Psychiatry Research Review™

Making Education Easy

Issue 47 - 2018

In this issue:

Abbreviations used in this issue:

ADHD = attention-deficit/hyperactivity disorder;
CBT = cognitive behavioural therapy; **CVD** = cardiovascular disease
HAM-D = Hamilton Depression Rating Scale;
MADRS = Montgomery-Åsberg Depression Rating Scale;
OR = odds ratio; **PTSD** = post-traumatic stress disorder;
RCT = randomised controlled trial.

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Welcome to issue 47 of Psychiatry Research Review.

Intriguing findings are reported in this issue from a US study, which suggests that hormonal therapy might mitigate the increased risk of depressive symptoms that accompany the menopause transition and early postmenopausal period. The study included 172 perimenopausal and early postmenopausal women. Fewer of the women treated with transdermal oestradiol and intermittent micronised progesterone developed clinically significant depressive symptoms as compared with the women receiving placebo.

Another paper reporting on the risk of congenital malformations associated with intrauterine exposure to stimulant medications yields valuable findings in relation to the risks and benefits of treatment for ADHD in women of reproductive age and during early pregnancy. It suggests that there might be a small increase in the risk of cardiac malformations with methylphenidate. In contrast, there were no increased risks of any malformations in infants exposed to amphetamines.

I hope you find these papers useful to you in your practice and I welcome your comments and feedback.

Kind Regards,

Associate Professor Ajeet Singh

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The effect of a single dose of intravenous ketamine on suicidal ideation: a systematic review and individual participant data meta-analysis

Authors: Wilkinson ST et al.

Summary: This systematic review examined individual participant data from 10 intervention studies that examined the effects of a single dose of ketamine on suicidal ideation and used either saline or midazolam as a control treatment. The analysis included only depressed patients who had suicidal ideation at baseline (n=167). The analysis included suicide items from clinician-administered (the MADRS or the HAM-D) and self-report scales (the Quick Inventory of Depressive Symptomatology–Self Report [QIDS-SR] or the Beck Depression Inventory [BDI]), obtained for up to 1 week after ketamine administration. Ketamine was associated with a rapid, significant reduction in suicidal ideation within 1 day and for up to 1 week on both the clinician-administered and self-report outcome measures. Effect sizes were moderate to large (Cohen's d=0.48–0.85) at all time points after dosing. In a sensitivity analysis, ketamine provided significant benefits as compared with control treatments on the individual suicide items of the MADRS, the HAM-D and the QIDS-SR, but not the BDI. In analyses that adjusted for concurrent changes in severity of depressive symptoms, the effect of ketamine on suicidal ideation remained significant.

Comment: The ketamine story is not going away – suggesting there may be some genuine clinically translatable signal to the usual background noise of non-translatable publications. This short-term (one week) comparator study of injected low-dose (sub-anaesthetic) ketamine versus saline or midazolam demonstrated reduced suicidal ideations manifesting rapidly and lasting up to a week. A moderate-to-large effect size was noted – needed for clinically meaningful translation. Inclusion of a midazolam limb was valuable – helping to tease out non-specific anxiolytic effects. If ketamine translated to clinical use, it will present many implementation issues. It is a substance with abuse risk. Parenteral administration carries medical risk and associated costs of implementation – potentially offset if the hospital admission rate is reduced. Rapid loss of benefits will necessitate close review of the patient. Failure to offer it to a suicidal patient creates both clinical and medicolegal complexities once/if it enters practice guidelines. Clinicians should keep an eye on the ketamine story, but cautiously await practice guideline and FDA/TGA level approval before ever considering clinical use.

Reference: Am J Psychiatry. 2018;175(2):150-8

Abstract

Efficacy and safety of intranasal esketamine adjunctive to oral antidepressant therapy in treatment-resistant depression

Authors: Daly EJ et al.

Summary: This phase 2 study randomised 67 patients (mean age, 44.7 years) with treatment-resistant depression to placebo (n=33), intranasal esketamine 28 mg (n=11), 56 mg (n=11), or 84 mg (n=12), as twice-weekly double-blind treatment from days 1–15 (period 1), followed by optional open-label treatment from days 15–74 (period 2). During the open-label phase, dosing frequency was reduced from twice weekly to weekly, and then to every 2 weeks. In period 2, 28 placebo-treated participants with moderate-to-severe symptoms were re-randomised to 1 of the 4 treatment arms; those with mild symptoms continued receiving placebo. Participants continued their existing antidepressant treatment during the study. After completing study treatment, patients were followed-up for 8 weeks. The primary efficacy end point was change from baseline to day 8 (each period) in the MADRS total score. In all 3 esketamine groups, the change (least squares mean difference vs placebo) in MADRS total score (both periods combined) was superior to placebo (esketamine 28 mg: −4.2, p=0.02; 56 mg: −6.3, p=0.001; 84 mg: −9.0, p<0.001) and demonstrated a significant ascending dose-response relationship (p<0.001). Improvement in depressive symptoms appeared to be sustained (−7.2) despite reduced dosing frequency in the open-label phase. Three esketamine-treated participants during the double-blind phase (vs none receiving placebo) and 1 esketamine-treated patient during the open-label phase had adverse events that led to study discontinuation (1 event each of syncope, headache, dissociative syndrome, and ectopic pregnancy).

Comment: As is often the case, a promising signal in the academic literature is turned into a commercially implementable product by industry. The main drawback with subcutaneous esketamine is the adverse effect profile (such as hypotension and tachycardia) and the associated time and cost to monitor patients. Furthermore, many patients have needle phobia. So, the opportunity for simple intranasal delivery is interesting – a parenteral route is needed, given the poor oral CNS bioavailability due to extensive hepatic metabolism. Despite the modest sample size in the RCT, a significant improvement in depressive symptoms was noted – sustained for eight weeks, and consistent with robust effect size. There was a strong dose-effect relationship noted – better outcomes with higher doses, likely reflecting better CNS bioavailability. As this was a phase II study and esketamine has been patented to enable potential commercial returns on large R&D outlays, if intranasal esketamine reaches market post-FDA/TGA approval, the era of ketamine in acute suicidality will be upon us. Teasing out acute suicidality from chronic suicidality (such as in borderline personality disorder) will be crucial, and something best discerned by suitably experienced psychiatrists, given the clinical and medicolegal implications. RANZCP and other peak bodies will need to establish expert panels to guide implementation, should such agents become clinically available.

Reference: JAMA Psychiatry. 2018;75(2):139-48
Abstract

Trial of prazosin for post-traumatic stress disorder in military veterans

Authors: Raskind MA et al.

Summary: In this study, 304 veterans from 13 Department of Veterans Affairs medical centres who had chronic PTSD and reported frequent nightmares were randomised to receive prazosin (n=152) or placebo (n=152) for 26 weeks; study treatment was administered in escalating divided doses over the course of 5 weeks to a daily maximum of 20 mg in men and 12 mg in women. After week 10, participants continued to receive prazosin or placebo for an additional 16 weeks. The primary outcome measures consisted of the change in score from baseline to 10 weeks on the Clinician-Administered PTSD Scale (CAPS) item B2 ("recurrent distressing dreams"; scored from 0 to 8, with higher scores indicating more frequent and more distressing dreams); the change in score from baseline to 10 weeks on the Pittsburgh Sleep Quality Index (PSQI; scored from 0 to 21, with higher scores indicating worse sleep quality); and the Clinical Global Impression of Change (CGIC) score at 10 weeks (scored from 1 to 7, with lower scores indicating greater improvement and a score of 4 indicating no change). No significant between-group differences were found at 10 weeks in the mean change from baseline in the CAPS item B2 score (between-group difference, 0.2; p=0.38), in the mean change in PSQI score (between-group difference, 0.1; p=0.80), or in the CGIC score (between-group difference, 0; p=0.96). These findings were not significantly different at 26 weeks and there were no between-group differences for any other secondary outcomes. At 10 weeks, the mean difference between the prazosin and placebo groups in the change from baseline in supine systolic blood pressure was a decrease of 6.7 mm Hg. New or worsening suicidal ideation occurred in 8% of the participants assigned to prazosin and in 15% of those assigned to placebo.

Comment: Chronic PTSD is a common and disabling condition facing many patients – particularly returned service men. In this prospective RCT, 304 US veterans with chronic PTSD were randomised to the α1-adrenoreceptor antagonist and blood pressure agent prazosin versus placebo. They were assessed with a battery of rating scales over a six-month follow-up period, in particular looking for reduction in nightmares – something prazosin has previously been associated with alleviating. There was no difference noticed between groups. This is important, as a growing thread of clinicians have started to offer prazosin to such patients. As it is a blood pressure-lowering agent, there is potential risk should an overdose arise. The study used a robust dosing schedule – helping ensure under-dosing was not a contributing factor to the negative finding. This finding will help shape practice behaviour away from trialling prazosin in such patients, but such patients are still left with the debilitating impacts of chronic insomnia – sometimes less than ideally tackled with off-label use of a sedating atypical antipsychotics due to lack of better alternatives.

Reference: N Engl J Med. 2018;378(6):507-17
Abstract

Efficacy of transdermal estradiol and micronized progesterone in the prevention of depressive symptoms in the menopause transition

Authors: Gordon JL et al.

Summary: This study enrolled 172 community-dwelling, euthymic perimenopausal and early postmenopausal women aged 45–60 years and randomised them to receive transdermal oestradiol (TE; 0.1 mg/day) or placebo for 12 months. The TE group also received oral intermittent micronised progesterone (IMP; 200 mg/day for 12 days every 3 months); identical placebo pills were administered to the placebo group. Forty-three women developed clinically significant depressive symptoms. Placebo recipients were more likely than those treated with TE+IMP to score ≥16 on the Center for Epidemiological Studies–Depression Scale (CES-D) at least once during the study (32.3% vs 17.3%; OR, 2.5; 95% CI, 1.1 to 5.7; p=0.03) and they had a significantly higher mean CES-D score across the 12-month intervention (p=0.03). Baseline reproductive stage moderated the effect of treatment (β, −1.97; p=0.03), in that TE+IMP was associated with mood benefits over placebo among women in the early menopause transition (β, −4.2; p<0.001), but not the late menopause transition (β, −0.9; p=0.23) or in the postmenopausal period (β, −0.3; p=0.92). Stressful life events in the 6 months preceding enrolment also moderated the effect of treatment on mean CES-D score; the mood benefits of TE+IMP increased with a greater number of events (β, 1.22; p=0.003). Treatment effects were not moderated by baseline oestradiol levels, baseline vasomotor symptoms, history of depression, or history of abuse.

Comment: This is a very interesting study with potential future public health implications. It is the first study testing whether hormone therapy can prevent the onset of perimenopausal and early postmenopausal depressive symptoms. Interestingly, over the three-month follow-up period, around 1 in 5 of all subjects developed clinically significant *de novo* depressive symptoms. Subjects on placebo had a 1.9-fold higher rate of developing depressive symptoms. Larger and longer studies will be needed to gauge both the efficacy and safety of such approaches before widespread public health level implementation arises. There is on the one hand a risk of over-medicalising a natural stage of life, but on the other hand there is a risk of missing an opportunity to prevent treatable suffering. The study has an interesting side finding, in that women with an excess of stressful life events in the six months prior to the study were more likely to develop depressive symptoms – such findings are likely best characterised as adjustment disorder with depressed mood rather than major depression *per se*. In such cases, psychosocial measures may be preferred to pharmacological ones.

Reference: JAMA Psychiatry. 2018;75(2):149-57
Abstract

*Efficacy demonstrated by statistically significant change from baseline vs placebo in PANSS total score at 6 weeks in two pivotal studies; in one, the 2 mg/day primary endpoint was not met. In a 52-week maintenance study, time to impending relapse was statistically significantly increased with REXULTI vs placebo[1]

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*Please note updated information in italics.

References: 1. REXULTI® Australian Approved Product Information. 2. Department of Health. Pharmaceutical Benefits Scheme. Available at: www.pbs.gov.au.

Association between methylphenidate and amphetamine use in pregnancy and risk of congenital malformations: a cohort study from the International Pregnancy Safety Study Consortium

Authors: Huybrechts KF et al.

Summary: This investigation into the risk of congenital malformations associated with intrauterine exposure to stimulant ADHD medications in the first trimester included 1,813,894 pregnancies nested in the 2000–2013 US Medicaid Analytic eXtract, with replication of initial safety signals in 2,560,069 singleton pregnancies from Nordic Health registries (Denmark, Finland, Iceland, Norway, and Sweden; 2000–2013). In the US data, 35.0 per 1,000 infants not exposed to stimulants were diagnosed as having congenital malformations, compared with 45.9 per 1,000 infants for methylphenidate and 45.4 for amphetamines. For cardiac malformations, the risks were 12.7, 18.8 and 15.4 per 1,000 infants, respectively. The adjusted relative risks for methylphenidate were 1.11 (95% CI, 0.91 to 1.35) for any malformations and 1.28 (95% CI, 0.94 to 1.74) for cardiac malformations. The associations with malformations overall and with cardiovascular malformations were null for amphetamines: 1.05 (95% CI, 0.93 to 1.19) and 0.96 (95% CI, 0.78 to 1.19), respectively. Sensitivity analyses accounting for proxies of unmeasured confounders and increasing the specificity of the exposure and outcome definitions confirmed these findings. Replication of the analyses for methylphenidate using the Nordic data yielded a relative risk of 1.28 (95% CI, 0.83 to 1.97) for cardiac malformations, resulting in a pooled estimate for first-trimester methylphenidate exposure from the US and Nordic data of 1.28 (95% CI, 1.00 to 1.64).

Comment: As robust epidemiological data comes to light, clinicians need to keep abreast of such data to best guide patients on shared decision-making in relationship to psychotropics and pregnancy. Furthermore, prescribers must be mindful of unplanned pregnancies in women of childbearing age for whom they prescribe psychotropics and regularly counsel about the need to use contraception. This very large and methodologically robust study examined the risk of congenital malformations associated with intrauterine exposure to stimulants. Relative risk was used as a more robust and easy-to-interpret statistical measure versus the odds ratio, which can inflate seeming effect sizes and is a less intuitive measure of different rates of an outcome between groups. A significantly increased risk of cardiac malformations (1.28-fold) and any malformation (1.11-fold) were noted for use of methylphenidate but not for amphetamines. This is a clinically very useful finding, as one can make the strong case that if a stimulant is to be used in a woman of childbearing age, amphetamine is preferred to methylphenidate.

Reference: JAMA Psychiatry. 2018;75(2):167-75
Abstract

Association of cumulative childhood adversity and adolescent violent offending with suicide in early adulthood

Authors: Björkenstam E et al.

Summary: This population-based cohort study included 476,103 individuals (48.7% female) born in Sweden between 1984 and 1988 who were prospectively followed up from 20 years of age until 31 December 2013, with respect to suicide. In analyses adjusting for demographics and psychiatric disorder, individuals with a history of childhood adversity who were convicted of violent offending (defined as being convicted of a violent crime between the ages of 15 and 19 years) were at greater risk of suicide compared with those with no violent offending (adjusted incidence rate ratio [IRR], 8.5; 95% CI, 4.6 to 15.7). Adolescent violent offending partly mediated the association between childhood adversity and suicide.

Comment: Experienced clinicians will be very aware of the large public health impact child maltreatment has. In this epidemiological study of close to half a million people, the researchers explored whether adolescent violent offending mediates the association between childhood maltreatment and suicide in early adulthood. The study found that individuals with childhood maltreatment had higher rates of violent offending and suicide and, not surprisingly, subjects with violent offending had the highest rate of suicide – violence turned on one's self. The myriad psychiatric problems (such as cluster B personality disorders) stemming from childhood maltreatment are conditions of prevention. Societal measures to reduce pressures on families and increase supports are ever needed, along with family planning among those ill-prepared (materially/emotionally) to adequately nurture children. However, basic human rights to have children and rising fiscal pressures on families in a low economic growth era present very major challenges. Alas, it is likely childhood maltreatment and cluster B personality dynamics will remain and become an increasing factor in psychiatric formulation and care. Sometimes the best we can do is not to add to harm through overly biological formulations and exposure to polypharmacy in this group.

Reference: JAMA Psychiatry. 2018;75(2):185-93
Abstract

Childhood trauma Is associated with poorer cognitive performance in older adults

Authors: Petkus AJ et al.

Summary: These researchers examined the association between childhood trauma, cortisol, and cognitive performance in two samples of older adults: a discovery sample of 57 older adults with generalised anxiety disorder and 19 psychiatrically healthy age-equated comparison subjects who were referred largely through primary care clinics between 2004 and 2006; the replication sample consisted of 48 older adults with DSM-IV anxiety or depressive disorders who were recruited between 2012 and 2013. Childhood trauma was self-reported using the Early Trauma Inventory Self-Report–Short Form. Both samples participated in a neuropsychological assessment. Across both samples, childhood trauma was significantly associated with worse performance on measures of processing speed, attention, and executive functioning. The effect of the association between childhood trauma and worse cognitive performance was larger in analyses specifically examing general, physical, and sexual traumatic events (all $p<0.05$). Cortisol levels did not explain the association between childhood trauma and cognitive functioning.

Comment: This is an interesting study. Despite the small sample size and vulnerability to type I statistical error, it is an interesting paper nonetheless. The basic finding of poorer cognitive outcomes independent of mood/anxiety factors being associated with childhood maltreatment is of much interest. The study did not find differential cortisol levels (as a measure of dysregulation of the hypothalamic-pituitary-adrenal axis) to be relevant in the sample. This suggests that other mechanisms may play a role in the impaired cognition noted among subjects with childhood trauma. While depression and anxiety can affect cognition, the finding of poorer cognition in both groups and with matched controls suggests a direct impact of the trauma on cognitive performance. This may be mediated biologically, or potentially psychologically via dissociative phenomena – but the latter are usually only seen in subjects with marked trauma-related diagnoses; such cases were not included in the study. It will be interesting to see if a literature emerges around childhood trauma being a risk factor for dementia. If so, it's yet another signal in the literature pointing to the adverse impacts of childhood trauma on whole-of-life health outcomes.

Reference: J Clin Psychiatry. 2018;79(1):16m11021
Abstract

Independent commentary by Associate Professor Ajeet Singh (MBBS(Melb), MPsych(Melb), MD(Melb), FRANZCP), an academic private psychiatrist with interests in mood disorders, pharmacogenetics, transcranial magnetic stimulation, and medical innovation. He is based at The Geelong Clinic, and teaches at Deakin Medical School. His research has focused on genetically-guided prescribing (pharmacogenetics) of antidepressants, particularly the role of the blood-brain-barrier. He is an academic member of the Clinical Pharmacogenetics Implementation Consortium (CPIC) and member of the Genetic Tests in Psychiatry Taskforce, International Society of Psychiatric Genetics (ISPG). He has recently won awards in multiple start-up competitions, leading his team to win The Melbourne University Accelerator Contest in 2016 for his start-up CNSDose.

Virtual-reality-based cognitive behavioural therapy versus waiting list control for paranoid ideation and social avoidance in patients with psychotic disorders: a single-blind randomised controlled trial

Authors: Pot-Kolder RMCA et al.

Summary: This Dutch study randomly assigned 116 outpatients aged 18–65 years with a DSM-IV-diagnosed psychotic disorder and paranoid ideation in the past month to virtual-reality-based cognitive behavioural therapy (VR-CBT; n=58) (in addition to treatment as usual) or to a waiting list control group (treatment as usual; n=58). VR-CBT consisted of 16 individual therapy sessions (each lasting 1 h). The primary outcome was social participation, operationalised as the amount of time spent with other people, momentary paranoia, perceived social threat, and momentary anxiety. At the 3-month post-treatment assessment, VR-CBT failed to significantly increase the amount of time spent with other people when compared with treatment as usual. Momentary paranoid ideation (b=−0.331, p<0.0001; effect size −1.49) and momentary anxiety (−0.288, p=0.0002; −0.75) were significantly reduced in the VR-CBT group compared with the control group at the post-treatment assessment; these improvements were maintained at a 6-month follow-up visit.

Comment: Patients with residual psychotic symptoms suffer a significant ongoing burden of disease. An important component of this stems from residual paranoid ideations and associated anxiety, depression, and social isolation. A vicious cycle of paranoia, social isolation, and entrenched paranoia can arise, impeding optimal psychosocial recovery. In this comparator trial of 116 patients with residual paranoid symptoms, there was no benefit from the virtual-reality-based CBT intervention. This is unfortunate, as such systems are scalable and cost-effective if an effect is noted. It is likely that further systems will be developed to automate and scale CBT and related therapies. The issue clinically will be the utility of such systems in improving outcomes. The study did identify reduced paranoid and anxious symptoms in the virtual-reality-based CBT limb, and if this translates to a cost-of-care saving, an economic value proposition for the system may arise. As artificial intelligence (AI) systems improve, it will be interesting to see if low-cost scalable cloud-based machine learning CBT and related psychological therapies start to make a clinical impact or not – to date, early systems have been largely disappointing, in part due to a lack of AI-powered natural language programming interfaces.

Reference: Lancet Psychiatry. 2018;5(3):217-26
Abstract

Clinical and cost-effectiveness of an intervention for reducing cholesterol and cardiovascular risk for people with severe mental illness in English primary care: a cluster randomised controlled trial

Authors: Osborn D et al.

Summary: This cluster RCT involved 327 people with severe mental illnesses (schizophrenia, bipolar disorder, or psychosis) across 76 general practices in England. Participants were aged 30–75 years and had elevated cholesterol concentrations (5.0 mmol/L) or a total:HDL cholesterol ratio of ≥4.0 mmol/L and ≥1 modifiable CVD risk factors. Thirty-eight general practices, including 155 patients, were randomly assigned to the Primrose intervention, consisting of up to 12 appointments over 6 months with a trained primary care professional involving manualised interventions for CVD prevention (i.e. adhering to statins, improving diet or physical activity levels, reducing alcohol, or quitting smoking). The remaining 38 general practices (including 172 patients) received treatment as usual (feedback of screening results only). Mean total cholesterol concentration data at 12 months were available for 137 (88%) participants in the Primrose intervention group and 152 (88%) participants in the treatment-as-usual group; no between-group difference was observed (5.4 mmol/L for Primrose vs 5.5 mmol/L for treatment as usual; p=0.788). Mean cholesterol decreased over 12 months in both groups (−0.22 mmol/L for Primrose vs −0.36 mmol/L for treatment as usual). The Primrose intervention resulted in significantly lower total healthcare costs (£1,286 vs £2,182 in the treatment-as-usual group; p=0.012) and psychiatric inpatient costs (£157 vs £956; p=0.018).

Comment: This is an interesting study – measures to improve general health outcomes among patients with severe mental illness is a key public health focus. A cluster randomised trial in general practices across England involved 327 subjects. The intervention group involved a set number of GP reviews and a checklist of metabolic syndrome-related interventions, and this was compared to *ad hoc* care as usual. No significant difference in cholesterol levels was found for the intervention group over care as usual, suggesting care as usual was pretty effective. However, the intervention group had lower admission rates for psychiatric problems, possibly mediated by a greater number of GP visits and more time per visit. Generic supportive psychotherapy can make a difference to mental state stability, and this may be part of the observed effect. Longer and larger studies will be needed to determine if prescriptive increased GP vigilance of the general health of patients with severe mental illness yields benefits, but intuitively, ensuring patients with psychiatric illness regularly see their GP makes good clinical sense.

Reference: Lancet Psychiatry. 2018;5:145-54
Abstract

Long-term acute-phase treatment with antidepressants, 8 weeks and beyond: a systematic review and meta-analysis of randomized, placebo-controlled trials

Authors: Henssler J et al.

Summary: This systematic review of the published literature up to March 2014 identified 104 double-blind, randomised studies lasting ≥8 weeks that compared antidepressant monotherapy to placebo in a total of 35,052 adult patients with acute depressive disorder. The primary outcome was the standardised mean difference (SMD) between antidepressant and placebo. Active treatment was statistically significantly superior to placebo, with consistent effect sizes (SMD) after 8, 12, 16, 20 and 24 weeks of 0.27, 0.34, 0.24, 0.31 and 0.34, respectively. Results remained stable across secondary outcomes (response, remission, and dropouts), and in subgroup and sensitivity analyses.

Comment: This is an important study, as it sheds robust empirical light on the utility of antidepressants for major depression during prolonged (greater than 8 weeks) treatment. Many studies of antidepressants only last 8 weeks due to funding limitations and loss of statistical power from recruit dropout-related attrition. This meta-analysis explored 104 studies that included 35,052 patients assessed and treated for more than 8 weeks (over 6 months in some cases). The study found that for up to 6 months, antidepressants significantly separated from placebo for reducing total depressive symptoms. This finding helps complement the findings of Ciprian et al. published in the *Lancet* earlier this year – whose very large meta-analysis robustly helped put to rest the debate of whether antidepressants were just placebos. For moderate-to-severe depression, antidepressants do have efficacy – especially where an experienced clinician has avoided common misdiagnoses of adjustment disorder with depressed mood and persistent depressive disorder (often related to childhood maltreatment) before initiating an antidepressant. Alas, in the modern era, therapeutic trials of antidepressants in the face of non-specific depressive presentations are common – underpinning the high population rates of antidepressant prescriptions despite psychosocial interventions being more appropriate in many cases.

Reference: J Clin Psychiatry. 2018;79(1):15r10545
Abstract

