

femoris 3+, positive left (L) Hoffman's reflex. Chemosensory Testing: Olfaction: Brief Smell Identification Test: 12 (normosmia). Retronasal Olfactory Testing: Retronasal Smell Index: 1 (Anosmia). Gustatory Testing: Propylthiouracil Disc Taste Test: 10 (normogeusia). Waterless Empirical Taste Test: sweet: 4, sour: 3, salty: 7, bitter: 5, brothy: 0, total: 30 (ageusia to umami, otherwise normogeusia). Neuropsychiatric Testing: Go-No-Go Test: 2/6 (abnormal).

**Discussion.** Perhaps hypergeusia may not have been true hypergeusia but a misperception of retronasal smell associated hyperosmia with physiologic synesthesia manifested as taste. Peradventure, the perceived hypergeusia, is just one component of a generalized delusional paradigm, where many sensory perceptions are intensified. The perceived delusional hyperosmia may be intensification of the sensory misperception due to an underlying dysgeusia. This may represent a variant of the two-factor hypothesis of delusions whereby a distorted sensory perception is then misrepresented in a delusion. Dysfunction of the right hemisphere, which normally acts to censor the left, allows the delusion to manifest. While two different anatomical abnormalities (one left and one right hemisphere) have been postulated to be the foundation of such delusions, it is distinctly possible that a single lesion of the inferior parietal lobule may be sufficient for both sensory distortions to be produced as well as loss of inhibition of delusional interpretation of distorted sensation of the frontal lobe by the right parietal lobe, yclept the sensorialist hypothesis. In those who present with hypergeusia, search for delusional origin is warranted and in those who present with delusions, query as to perceived hypergeusia may be revealing.

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## Number Needed to Treat and Number Needed to Harm From Two Phase 3 Studies of Sublingual Dexmedetomidine for Treating Acute Agitation in Patients With Schizophrenia and Bipolar Disorder

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### Abstract

**Background.** Episodes of acute agitation can occur in individuals who suffer from schizophrenia or bipolar disorder and these can be a significant challenge for patients and for those who provide care to them. Sublingual dexmedetomidine is a selective alpha<sub>2</sub>-adrenergic receptor agonist that was recently approved by the US Food and Drug Administration for the treatment of agitation in adults with schizophrenia or bipolar disorder. The sublingual

form of dexmedetomidine does not undergo first-pass hepatic metabolism, thus resulting in greater absorption than when ingested. In two Phase 3 studies of adults with schizophrenia or bipolar disorder, sublingual dexmedetomidine significantly reduced acute agitation at 2 hours, as measured by the five-item Positive and Negative Syndrome Scale-Excited Component (PEC). When initially appraising the potential utility of a new medication, number needed to treat (NNT) and needed to harm (NNH) can be helpful to assess the size of the treatment effect and, hence, clinical relevance.

**Objective.** Calculation of NNT and NNH through post hoc analysis of Phase 3 data.

**Methods.** Post hoc analysis of data were performed on data from two double-blind, randomized, placebo-controlled studies of sublingual dexmedetomidine in adults with schizophrenia or bipolar disorder experiencing acute agitation. Patients were randomized to a single dose of sublingual dexmedetomidine 180 µg, 120 µg, or placebo. The primary endpoint was mean change from baseline in the PEC total score. A therapeutic response was defined as a ≥40% reduction from baseline in PEC total score at 2 hours. NNT was calculated for PEC response rate for sublingual dexmedetomidine versus placebo. NNH was calculated using the incidence of adverse events for sublingual dexmedetomidine versus placebo. Likelihood to be helped or harmed (LHH) was calculated as the ratio of NNH to NNT.

**Results.** NNT (95% CI) was 3 (2, 3) for 180 mcg and 3 (3, 4) for 120 ug in patients with schizophrenia and 3 (2, 3) for 180 mcg and 4 (3, 6) for 120 ug in patients with bipolar disorder. NNH was greater than 10 for all AEs except somnolence, where NNH was 7 (5, 10) for all doses pooled from both studies. LLH values were greater than 1 for efficacy versus applicable tolerability outcomes in all cases.

**Conclusions.** This post hoc analysis demonstrated favorable NNT and NNH values for sublingual dexmedetomidine. In all instances therapeutic response was encountered more frequently than any adverse event. These values compare favorably to similar analyses for other approved agents for the treatment of agitation associated with schizophrenia or bipolar disorder, including intramuscular and inhaled formulations.

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## Clinical Determinants, Patterns, and Outcomes of Antipsychotic Medication Prescribing in the Treatment of Schizophrenia and Schizoaffective Disorder: A Naturalistic Cohort Study

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**Abstract**

**Background.** Schizophrenia affects individuals, families, and systems, with treatment primarily being antipsychotic medications. Long-acting injectable (LAI) antipsychotics are increasingly being used. This study sought to identify predictors of antipsychotic choice, in terms of formulation (LAI vs oral) and class (FGA vs SGA), and clinical outcomes.

**Methods.** 123 patients who received LAI antipsychotics were diagnosis-matched to patients who received oral antipsychotics. Sociodemographic and clinical factors were extracted from the medical record, including indicators of illness severity. Groups were compared with Chi-Square and t-tests, and logistic regression models were used to identify independent predictors of antipsychotic choice.

**Results.** Patients that received LAIs had longer admissions, more complex discharges, and greater illness severity; however, there were no differences in readmission rates. Independent predictors of LAIs included younger age, being single, and longer admission. Patients who received FGA LAIs were more likely to use substances and be undomiciled compared to SGA LAIs, with the only predictor being older age. Oral FGAs were more likely than oral SGAs to be prescribed to older and female patients, as well as those with co-occurring substance use, complex discharges, and longer admissions.

**Conclusions.** Illness severity and duration of illness appear to drive choice of LAI vs. oral antipsychotic medication and FGA vs. SGA. While LAIs were prescribed to patients with greater illness severity, readmission rates were equivalent to those receiving oral medication, supporting the use of LAI in patients with greater illness severity. Rationales for prescribing LAIs to younger patients and FGAs to older patients are discussed.

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## Complete *in vitro* Dissolution of Valbenazine as Either Whole Capsules or Crushed Capsule Contents

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**Abstract**

**Introduction.** Tardive dyskinesia (TD) is a persistent and potentially disabling movement disorder associated with exposure to antipsychotics and other dopamine receptor blocking agents. Three valbenazine capsule strengths (40 mg, 60 mg, 80 mg) are approved for the once-daily treatment of TD. However, some patients with TD, especially in elderly populations, have trouble swallowing due to orolingual movements. This study was conducted to evaluate two different dissolution methods for valbenazine: whole intact capsules versus crushed capsule contents.

**Methods.** Samples were prepared using two commercial lots (Lot-A, Lot-B) for two doses (40 mg, 80 mg), with six replicate

samples per lot and dose. The whole capsules were weighed, put into a sinker, and added to a dissolution bath containing 900 mL of 0.1N HCl at  $37 \pm 0.5^\circ$  Celsius. Testing on the crushed capsule contents commenced after opening the capsules, weighing and crushing the contents, and transferring the contents to the dissolution bath. Samples were collected (at 10, 15, 20, 30, 45, and 60 min) with a paddle speed of 50 rpm and analyzed using high performance liquid chromatography. Standards were prepared at nominal concentrations of 0.044 mg/mL (for 40 mg) and 0.089 mg/mL (for 80 mg).

**Results.** Capsules were opened easily by manual manipulation, and contents were crushed easily between spoons. Very rapid (>85% in 15 min) and complete drug release was observed in all samples, independent of capsule strength (40 mg, 80 mg) or preparation (whole intact capsule or crushed capsule contents). For 40-mg capsules, average percent release at first and last collection timepoints were as follows (whole vs crushed): 10 min (98.4% vs 98.6% [A], 93.7% vs 97.6% [B]); 60 min (102.3% vs 100.5% [A], 100.9% vs 100.6% [B]). Results for 80-mg capsules were as follows: 10 min (98.2% vs 99.6% [A], 99.4% vs 97.9% [B]); 60 min (102.0% vs 101.6% [A], 103.2% vs 100.9% [B]).

**Conclusions.** Crushing the capsule contents did not impact the *in vitro* dissolution performance of valbenazine. Many patients with TD, particularly elderly patients, have difficulty swallowing and may benefit from alternative delivery methods for valbenazine, especially if other TD medications cannot be crushed. More research is needed to better understand if and how crushing the capsule contents of valbenazine affects their stability when mixed with food or delivered through a feeding tube.

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## Digital CBT-I Treatment Improves Sleep and Reduces Anxiety and Depression Symptoms in Adults With Chronic Insomnia: Interim Analysis of DREAM Study

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**Abstract**

**Introduction.** Chronic insomnia (CI) often co-occurs with depression and anxiety, and treatment may positively impact mood. This ongoing study collected real-world data on changes in insomnia, depression, and anxiety symptoms among adults with CI treated with a prescription digital therapeutic (PDT) delivering cognitive-behavioral therapy for insomnia (CBT-I; Somryst, previously SHUTi).

**Methods.** This prospective, single-arm, pragmatic clinical study enrolled adults ( $\geq 18$  years) in the US with CI and mobile device access. The PDT consists of six core modules completed over