## Practical Psychopharmacology with Dr. Goldberg

Maddison Ulrich Hussey, M.D., David Puder, M.D.

Dr. Joseph F. Goldberg is a psychiatrist and clinician researcher with over 180 publications and 3 books. This article focuses on his newest book, *Practical Psychopharmacology: Translating Findings From Evidence-Based Trials into Real-World Clinical Practice*. *In this article, we discuss psychopharmacology and his approach to psychiatry.*

"The physician approach of psychopharmacology is knowing the entirety of the drug's effects on the body and the body's effect on the drug." - Dr. Goldberg

David Puder, M.D. has no conflicts of interest to report.
Joseph Goldberg, M.D. has the following conflicts of interest:

- Consultant: BioXcel, Jazz Pharmaceuticals, Lundbeck, Otsuka, Sage Pharmaceuticals, Sunovion
- Speakers bureau: Abbvie, Alkermes, Intracellular Therapies, Sunovion

Maddison Ulrich Hussey, M.D., has no conflicts of interest to report.

This article is further discussed in the podcast "Psychiatry & Psychotherapy" **Episode 131** found on **iTunes**, **Google Play**, **Stitcher**, **Overcast**, **PlayerFM**, **PodBean**, **TuneIn**, **Podtail**, **Blubrry**, **Podfanatic**

# Pramipexole in Treatment-Resistant Bipolar Depression

Dr. Goldberg published a preliminary randomized, double-blind, placebo-controlled study in 2004 that added pramipexole to mood stabilizers for treatment-resistant bipolar depression (Goldberg et al., 2004). Twenty-two patients diagnosed with bipolar depression were given either placebo or pramipexole in addition to the lithium, divalproex, carbamazepine, lamotrigine, and/or topiramate they had already been taking for at least a month. They defined treatment resistance as patients who "had not responded to at least two adequate trials of standard antidepressants with concomitant mood stabilizers during the current episode". The dose of pramipexole was increased every 3-5 days "until 1) achievement of primary endpoint (defined as a reduction of 50% or more from baseline in Hamilton depression scale score for at least 2 successive weeks), 2) drug intolerance, or 3) 6-week protocol completion." They found that "eight (67%) of 12 patients taking pramipexole and two (20%) of 10 taking placebo had an improvement of at least 50% in their Hamilton depression scale scores. The mean percentage of improvement from baseline Hamilton depression scale scores was greater for patients taking pramipexole (48%) than for those taking placebo (21%). Mean improvements in CGI severity

were also greater with pramipexole than placebo." They concluded that pramipexole was safe and effective as an adjunct treatment for patients with treatment-resistant bipolar depression.

Dr. Goldberg explains that his thought process for choosing pramipexole was trying to target symptoms of anhedonia, anergia, and apathy with a D2/D3 agonist. Pramipexole also improves cognitive functioning. He also notes that a large contributor to the lack of continued research in pramipexole is simply that the patent expired.

## Further studies on pramipexole

A later study by Jan Fawcett in 2016 also looked at pramipexole as an option for patients experiencing treatment-resistant episodes of both unipolar and bipolar depression (Fawcett et al., 2016). This study followed 42 patients and defined treatment resistance as "having failed to respond to at least four adequate antidepressant medication trials" including ECT. They found that out of "42 patients, 20 remitted (47.6%), 12 responded (28.6%), two did not respond (4.8%), and eight could not tolerate the drug (19.0%). Intolerance was encountered early, often at a low dosage and usually due to nausea. Of the eight patients who had failed to benefit from ECT (two had bipolar disorder), four responded and four remitted with pramipexole." The following table provided some guidelines from the study in administering pramipexole:

TABLE 1. Practical Guidance in the Use of Pramipexole in Treatment-Resistant Depressive Episodes (Fawcett et al., 2016):

- Slower titration rate in younger patients
- Starting dose not more than 0.125–0.50 mg/day h.s.
- Dose only once a day at bedtime, unless patient has trouble with sleep (rare)
- Therapeutic dose range, 1.0–5.0 mg/day
- Common adverse events: nausea, sleepiness, dizziness, tremors, compulsive behaviors, sleep attacks
- Depressive episodes that are associated with severe anhedonia, lack of motivation, inability to initiate behaviors, and unreactive mood are likely good candidates
- Expected benefit, if it occurs, by 4 weeks at maximally tolerated dose
- Avoid abrupt discontinuation because the risk of dopamine agonist withdrawal syndrome may be as high as 1 in 7
- When nausea is encountered, reduce the dosage, then try raising it again after 1–2 weeks

Maddison Ulrich Hussey, M.D., David Puder, M.D.

# Sometimes Medications Are Not The Full Answer

## Diet Can Give An “Anti-Helplessness Stance”

Dr. Goldberg notes in our discussion that there is likely a benefit from the patient simply proactively making changes to their lifestyle, taking an “anti-helplessness stance” in their outcome.

The SMILES trial, done by Jacka et al. in 2017, implemented dietary changes as a treatment for major depression. “There were 31 in the diet support group and 25 in the social support control group who had complete data at 12 weeks. The dietary support group demonstrated significantly greater improvement between baseline and 12 weeks on the MADRS than the social support control group, $t(60.7) = 4.38$, $p < 0.001$, Cohen’s $d = –1.16$. Remission, defined as a MADRS score <10, was achieved for 32.3% (n = 10) and 8.0% (n = 2) of the intervention and control groups, respectively ($\chi 2$ (1) = 4.84, p = 0.028); number needed to treat (NNT) based on remission scores was 4.1 (95% CI of NNT 2.3–27.8)” (Jacka et al., 2017b).

## Polypharmacy Is Common And Often Not The Most Effective Option

Throughout our reading of Dr. Goldberg’s work is a fight for simplicity and a scientific approach of finding the right medication with the least side effects.

One of Dr. Goldberg’s clinical interests that has influenced his research is polypharmacy. In Dr. Goldberg’s 2009 article titled, “Depressive Illness Burden Associated With Complex Polypharmacy in Patients With Bipolar Disorder: Findings From the STEP-BD”, the study aimed at analyzing profiles of patients with bipolar disorder who were receiving multi-drug treatment regimens. This study concluded that:

1. “Complex polypharmacy involving at least 4 medications occurs in approximately 1 in 5 individuals with bipolar disorder.”
2. “Use of traditional mood stabilizers is associated with fewer cotherapies.”
3. “Complex regimens are especially common in patients with substantial depressive illness burden and suicidality, for whom simpler drug regimens may fail to produce acceptable levels of response.”

Looking at specific medications, they found “complex polypharmacy was least often associated with lithium, divalproex, or carbamazepine and most often associated with atypical antipsychotics or antidepressants. Contrary to expectations, a history of psychosis, age at

onset, bipolar I versus II subtype, history of rapid cycling, prior hospitalizations, current illness state, and history of alcohol or substance use disorders did not significantly alter the risk profiles for receiving complex regimens" (Goldberg et al., 2009).

After this study, a resident working with Dr. Goldberg published a literature review that looked at extensive polypharmacy in patients with bipolar disorder and their contributing factors (Kim et al., 2021). This review found that of more than 13,800 patients across 49 studies, over 22% were taking 4 or more medications. They noted that "studies do not point to better outcomes for patients receiving more complex drug regimens, suggesting likely confounding by indication, high severity, or comorbid conditions." The study compiled contributing factors to polypharmacy, summarized in the following table (Kim et al., 2021):

**Table 2. Clinical Characteristics Associated With Complex Polypharmacy in Bipolar Disorder Patients**

| Characteristic | Observations |
|---|---|
| Sex | Female[6,23] |
| Race | White[6] |
| Age | Above 50 years in some studies,[19] ; no relation between age and medication number in others[1,16,29] |
| Psychosis | Present more often than absent[6,35] |
| Bipolar disorder subtype | Remission less likely in complex pharmacotherapy subjects with bipolar I than with bipolar II disorder diagnoses[13] |
| Medication dosage | Generally lower than in monotherapy[40] |
| Depressive illness burden | High[15] |
| Treatment adherence | Lower than with fewer medications[33] |
| Association with adverse effects | No clear additive burden[33] |
| Comorbid personality disorders | Borderline personality disorder[6] |
| Other comorbid psychiatric conditions | Posttraumatic stress disorder[6]; remission less likely in complex pharmacotherapy subjects with social or generalized anxiety disorder[33] or other anxiety disorders[18] |
| History of suicide attempts | Typically ≥ 1[15,18] |
| Personality traits | Low levels of extraversion, conscientiousness, and openness[5,31] |

It is important to try to minimize complex polypharmacy when possible to avoid unnecessary side effects and medication costs. Dr. Goldberg notes in the podcast that when handling patients with complex polypharmacy, it is beneficial to go through the list and ask the patient what each drug is actually doing for them. This helps with adherence to the medications, and promotes patient autonomy. The bottom line for patient care should be the measure of the *patient's* satisfaction with their care, not ours.

Also of note, that effective treatment, like partial programs often lead to less medication over time. One study by Bateman and Fonagy found that patients with borderline personality disorder had much fewer medications than those in standard care in the five-year follow up after treatment (Bateman & Fonagy, 2010). Note in the below table, that those who received treatment had 0.02 years out of 5 years on three or more drugs, whereas those in the treatment as usual group had 1.9 years out of 5 years on three or more drugs.

Maddison Ulrich Hussey, M.D., David Puder, M.D.

**TABLE 1. Effect Sizes for Primary and Secondary Outcomes for Mentalization-Based Treatment by Partial Hospitalization/Group Therapy and Treatment as Usual Groups Over 5 Years Postdischarge**

| Measure | Mentalization-Based Treatment by Partial Hospitalization/Group Therapy (N=22) | | Treatment as Usual (N=19) | | Analysis | | | Effect Size[a] | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Test | df | p | d | 95% CI |
| Suicide attempts | | | | | | | | | |
| Total number | 0.05 | 0.9 | 0.52 | 0.48 | U=73, z=3.9 | | 0.00004 | 1.4 | 1.3 to 1.5 |
| | N | % | N | % | Test | df | p | d | 95% CI |
| Any attempt | 5 | 23 | 14 | 74 | $\chi^2$=8.7 | 1 | 0.003 | 2.0 | 1.4 to 4.9 |
| Zanarini Rating Scale for Borderline Personality Disorder[b] | | | | | | | | | |
| Positive criteria | 3 | 14 | 13 | 87 | $\chi^2$=16.5 | 1 | 0.000004 | 1.4 | 1.2 to 2.4 |
| | Mean | SD | Mean | SD | Test | df | p | d | 95% CI |
| Total | 5.5 | 5.2 | 15.1 | 5.3 | F=29.7 | 1, 35 | 0.000004 | 1.80 | 0.14 to 3.50 |
| Affect | 1.6 | 2.0 | 3.7 | 2.0 | F=9.7 | 1, 35 | 0.004 | 1.10 | 0.41 to 1.70 |
| Cognitive | 1.1 | 1.4 | 2.5 | 2.0 | F=6.9 | 1, 35 | 0.02 | 0.84 | 0.30 to 1.40 |
| Impulsivity | 1.6 | 1.8 | 4.1 | 2.3 | F=13.9 | 1, 35 | 0.001 | 1.20 | 0.59 to 1.90 |
| Interpersonal | 1.5 | 1.7 | 4.7 | 2.3 | F=23.2 | 1, 35 | 0.00003 | 1.6 | 1.0 to 2.3 |
| GAF score[c] | 58.3 | 10.5 | 51.8 | 5.7 | F=5.4 | 1, 35 | 0.03 | 0.75 | –1.90 to 3.40 |
| | N | % | N | % | Test | df | p | d | 95% CI |
| GAF score >61 | 10 | 46 | 2 | 11 | $\chi^2$=6.5 | 1 | 0.02 | 3 | 2 to 12 |
| | Mean | SD | Mean | SD | Test | df | p | d | 95% CI |
| Number of days of hospitalization[c] | 0.27 | 0.71 | 6.2 | 5.6 | U=25.5, z=5.1 | | 0.00000002 | 1.50 | 0.36 to 2.70 |
| Number of emergency room visits[c] | 0.77 | 1.10 | 6.4 | 5.7 | U=66.0, z=3.9 | | 0.00003 | 1.40 | 0.21 to 2.63 |
| Number of years of employment[c] | 3.2 | 2.3 | 1.2 | 1.9 | F=8.9 | 1, 35 | 0.005 | 0.94 | 0.29 to 1.60 |
| Number of years of further treatment[c] | | | | | | | | | |
| Further psychiatric outpatient treatment | 2.0 | 1.9 | 3.6 | 1.5 | F=8.5 | 1, 35 | 0.006 | 0.93 | –4.00 to 1.50 |
| Further therapy 36 months postintake | 0.48 | 1.10 | 0.55 | 0.83 | F=0.6 | 1, 35 | n.s. | 0.07 | –0.23 to 0.37 |
| Further assertive outreach treatment | 0.39 | 0.51 | 2.7 | 1.8 | U=33.5, z=4.68 | | 0.0000002 | 1.8 | 1.4 to 2.2 |
| Medication (years)[c] | | | | | | | | | |
| Antidepressants | 1.1 | 1.8 | 3.3 | 2.3 | F=11.6 | 1, 35 | 0.002 | 1.10 | 0.45 to 1.70 |
| Antipsychotics | 0.16 | 0.28 | 3.1 | 2.1 | U=9.0, z=5.4 | | 0.0000000005 | 2.04 | 1.60 to 2.50 |
| Mood stabilizers | 0.11 | 0.26 | 1.8 | 2.1 | U=105.0, z=3.2 | | 0.001 | 1.17 | 0.73 to 1.60 |
| Three or more drugs (including hypnotics) | 0.02 | 0.11 | 1.9 | 1.9 | U=58.5, z=4.6 | | 0.0000009 | 1.45 | 1.10 to 1.80 |

[a] For frequency variables, data effect sizes are stated as numbers needed to treat with Newcombe-Wilson 95% confidence intervals.
[b] Number for treatment as usual=15.
[c] Number for treatment as usual=18.

## The importance of profiling patients

Next in the discussion, Dr. Goldberg explains his thoughts on the study by Ghaemi et al., “Citalopram for Acute and Preventive Efficacy in Bipolar Depression (CAPE-BD): A Randomized, Double-Blind, Placebo-Controlled Trial”. This study found that adding citalopram to a mood stabilizer **did not add** a significant benefit to the patient’s treatment (Ghaemi et al., 2021). Dr. Goldberg points out that randomized clinical trials only include diagnoses that fit DSM

criteria. In clinical practice, if we are looking at patients who do not truly fit the bipolar criteria, we are extrapolating the results. In Dr. Goldberg's view, it is necessary to determine each patient's "profiling candidacy" for antidepressants when treating bipolar depression. His criteria for a bipolar patient who is a good candidate for adding an antidepressant to treatment is:

1. Bipolar disorder type 2 is better than bipolar type 1.
2. The patient has NO mixed features.
3. The patient has had no recent mania, aka they were previously euthymic before the current depressive episode.
4. The patient has no rapid cycling (4 episodes in the past year).
5. The patient has never historically become manic after taking an antidepressant.

This demonstrates the importance of describing patients as much as possible to choose the right medications, going "beyond just the diagnosis". This concept is a large focus of Dr. Goldberg's latest book.

# Moderators of Treatment Outcome

In this podcast, Dr. Puder and Dr. Goldberg also delve into Chapter 5 of Dr. Goldberg's book, *Practical Psychopharmacology*, titled, "Tailoring the Fit: Moderators and Mediators of Treatment Outcome". Helena Chmura Kraemer, Ph.D. has done a lot of work in bringing awareness to the importance of moderators and mediators in clinical research and in clinical practice (Kraemer, 2016). Dr. Goldberg uses her research to guide the discussion on moderators and mediators in his book. He defines moderators as "patient baseline characteristics that influence outcome" (pre-treatment factors). He defines mediators as factors that affect outcome after treatment starts, aka "things that muck up good outcomes".

For example, antidepressants are the gold standard first-line treatment choice for patients with major depression. However, most antidepressants do not work as well when the moderator of anxiety is also present. Dr. Goldberg points to a study done by Thase et al, which looked at treating patients with vilazodone who have major depression and severe comorbid anxiety. The study noted that "82% of the pooled study group met the criteria for anxious depression compared with only about 50% of STAR*D participants" (Thase et al., 2014). They found that vilazodone worked significantly better than placebo for this subgroup of patients. Paying attention to moderators will help guide treatment decisions, especially in more complicated patients.

Maddison Ulrich Hussey, M.D., David Puder, M.D.

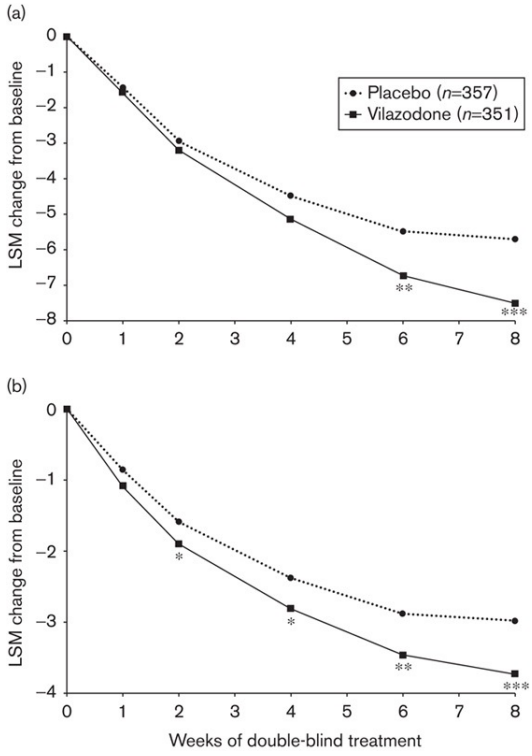


Fig. 1

Mean changes in (a) HAMA total and (b) HAMD17 Anxiety/Somatization subscale scores over 8 weeks of treatment in patients with anxious depression. HAMA, Hamilton Anxiety Rating Scale; HAMD17, 17-item Hamilton Depression Rating Scale; LSM, least squares mean. *P<0.05; **P<0.01; ***P≤0.001 versus placebo (Thase et al., 2014).

Next, we will highlight some of the specific moderators Dr. Goldberg outlines in his book.

# Dr. Goldberg's List of Moderators (J. Goldberg & Stahl, 2021):

1. Baseline severity
2. Age
3. Early age at onset
4. Chronicity
5. Episode number
6. Duration of untreated illness
7. Sex
8. Race and ethnicity
9. History of suicide attempts
10. Baseline anxiety
11. Childhood trauma
12. Resilience
13. Past treatment response
14. Familiality
15. Patient treatment preference
16. Elevated inflammatory markers
17. Psychosocial context
18. Illness subcharacteristics

# Practical Psychopharmacology with Dr. Goldberg

Maddison Ulrich Hussey, M.D., David Puder, M.D.

## Baseline severity

Baseline severity is a crucial variable to consider. For example, patients with more severe symptoms of depression are not placebo responsive, whereas mild depression is more placebo responsive. Thus, it will be more difficult to differentiate the effect of placebo from the drug in mild depression. Conversely, more severe patients who improve on a drug are showing a more durable response (that might take longer to achieve).

For example, the reason that lamotrigine is not FDA approved for bipolar depression is that in the study trials, the placebo response was very high in mildly depressed bipolar patients (Geddes et al., 2009). When clinical trials enroll more moderately ill patients, they may be muddying the effects of the trial with the higher placebo effect due to the mild severity of patients enrolled. As Goldberg explains in his book, “high baseline severity in RCTs can often be a predictor of better response to an active drug, not simply by suppressing placebo responsivity but by allowing for greater variance in the active treatment arm with which to see clinically meaningful change” (J. Goldberg & Stahl, 2021).

## Baseline anxiety

The comorbidity of anxiety is widely underappreciated. A review by Bagby et al. notes, “There are relatively few studies in which the existence of a comorbid anxiety disorder was not predictive of nonresponse” (Bagby et al., 2002).

## Past treatment response

Looking at moderators will help you treat the patient more effectively, especially looking at the number of failed responses in the current episode. In Dr. Goldberg’s opinion, this is the most important moderator to consider. It is important to clarify the adequacy of past trials before ruling out these drugs in treatment. Why did they stop taking the medication? Were they on the drug long enough?

Furthermore, we must be realistic with the patient about the probability of success. In a paper titled, “When Further Pharmacotherapy is Futile”, Goldberg notes that “declaring pharmacologic futility (...) means embracing the here-and-now reality of existing treatment limitations, fostering resilience, planning realistic goals, and breaking free from unreasonable expectations. Remission always remains the ideal outcome, but overzealous efforts to attain overidealized goals ultimately make perfection the enemy of the good” (J. F. Goldberg, 2018).

This paper looks at the question, “How do you maintain hope when the patient has tried many different treatments and is still not getting better?” Each treatment trial raises the risk of an “operant conditioning paradigm”, meaning therapy failure is demoralizing for patients. Goldberg lays out some goals of therapy for the clinician in this situation:

## Practical Psychopharmacology with Dr. Goldberg

Maddison Ulrich Hussey, M.D., David Puder, M.D.

- “Sustaining a sense of hope by redirecting efforts away from repeated failures of relentless pharmacology trials and instead toward more aggressive psychotherapeutic/psychosocial treatment modalities
- Providing an honest appraisal of prognosis and its modifiable versus non modifiable determinants
- Eliminating medications of no obvious benefit that may contribute to the cumulative burden of adverse effects (particularly those that may have already imposed significant metabolic or cardiovascular hazards) or potential undesired pharmacokinetic interactions
- Helping patients differentiate acceptable from unacceptable residual symptoms or adverse drug effects
- Educating patients and families about the role of pharmacotherapy as an adjunct to psychosocial therapies, rather than the reverse
- Reorienting the goals of treatment away from disease modification and instead toward alternative outcome states, such as avoiding suicide attempts, managing chronic suicidal thinking, and avoiding emergency department visits or hospitalizations unless absolutely necessary
- Strengthening patients’ capacity for resilience and ways to hone skills for coping with a chronic and possibly permanent condition
- Developing a philosophically aligned interdisciplinary treatment team (e.g., psychotherapist, pharmacologist, case manager, primary care provider) with a convergent perspective about the goals of treatment
- Gently redirecting unrealistic expectations or magical thinking that new therapies will likely produce dramatically transformative effects and fostering their cautious rather than overzealous undertaking
- Maintaining a focus on quality of life and the pursuit of reasonable personal goals in light of, rather than as prevented by, persistent symptoms
- Recognizing the value of small gains or modest improvements (such as inroads made in insomnia, or impulsive aggression, or the ability to perform part-time volunteer work)
- Helping steer patients away from potentially exploitative, costly, unnecessary evaluations that fall outside the mainstream or the pursuit of unfounded remedies with which potential hazards exceed expectable benefits (including inappropriate or non-evidence-based dosing of controlled substances)
- Permitting oneself, as a clinician, the humility to accept that not all mental health disorders are biologically remediable and that even dire outcomes such as completed suicide are sometimes unpreventable despite excellent care” (J. F. Goldberg, 2018).

Dr. Goldberg also suggests asking, “Is my diagnosis right?” when looking at non response. Check for other causes for this patient’s symptoms (drug use, thyroid disease, somatization, etc.). This is necessary to then be able to map out what is viable for treatment.

When assessing treatment response, Dr. Goldberg notes that at least a measurable improvement of 20% in the first 2 weeks is a good indicator of future success for medications for

major depressive disorder, bipolar depression, schizophrenia, panic disorder and generalized anxiety disorder. This measure comes from a study done in 2009 by Szegedi et al. The study concluded that “the high negative predictive values indicate little chance of stable response or stable remission in the absence of improvement within 2 weeks. A lack of improvement during the first 2 weeks of therapy may indicate that changes in depression management should be considered earlier than conventionally thought” (Szegedi et al., 2009). Thus, if the patient is showing no improvement after 2 weeks, following up a lack of change with things like a dosage change, augmentation, or substitutions is indicated.

When assessing a patient’s improvement, it is important to assess “measurable improvement”. We need to use a metric to avoid subjectivity. Most often for depression, clinicians use the PHQ9 to monitor improvement. Interestingly, there is no research to support that the PHQ9 can measure change over time, as it was made as a screening tool for depression. If we want to use a more appropriate scale, clinicians can use scales sensitive to change over time like the Montgomery-Asberg Depression Rating Scale (MADRS) or the Quick Inventory of Depressive Symptomatology (QIDS). He notes one could even try asking the patient to fill out a visual analog scale of daily ratings of symptoms from 1-10. Dr. Goldberg does admit that this will be time consuming during regular psychiatric appointments, and he himself does use the PHQ9 to monitor patient progress.

## Psychosocial context

Dr. Goldberg notes somatization as another important moderating factor, stating that “patients who are very somatically preoccupied are very difficult to treat.” He references the “nocebo effect”, defined as adverse effects from innocuous substances. The clinician runs the risk of worsening a patient’s status due to side effects of new medications. Clinicians also need to differentiate serious from “annoying” side effects when determining whether to continue a medication. Goldberg notes that opposing mechanisms or disparate symptoms indicate somatization over side effects. It is necessary to use supportive psychotherapy to empathize and use therapeutic alliance to your benefit when having these discussions with patients experiencing somatization.

A study done by McKay et al. in 2006 looked at the contribution of the psychiatrist in depression treatment outcomes. They concluded, “in this study, both psychiatrists and treatments contributed to outcomes in the treatment of depression. However, given that psychiatrists were responsible for more of the variance in outcomes it can be concluded that effective treatment psychiatrists can, in fact, augment the effects of the active ingredients of anti-depressant medication as well as placebo” (McKay et al., 2006).

*Acknowledgments:*
*This article was supported by “Mental Health Education & Research”.*

# Practical Psychopharmacology with Dr. Goldberg

Maddison Ulrich Hussey, M.D., David Puder, M.D.

**References:**

Bagby, R.M., Ryder, A.G., & Cristi, C. (2002, July). Psychosocial and clinical predictors of response to pharmacotherapy for depression. *Journal of psychiatry & neuroscience : JPN, 27*(4), 250-257.

BATEMAN, A., & FONAGY, P. (2010). Mentalization based treatment for borderline personality disorder. *World Psychiatry, 9*(1), 11–15. https://doi.org/10.1002/j.2051-5545.2010.tb00255.x

Fawcett, J., Rush, A. J., Vukelich, J., Diaz, S. H., Dunklee, L., Romo, P., Yarns, B. C., & Escalona, R. (2016). Clinical Experience With High-Dosage Pramipexole in Patients With Treatment-Resistant Depressive Episodes in Unipolar and Bipolar Depression. *American Journal of Psychiatry, 173*(2), 107–111. https://doi.org/10.1176/appi.ajp.2015.15060788

Geddes, J. R., Calabrese, J. R., & Goodwin, G. M. (2009). Lamotrigine for treatment of bipolar depression: independent meta-analysis and meta-regression of individual patient data from five randomised trials. *British Journal of Psychiatry, 194*(1), 4–9. https://doi.org/10.1192/bjp.bp.107.048504

Ghaemi, S. N., Whitham, E. A., Vohringer, P. A., Barroilhet, S. A., Amerio, A., Sverdlov, O., & Patkar, A. A. (2021). Citalopram for Acute and Preventive Efficacy in Bipolar Depression (CAPE-BD). *The Journal of Clinical Psychiatry, 82*(1). https://doi.org/10.4088/jcp.19m13136

Goldberg, J. F. (2018). When Further Pharmacotherapy Seems Futile. The Journal of Clinical Psychiatry, 80(1). https://doi.org/10.4088/jcp.18ac12276

Goldberg, J. F., Burdick, K. E., & Endick, C. J. (2004). Preliminary randomized, double-blind, placebo-controlled trial of pramipexole added to mood stabilizers for treatment-resistant bipolar depression. *American Journal of Psychiatry*, *161*(3), 564-566. https://doi.org/10.1176/appi.ajp.161.3.564

Goldberg, J. F., Brooks III, J. O., Kurita, K., Hoblyn, J. C., Ghaemi, S. N., Perlis, R. H., ... & Thase, M. E. (2009). Depressive illness burden associated with complex polypharmacy in patients with bipolar disorder: findings from the STEP-BD. *Journal of Clinical Psychiatry*, *70*(2), 155. https://www.psychiatrist.com/jcp/bipolar/depressive-illness-burden-associated-complex-polypharmacy/

Goldberg, J., & Stahl, S. (2021). *Practical Psychopharmacology (Translating Findings From Evidence-Based Trials into Real-World Clinical Practice)* (1st ed.). Cambridge University Press.

Jacka, F. N., O'Neil, A., Opie, R., Itsiopoulos, C., Cotton, S., Mohebbi, M., Castle, D., Dash, S., Mihalopoulos, C., Chatterton, M. L., Brazionis, L., Dean, O. M., Hodge, A. M., & Berk, M. (2017). A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial). *BMC Medicine, 15*(1). https://doi.org/10.1186/s12916-017-0791-y

Kim, A. M., Salstein, L., & Goldberg, J. F. (2021). A Systematic Review of Complex Polypharmacy in Bipolar Disorder. *The Journal of Clinical Psychiatry, 82*(3). https://doi.org/10.4088/jcp.20r13263

# Practical Psychopharmacology with Dr. Goldberg

Maddison Ulrich Hussey, M.D., David Puder, M.D.

Kraemer, H. C. (2016). Messages for Clinicians: Moderators and Mediators of Treatment Outcome in Randomized Clinical Trials. *American Journal of Psychiatry, 173*(7), 672–679. https://doi.org/10.1176/appi.ajp.2016.15101333

McKay, K. M., Imel, Z. E., & Wampold, B. E. (2006). Psychiatrist effects in the psychopharmacological treatment of depression. *Journal of Affective Disorders, 92*(2–3), 287–290. https://doi.org/10.1016/j.jad.2006.01.020

Szegedi, A., Jansen, W. T., van Willigenburg, A. P. P., van der Meulen, E., Stassen, H. H., & Thase, M. E. (2009). Early Improvement in the First 2 Weeks as a Predictor of Treatment Outcome in Patients With Major Depressive Disorder. *The Journal of Clinical Psychiatry, 70*(3), 344–353. https://doi.org/10.4088/jcp.07m03780

Thase, M. E., Chen, D., Edwards, J., & Ruth, A. (2014). Efficacy of vilazodone on anxiety symptoms in patients with major depressive disorder. *International Clinical Psychopharmacology, 29*(6), 351–356. https://doi.org/10.1097/yic.0000000000000045