Published in final edited form as:

Ann Behav Med. 2014 June ; 47(3): 253–254. doi:10.1007/s12160-013-9581-8.

Is the glass half full or half empty? Treatment of depression and HIV/AIDS treatment adherence: a comment on Sin and DiMatteo

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In 2000, DiMatteo and colleagues published a major meta-analysis of 30 years of observational research relating depression and treatment adherence in various chronic illnesses; 12 studies were identified and none focused on HIV/AIDS (1). Twelve years later, a meta-analysis limited to treatment adherence in HIV/AIDS collected 95 studies (2). The new meta-analysis by Sin and DiMatteo (3) reflects the current state of the science in this rapidly growing literature and makes a timely contribution to future progress. Analyses test whether treatment of depression in individuals with HIV/AIDS would result in improved antiretroviral (ART) adherence. They include 29 observational and experimental studies, which vary considerably in their measurement and treatment methods. Although a significant relationship between depression treatment and better ART adherence was found overall, the effect was quite variable. Thus, comprehensive moderator analyses provide an important guide to evaluating the evidence.

Three findings most relevant to future work emerge. First, treatments specifically targeting depression are more likely to be associated with ART adherence than those that address depression as a secondary matter. Second, treatments of longer duration are significantly more likely to be associated with adherence than shorter treatments. Third, and most important, observational studies are likely to yield stronger effects than randomized controlled trials (RCTs). In fact, among RCTs, included because they employed at least one intervention element aimed at reducing depression or distress, the effect was not significant. Methodological limitations of these trials suggest a closer look is warranted.

Of the 15 RCTs, only 2 used a diagnosis of a depressive disorder as an entry criterion (4,5); one used a positive screening result for major depressive disorder (MDD) (6). Those remaining did not require that participants endorse any depression; 7 did not even measure depression. Trials infrequently used formal, empirically supported depression treatments, with the following exceptions. One trial tested collaborative stepped care, where antidepressant pharmacotherapy was the most common treatment (6); two smaller trials used 10-12 individually-delivered sessions of cognitive behavioral therapy (CBT) for depression, adapted to also address ART non-adherence as a primary, well-measured outcome (4,5).

This makes it impossible to isolate depression treatment-related adherence effects but may

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also explain why these trials are unique among those reviewed in achieving significant effects on both depression and adherence (4,5). However, maintenance of adherence effects over time may be challenging, at least in certain populations (5). Collaborative care, focused more exclusively on depression treatment, improved depression more quickly than active monitoring. However, by 12 months, depression improvements in the intervention group were met by equivalent gains among controls. The trial had no impact on adherence to ART or pharmacotherapy, secondary outcome effects for which it may have been underpowered (6). Thus, regarding causal effects of depression treatment on ART adherence, evidence is actually quite limited. Inconsistencies with measurement of depression and adherence likely also contributed to effect variability among observational studies (3).

To improve the evidence base, greater precision is needed in the conceptualization and measurement of depression (e.g., psychiatric condition vs. emotional distress). Although depression is most often described as a problem of psychiatric comorbidity in HIV/AIDS, most studies use self-report screeners with high false-positive rates or questionnaires more reflective of general emotional distress than a psychiatric condition (7,2). For example, only 6% of studies relating depression and ART adherence used structured clinical interviews for depression (2), the recognized gold standard. Imprecision in measurement and sample specification is likely to limit progress unless better concordance between constructs and measures is achieved (See, 7,2). Further trials are needed to rigorously evaluate the effects of depression treatment on ART adherence and other health outcomes. However, empirical evidence and clinical reasoning both suggest that treatment of depression may be necessary but insufficient to improve ART adherence, as it appears to be for treatment adherence in other illnesses (e.g., 8) and for other health behaviors in HIV/AIDS, such as sexual risk (9). Also, available data do not rule out non-causal or reverse causality models (3,10). One well-designed trial targeting depression and ART adherence as primary outcomes is currently underway in adults meeting MDD diagnostic criteria (11). Interventions are also needed to address emotional distress that does not fit the conceptual model of a comorbid psychiatric condition. To guide the refinement of these approaches and increase their chances for translation, work is needed to evaluate hypothesized mechanisms linking depression and emotional distress with treatment non-adherence. Treatments that synthesize intervention elements for depression and distress with those aimed at addressing a fuller set of relevant facilitators and barriers to treatment adherence are likely to have the greatest impact on research and practice.

Acknowledgments

Dr. Gonzalez's efforts on this study were partially supported by grants from the National Institutes of Health (DK020541 and DK098742).

Conflict of Interest: Dr. Gonzalez is supported by an NIDDK grant to integrate the treatment of distress with self-management support in adults with type 2 diabetes. He trained and collaborated with Dr. Safren on NIH-supported trials of cognitive behavioral therapy for adherence and depression in HIV/AIDS and diabetes. He receives royalties from Oxford University Press, as a co-author of therapist and client manuals for cognitive behavioral therapy for adherence and depression in chronic illness.

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