



Official reprint from UpToDate®

www.uptodate.com © 2023 UpToDate, Inc. and/or its affiliates. All Rights Reserved.

Wolters Kluwer

Substance use disorder in adolescents: Psychosocial management

AUTHOR: [Oscar Bukstein, MD](#)**SECTION EDITORS:** [David Brent, MD](#), [Andrew J Saxon, MD](#)**DEPUTY EDITOR:** [Michael Friedman, MD](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

Literature review current through: **Oct 2023**.

This topic last updated: **Apr 18, 2022**.

INTRODUCTION

Substance use is pervasive and endemic among adolescents in the United States. Although most use by adolescents will attenuate over time, many youth who use alcohol and other drugs suffer negative health and social consequences. Some advance to more severe levels of use and impairment, meeting DSM-5 criteria for substance use disorders (SUDs) during adolescence or later as adults.

Although the general approach to the treatment of adolescents with SUD is similar in some respects to the assessment and treatment of adults with SUD, developmental considerations require an assessment and interventional approach tailored to the cognitive, social, and legal status of adolescents. (See "[Substance use disorder in adolescents: Epidemiology, clinical features, assessment, and diagnosis](#)".)

This topic reviews treatment of SUD in adolescents. The epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis are reviewed separately. Treatment of specific SUDs in adults are also reviewed separately.

- (See "[Substance use disorder in adolescents: Epidemiology, clinical features, assessment, and diagnosis](#)".)
- (See "[Opioid use disorder: Pharmacologic management](#)".)
- (See "[Opioid use disorder: Psychosocial management](#)".)

- (See ["Opioid withdrawal: Clinical features, assessment, and diagnosis"](#).)
 - (See ["Cannabis use disorder: Clinical features, screening, diagnosis, and treatment"](#).)
 - (See ["Cannabis withdrawal: Epidemiology, clinical features, diagnosis, and treatment"](#).)
 - (See ["Management of moderate and severe alcohol withdrawal syndromes"](#).)
 - (See ["Stimulant use disorder: Treatment overview"](#).)
 - (See ["Alcohol use disorder: Treatment overview"](#).)
 - (See ["Management of smoking and vaping cessation in adolescents"](#).)
-

APPROACH TO TREATMENT

Our approach to selecting treatment for substance use disorder in adolescents is reviewed separately. (See ["Substance use disorder in adolescents: Treatment overview"](#).)

INTERVENTIONS

Psychosocial interventions for adolescents with substance use disorder (SUD) generally have one or more of the following goals:

- Advancing motivation for treatment and abstinence or reduced use
- Developing skills to achieve and maintain abstinence or reduced use
- Enhancing external control of behavior, usually through parenting strategies
- Identifying prosocial peers and activities to replace deviant ones

Most psychosocial interventions for adolescents with good evidence of efficacy are modifications of similar interventions for adults, such as cognitive-behavioral therapy (CBT) [1,2], motivational interviewing [3,4], and contingency management [5]. (See ["Substance use disorders: Psychosocial management"](#) and ["Substance use disorders: Motivational interviewing"](#) and ["Substance use disorders: Training, implementation, and efficacy of treatment with contingency management"](#).)

Family-based treatment — Family-based treatment interventions with empirical support in treating adolescents with SUD take an ecologic approach to treatment, which directly targets both intrafamilial relationships and the multiple interacting systems (eg, school, peer, juvenile justice) within which adolescents develop. The treatments include multidimensional family therapy, functional family therapy, brief strategic family therapy, and multisystemic family therapy.

All of these treatment models focus on improving:

- Adolescent functioning in family and social contexts.
- Parental monitoring and supervision skills.
- Communication between family and social systems (eg, schools).
- Adolescents' coping, communication, decision-making, and problem-solving skills associated with substance use.

Yet the models have different emphases and structural differences:

- Multidimensional family therapy – Youth learn coping, problem-solving, and decision-making skills, and the family learns ways to enhance family functioning.
- Functional family therapy – Uses more behavioral approaches, such as modifying family members' behavior using contingency management techniques, communication, problem solving, and behavioral contracts.
- Brief strategic family therapy – The clinician establishes a relationship with each family member, observes how the members behave with one another, and assists the family in changing negative interaction patterns.
- Multisystemic family therapy – Antisocial behaviors, delinquency, and substance problems are seen within the larger context of multiple systems of influence, including multiple social-ecological factors such as individual, family, peer, school, and community influences. Treatment in multisystemic family therapy is often intensive, using multiple sessions and hours per week.

Family based interventions are the most strongly supported of psychosocial interventions for adolescents with SUD. A meta-analysis of 24 clinical trials with 2090 adolescents with SUD compared family-based therapy with treatment as usual or another manualized intervention. The family therapies were based on one of four models: multidimensional family therapy, brief strategic family therapy, multisystemic therapy, and functional family therapy [6]. The family therapies led to modestly improved substance use outcomes (days of use/month; urine drug screens) compared with the control groups.

As an example, a randomized clinical trial compared multidimensional family therapy, an adolescent skills-based group therapy, with a family education group intervention in 182 young teens with SUD [7]. Multidimensional family therapy consisted of 16 sessions provided weekly in an office-based setting over an average of five months. The multifamily educational intervention consisted of groups of three to four families during a 16-week period. Individual

crisis sessions were available to families on request of the family or the therapist in the case of emergencies. Skill-building exercises were conducted in groups of six and eight adolescents and led by two therapists for 90 minutes. At 6 and 12 months, all three groups showed improvement in symptoms and prosocial functioning, with multidimensional family therapy showing superior improvement overall.

Motivational interviewing — Motivational interviewing is a counseling approach in which clinicians use a patient-centered stance paired with eliciting techniques to help patients explore and resolve their ambivalences about changing behaviors that are not healthy. Motivational interviewing in adolescents uses the same approach and techniques used in adults. The theoretical foundation and components of motivational interviewing, along with its efficacy in adults, are reviewed separately. (See "[Substance use disorders: Motivational interviewing](#)".)

Motivational interviewing is generally provided in one to four sessions of 15- to 45-minute duration. A minimum duration of 20 minutes appears to be needed, with greater efficacy associated with more sessions. Although tested as a stand-alone intervention in clinical trials, motivational interviewing-based interventions are commonly combined with other interventions such as CBT. (See '[Cognitive-behavioral therapy \(CBT\)](#)' below.)

Motivational enhancement therapy (MET), a four or more session variant of motivational interviewing, includes structured, specific assessment of the patient's substance use (including quantitative assessment of consumption) and personalized risk feedback [8].

Randomized clinical trials have shown motivational interviewing to be modestly efficacious in reducing alcohol use. A meta-analysis of 22 randomized controlled trials compared motivational interviewing with treatment as usual in adolescents with risky alcohol use with or without a consequence [9]. Motivational interviewing was effective in reducing number of alcohol use days per month (1.1 fewer days per month, 95% CI -2.2 to -0.3). The strength of the evidence was moderate. Motivational interviewing was also effective in reducing the number of heavy alcohol use days per month versus treatment as usual (0.7 fewer heavy days per month, 95% CI -1.6 to 0.02). The strength of the evidence was low. Other meta-analyses have noted similar findings for the effects of motivational interviewing/MET on alcohol consumption in adolescents and young adults [9-13].

Results from meta-analysis evaluating the effects of motivational interviewing on use of drugs other than alcohol in adolescents are mixed [9,12,13]. As an example, in the meta-analysis described above, motivational interviewing had no effect on the frequency of cannabis use, but it did reduce overall substance-related consequences in those adolescents who used cannabis [9].

Motivational interviewing/MET may have limited effectiveness in those adolescents with more severe levels of substance use or with SUD.

Cognitive-behavioral therapy (CBT) — CBT for SUD in adolescents focuses on:

- Enhancing adolescent coping, problem solving, and decision-making skills related to substance use;
- Teaching skills to help adolescents cope with cravings and overcome temptations to use substances (eg, drug refusal skills, avoiding high-risk situations);
- Improving interpersonal relationships (eg, communication, anger management, and mood regulation skills);
- Reducing risky behaviors associated with substance use (eg, HIV/sexual risk behaviors, riding with or driving while intoxicated).

CBT for SUD may be delivered individually to adolescents or in a group format. The theoretical foundation and components of CBT for SUD, along with its efficacy in adults, are reviewed separately. (See ["Substance use disorders: Psychosocial management", section on 'Cognitive-behavioral therapy'](#).)

Three randomized clinical trials with a total of 246 adolescents compared CBT with psychoeducational groups or usual care for SUD, finding that adolescents assigned to receive CBT reported a greater reduction in substance use compared with control groups [14-16]. As an example, a trial randomly assigned 224 adolescents to receive either CBT or multidimensional family therapy. Both interventions produced reductions in reported substance use days during the past month from pretreatment to 6- and 12-month follow-up assessments, although there appeared to be continued improvement over time in the family therapy condition, compared with some leveling off in substance-use reductions in the CBT condition after the six-month follow-up [16].

Contingency management training — Contingency management involves motivational incentives and is based on operant behavioral principles [5]. In contingency management, immediate rewards or incentives (ie, voucher payments or prize drawings) are provided to increase the frequency of reinforced behaviors (eg, abstinence, treatment compliance).

The theoretical foundation and components of contingency management for SUD, along with its efficacy in adults, are reviewed in detail separately. Contingency management differs in adolescents compared with adults in the nature of the awards, eg, youth relevant store payment cards, tickets to youth-oriented events. (See ["Substance use disorders: Principles,](#)

components, and monitoring during treatment with contingency management" and "Substance use disorders: Training, implementation, and efficacy of treatment with contingency management".)

Clinical trials, on balance, support the short-term efficacy of contingency management for substance use problems in adolescents. Of seven clinical trials in this population, four with a total of 462 patients found contingency management led to greater abstinence compared with controls [17-20]. Three trials with a total of 165 patients found no difference in abstinence between contingency management and control groups [21-23].

The theoretical foundation and components of mutual help groups for SUD, along with their efficacy in adults, are reviewed in detail separately. (See "Alcohol use disorder: Psychosocial management", section on 'Mutual help groups'.)

Screening and brief intervention — Brief intervention for unhealthy alcohol use can be delivered as an individual intervention or coupled with population-based screening (eg, in a primary care practice) to identify adolescents with unhealthy alcohol use who may benefit from treatment.

Screening and brief intervention are described in detail separately, along with data on their efficacy in adults. (See "Screening for unhealthy use of alcohol and other drugs in primary care" and "Brief intervention for unhealthy alcohol and other drug use: Goals and components" and "Brief intervention for unhealthy alcohol and other drug use: Efficacy, adverse effects, and administration".)

Brief intervention for unhealthy alcohol use (but not unhealthy drug use) in adolescents has been found to lead to small reductions of alcohol use in clinical trials. A meta-analysis of 19 randomized clinical trials and five studies with controlled quasi-experimental designs compared the efficacy of brief intervention with no treatment, a wait-list control, or some form of routine treatment as usual in 172 adolescents (age 11 to 18) and 1691 young adults (age 19 to 30) with unhealthy drinking [24]. Brief interventions led to very modest reductions in alcohol consumption and alcohol-related problems among adolescents (effect size = 0.27 and 0.19) and young adults (effect size = 0.17 and 0.11). The effects persisted for up to one year after intervention and did not vary across participant demographics, intervention length, or intervention format.

Results from the 19 randomized trials were not analyzed separately. Brief intervention led to superior outcomes compared with control conditions in nine of the trials.

As an example, a randomized clinical trial compared two brief intervention conditions in 315 adolescents with alcohol and drug use disorder who were identified by screening in a school setting [25,26]. Ninety percent of the sample met DSM-IV diagnostic criteria for an SUD during prior year SUD (primarily alcohol or cannabis use disorder). All of the 32 students who did not meet criteria for any SUD reported either one or two dependence criteria for at least one substance. Adolescent participants and their parents were randomly assigned to receive one of three brief interventions:

- Two adolescent-only sessions
- Two adolescent-only sessions and one parent-only session
- An assessment only control condition

Adolescents and parents were assessed at intake and at 6 and 12 months following the completion of the intervention with the primary outcome measure the percent abstinent in the previous 90 days. After six months, adolescents in both actively treated groups showed greater reductions in drug use behaviors compared with the control group. For previous 90-day alcohol use, a greater percentage of adolescents were abstinent in the two actively treated groups compared with the control groups (53.5 and 47.3 versus 26.1 percent). For previous 90-day cannabis use, a greater percentage of adolescents were abstinent in the two actively treated groups compared with the control group (51.0 and 62.5 versus 37.0 percent). Youth receiving the child/parent intervention had better outcomes compared with the adolescent-only group.

Clinical trials are insufficient to determine the efficacy of brief interventions in adolescents with mild or moderate/severe alcohol use disorder.

In our clinical experience, brief intervention is useful as a first step intervention that includes assessing the patient's recognition of a problem with alcohol and his or her willingness for treatment.

The United States Preventive Service Task Force, which recommends screening and brief intervention for adults with unhealthy drinking in primary care, did not include adolescents with alcohol use disorder in its review of the intervention [27]. The American Academy of Pediatrics recommends screening and brief intervention for adolescents with unhealthy drinking [28].

School-based treatment — SUD treatment can be provided to adolescents in schools, including recovery high schools, which are specifically designed to provide secondary education, SUD education, and support to adolescents "in recovery." Other than brief interventions administered in schools, there is scant literature on school-based interventions in such recovery environments.

While not supported by randomized clinical trials, attendance at recovery high schools has shown benefit in improving substance use and related outcomes [29]. Recovery high schools are generally used by adolescents who have had difficulty with community-based treatment and need extra supports beyond specific SUD treatment.

In a meta-analysis of individual, family, and school-based prevention interventions designed to decrease multiple risk behaviors, universal school-based interventions reduced alcohol use by 28 percent (odds ratio 0.72, 95% CI 0.56-0.92; eight studies, n=8751, moderate evidence quality) versus no intervention or treatment as usual [30].

School-based programs aimed at prevention of alcohol use in adolescents appear to have efficacy in reducing risky drinking and alcohol-related harms into adulthood. In a long-term follow-up study, 2190 students from 26 high schools participated in a cluster randomized trial in which schools were randomized to deliver one of three different prevention interventions for alcohol misuse (universal web-based prevention of alcohol use, group sessions for individuals with high-risk personality profiles, or a combination of the two – with students within the combination schools invited to universal or high-risk intervention as appropriate for the individual student) versus active control (ie, health education as usual) [31]. At seven-year follow-up, students in all three intervention groups had reduced odds of alcohol-related harms compared with the control group (universal prevention: odds ratio 0.25, 95% CI 0.11-0.55; high-risk groups: odds ratio 0.13, 95% CI 0.05-0.31; combination: odds ratio 0.33, 95% CI 0.19-0.58). Additionally, at follow-up, lower risk of hazardous alcohol use and monthly binge drinking was seen for the universal web prevention intervention, and lower risk of hazardous alcohol use and weekly alcohol use was seen for the high-risk personality profile intervention. No added benefit was observed by delivering the combined interventions.

Addiction counseling — Addiction (or drug/alcohol) counseling is a widely used treatment for SUD in both individual and group formats. The content of counseling varies; its efficacy as commonly delivered has not been tested in clinical trials in adolescents. Evidence-based models of addiction counseling have been developed but are not widely available [32]. The components and administration of addiction counseling are reviewed separately. (See "[Substance use disorders: Psychosocial management](#)", section on 'Addiction counseling'.)

Mutual help groups — Although not professionally provided treatment, mutual help or self-help groups are an important part of treatment of adolescents with SUD, and are generally recommending by treating clinicians. Twelve-step groups such as Alcoholics Anonymous and Narcotics Anonymous are the most widely available, though some object to their spiritual component, including a focus on a “higher power.” Narcotics Anonymous groups may also be

problematic as some advocate against the use of therapeutic medications such as opioid agonists for opioid use disorder.

These problems are addressed by nonreligious programs such as Self-Management and Recovery Training. Adolescents are best off in groups composed of peers and young adults. In areas where only older adult groups are available, the clinician will need to assess the adolescent's receptiveness and perceived benefit.

There are no randomized trials of the efficacy of mutual help groups for SUD in adolescents. Trials in adults are limited in number and methodologies and have yielded mixed results.

The theoretical foundation and components of mutual help groups for SUD, are reviewed in detail separately. (See ["Alcohol use disorder: Psychosocial management", section on 'Mutual help groups'](#).)

Facilitating mutual help group engagement — Interventions such as 12-step facilitation are designed to help patients with SUDs to engage in mutual help groups. There have been no randomized clinical trials of these interventions in adolescents, and results from trials in adults have been mixed. (See ["Substance use disorders: Psychosocial management", section on 'Facilitating mutual help group engagement'](#).)

MULTIMODAL APPROACHES

Several psychosocial interventions that combine multiple modalities have been customized to the needs of adolescents with substance use disorder (SUD) and tested in clinical trials. No one combination of interventions has been found to be more effective than others.

Adolescent assertive continuing care — Adolescent assertive continuing care (ACC) integrates acute treatment in the context of long-term monitoring and support. Components of the intervention include:

- Case management
- Routine and as needed home visits
- Help linking the adolescent to necessary services
- Transportation to needed services
- Prosocial activities or potential jobs
- Advocacy to access services
- Monitoring lapse cues and attendance
- Social support for coping with lapses or other challenges

ACC is similar to care management interventions developed for other chronic/recurring diseases such as asthma or diabetes [33].

The theoretical foundation and components of continuing care for SUD, and its efficacy in adults, are reviewed separately. (See ["Continuing care for addiction: Components and efficacy"](#) and ["Continuing care for addiction: Implementation"](#).)

ACC after residential treatment has been tested in two randomized clinical trials with 520 adolescents with an SUD [19,34]. Assignment to ACC led to greater continuing care linkage, retention, and longer-term abstinence from marijuana. As an example, a trial randomly assigned 183 youth aged 12 to 17 years old with an active DSM-IV alcohol or other drug disorder to receive either ACC or usual continuing care for 90 days following discharge from residential treatment [19,34]. Over that period, a greater percentage of youth in the ACC group reported abstinence from marijuana use compared with the control group.

Adolescent community reinforcement approach — The adolescent community reinforcement approach (A-CRA) is a cognitive-behavioral therapy (CBT)-based intervention that aims to make abstinence more rewarding than continued use [35-38]. In the A-CRA, the clinician helps the youth and his or her family to develop social and recreational activities to compete with time spent using alcohol and drugs [39].

The A-CRA includes individual CBT sessions for the adolescent, sessions with the caregivers alone, and sessions with the youth and caregivers together. An array of different therapeutic procedures focus on various skills and life areas, including relapse prevention, relationship skills, communication skills, problem solving, goal setting and working through barriers to completion, analysis of using behaviors, making non-substance-using friends, engaging in satisfying social and leisure activities that do not involve substance use, sampling new activities, and assignment of homework. There are also optional procedures for coping with a lapse, anger management, and job finding.

The theoretical foundation, components, and efficacy of the CRA for adults are reviewed separately. (See ["Substance use disorders: Psychosocial management"](#), [section on 'Community reinforcement approach'](#).)

The A-CRA appears to be an efficacious intervention for adolescents with an SUD. A clinical trial randomly assigned 180 homeless, runaway adolescents, and young adults (mean age 19.21 years) to either the A-CRA or treatment as usual. Youth assigned to the A-CRA, compared with treatment as usual, reported reduced substance use and depression and increased social stability [40].

Other trials have compared the A-CRA to other active interventions finding little difference in substance use outcomes [1] or tested the A-CRA in conjunction with adolescent assertive continuing care, finding superior substance use outcomes compared with treatment as usual [41]. (See '[Adolescent assertive continuing care](#)' above.)

Intervention combinations — Motivational interviewing and contingency management are typically added on to other “platform” interventions, such as CBT or family based treatment. These combinations of add-on and platform interventions have not been clearly shown to lead to superior outcomes compared with platform interventions alone.

Motivational interviewing and contingency management are typically added on to a “platform” intervention, such as CBT or family based treatment [1]. Clinical trials have not compared combined motivational interviewing plus CBT with CBT alone. The addition of motivational enhancement therapy/motivational interviewing and contingency management as add-on interventions have not established themselves as clearly better than the platform evidence-based therapies alone, although a meta-analysis of the combined MET/CBT found that the combined intervention was superior to CBT alone in reducing substance use (effect size 0.59; 95% CI -1.88 to 3.07) [42].

Contingency management is also used in combination with other interventions, though without supporting evidence from clinical trials. A trial of 153 adolescents with cannabis use disorder, subjects were randomized to receive 14 weeks of either MET/CBT, MET/CBT plus abstinence-based contingency management, or MET/CBT plus contingency management and parent training [43]. The addition of contingency management, but not parent training, improved cannabis abstinence during the study. No differences were seen among intervention groups at one-year follow-up.

Others — Longer-term treatment for adolescents with SUD in residential programs, therapeutic communities, and wilderness/adventure programs such as Outward Bound may be available for some adolescents with SUD who have failed less intensive treatment. There are no randomized clinical trials of the efficacy of these interventions in adolescents. Observational study of substance use before and after these programs (more extensive for therapeutic communities) provides limited support for them [44].

Some experts have questioned whether some wilderness/adventure programs might be not only ineffective but potentially harmful to youth, who may be essentially incarcerated and cut off from contact with anyone.

COMMUNICATION ABOUT ADOLESCENT CARE

Adolescents are more likely to provide truthful information in treatment if they believe that the information obtained will not be shared.

At the beginning of the initial contact with an adolescent, the clinician should review exactly what information the clinician is obliged to share and with whom, including:

- An adolescent's expression of potential danger to self or others would require that the clinician inform a responsible adult, usually the parents, in order to keep the teenager or others safe.
- In general, the clinician's recommendations for treatment and clinical impressions would be shared with parents, though there may be some circumstances in which this would not be helpful.

The clinician should be knowledgeable about local and federal laws that limit the information that may be released. Most states have confidentiality laws that restrict information that the clinician may share unless the adolescent provides consent, information about deviant behavior such as selling drugs, who sells drugs to the adolescent, and peer behaviors that include drug use and other antisocial behaviors. Other clinicians, teachers, and parents, are legally permitted to provide information to the assessing/treating clinician.

SUMMARY AND RECOMMENDATIONS

- Our approach to selecting treatment for substance use disorder (SUD) in adolescents is reviewed separately. (See "[Substance use disorder in adolescents: Treatment overview](#)".)
- Motivational interviewing is a counseling approach in which a patient-centered stance and eliciting techniques are used to help patients resolve ambivalence about reducing or stopping substance uses. Randomized clinical trials have shown motivational interviewing to be modestly efficacious in reducing alcohol use. (See '[Motivational interviewing](#)' above.)
- Cognitive-behavioral therapy (CBT) for SUD in adolescents focuses on enhancing adolescent coping, problem solving, and decision-making skills related to substance use; teaching skills to help adolescents cope with cravings and overcome temptations to use substances; and improving interpersonal relationships. Multiple clinical trials have shown CBT to be efficacious in reducing use compared with psychoeducation or usual care. (See '[Cognitive-behavioral therapy \(CBT\)](#)' above.)

- Contingency management when added to, for example, group addiction counseling, uses motivational incentives to reduce substance use, based on principles of operant behavioral conditioning. Although mixed results have been found, clinical trials, on balance, support the short-term efficacy of contingency management for substance use problems in adolescents. (See '[Contingency management training](#)' above.)
- Family-based treatment interventions – including multidimensional family therapy, functional family therapy, brief strategic family therapy, and multisystemic family therapy – are the most strongly supported of psychosocial interventions for adolescents with SUD. (See '[Family-based treatment](#)' above.)
- Brief intervention is useful as a first step intervention for adolescents with a mild alcohol use disorder that includes assessing the patient's recognition of a problem with alcohol, as well as his or her willingness for treatment. (See '[Screening and brief intervention](#)' above.)
- While not adequately tested for efficacy, SUD treatment can be provided to adolescents in schools. Specifically designed recovery high schools provide secondary education, SUD education, and support to adolescents "in recovery." Observational trials have shown associations between recovery high school attendance and reduced substance use. (See '[School-based treatment](#)' above.)
- Addiction counseling and mutual help groups are widely available treatments for SUD and are available specifically for adolescents. While evidence-based models of addiction counseling have been tested, addiction counseling as typically provided and mutual help groups have not been sufficiently tested for efficacy in adolescents with SUD. They can be helpful in our clinical experience. (See '[Mutual help groups](#)' above and '[Addiction counseling](#)' above.)
- Several psychosocial interventions that combine multiple modalities have been developed to meet needs of adolescents with SUD. Adolescent assertive continuing care and the adolescent community reinforcement approach have been found to be efficacious in clinical trials compared with treatment as usual. No one combination of interventions has been found to be more effective than others. (See '[Multimodal approaches](#)' above.)

Use of UpToDate is subject to the [Terms of Use](#).

