

Evidence-based Synthesis Program (ESP)

Interventions to Improve Pharmacological
Adherence among Adults with Psychotic
Spectrum Disorders, Bipolar Disorder, and
Posttraumatic Stress Disorder

A Systematic Review

VA Portland Healthcare System

July 18, 2016

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Acknowledgements

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Disclosure

This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Center located at the Portland VA Medical Center funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

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VA Evidence-based Synthesis (ESP) Program Overview

- Sponsored by VA Quality Enhancement Research Initiative (QUERI) Program.
- Established to provide timely and accurate syntheses/reviews of healthcare topics identified by VA clinicians, managers and policy-makers, as they work to improve the health and healthcare of Veterans.
- Builds on staff and expertise already in place at the Evidence-based Practice Centers (EPC) designated by AHRQ. Four of these EPCs are also ESP Centers:
 - Durham VA Medical Center; VA Greater Los Angeles Health Care System; Portland VA Medical Center; and Minneapolis VA Medical Center.

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- Provides evidence syntheses on important clinical practice topics relevant to Veterans, and these reports help:
 - develop clinical policies informed by evidence,
 - the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
 - guide the direction for future research to address gaps in clinical knowledge.
- Broad topic nomination process – e.g. VACO, VISNs, field – facilitated by ESP Coordinating Center (Portland) through online process:

<http://www.hsrd.research.va.gov/publications/esp/TopicNomination.cfm>

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- Steering Committee representing research and operations (PCS, OQP, ONS, and VISN) provides oversight and guides program direction.
- Technical Advisory Panel (TAP)
 - Recruited for each topic to provide content expertise.
 - Guides topic development; refines the key questions.
 - Reviews data/draft report.
- External Peer Reviewers & Policy Partners
 - Reviews and comments on draft report
- Final reports posted on VA HSR&D website and disseminated widely through the VA.

<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>

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- What is your primary role in VA?
 - Pharmacist
 - Mental health clinician
 - Researcher
 - Administrator, manager or policy-maker
 - Other

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Current Report

Interventions to Improve Pharmacological Adherence
among Adults with Psychotic Spectrum Disorders,
Bipolar Disorder, and Posttraumatic Stress Disorder
(November 2015)

Full-length report available on the ESP website (intranet only):

<http://vaww.hsrd.research.va.gov/publications/esp/PharmaAdherence.cfm>

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Overview of Today's Presentation

- Background
- Scope of the review
- Results
- Future research
- Implications for VA
- Discussion/Q&A

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Medication Adherence Topic Nomination

- Original topic nomination focused on medication adherence for chronic conditions
- 2012 AHRQ review looked all conditions except HIV and SMI (included depression)
 - Strongest evidence related to reduced copays across conditions, self-management for asthma, collaborative care/case management for depression, pharmacist led hypertension approaches, and education, reminders, and pharmacist led multicomponent interventions
 - <https://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1248>

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Background

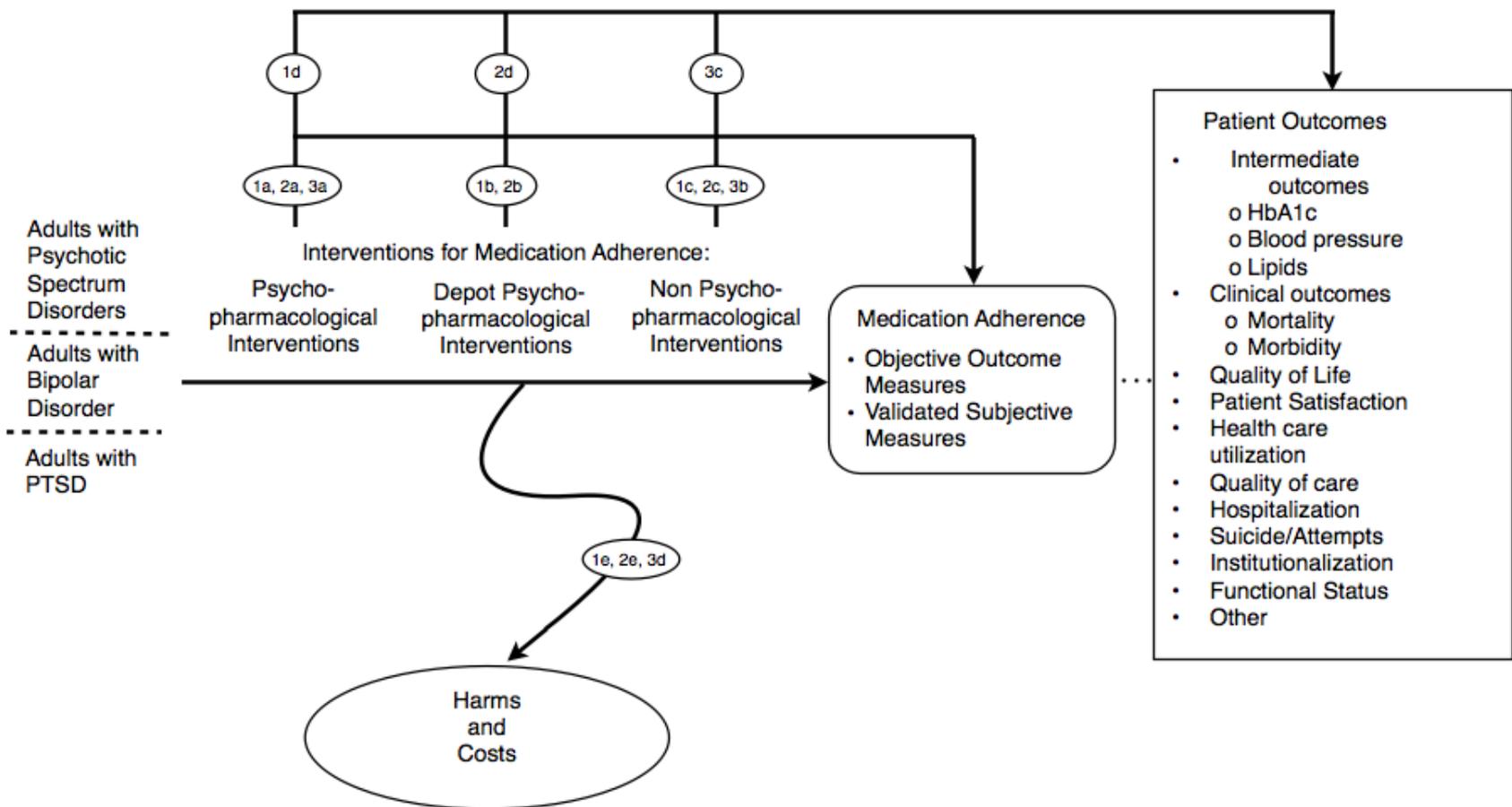
- ❑ Adherence to medication among individuals with serious mental illness is often low.
- ❑ Adherence among individuals with schizophrenia is estimated to be between 25-50%
- ❑ Reported rates of adherence among individuals with bipolar disorder is 30-57%
- ❑ Medication non-adherence is one of the strongest predictors of poor outcomes in people with schizophrenia and bipolar disorder.
- ❑ Individuals with serious mental illness have a higher prevalence of comorbid non-psychiatric conditions

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Scope of the Review

- ❑ For individuals with psychotic spectrum disorders, bipolar disorder, and PTSD, summarize the evidence related to:
 - ❑ Effectiveness of medication adherence interventions on both psychopharmacological and non-psychopharmacological adherence
 - ❑ Effect on patient outcomes
 - ❑ Related costs and intervention-associated harms

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Methods

- Search Strategy
 - ❑ Searched MEDLINE, PubMed, PsycINFO, EMBASE, CINAHL, and CCRT from database inception to January, 2015
 - ❑ Evaluated reference lists of identified systematic and nonsystematic reviews
 - ❑ Searched ClinicalTrials.gov, ICTRP, ISRCTN Registry, Conference Papers Index, and Dissertation and Theses Global for grey literature

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Methods

- Study Selection
 - Included studies of adults examining:
 - Interventions designed to improve medication adherence in general mental health settings
 - Reported a patient outcome and an objective or validated subjective measure of adherence
 - Included RCTs, NRCTs, methodologically rigorous observational studies, including before/after studies with at least 3 time points that controlled for time
 - 10% of titles/abstracts and 100% of full text were dual reviewed

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Methods

- Quality Assessment
 - ❑ Two reviewers independently assessed the quality of each study using the risk of bias ROB tool developed for AHRQ Evidence-based Practice Centers
 - ❑ Disagreements were resolved through discussion or by a third reviewer
 - ❑ Studies were given an assessment of low, medium, high, or unclear ROB

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Overall Results

- Our search for literature resulted in 7,944 studies. After abstract and full text review, 24 studies from 25 publications met inclusion criteria
 - Psychotic spectrum disorders (20 studies, 21 publications)
 - Bipolar disorder (4 studies)
 - PTSD (no studies identified)

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Key Findings

- ❑ For psychotic spectrum disorders (20 studies, 21 publications):
 - ❑ Interventions involving family members (3 studies) show a generally positive effect on adherence (SOE: low), and studies report positive effects on symptom severity and function, with fewer hospital admissions and a longer time to relapse.
 - ❑ Interventions involving technology (4 studies) report a positive effect on medication adherence (SOE: low). SMS (2 studies) had a positive effect on symptom severity and quality of life. The effects of e-Monitoring (2 studies) on patient outcomes were mixed.
 - ❑ Interventions combined with a depot antipsychotic (2 studies) found limited effect (SOE: insufficient). There was insufficient evidence for all other types of interventions.

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Key Findings

- ❑ For bipolar disorder (4 studies):
 - ❑ Interventions involving psychoeducation (2 small studies) showed a positive effect on medication adherence (SOE: insufficient) and reductions in depression, mania, hospital readmissions, and global functioning. Evidence for other types of interventions were also insufficient.
- ❑ PTSD - No studies were identified

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Psychotic Spectrum Disorders

Type of Intervention	Study Design (Combined N) ^a	Findings	Strength of Evidence	Comments
Family Interventions	3 RCTs (N=497)	Better adherence with family interventions as measured by clinician rating/blood plasma and pharmacy records/family-report as compared to usual care in 2 studies (moderate ROB). No difference when controlling for time in a third study examining a culturally modified family intervention as compared to the standard family intervention and monthly sessions (moderate ROB).	Low	Heterogeneity among interventions.
Technology Interventions	4 RCTs (N=534)	Mixed findings on e-monitoring/MEMS: better adherence in one study as compared to pill counts and self-reported adherence (high ROB), conflicting results in one study as compared to a pharmacy-based intervention and usual care (low ROB). Telephone plus SMS resulted in nonsignificant adherence improvement versus telephone or SMS alone (moderate ROB); SMS alone resulted in significantly better adherence than usual care (moderate ROB).	Low	Mixed findings and heterogeneous interventions.
Adherence Intervention Plus Depot Antipsychotic	1 Trial (randomization unclear) (N=57); 1 Prospective Cohort (N=30)	Findings indicated improved adherence related to the use of depot antipsychotic injections plus a behavioral multicomponent intervention (compared to usual care or no comparator) as measured by injection visits up to one year, and TRQ, Morisky scale, DAI, and AMQ up to 25 weeks (moderate ROB).	Insufficient	Heterogeneity among interventions; ROB due to study design.
Pharmacist led Intervention	1 Prospective Cohort w/post hoc comparison (N=30)	No significant difference over time or between groups (high ROB).	Insufficient	Evidence from only one study; potential ROB due to study design flaws.
System level Intervention	1 NRCT (N=70)	Nonsignificant trend towards better adherence for the system-level intervention, compared with Compliance Therapy (moderate ROB).	Insufficient	Evidence from only one study.

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Psychotic Spectrum Disorders

Type of Intervention	Study Design (Combined N) ^a	Findings	Strength of Evidence	Comments
Multicomponent Behavioral Interventions				
Behavioral Multicomponent Adherence Therapy	2 RCTs (N=570)	Mixed findings: one study (low ROB) reported better adherence compared to usual care on the MAQ and SAI-C at 12 months, and the other (low ROB) reporting no difference from usual care on the CDR, DAI-30, and MARS at 12 weeks post-discharge.	Insufficient	Evidence from only 2 studies, with mixed findings.
Behavioral Multicomponent Compliance Therapy	2 RCTs (N=130); 1 NRCT (N=70); 1 Prospective Cohort (N=30)	Mixed findings: better MARS scores with Compliance Therapy at one month but not 6 months in one study (high ROB); better DAI and adherence scores as compared with routine management plus supportive counseling through 18-month follow-up in one study (high ROB); no benefit to Compliance Therapy up to 6 months in 2 studies (compared to nonspecific counseling and Compliance Therapy; moderate ROB).	Insufficient	Inconsistent findings among 4 studies. ROB due to study design.
Other Behavioral Multicomponent	1 RCT (N=88)	No difference between CBT plus MI and group psychoeducation plus MI groups (moderate ROB).	Insufficient	Evidence from only one study.
Other Interventions				
Motivational Interviewing (MI)	1 RCT (N=114)	One study found no benefit of MI over usual care as measured by the MAQ or DAI (low ROB).	Insufficient	Evidence from only one study.
Cognitive Adaptation Training (CAT)	2 RCTs (N=247)	One study found that both CAT and Pharm-CAT resulted in better adherence than usual care, with no difference between the two (moderate ROB). The second study comparing Pharm-CAT to e-monitoring reported mixed results (low ROB).	Insufficient	Evidence from 2 studies that used different comparators.
Shared Decision Making	1 RCT (N=107)	One study found no benefit to a shared decision making over usual care as measured by the MARS and plasma levels (high ROB).	Insufficient	Evidence from only one single study.

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Bipolar Disorder

Type of Intervention	Study Design (Combined N)	Findings	Strength of Evidence	Comments
Psychoeducation (individual/group)	1 RCT (N=108); 1 NRCT (N=45)	Both individual and group psychoeducation resulted in better medication adherence than pharmacotherapy alone or pharmacotherapy with standard psychotherapy (moderate ROB).	Insufficient	Evidence from only 2 studies, external validity concerns due to setting.
Psychoeducation Plus Problem Solving	1 RCT (N=164)	There was no improvement in medication adherence associated with the intervention as compared to usual care (moderate ROB).	Insufficient	Evidence from only one study. Only 75% of the intervention group and 81% of the control group participated in baseline plus one other assessment, and only 49% of the intervention group participated in most or all of the group sessions, with 37% never participating.
Customized Behavioral Multicomponent	1 Prospective Cohort (N=43)	Customized adherence enhancement (CAE) was associated with better adherence and attitudes towards medication at 3 and 6 months (moderate ROB).	Insufficient	Evidence from only one study; ROB due to study design.

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Discussion

- ❑ In general, interventions were heterogeneous, and findings were mixed.
- ❑ Interventions involving family members, and those involving technology for individuals along the psychotic spectrum show promise; however, due to a lack of consistent benefit across studies, we rated the strength of evidence as low.
- ❑ Other interventions varied widely, and the evidence was insufficient. There were few studies examining the same interventions, sample sizes were small, and in general, there were methodological flaws.
- ❑ The evidence was insufficient for all interventions for individuals with bipolar disorder.
- ❑ We identified no studies examining medication adherence in individuals with PTSD.
- ❑ Other than technology-based interventions, most were flexible and allow for adaptation to different settings and patients. While interventions for medication adherence have been found effective for other conditions, more research is needed to better understand whether they are effective with individuals with serious mental illness.

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Future Research

- ❑ Future research with an active comparator is needed. Many studies compared to usual care. Given the type of intervention, it is possible that added interaction/increased attention may have an effect.
- ❑ More research is needed examining interventions accompanying depot antipsychotics to determine if any improvement in adherence or patient outcome is associated with depot or the intervention, or the degree of improvement in this population relates to low baseline levels.
- ❑ In general, future research should also include larger RCTs of adequate duration. Given that many of the interventions are multicomponent and complex, and that they are implemented in a wide range of settings, standardization of the interventions would improved the ability to replicate and evaluate effectiveness.

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Future Research

- ❑ No research we identified evaluated the effect on non psychopharmacological medication. Considering high rates of comorbid conditions, more research should examine whether medication adherence interventions for one condition spill over to others.
- ❑ Medication adherence is measured using a wide range of objective and subjective measures. The identification of a gold standard is warranted.
- ❑ No identified studies examined harms associated with interventions for medication adherence. While the risks associated with these types of interventions may be low, research is necessary to better weigh the potential benefits and harms.

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Questions?

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The full report and cyberseminar presentation is available on the ESP website:

<http://www.hsrd.research.va.gov/publications/esp/>