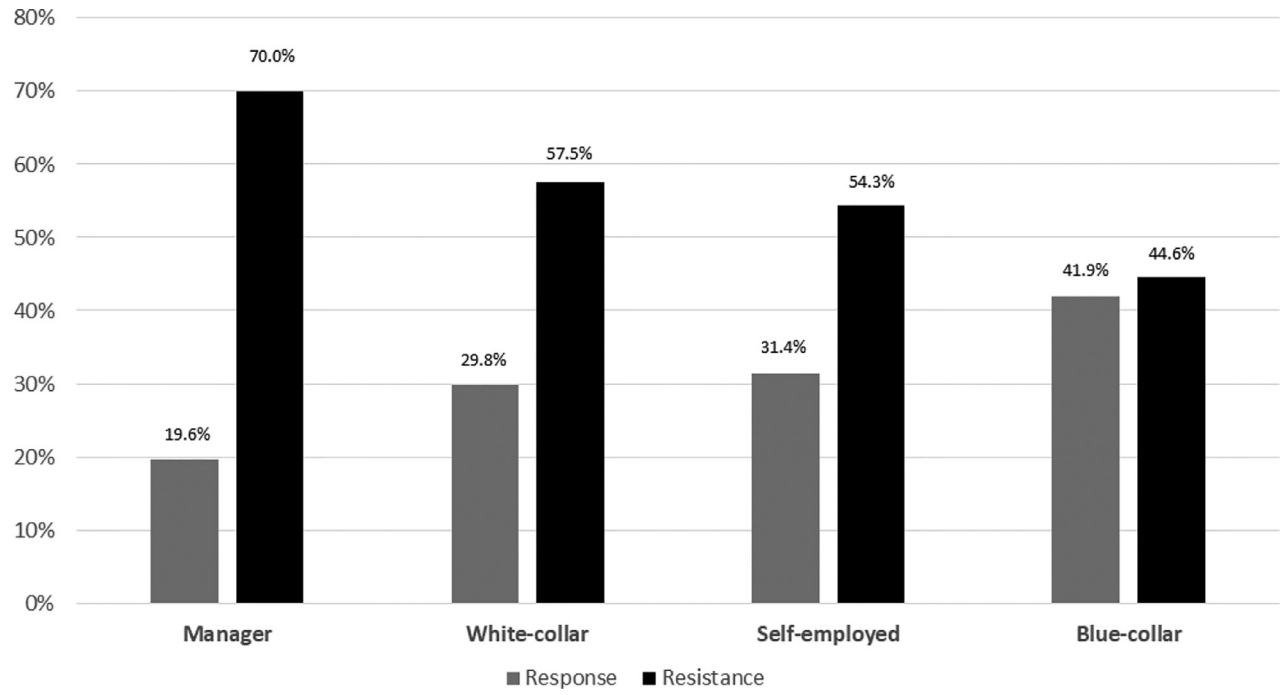


Fig. 1 Rates of response and resistance to treatments for depression stratified for occupational categories.

2.3. Statistical analysis

Data analysis was performed using the software SPSS, version 23 (IBM Corp., 2015). Standard statistics for categorical and continuous data were performed as appropriate (Chi-sq test, Student T-test, one-way analysis of variance). The association between occupational category and response/resistance to treatment was analyzed by the Chi-square test with post-hoc comparisons among pairs of occupational categories. Binomial regression models were run to control for socio-demographic differences (sex, age and education). All the p-values were two-tailed, and the significance level was defined as $p \leq .05$.

3. Results

Sociodemographic and clinical variables of the sample, stratified for occupational category are reported in Table 1. As expected, Managers had mostly a high educational level (46% university or more). White collars were younger on average (47 ±10 years) and predominantly females (71%). No significant differences were observed in terms of ethnicity, marital status, suicide ideation and type of treatment administered.

In the whole sample, the global rate of response to treatments for depression was 31% and resistance rate was 57%. Blue-collars had the highest rate of response (42%), significantly higher than White-collars (30%, p=.004) and Managers (20%, p=.005), but not than Self-employed (31%, p=.17). Blue collars also had the lowest rate of resistance to treatments (45%), significantly lower than White-collars (58%, p=.010) and Managers (which had the highest rate: 70%, p=.012), but not significantly different from that of Self-employed (54%, p=.26) (Table 1 and Fig. 1). Controlling for variables that differentiated individuals in the different professional categories and were potentially able to affect the treatments outcome (gender, age, education and treatment class), differences among occupational categories remained significant for both response and resistance to treatments for depression (Table 2). Treatment with "Other" antidepressant agents (but not selective noradrenaline reuptake inhibitors, Noradrenergic and specific serotoninergic drugs -SNRI/NaSSA- and Selective serotonin reuptake inhibitors -SSRI) were associated with poorer response and, as a trend, more resistance than treatment with Tricyclic and tetratricyclic drugs -TCA/TeCA-. Age, gender and educational level did not impact on treatment outcomes.

4. Discussion

The results of our analysis are in line with our previous finding of a worse response to treatments for MDD in the patients employed in a high occupational position (Mandelli et al., 2016), as well as in line with the finding by (Cheng et al., 2007) regarding a greater chance of remission in those in low occupational levels. In this sample, Managers had indeed the lowest absolute rate of response to treatments for depression and the highest absolute rate of treatment resistance than all occupational categories, at the opposite of Blue-collar workers. The lack of differences of White collars and Self-employed workers from Managers can be explained by a poor differentiation of occupational position level when using broad categories such as 'White-collar' and 'Self-employed', which can include from high to middle occupational positions.

Indeed, at the time of recruitment of this sample, we followed a traditional classification, which makes a basic distinction between managers, employees, blue-collar workers and self-employed. In contrast, in our previous investigation (Mandelli et al., 2016) and in (Cheng et al., 2007),

Table 2 Occupational category regressed on outcome variables, including potential confounders in the model (binomial logistic regression).

Response					
	B	S.E.	Wald Chi-sq.	p-value	Exp(B)
Sex[a]	<0.01	.18	<0.01	.99	1.00
Age	< −0.01	<0.01	.05	.83	1.00
Education	.02	.10	.03	.87	1.02
Antidepressant[b]			16.53	.001	
SSRI	.06	.37	.03	.87	1.06
SNRI/NaSSA	.56	.40	1.93	.17	1.75
Others	.98	.42	5.39	.020	2.67
Occupational category[c]			11.20	.010	
Manager	1.22	.44	7.72	.005	3.41
White-collar	.64	.24	7.36	.007	1.90
Self-employed	.32	.35	0.84	.36	1.38
Resistance					
Sex[a]	.10	.20	.23	.63	1.10
Age	<0.01	<0.01	<0.01	.97	1.00
Education	.03	.12	.06	.82	1.03
Antidepressant[b]			14.73	.002	
SSRI	.13	.41	.09	.76	1.13
SNRI/NaSSA	−0.49	.44	1.26	.26	.61
Others	−0.79	.46	2.91	.09	.45
Occupational category[c]			9.44	.024	
Manager	−1.22	.48	6.42	.011	.29
White-collar	−0.68	.27	6.27	.012	.51
Self-employed	−0.31	.40	.61	.44	.74

In logistic regression, B is the coefficient for the constant ("intercept") in the null model; S.E. is the standard error around the coefficient for the constant; Wald Chi-sq. tests the null hypothesis that the constant equals 0; Exp(B) is the exponentiation of the B coefficient, which is an odds ratio.

Abbreviations: SSRI, Selective serotonin reuptake inhibitors; SNRI, Selective noradrenaline reuptake inhibitors; NaSSA, Noradrenergic and specific serotoninergic drugs; TCA, tricyclic drugs; TeCA, tetratricyclic drugs

[a] The reference category is 'male'

[b] The reference category is 'TCA/TeCA'

[c] The reference category is 'blue-collar'

occupational levels were collected and ranked according to a system based on 'occupational prestige' (Hollingshead, 1975), which allowed to stratify the occupational level more subtly. However, on the whole, the findings are consistent, and support a role of the occupational level in the process of recovery from MDD, and specifically a poorer treatment outcome in subjects employed in high occupational levels. This is a brand new and exciting finding which may lead to a series of measures to be adopted in workplaces in order to reduce this, until now, neglected detrimental effect.

As mentioned in the introduction, since the absence of more specific assessments of the psychosocial characteristics of work environments, this study does not allow to provide explanations of the results obtained. A number of mediating factors are likely to occur, but this study did not evaluate them, since the sample was originally recruited for other purposes. Therefore, any discussion of possible mediating factors would be speculative now. However, specific stressful psychosocial factors in high occupational positions, such as high demand and workload, pressure, competition, social isolation at work and poor work-life balance, might represent critical impediments to the healing process. Further, personal attributes, difficulties in adapting to the depressive state and stigma of mental illness, along with transient side effects of drugs on mental functioning, may complicate the adherence to treatments. For a more detailed discussion of the many factors that can intervene we refer the reader to a recent opinion article (Mandelli et al., press). Future focused scientific investigation must clarify these and several other potential risk factors for poor response to the treatments for depression in middle-high occupational levels.

A number of other limitations should be taken into account. Patients were recruited from university/academic psychiatric treatment settings, so that they might not be representative of MDD patients in primary care settings. Further, the sample was recruited within the context of a project on resistant depression (Dold et al., 2017; Souery et al., 2007) and it might have a selection bias towards non-response. Further, we considered "adequate" a treatment based on a minimum duration of at least 4 weeks (at pharmacological doses according to international guidelines (National Institute for Health and Care Excellence (NICE), 2009)). However, the response rates observed in our sample (20–42%) were in line with recent evidence (37% response rate to second-generation antidepressants over 6–12 weeks of treatment (Gartlehner et al., 2011)). Though, the sample was balanced regarding the number of non-responders

or resistant patients, so that the project context should not have influenced the main outcomes (response and resistance). Other definitions of response and resistance may also produce different findings, as well as longer a follow up, further studies on big data or national registry datasets may confirm the present results. The sample may be not sufficiently large to detect smaller differences among subjects in the different occupational categories. The employment categories were equivocal and not standardized as in our previous study, being here probably accurate for high Managers and Blue-collar workers only. Moreover, the size of the samples was unbalanced, with an over-representation of white-collar workers and a low number of managers, but also blue collars and self-employed workers. These are a major limitation of the present study, along with the lack of evaluation of stress at work and other risk factors. Especially, a systematic assessment of the impact of possible cognitive side effects, in the different occupational categories, was not possible. Finally, the sample was predominantly composed by Caucasian Europeans (>95%): this limits variable ethnic effects in terms of occupational disadvantage, but results can be generalised with confidence only to Europeans.

In conclusion, the findings of this study substantially confirm the already observed negative effect of being employed in high-middle occupational levels on the outcome of treatment for depression. Occupational factors therefore play a critical role in both the risk and the recovery process in MDD. The nature and impact of these factors deserve further investigation in larger and better characterized samples.

Authors disclosure

Expert Platform on Mental Health – Focus on Depression.

Role of funding source

This article was not supported by external funding.

Contributors

All authors contributed substantially to and have approved the final manuscript.

Conflict of interest

None.

Acknowledgements

None.

References

APA, 2000. Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Association, Washington, DC.

Bonde, J.P., 2008. Psychosocial factors at work and risk of depression: a systematic review of the epidemiological evidence. Occup. Environ. Med. 65, 438–445.

Cheng, I.C., Liao, S.C., Lee, M.B., Tseng, M.M., 2007. Predictors of treatment response and length of stay for inpatients with major depression. J. Formos. Med. Assoc. 106, 903–910.

Dold, M., Bartova, L., Souery, D., Mendlewicz, J., Serretti, A., Porcelli, S., Zohar, J., Montgomery, S., Kasper, S., 2017. Clinical characteristics and treatment outcomes of patients with major depressive disorder and comorbid anxiety disorders - results from a European multicenter study. J. Psychiatr. Res. 91, 1–13.

Ekman, M., Granstrom, O., Omerov, S., Jacob, J., Landen, M., 2013. The societal cost of bipolar disorder in Sweden. Soc. Psychiatry Psychiatr. Epidemiol. 48, 1601–1610.

Ervasti, J., Joensuu, M., Pentti, J., Oksanen, T., Ahola, K., Vahtera, J., Kivimaki, M., Virtanen, M., 2017. Prognostic factors for return to work after depression-related work disability: a systematic review and meta-analysis. J. Psychiatr. Res. 95, 28–36.

Evans-Lacko, S., Koeser, L., Knapp, M., Longhitano, C., Zohar, J., Kuhn, K., 2016. Evaluating the economic impact of screening and treatment for depression in the workplace. Eur. Neuropsychopharmacol. 26, 1004–1013.

Gartlehner, G., Hansen, R.A., Morgan, L.C., Thaler, K., Lux, L., Van Noord, M., Mager, U., Thieda, P., Gaynes, B.N., Wilkins, T., Strobelberger, M., Lloyd, S., Reichenpfader, U., Lohr, K.N., 2011. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis. Ann. Intern. Med. 155, 772–785.

Global Burden of Disease Study 2013 Collaborators, 2017. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 390, 1211–1259.

Harvey, S.B., Modini, M., Joyce, S., Milligan-Saville, J.S., Tan, L., Mykletun, A., Bryant, R.A., Christensen, H., Mitchell, P.B., 2017. Can work make you mentally ill? A systematic meta-review of work-related risk factors for common mental health problems. Occup. Environ. Med. 74, 301–310.

Hees, H.L., Koeter, M.W., Schene, A.H., 2012. Predictors of long-term return to work and symptom remission in sick-listed patients with major depression. J. Clin. Psychiatry 73, e1048–e1055.

Hollingshead, A.B., 1975. Four Factor Index of Social Position. Department of Sociology, Yale University, New Haven, CT.

IBM Corp., 2015. IBM SPSS Statistics, Release 23.0.0.0 ed.

Joyce, S., Modini, M., Christensen, H., Mykletun, A., Bryant, R., Mitchell, P.B., Harvey, S.B., 2016. Workplace interventions for common mental disorders: a systematic meta-review. Psychol. Med. 46, 683–697.

Kautzky, A., Dold, M., Bartova, L., Spies, M., Vanicek, T., Souery, D., Montgomery, S., Mendlewicz, J., Zohar, J., Fabbri, C., Serretti, A., Lanzenberger, R., Kasper, S., 2018. Refining prediction in treatment-resistant depression: results of machine learning analyses in the TRD III sample. J. Clin. Psychiatry 79.

Lee, Y., Rosenblat, J.D., Lee, J., Carmona, N.E., Subramaniapillai, M., Shekotikhina, M., Mansur, R.B., Brietzke, E., Lee, J.H., Ho, R.C., Yim, S.J., McIntyre, R.S., 2018. Efficacy of antidepressants on measures of workplace functioning in major depressive disorder: a systematic review. J. Affect Disord. 227, 406–415.

Lepine, J.P., Briley, M., 2011. The increasing burden of depression. Neuropsychiatr. Dis. Treat. 7, 3–7.

Mandelli, L., Serretti, A., Porcelli, S., Souery, D., Mendlewicz, J., Kasper, S., Montgomery, S., Zohar, J., 2019. Opinion paper: poor response to treatment of depression in people in high occupational levels.. Psychol. Med.

Mandelli, L., Serretti, A., Souery, D., Mendlewicz, J., Kasper, S., Montgomery, S., Zohar, J., 2016. High occupational level is associated with poor response to treatment of depression. Eur. Neuropsychopharmacol. 26, 1320–1326.

Mathers, C.D., Loncar, D., 2006. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 3, e442.

Montgomery, S.A., Asberg, M., 1979. A new depression scale designed to be sensitive to change. Br. J. Psychiatry 134, 382–389.

National Institute for Health and Care Excellence (NICE), 2009. Depression in adults: Recognition and Management. NICE (Ed.).

Schosser, A., Serretti, A., Souery, D., Mendlewicz, J., Zohar, J., Montgomery, S., Kasper, S., 2012. European Group for the Study of Resistant Depression (GSRD)–where have we gone so far: review of clinical and genetic findings. Eur. Neuropsychopharmacol. 22, 453–468.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Suppl 20), 22–33 quiz 34-57.

Souery, D., Calati, R., Papageorgiou, K., Juven-Wetzler, A., Gailledreau, J., Modavi, D., Sentissi, O., Pitchot, W., Papadimitriou, G.N., Dikeos, D., Montgomery, S., Kasper, S., Zohar, J., Serretti, A., Mendlewicz, J., 2015. What to expect from a third step in treatment resistant depression: A prospective open study on escitalopram. World J. Biol. Psychiatry 16, 472–482.

Souery, D., Oswald, P., Massat, I., Bailer, U., Bollen, J., Demyttenaere, K., Kasper, S., Lecrubier, Y., Montgomery, S., Serretti, A., Zohar, J., Mendlewicz, J., 2007. Clinical factors associated with treatment resistance in major depressive disorder: results from a European multicenter study. J. Clin. Psychiatry 68, 1062–1070.

Theorell, T., Hammarstrom, A., Aronsson, G., Traskman Bendz, L., Grape, T., Hogstedt, C., Marteinsdottir, I., Skoog, I., Hall, C., 2015. A systematic review including meta-analysis of work environment and depressive symptoms. BMC Public Health 15, 738.

Vemer, P., Bouwmans, C.A., Zijlstra-Vlasveld, M.C., van der Feltz-Cornelis, C.M., Hakkaart-van Roijen, L., 2013. Let's get back to work: survival analysis on the return-to-work after depression. Neuropsychiatr. Dis. Treat. 9, 1637–1645.

Wan Mohd Yunus, W.M.A., Musiat, P., Brown, J.S.L., 2018. Systematic review of universal and targeted workplace interventions for depression. Occup. Environ. Med. 75, 66–75.

World Health Organization, 2017. Depression and Other Common Mental Disorders. Global Health Estimates. WHO.