Assessment of suicidal ideation and behavior in clinical trials: challenges and controversies

Clinical Trial Perspective

The association between several psychoactive medications and suicidal adverse events, as well as the recent focus on treatment of suicidal behaviors, has resulted in increased attention on the assessment of suicidal ideation and behavior within clinical trials. Measurement of suicidal adverse events is now required in clinical trials of a range of medications. The Columbia Suicide Severity Rating Scale is the leading measure of suicidal adverse events. It is brief, measures both suicidal ideation and behavior, contains definitions of each term and has promising psychometric properties. While such measures may assist clinical trial staff, suicidal events remain a challenge to assess. Clinical trial design features from studies of interventions for suicidal patients may guide the design of trials in which assessment of suicidal adverse events is now required, including patient selection, safety plans for at-risk patients, flexible treatment algorithms and clear assessment protocols and referral pathways.

Keywords: assessment • clinical trial • Columbia Classification Algorithm of Suicide Assessment • Columbia Suicide Severity Rating Scale • suicidal adverse event • suicidal behavior • suicidal ideation

In recent years there has been increasing interest in the assessment and management of suicidal ideation and behavior within clinical trials. This has occurred following empirical findings demonstrating an association between a number of psychotropic and non-psychotropic medications and suicidal adverse events [1,2,10], increased public awareness of this association and legal cases over patients who die by suicide on these medications. In addition, suicidal thoughts and behaviors have now become the primary focus for psychopharmacological and psychotherapeutic intervention studies, independent of the underlying psychiatric disorder [2–5]. This attention has prompted advances in the assessment and management of suicidal ideation and behavior; however, clinical and research challenges remain. This paper provides researchers and clinicians with a background to the need for measurement of suicidal adverse events in clinical trials and provides an overview of current thinking regarding assessment of suicidal events from both regulatory and clinical perspectives. Consideration is also given to contemporary methods of managing suicidal patients within clinical trials that are now enabling the ethical participation of those with an elevated yet acceptable risk of suicide. Current challenges facing clinicians who are assessing and managing suicide risk within clinical trials are also discussed.

The emergence of suicidal adverse events

In 2003, concern was raised regarding suicidal adverse events occurring in a greater number of children treated with paroxetine compared with placebo [6]. Subsequent investigation using aggregated placebo-controlled clinical trial data,
by the UK Committee on Safety of Medicines, confirmed that significantly more suicidal adverse events had occurred in those treated with paroxetine compared with placebo [102]. This finding precipitated a wider investigation by both the US FDA and the Committee on Safety of Medicines into the safety of antidepressants in children and adolescents, and later in adults too. The emergence of concern regarding suicidal adverse events was somewhat unexpected for multiple reasons. The aim of antidepressants is to treat depressive disorder and therefore reduce a known risk factor for suicide and suicidal behavior. Emerging evidence from epidemiological studies suggested that antidepressants prescriptions were associated with declining suicide rates [7]. Furthermore, following earlier reports of a link between fluoxetine and suicidal adverse events in the early 1990s (8,9), a prior investigation by the FDA concluded that there was no association [10]. The unanticipated nature of these adverse events meant no standardized method of assessing, defining or classifying suicidal adverse events had been implemented within these clinical trials. This meant that data were incomplete and inconsistent [11] and required classification using a standardized system prior to being used in safety analyses. The FDA commissioned a team from Columbia University to complete this task [11]. A systematic approach to the categorization of suicidal ideation and behavior was created, The Columbia Classification Algorithm of Suicide Assessment (C-CASA) [11]. The C-CASA classifies events into one of nine classes: completed suicide, suicide attempt, preparatory actions toward imminent suicidal behavior, suicidal ideation, self-injurious behavior intent unknown (fatal or non-fatal), not enough information, self-injurious behavior without suicidal intent, or other (accident, psychiatric or medical) [11]. The ‘intent unknown’ and ‘not enough information’ categories were required given that the level of detail in some narratives made it impossible to determine if an event was suicidal or not. The classification of adverse events by the Columbia team also revealed that when a standardized system was not used within clinical trials, biases toward classifying events as suicide attempts was evident, with 45 of 78 events (57.7%) reclassified by the Columbia team as not being suicide attempts [11]. However, errors in classifying events that were clearly suicidal as being not suicidal were also evident, with 26 of 377 (6.9%) previously unidentified suicidal events detected by the Columbia team [11]. The FDA’s subsequent analyses revealed that those treated with antidepressants experienced a risk of suicidal ideation or behavior that was double that of those treated with a placebo, with 14 more cases of suicidal ideation or behavior per 1000 patients detected in the antidepressant group [1,103]. In October 2004, the FDA raised a Public Health Advisory regarding the relationship between antidepressant drugs and increased suicidal risk in children and adolescents, which was later updated to include information regarding risk in young adults established in subsequent analyses [103].

Subsequent to the investigation of pediatric antidepressants, reports regarding suicidal adverse events occurring in other medications triggered an FDA-initiated investigation. Medications included anti-epileptic drugs [104], montelukast sodium (asthma) and other drugs that act on the leukotriene pathway [105]: rimonabant [106], atomoxetine [107] and varenicline [108]. Consistent across all clinical trials of these drugs was that none of them were designed to measure suicidal adverse events, necessitating the post hoc classification of suicidal events using the C-CASA prior to conducting safety analyses.

The warnings issued by Drug Regulatory Boards regarding increased risk with active treatment compared with placebo appear to have resulted in some unintended consequences, some being predictable, such as the international decline in child and adolescent antidepressant prescription rates [12–15], but others less predictable, such as declining depressive disorder diagnosis rates in children and adolescents [16]. Following the decline in antidepressant prescriptions, concern was also raised regarding an associated increase in suicide rates [17]; however, this relationship was not borne out with the release of further suicide data.

Responding to suicidal ideation & behavior within clinical trials

The systematic and prospective collection of suicidal adverse event data will lead to more complete datasets to inform drug safety analyses and will allow better detection of patients who are at risk, compared with the retrospective classification of spontaneously reported suicidal events [18]. In order to address this and other issues within clinical trials, the FDA released a draft guidance for industry on prospective assessment of suicidal events in clinical trials and sought comment from stakeholders, including the pharmaceutical companies and academics [18]. The FDA guidance provides recommendations, but in this draft form they are not binding. The guidance discusses the need for actively querying participants about suicidal adverse events in contrast to the collection of spontaneously reported events. When assessing and treating patients, clinicians can be reluctant to enquire about suicidal thoughts and behaviors, believing that to do so may incite the patient to consider suicide; however, empirical evidence has found that asking about suicide does not prompt suicidal thinking [19]. The FDA have recommended that assessment of suicidal
events occurs at baseline and at each subsequent study visit, noting that early stages of treatment or times of dose change may be periods of highest risk [18]. While this approach is sensible and optimizes patient safety, Oquendo et al. acknowledge that as frequent monitoring may increase safety and therefore reduce suicidal events, the practice diverges from ‘real-world’ practice, where monitoring may not be carried out as diligently or frequently, which will reduce the generalizability of findings [20]. The FDA recommends that suicidal events be classified into the categories of suicidal ideation and suicidal behavior specified by the C-CASA. This recommendation addresses the problematic lack of standardized terms and definitions for suicidal events [21–23], which has limited the field of suicide research for many years [24]. Agreed upon terms and definitions are essential to the development of psychometrically sound assessment measures. Such consistency allows researchers, clinicians and patients to communicate effectively about suicidal ideation and behavior. Moreover, consistency in terms and definitions is essential for the aggregation of datasets from randomized controlled trials. This is required since clinical trials traditionally aim to determine treatment efficacy and are not sufficiently powered to detect rare occurrences such as suicidal events [25]. The Center for Disease Control and Prevention recently released a document featuring the definitions of suicidal ideation and behavior found in the C-CASA [26], in order to assist with the collection of uniform data in surveillance efforts, pointing to further consistency in how the field defines suicidal ideation and behavior. It is noted in this document that the term ‘suicide’ is now preferred to ‘completed suicide’ as used previously [27]. Moreover, different suicidal events and behaviors are associated with different levels of risk for suicide and suicide attempt. For example, Kessler et al. found that suicidal ideation with a plan was a stronger risk factor for later suicide attempt than suicidal ideation without a plan [27]. Moreover, different suicidal events also require different levels of intervention. For example, passive suicidal ideation may trigger outpatient treatment, whereas active ideation with a plan and intent with a past history of suicidal behavior is more likely to require inpatient admission.

The FDA draft guidance states that suicidal ideation and behavior should be assessed in clinical trials of all medications for psychiatric indications, antiepileptic drugs and neurological drugs with central nervous system activity, as well as a range of other medications for which concerns regarding suicidal adverse events have been raised. These other medications include isotretinoin and other tretinoins, β-blockers, reserpine, smoking cessation and weight-loss drugs [18].

### Measurement

A large number of self- and clinician-rated measures exist for the assessment of suicidal ideation, suicidal behavior and associated constructs, such as hopelessness. Self-report measures are useful in supplementing an assessment of risk but tend to err toward over-estimating risk leading to high false-positive rates [28], and only some have evidence of predictive validity, a notable example being the Suicidal Ideation Scale [29]. Comprehensive reviews of existing measures are available elsewhere [25,30,31].

#### Suicidal adverse events

For the prospective measurement of suicidal adverse events, the FDA recommends the use of assessment measures that collect data points as specified by the C-CASA. According to a recent consensus statement on the measurement of suicidal adverse events, it was reported that only the Columbia Suicide Severity Rating Scale (C-SSRS) met this criterion [25]. Few measures have been designed to specifically determine suicidal ideation and behavior within clinical trials. Measures used to assess adverse events need to be administered by a wide variety of health professionals and clinical trial staff, and should also be relatively brief, yet address the range of both suicidal ideation and behavior. With endorsement from the FDA [18] and others [32], the C-SSRS is currently the leading measure (this is reviewed below). However, some others have been used within clinical trials to detect suicidal events, such as the Sheehan Suicidality Tracking Scale, which is derived from the Mini International Neuropsychiatric Interview [33].

#### The Columbia Suicide Severity Rating Scale

The C-SSRS was developed in 2008 within a National Institute of Mental Health-funded clinical trial designed to evaluate treatments for youth suicide attempters [34], in response to the need for a low burden measure of the full spectrum of both suicidal ideation and behavior. The C-SSRS is a brief, semi-structured, clinician-administered questionnaire designed to track severity and change in suicidal ideation and behavior over time. The C-SSRS is suited to administration within a clinical trial in order to determine suicidal adverse events and has been used widely for this purpose. The C-SSRS assesses both passive and active suicidal ideation (nonspecific, method but no intent or plan, method and intent but no plan and method, intent and plan) and suicide attempt, interrupted attempt, aborted attempt and preparatory acts and nonsuicidal self-injurious behavior. The C-SSRS...
Clinical Trial Perspective

Melvin, Gordon & Freake

features a definition for each of the terms in order to guide clinicians during administration. Each type of ideation and behavior is complemented by suggested probes. Presence of suicidal ideation triggers five items regarding the intensity of ideation (frequency, duration, controllability, deterrents and reasons for ideation). Presence of suicide attempt triggers the rating of lethality or potential lethality of the attempt(s). While the C-CASA features categories that accommodate events of ‘unknown intent’ or for which not enough information is present, these have not been included in this prospective tool as it is the clinician’s task to make a determination even though, at times, intent may be difficult to determine [36]. A recent study reported on the psychometric properties of the C-SSRS using data from three studies [36]. Findings showed that the measure has good convergent and divergent validity and, importantly, good predictive validity with worst point lifetime suicidal ideation and ideation with at least some intent to die, both predictive of suicide attempt [36]. Comparison of C-SSRS rating with Columbia Suicide History Form ratings revealed very high levels of sensitivity and specificity; however, both rating were made by the same investigator. The C-SSRS has been translated into over 100 languages and dialects but requires further cross-cultural validation given the cultural differences involved with suicide and suicidal behavior [35]. The measure has been used in clinical medication trials (Phases I–IV) for psychiatric (e.g., depression, schizophrenia, personality disorders or apathy), neurological (e.g., epilepsy or chronic headache) and other medical conditions (e.g., diabetes, cardiovascular disease or obesity) [109]. Importantly, accessible training is available for C-SSRS, which aids consistency of administration.

As well as the clinician-administered version, the C-SSRS can be administered over the telephone by centralized raters and automated telephone systems. Known as the eC-SSRS, the system uses interactive voice response and the presence of any suicidal content triggers the involvement of a clinician [37]. The first study of the eC-SSRS suggested that it was feasible with inter-rater agreement between the eC-SSRS and an interviewer being greater than between two interviewers. Interactive voice response technology has the advantage of providing consistent administration of the assessment measure [37] but concerns exist regarding the patient’s ability to correctly determine their suicidal intent using the eC-SSRS compared with a clinician’s judgment [35]. Anecdotally, eC-SSRS was preferred by some patients due to its privacy and unbiased questioning, while in contrast other patients found it to be a disconnected experience, which did not allow for clarification of responses or rephrasing of questions [37]. The eC-SSRS has been used in studies of multiple disorders, including major depression, insomnia, epilepsy, post-traumatic stress disorder and fibromyalgia. An analysis of 35,244 eC-SSRS assessments from 14 clinical studies (seven major depressive disorder studies) found that average administration time for those who reported active suicidal ideation with some intent or any suicidal behavior was 7.7 min, while those without intent took 3.5 min [38]. Suicidal ideation was reported by 14.6% and suicidal behavior by 1.4% at follow-up appointments. In terms of predicting suicidal behavior, those with lifetime ideation with intent to act or prior suicidal behavior were four-to five-times more likely to report suicidal behavior during the study, while those with both were 7.6-times more likely to report suicidal behavior. These findings along with the predictive validity findings from Posner et al. provide some guidance on the complex question of at what point patients should be excluded due to risk of suicidal behavior [36].

Clinical trials targeting suicidal or self-harming patients

Outcome measure selection within clinical trials depends on the aim of the study. For example, intervention studies that have treated suicide attempters tend to focus on time to suicidal event or attempt as their primary outcome [2–4], as assessed by clinical interview or C-SSRS. Similarly, trials that have treated individuals who have self-harmed (with or without suicidal intent), assess self-harm as the primary outcome of interest [39,40]. The Scale for Suicidal Ideation is a 19-item interviewer administered measure of a patient’s plans, thoughts and intention to die by suicide [41], which has been popular in recent key studies [2–4,42]. In pediatric trials, the 30-item self-report Suicidal Ideation Questionnaire has been used in multiple studies [3,39,43].

Alternatives to clinical trial data

Following the FDA analyses, other studies using different methodologies and datasets have contributed to the debate around the association between suicidal adverse events and a range of medications. For example, Valuck et al. found no significant risk of suicide attempts among adolescents taking antidepressants in a large longitudinal health insurance database (n = 24,000) [44]. Using observational data from a large sample representative of the UK population, Arana et al. found no increased risk of suicide attempt or suicide in patients with epilepsy who were taking antiepileptic drugs, but did find an association in those with depression who were taking antiepileptics and those who did not have epilepsy, depression or bipolar disorder who
were taking antiepileptic drugs for other indications [45]. These findings point to the utility of using other study methodologies to inform medication safety, particularly when assessing rare events. However, these studies also appear to be limited by some of the same issues as clinical trials, including a lack of clear definition of suicidal events. In the future, improved data collection will be achieved by prospective measurement of suicidal events within clinical trials, providing a more complete dataset for safety analyses, and data from a range of sources (e.g., epidemiological studies or administrative databases) that use standardized suicide terminology may be considered in order to provide a more complete assessment of the risks and benefits of treatments [25].

Clinical issues
Despite the recent advances in the protocols for assessing suicidal ideation and behavior within clinical trials, several clinical challenges still remain [46]. Multiple studies have reported that agreement between clinicians on ratings of suicide behavior and risk are low [47,48]. Some have found that better, yet modest, inter-rater reliability was achieved, possibly due to the existence of standardized protocols and training procedures [49,50]; however, providing a standard definition of suicide attempt to one group of clinicians did not result in greater inter-rater agreement within that group, than in a group without the definition [49]. Suicidal intent is known to be difficult to assess, yet it is critically important in determining suicidal from nonsuicidal behavior. While sometimes obvious due to the lethality of means (e.g., jumping from a high place or a massive overdose), intent can also be ambiguous, denied due to shame or unclear due to the impulsive nature of an attempt [53]. Furthermore, acutely suicidal individuals with intent and plans may deny active suicidal ideation in an effort to prevent barriers, such as inpatient admission, from interfering with their plans to die. Future psychometric evaluations of suicide measures should evaluate the capacity for trained raters to correctly rate suicidal ideation, behavior and particularly intent.

A further clinical challenge to assessing suicidal ideation and behavior is the stigma that is typically attached to the reporting of such thoughts or behaviors [54]. To admit to suicidal thoughts may be perceived as a moral foible or character fault. Patients who have made a suicide attempt may attempt to minimize or dismiss the attempt as not being serious in order to reduce embarrassment.

It ought to be noted that assessing suicidal ideation and behavior as an adverse event does not equate to a full suicide risk assessment. Once any suicidal ideation or behavior is detected, a risk assessment performed by a mental health professional or a suitably trained health professional is needed. Risk assessment involves a review of other known predisposing bio–psycho–social risk factors for suicide, such as recent life stressors, access to lethal means, male gender, unemployment, impulsivity, aggression, hopelessness, family history of suicide, history of abuse and psychiatric disorder, such as major depressive disorder, alcohol use disorder, eating disorder, schizophrenia and borderline personality disorder [55,56]. Hence, measures used to detect suicidal adverse events may supplement or trigger an assessment of suicide risk. The challenge of risk assessment is compounded by the lack of current understanding as to how the various risk factors interact. Study investigators and clinicians face significant challenges, given that suicidal behavior is not a diagnosis, but the final common pathway with a heterogeneous etiology [57]. The proportion of study participants requiring a suicide risk assessment during a clinical trial will vary with the study population. For example, in a depressed sample, risk assessments may be quite common compared with a non-psychiatric condition where it may be very rare. An estimate of the proportion of participants likely to need a fuller risk assessment might be best determined through pilot data or prior studies and would provide investigators with an estimate of the resources required. For some studies, particularly of non-psychiatric conditions, training of study health professionals in suicide risk assessment may be required, in order to ensure capacity to provide assessments is sufficient. Alternatively, an external agency may be engaged to provide risk assessments.

Management of suicide risk within clinical trials
Inclusion of suicidal or potentially suicidal patients within a clinical trial raises multiple professional and ethical issues for researchers and study clinicians in terms of patient safety and patient rights [20]. The mitigation of suicidal risk within clinical trials is achieved through study design features, use of protocols that reflect robust assessment and management of any risk, the use of best practice management guidelines and engagement of the patient in relevant usual care services. These practices enable the provision of ethical, high-quality care, whilst treating suicidal patients, or those who may be at risk of suicidal adverse events, within clinical trials. Trial protocols drawn from psychiatric studies that have targeted suicidal behavior as the focus of intervention [3] and consensus guidelines [25] may also be useful to inform non-psychiatric studies that are now required to assess for suicidal adverse events.

A crude approach to reducing risk is the exclusion of all participants with current or historical suicidal ideation or behavior. However, this creates a highly
selected sample and does not reflect real-world practice, as it is likely to exclude the sickest patients. Furthermore, this may lead to complacency and a lack of vigilance for those patients whose suicidal ideation or behavior first arises during the study. The issue of highly selected samples is a known problem within depression research, where trial samples do not reflect the typical presentation of the disorder [54–56]. Exclusion of suicidal patients also creates the problem of a lack of equity, in that fewer studies including suicidal patients will likely equate with fewer evidence-based treatments for this population. While those deemed to be at acute risk of suicide should not be included in clinical trials [25], there is no current, agreed-upon formula for estimating acceptable risk within clinical trials. Each study protocol needs to include a clearly defined and appropriate level of risk that can reasonably be managed within the study.

Several methods have been used to mitigate and, in part, address suicide risk in clinical trials. The design of the study is a powerful way to address this issue. Studies that have investigated treatments that have targeted patients who have attempted suicide or self harmed, have compared standard treatment (treatment as usual) with standard treatment and an enhanced intervention [40] or compared evidence-based drug treatment with a similar drug [4], thereby addressing suicide risk through the provision of usual care. Other studies have compared the experimental intervention (e.g., rapid response outpatient treatment [57], dialectical behavior therapy [58] or cognitive therapy [2]) with standard treatment or an enhanced standard treatment. The use of a placebo control for suicidal patients is to be avoided, due to the unacceptable risk involved with this type of control [33]. Further studies appear to have mitigated the suicide risk by using a quasi-experimental design; for instance, those at-risk adolescents with the greatest clinical need allocated to the most intensive treatment [59] or allowing for the patient to chose their treatment [34,60]. Box 1 describes additional strategies that may be employed within clinical trials to moderate suicide risk.

Future perspective
Adoption of standardized terms and definitions for suicidal ideation and behavior across the field is emerging but urgent. It will provide a common language for clinicians, researchers and patients alike and will facilitate aggregation of smaller datasets and comparison between studies.

Use of standardized, prospective measurement of suicidal adverse events within clinical trials will greatly improve the quality of data available to medication safety analyses and ultimately enhance patient outcomes. It is possible that analyses using this higher quality data may lead to different conclusions regarding the risk of medications than those that exist today.

Other sources of data (e.g., large observational databases) will, at least, supplement data derived from clinical trials in determining medication safety.

While predicting suicide is not currently possible,
Assessment of suicidal ideation & behavior in clinical trials

Executive summary

Emergence of suicidal adverse events
- The detection of suicidal adverse events prompted the development of systems to classify these events.

Measurement of suicidal adverse events
- Systematic, prospective monitoring for suicidal adverse events is now required for a range of medications identified as being of concern.

Columbia Suicide Severity Rating Scale
- At present, the only assessment measure of the US FDA-recommended suicidal ideation and behavior data points is the Columbia Suicide Severity Rating Scale.
- Psychometric properties of the Columbia Suicide Severity Rating Scale are promising and a computer automated version is available.

Clinical issues
- Assessment of suicidal ideation and behavior is a complex task. Inter-rater reliability may be low, suicidal intent may be hidden and stigma may influence reporting of suicidal ideation and behavior.

Management of suicide risk within clinical trials
- Clinical trials designed to treat suicidal patients possess design features that aim to mitigate and respond to suicide risk. Some of these design features may be useful in clinical trials that are now required to monitor for suicidal adverse events.

Paper's of special note have been highlighted as:
- of interest
- of considerable interest

References
Papers of special note have been highlighted as:


Further psychometric and cross-cultural evaluation of measures of suicidal ideation and behavior, such as the Columbia Suicide Severity Rating Scale, will likely improve the measurement of suicidal adverse events and, potentially, the capacity to predict suicide risk.

While prioritizing patient well-being and ethical research guidelines, clinical trials will be far more inclusive of patients with current or historical suicidal ideation or behavior, due to rigorous monitoring and adequate protocols that enable a prompt response to any clinical emergency. As a result, study outcomes will be able to be generalized and suicidal patients will be a less marginalized population.

Financial & competing interests disclosure
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancy, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.
272

Clinical Trial Perspective  Melvin, Gordon & Freake


■ Key document that describing the US FDA’s thinking on the measurement of suicidal adverse events.

■ Describes the methods that enable suicidal patient participation in clinical trials.

■ Key review of issues related to suicidal adverse events developed by an expert panel.
35 Freudenthal S. Challenges of assessing intent to die: can suicide attempters be trusted? Omega 55(1), 57–70 (2007).

■ First description of the psychometric properties of the Columbia Suicide Severity Rating Scale.

■ Describing interactive voice response version of the Columbia Suicide Severity Rating Scale.
46 Rudd MD. Suicidality in clinical practice.
55 Zimmerman M, Chelminsiki I, Posternak MA. Generalizability of antidepressant efficacy trials: differences between depressed psychiatric outpatients who would or would not qualify for an efficacy trial. Am. J. Psychiatry 162, 1370–1372 (2005).

Websites

- Summarizes the FDA’s findings on antidepressants and suicidal adverse events and changes to product information.
105 US FDA. Updated information on leukotriene inhibitors: montelukast (marketed as Singulair), zafirlukast (marketed as Accolate) and zileuton (marketed as Zyflo and Zyflo CR) (2009). www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/drugsafetyinformationforhealthcareprofessionals/ucm165489.htm
109 Center for Suicide Risk Assessment. Columbia-Suicide Severity Rating Scale (C-SSRS). Columbia University Medical Center. www.cssrs.columbia.edu/uses_cssrs.html