The validity of the Columbia–Suicide Severity Rating Scale (C-SSRS) relative to other measures of suicidal ideation and behavior and the internal consistency of its intensity of ideation items were analyzed in three multisite studies, which are described here, along with the measures used.

Study 1

The Treatment of Adolescent Suicide Attempters study was a multisite feasibility study designed to develop and evaluate treatments to prevent suicide reattempts. The sample, methods, treatment, and initial outcomes of this study have been described in previous reports (1-3).

Participants

Participants were recruited from adolescent inpatient units, partial hospitals, and from general and specialty outpatient programs for depressed suicidal teenagers. Before entry into the study, informed consent/assent was obtained. Inclusion criteria were: adolescents aged 12 to 18 years who had made a suicide attempt or interrupted attempt within 90 days prior to intake; diagnosis of a major unipolar mood disorder (major depression, N=106; dysthymic disorder, N=1; depression not otherwise specified, N=4; or both major depression and dysthymic disorder, N=13); presence of at least moderate symptoms of depression, as defined by Children's Depression Rating Scale-Revised (CDRS-R) scores >=36; and they were required to be living with a parent or guardian who agreed to participate in the treatment. Exclusion criteria included diagnoses of substance dependence, bipolar disorder, psychosis or a developmental disorder.

Methods

This research project began as a three-arm randomized trial of pharmacotherapy, a cognitive-behavioral therapy designed for suicidal adolescents, and a combination of the two. Subsequently, a feasibility design was adopted allowing participants to be either randomized or to choose their preferred treatment. Participants were evaluated by an Independent Evaluator at baseline and at treatment weeks 6, 12, 18 and 24. The Columbia Suicide History Form (CSHF), the C-SSRS, Beck's Scale of Suicidal Ideation (SSI) and Beck's Lethality Scale (BLS) were administered at baseline, weeks 6, 12, 18, and 24, as well as during intervening unscheduled visits.

A total of 126 patients consented, were screened, and enrolled in the study. After two patients withdrew prior to baseline assessment, 124 participants were evaluated and reported on in this supplement. Mean age was 15.8 years (SD=1.5); 28 (22.6%) were male; 83 (66.9%) were White; 16 (12.9%) were African American; 19 (15.3%) were Hispanic; and 6 (4.8%) were "other". Fifteen (12%) participants made a suicide attempt during treatment. For a more detailed description of participant characteristics, refer to Brent et al., 2009 (3).

Ninety-six participants (77.4%) were assessed at week 12, 87 participants (70.2%) were evaluated at week 18, and 83 participants (66.9%) at week 24. Analyses were based on the intent-to-treat model and included the 124 patients who began treatment. Attrition between the study visits was due to participants refusing to continue both the study's treatment and assessments. Participants who refused treatment but continued with assessments were included in the analyses. As previously reported, participants who remained in the study for longer than median duration compared to those who were followed for less than the median, were similar on all baseline predictors of suicidal events except income (3).

Study 2

Study 2 (4) was a randomized, double-blind, placebo-controlled trial of escitalopram to treat depression in adolescent patients with major depressive disorder. The study resulted in FDA approval of the use of escitalopram to treat adolescents with major depressive disorder.

Participants

Participants were male and female adolescent outpatients (aged 12 to 17 years) with Major Depressive Disorder for at least 12 weeks. Diagnosis was established at screening by agreement of two independent clinicians through the use of the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version. In addition, the patients were required to have a score of at least 45 on the Children's Depression Rating Scale-Revised (CDRS-R) at both the screening and baseline visits and a score of at least 4 on the Clinical Global Impressions-Severity (CGI-S) Scale at baseline. In addition, participants were required to have a score of 80 or higher on the Kaufman Brief Intelligence Test at screening and to have normal physical examination, laboratory tests, and electrocardiogram (ECG) results.

Patients considered a suicide risk by the investigator, including those who had active suicidal ideation, had made a suicide attempt, or had been hospitalized because of a suicide attempt, were not eligible for the study. Other exclusion criteria included an Axis I diagnosis other than MDD, a history of psychosis or current psychosis, a history of mania or hypomanic episodes, a personality disorder, or co-morbidity with substance abuse, attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, posttraumatic stress disorder, bipolar disorder, pervasive developmental disorder, mental retardation, conduct disorder, oppositional defiant disorder, bulimia or a seizure disorder. Patients with a first-degree relative

with bipolar disorder were not enrolled. The exclusion criteria also included those who were taking other psychotropic medication or had been treated with any antidepressant or anxiolytic medication within two weeks of baseline (four weeks for fluoxetine), any neuroleptic or stimulant within six months of screening, or any investigational drug within 30 days or five half-lives before screening. Those with hypersensitivity to escitalopram or involvement in clinical studies of citalopram or escitalopram were excluded, as were pregnant women, nursing mothers, and females who were not practicing reliable birth control.

584 patients were screened and 316 were assigned either to placebo (N=158) or escitalopram (N=158). 133 (84.7%) participants on placebo and 126 (81.3%) participants on escitalopram completed the study, with no significant differences between the treatment groups for premature discontinuation.

The mean age of the placebo group was 14.5 +/- 1.5, and 14.7 +/-1.6 in the escitalopram group. The placebo group was identified as 78.3% White and the escitalopram group as 72.9% White. Both groups were 59% female.

Method

Participants were randomly assigned to 8 weeks of double-blind treatment with escitalopram 10 to 20 mg/day (N=155) or placebo (N=157). After a placebo lead-in, patients were evaluated at a baseline visit to determine whether they continued to meet all entry criteria, after which eligible patients were randomly assigned (1:1) to double-blind, flexible-dose treatment with either escitalopram, fixed at 10 mg/day for the first three weeks of double-blind treatment and then potentially increased to 20 mg/day at the end of week 3 or 4, or placebo.

The primary efficacy parameter was the change from baseline to week 8 in the Children's Depression Rating Scale-Revised (CDRS-R) score using the last observation carried forward approach. Evaluations were scheduled at the end of 1, 2, 3, 4, 6, and 8 weeks of double-blind treatment. The Children's Depression Rating Scale-Revised was performed at the initial (screening) visit, baseline, and at the end of weeks 2, 4, 6, and 8 of double-blind treatment. The Clinical Global Impressions-Improvement (CGI-I) Scale and Clinical Global Impressions-Severity (CGI-S) were administered at all postbaseline study visits; the Clinical Global Impressions-Severity was also administered at baseline. The Children's Global Assessment Scale (CGAS) was administered at baseline and at the end of weeks 4 and 8 of the double-blind phase; the Children's Global Impressions-Severity was also administered on early termination. Suicidal ideation and behavior was assessed using patient self-report with the Suicidal Ideation Questionnaire-Junior High School Version (SIQ-JR) and with the Columbia-Suicide Severity Rating Scale.

Study 3

Participants

Participants for this study were recruited by clinical staff at psychiatric and medical emergency departments in affiliated hospitals at Columbia University (CU), the University of Pennsylvania (UPenn), and the University of Rochester (UR). Patients were recruited for a larger study that involved an evaluation of the identification and classification of recent suicide attempts and non-suicidal self-injurious behaviors by emergency department providers.

All potential participants were evaluated by a mental health professional in the emergency department. Permission was given for the research staff to approach patients to

determine if they met study criteria. Study inclusion criteria were as follows: (1) 18 years of age or older, (2) evaluated by a health care professional (physician or nurse) in the emergency department and willing to be approached by the research staff, and (3) understood and provided written informed consent to participate in the study. In addition, participants must have met criteria for one of three groups: (1) made a suicide attempt prior to the emergency department evaluation, (2) engaged in non-suicidal self-injurious behavior in the week prior to the emergency department evaluation, or (3) reported psychiatric symptoms and did not attempt suicide or engage in any non-suicidal self-injurious behavior prior to the emergency department evaluation.

A total of 237 participants were evaluated across three sites. Of the 237, 124 (52.3%) were identified as suicide attempters by the research staff, 31 (13.1%) were non-suicidal self-injurers, and 82 (34.6%) psychiatric patients did not make a suicide attempt or engage in a non-suicidal self-injurious behavior. There were no significant site differences in the proportions of the types of patients that were recruited. The mean age was 36 years (*SD*=12), and ranged from 18 to 79 years old. There were 136 (57.4%) females and 101 (42.6%) males; 121 (51.1%) Caucasians, 56 (24%) African Americans, 47 (20%) Hispanics, 2 (0.8%) Asians, 2 (0.8%) Native Americans, and 6 (2.5%) “Other” were unidentified in terms of ethnic background (data on race were missing for 3 subjects); 121 (51.1%) had never been married, 58 (24.5%) were married or partnered, 35 (14.8%) were divorced, 21 (8.9%) were separated, and 2 (0.8%) were widowed; 119 (50.2%) had a high school diploma; 107 (45.1%) were unemployed, 56 (23.6%) were employed, and 26 (11.0%) were disabled.

Methods

Eligible participants were identified by reviewing emergency department logs or electronic emergency department tracking databases, or they were referred directly to the study by emergency department providers. Written informed consent was obtained and enrolled participants were administered a battery of clinician-administered measures by research staff that included the C-SSRS, Scale for Suicide Ideation (SSI), Beck's Lethality Scale, and the Columbia Suicide History Form (CSHF). Participants were paid $50 for completing each research assessment interview. Research staff then classified patients as suicide attempters, non-suicidal self-injurers, or psychiatric controls, based upon the information obtained from the research instruments. Cases in which research staff was unsure about the correct classification were reviewed with the investigators and consensus was reached among the group.

Measures Used in the Study

Columbia Suicide Severity Scale (unpublished) (C-SSRS). This is a semi-structured instrument that provides for the identification and assessment of both suicidal ideation and behavior. The scale includes definitions of terms, questions, skip out criteria so that only relevant questions are asked, and allows for the integration of data from multiple sources.

The C-SSRS assesses five types of ideation: (1) wish to be dead, (2) non-specific active suicidal thoughts, (3) suicidal thoughts with methods, (4) suicidal intent, and (5) suicidal plan and intent. Severity rating(s) for suicidal ideation from 0 (no ideation) to 5 (active suicidal ideation with plan and intent) is assigned according to the appropriate type(s) reported within the designated time period. If the patient endorses any type of ideation, the Intensity of Suicidal

Ideation subscale is administered to assess the most severe type of ideation on the dimensions of frequency, duration, controllability, deterrents, and reasons for ideation. The intensity items are summed to create a Suicidal Ideation Intensity score ranging from 2 to 25.

The C-SSRS behavior item measures the full spectrum of suicidal behavior: suicide, actual attempts, interrupted attempts, aborted attempts, other preparatory acts or behavior (at the time of study 1, the scale did not include "suicide", but only the spectrum of attempts). Non-suicidal self-injurious behavior is also assessed (5). Self-injurious behaviors are assigned potential and actual lethality ratings based on the degree of potential versus actual medical damage. The actual lethality item is a compilation of the Beck Medical Lethality Rating Scale (6). The time periods for ideation and behavior ratings are amenable to the clinical need or study design (e.g., since last visit, past week, life time history).

Beck's Lethality Scale (6). This scale assesses the degree of medical lethality (physical damage) of a suicide attempt. The degree of medical damage is based on medical consequences, as well as type of treatment required. Good inter-rater reliability (r=0.8) has been reported for the scale (6).

Columbia Suicide History Form, CSHF (7). This is a semi-structured interview that elicits history of the individual's suicidal behavior. It assesses dangerous or life-threatening experiences, suicide attempts, interrupted attempts and aborted attempts, and asks specific questions concerning the circumstances surrounding any suicidal behavior (e.g., stimulus events, situation, whether alone or with others, whether communication of intent to others). Excellent inter-rater reliability (coefficient=0.97), as well as predictive and construct validity were reported for this scale (8).

Children's Depression Rating Scale-Revised (CDRS-R) (9) is an observer-rated scale which assesses the presence and severity of childhood depression. This scale is modeled after the Hamilton Depression Scale. The observer rates 17 symptom/content areas: school, work, capacity to have fun, social withdrawal, eating patterns, sleep patterns, excessive fatigue, physical complaints, irritability, guilt, self-esteem, depressed feelings, morbid ideation, suicidal ideation, weeping, facial expressions of affect, tempo of speech, and hyperactivity. Good inter-rater (r=0.82) and test-retest reliability (r=0.81) have been reported for the scale, as well as good convergent validity against the Global Rating of Depression scale (9).

Montgomery-Åsberg Depression Rating Scale (MADRS) (10) is a 10-item scale designed to be particularly sensitive to treatment effects. The observer rates 10 symptoms/content areas on a 0-6 scale, with regard to the state of the patient over the past week. The areas of assessment are: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulty, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts (available at: http://www.psy-world.com/madrs.htm).

Scale for Suicide Ideation, (SSI) (11) is a 21-item, interviewer-administered rating scale measuring the current intensity of patients' specific attitudes, behaviors, and plans to commit suicide on the day of the interview. The "worst prior" version of the scale inquires about the worst period of suicidal ideation over lifetime or since the last assessment. Individual items assess suicidal risk factors, such as the duration and frequency of ideation, sense of control over making an attempt, number of deterrents, and amount of actual preparation for a contemplated attempt. The severity of suicidal ideation is the sum of the first 19 items and was used in the

present analyses. The remaining two items address incidence and frequency of attempted suicide. Initial psychometrics properties were reported in Beck et al (11). A recent study of depressed adolescents documented discriminant and convergent validity of the Scale for Suicide Ideation total score and reported high internal consistency in a community sample (Cronbach's alpha=0.81) and in an outpatient sample (Cronbach's alpha=0.95) (12).

The Suicidal Ideation Questionnaire-Junior High School Version (SIQ-JR) (13) is a patient-rated questionnaire designed to identify thoughts about taking one's life. It consists of 15 items rated on a 7-point scale, with higher numbers reflecting greater seriousness of suicidal ideation and cognition.

The *Suicide Evaluation Board* was an independent, blinded panel of three experts in the treatment of patients with mood disorders who also make suicide attempts. All three experts were uninvolved in the study and blinded to diagnosis, clinical information, and treatment status. Using narratives created by the study independent evaluators, the Board members rated narratives independently and then came to consensus regarding classification. The Board's classifications: determined whether a death represented a suicide; determined whether self-damaging acts represented a suicidal or non-suicidal self-injury; determined whether hospitalizations or increased surveillance secondary to concerns about suicide represented interventions required to prevent imminent suicide attempt; and determined whether emergency evaluations were a result of significant suicide risk.

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