

From [Future Neurology](#)

Child and Caregiver Issues in the Treatment of Attention Deficit-Hyperactivity Disorder: Education, Adherence, and Treatment Choice

Maite Ferrin, MD, MSc; Eric Taylor, MA, MB, FRCP, FRCPsych, FMedSci

Abstract

There is much more to successful drug treatment than writing a prescription. In this article, we describe some of the 'holistic' aspects of the pharmacological treatment of attention deficit–hyperactivity disorder, with an emphasis on helping families to decide between psychological and pharmacological treatment and on the process of psychoeducation. Detailed accounts of drug and behavioral treatment in various circumstances are available elsewhere; however, the value and process of psychoeducation is sometimes underestimated or referred to in a cursory statement of the need for a good doctor–patient relationship. There has been little in the way of controlled trials, so no meta-analysis is attempted. Where possible (e.g., in reviewing the effects of psychological therapy and prediction of drug response), PubMed/Medline was searched for systematic reviews and randomized trials, but this article's conclusions should be taken as personal. These subjective views are based chiefly on experience in clinical practice, participation in focus groups with young people and their families and work with support groups.

Executive Summary

Assessment: Setting Therapeutic Targets

- *When setting therapeutic targets, these goals should be comprehensive and take into account not only the reduction of attention deficit–hyperactivity disorder (ADHD) core symptoms, but also the improvement in function and quality of life.*
- *When considering medication, the clinician has to consider that pharmacological treatments should be part of an overall treatment plan that is discussed responsively with the patient and their family.*
- *Predicting the response to medication is useful for advising families about the most likely outcomes of medications and thus to reassure them of the benefits of medication.*

Coexistent Problems in ADHD

- *Coexistent problems are the rule and not the exception in ADHD; for this reason, they need inclusion in treatment plans.*
- *Internalizing and externalizing problems: problems with conduct represent the most common condition associated with ADHD, whereas the internalizing problems probably remain underdiagnosed in this population. The choice of medication may be mediated by the profile of problems presented.*
- *Substance misuse and the choice of medication: there are implications for society at large from the widespread availability of cognitive-enhancing drugs. The prescriber needs to bear this in mind when considering treatment prescriptions.*

Attitudes Towards Treatment & Treatment Adherence in ADHD

- *Adherence to medication is often quite low, especially in teenage years, but is helped by detailed attention to tolerability and understanding of the disorder.*
- *Encouraging adherence to treatments, the role of education: behavioral and psychoeducational approaches are efficacious interventions and sometimes the first choice of treatment. These approaches are frequently underutilized by clinicians; however, recent guidelines have suggested a potential beneficial role of psychoeducational programs both once the diagnosis is made and later on during course of the treatment.*
- *Long-term effects of medication are not clear, so management should include periodic discontinuation to assess need.*

Future Perspective

- *Psychoeducation and other cognitive approaches are likely to be useful therapeutic agents for the multidimensional treatment of ADHD, especially when combined with the appropriate pharmacological treatments. For this purpose, evaluation of coexisting conditions with ADHD and a comprehensive assessment of the condition are required.*
- *In future, the choice of intervention may be informed by genomic testing and by the impact of medication on neuroimaging measures.*

Assessment: Setting Therapeutic Targets

Attention deficit–hyperactivity disorder (ADHD) is a complex disorder, or a set of disorders. The defining behaviors – consisting of impulsiveness, inattentiveness and restless activity – are not always the major impairment. The behaviors may, for instance, initiate a pattern of rejection or hostility from other people; inattentiveness may create a cognitively unstimulating environment for the sufferer.[1] Difficulties in classroom learning, poor peer or family relationships, aggressive behavior and personal distress may all be the aspects of the condition that are of most clinical concern. Therefore, the initial clinical assessment needs to set the goals of treatment for the individual ([Box 1](#)).[2]

Different people may place a different emphasis on these possible goals. For instance, parents may chiefly wish that the child’s achievement in school will improve, whereas the child’s priority might be to make better friendships and escape bullying. Both will want the clinician to recognize these goals. A diagnosis is usually valued, but a change in the diagnostic criteria is not necessarily the key change that is desired. The wise clinician will ensure that the goals are explicit and discuss which of them can realistically be expected to change. Furthermore, the different targets may have different dose–response characteristics. For example, parent rating scales may be less sensitive than teachers’ rating scales in some circumstances.[3] If the prescriber sets the dose according to the parental report only, an unduly high dose may be set in order to achieve satisfactory outcome, and the teacher may see excessive subduing of the child during daytime lessons. Although this is not common in clinical practice, it is sensible to ensure that monitoring the treatment outcome involves not only a rating scale of core symptoms, but also some consideration of the most salient goals, including reduction of functional impairment, parent–child and peer relationships, self-esteem and quality of life.[2]

Pharmacological Treatment: When is Medication Needed?

Medication can contribute to all of the aforementioned goals, especially the reduction of core symptoms. However, it is not the only way of helping. Behavior modification approaches also have a substantial effect size, as witnessed by systematic reviews using different methods.[4,5] A large-scale trial randomized children to receive careful medication, intensive behavioral treatment, the combination of both or treatment as usual.[6] Medication proved to be more powerful than behavioral treatment at 14 months, research treatment was better than routine and there were many advantages in adding medication to behavioral treatment, but few advantages in adding behavioral treatment to medication. On the other hand, adverse physical effects, such as growth reduction, were more common in those receiving medication,[7] and the longer-term effects remain in doubt (see later).[8,9]

Expert guidelines drawing on this evidence have come to different conclusions about the relative place of psychological and pharmacological interventions. The 2007 Practice Parameters of the American Academy of Child and Adolescent Psychiatry envisage medication as the usual treatment. Guidelines from the European Society of Child and Adolescent Psychiatrists[2] and from the National Institute of Clinical Excellence (NICE) in the UK[4] recommend a more restricted role for medication: as a first choice in severe cases, and otherwise only when psychological treatment has been unsuccessful, is infeasible or has been refused. For a list of different licensed and unlicensed medications used in ADHD, see [Box 2](#) .

Patients and their families are understandably confused by this disagreement between experts on such a fundamental point. Medication remains controversial in the press and broadcasting media. Indeed, some media accounts suggest that parents are at fault if they fall back on medication, being deficient in the ability to bring up their children without drugs. Careful explanation is therefore needed when a decision to medicate is contemplated. The decision itself should be made in the context of a responsive discussion involving the clinician, the child and the family; however, conflicts and tensions may arise. The duty of the clinician is to help the child. The attitudes of parents must be respected, but there will be times when the clinician should work hard to persuade a reluctant family of the value of treatment.

According to recent clinical guidelines on ADHD, the clinicians' work should be organized to provide optimal support for the child and the family. For this purpose, the following aspects are crucial: ensuring that children or adolescents and their parents are informed about the disorder, the different treatment options and the importance of medication compliance; an adequate follow-up on any effects of drug treatment by the clinician; compliance with national or local guidelines on the management of ADHD; and a specific plan for the continuation of care for adolescents moving into adult services.[4] For these reasons, when developing clinical services for children and adolescents with ADHD, a multidisciplinary team is usually required. The aim of multidisciplinary assessments is to undertake comprehensive and detailed evaluations of the individual from a wide range of biological, psychological, educational, developmental and social perspectives.[2,10] In addition, inadequate diagnosis or supervision of treatments and inadequacy of services has been related to cessation of treatment in young people with ADHD (see later). Child and adolescent psychiatrists and psychologists, pediatricians, specialized nurses, remedial disciplines, teachers and social workers work in different ways in different places, therefore clarity about roles should be developed.

Predicting the Response to Medication

Advising families about therapy would be easier if it were possible to predict the degree of response for the individual patient. In theory, there are several ways of predicting who will respond best to medication: clinical profiles, psychological testing, neuroimaging and psychophysiological measures have all been tried without yielding robust predictors,[11,12] and more recent attempts to predict on the basis of gene measurement have not yet been very successful. Any predictor would have to be powerful to be useful, because drug action is usually easy to monitor. Stimulant drugs work very rapidly, so a good estimate can be obtained by a single-dose trial or by trying the medication for a few days. This is likely to be a more effective process than the use of a biological marker with limited sensitivity and specificity.

However, there are some circumstances in which it is helpful to make a clinical prediction. An unsuccessful attempt at treatment may lead to a family losing trust in their adviser. A suggestion from a therapeutic trial may be perceived by a family as an indication of uncertainty in the adviser. Furthermore, the advent of a wider range of drugs, some of them slow to act, complicates the tactic of a therapeutic trial. A reanalysis of the Multimodal Treatment of Attention Deficit Hyperactivity Disorder (MTA) trial[13] did find some prediction of whether drug treatment would be markedly more effective than psychological treatment. A subtype of ADHD – hyperkinetic disorder – is the condition described in the International Classification of Diseases (10th revision), and requires not only the combined subtype of ADHD to be present, but also that diagnostic criteria are met in more than one setting (e.g., both home and school) and that the problems cannot be attributed to high levels of anxiety. Hyperkinetic disorder proved to be a moderator of treatment outcome on ratings of hyperactivity/impulsivity, total social skills score and internalizing symptoms. It may be a helpful way of counseling families on the likely outcomes of treatment; this information may be useful to reassure families of these children that medication is likely to work effectively.[2]

Coexistent Problems in ADHD

Internalizing & Externalizing Problems

Other problems present at the same time are sometimes termed ‘comorbidities’, but the term is misleading as it should refer to the simultaneous presence of distinct diseases. Many problems, such as oppositional defiance and emotional lability, are too common in ADHD to be regarded as separate illnesses.[14] Some two-thirds of referred school-age children with ADHD have at least one other psychiatric diagnosis (Table 1). These coexistent problems complicate the diagnostic process and can have an important impact on management and outcome. For these reasons, detecting a possible concurrent condition in children or adolescents with ADHD is particularly important.[15] The discussion of the effects of medication will need to take into account whether other problems are present in addition to the core of impulsiveness, inattention and overactivity. For most of these conditions, it is still correct to use antihyperactivity medication, but closer monitoring may well be needed.[2] High levels of anxiety tend to predict a poorer response to treatment,[12,16] but do not constitute a contraindication. Indeed, emotional problems are more likely to be improved than worsened by stimulants and atomoxetine (Table 1).

Problems with conduct, including oppositional defiant disorder (ODD) and aggressive or delinquent behavior or conduct disorder, represent the most frequent comorbidities with ADHD. In most studies, between 40 and 70% of the children presenting ADHD also have an ODD or a conduct disorder.[17] This percentage varies from one study to another, and probably with age: there are figures indicating

the existence of ODD in 30–60% of preadolescent children with ADHD, whereas 25–35% of adolescents with ADHD will present with antisocial conduct or antisocial personality disorder.[14] The development of oppositional and conduct problems (CPs) in ADHD has been reviewed in detail elsewhere.[18] The full reasons are not established, but the genetic influences on ODD and ADHD are usually similar; ADHD usually arises before CPs and the transition from ADHD to CPs is associated with high levels of critical expressed emotion from caregivers.[18] Therefore, we argue for a mediating role of hostile emotional atmospheres and for psychological as well as pharmacological interventions to enhance warmth and reduce negative emotions at home. It is possible that similar processes may contribute to the reduction of emotional lability. The choice of treatment may also be influenced by the profile of problems presented. A systematic review of the trials of treating labile emotions suggests that anti-ADHD medications may be helpful for brief emotional outbursts but remain contraindicated in bipolar disorders I and II.[19]

Substance Misuse

Substance misuse is a major associate of ADHD, and interventions to reduce it should be developed. A meta-analysis by Wilens and colleagues suggested not only that medication was not contraindicated in ADHD, but that it might actually be helpful.[20] However, perhaps it is effective treatment rather than medication *per se* that is useful. The powerful MTA study suggested that assignment to medication was neutral with regard to longer-term substance misuse, but that those treated with intensive behavior therapy were less at risk for drug misuse than other treatment groups.[21]

The presence – or the perceived risk – of substance misuse raises particular problems. Stimulant drugs are controlled substances: they affect dopamine and norepinephrine levels by blocking reuptake. These medications may also inhibit some of the metabolic enzymes that remove neurotransmitters from the synapse, such as the monoamine oxidases.[22] Their action to antagonize the dopamine transporter, and therefore to increase synaptic dopamine levels, is qualitatively similar to that of cocaine. Indeed, intravenous administration of stimulants is dangerously addictive. However, oral administration has a much slower time course and this seems to account for the lack of euphoria and potential for dependence.[23] Even in young people misusing cannabis there seems to be little risk of substance misuse escalating when a stimulant is prescribed.

The prescriber may want to discuss the choice of medication for patients who have misused drugs or have a close contact in the drug scene. Atomoxetine is not a euphoriant drug;[24] the preparation of Concerta[®] (Johnson & Johnson, NJ, USA) makes it difficult (but not impossible) to extract injectible methylphenidate; lisdexamfetamine (Vyvanse[®], Shire, Ireland, a recently approved drug in the USA) is said to be activated in the gut so should be inactive if injected or snorted.[25] However, families should not be led to think that alternative prescription removes all risks. Much of the misuse of stimulant medication is for cognitive enhancement by students who are presumably without a disability but seeking to improve their grades. This misuse can be served by all preparations

There is a black market in stimulants (and modafinil); in particular, some students who do not have a diagnosis of ADHD purchase the tablets as an aid to study. They believe that it helps to counteract fatigue and sharpen concentration. It is possible that those students have undiagnosed ADHD and are self-medicating.[26] However, the limited amount of data on the cognitive effects of stimulants is typically

developing people tend to suggest that they have a modest degree of cognitive enhancement in people without an illness. Furthermore, some students say that they will also take nonprescribed medication as a party drug. It is possible to pulverize some tablets and then inject or inhale the resulting powder for a euphoric 'high'.

There are implications for counseling and prescribing. Families are often fearful of drug treatment because of concerns about addiction. One can truthfully tell them that oral methylphenidate and atomoxetine are highly unlikely to give rise to dependence. Nevertheless, when there is a history of misuse, or a high risk of it, or another family member who is misusing, then our choice of medication is usually atomoxetine, which, to the best of our knowledge, carries no risk of dependence and no temptation to inject.

There are also implications for society at large from the widespread availability of cognitive-enhancing drugs. Other cognitive enhancers, such as nicotine analogs, AMPA receptor-mediated glutamatergic transmission and cAMP response element binding proteins, are likely to appear.[27] Should they be seen as methods of self-improvement or as cheating (analogous to the use of steroids in athletics)? Could they become coercive if employers or even teachers require their use? Will there be, short of coercion, a strong pressure to take them in order to compete effectively with people who do? These considerations should not lead to undue restriction for people who need the medicines. However, societies will need to consider how they react. In the UK, the NICE considered the issue and recommended that the attention-enhancing medicines should not be prescribed when the sole reason is the improvement of academic grades.[4]

Other Neurodevelopmental Conditions

In the presence of autism spectrum disorders, some of the common symptoms (stereotyped behaviors and social withdrawal) may be exacerbated by stimulants and indicate a need for low doses, careful dose adjustment and possibly a different class of drugs. Tics are not usually worsened by stimulants, but can be exacerbated in individual cases and so need to be checked, and sometimes a nonstimulant such as atomoxetine will be preferred.[28,29] The presence of epilepsy is sometimes seen as a contraindication to medication for ADHD. This is a pity, because there is very little evidence for any deleterious effects of the drugs on seizure frequency. Perhaps patients at particular risk for status epilepticus should receive dexamfetamine rather than another drug, but the suggestion is not backed up by good evidence.

The choice of medication should be influenced by knowledge of the effect sizes,[30] the speed of action, the convenience of administration, the potential adverse effects, the presence of other conditions (see previous section) and the preferences of the child and family. All of these need individual consideration and discussion. For example, an extended-release formulation of methylphenidate (such as Concerta) may have a slower onset of action in the morning, but a longer duration of activity through the day, than immediate-release tablets. It may therefore be preferred when the child is fearful of stigma from having to take tablets at school, or when the school is unwilling to administer, or conveys negative attitudes about, medication.[31] On the other hand, shorter-acting preparations may be preferred if the longer-acting one is disrupting sleep. If the beginning of the day is presenting particular problems at home, then it may be better for the child to take an immediate-release tablet (there is a relatively small amount of immediately released methylphenidate in the osmotic-release oral system preparation). The early stages of dosage adjustment should include consideration of diurnal fluctuation and tailoring the timing of doses and the

preparation of drug to give a profile of action over the day that best suits the individual.

On a longer time scale, atomoxetine differs from the stimulants in taking several weeks for the full action to appear, which will be a disadvantage for some families needing to see a quick change. On the other hand, it has a substantially longer action through the day, so the 'on-off' effects of the stimulants do not appear; this will be a considerable advantage for some families.[24]

Attitudes Towards Treatment & Treatment Adherence in ADHD

In chronic mental disorders, treatment nonadherence has an important impact both in the short term – affecting tolerability and efficacy of the treatments – but also in the long term, entailing a poorer medical outcome and a higher economic burden of disease.[32] For children and adolescents with ADHD, treatment adherence has been shown to be especially poor. **Reported levels of adherence average 50%, ranging from 35 to 81%, depending on the definition of adherence and the measure used.[33,34]** Since treatment adherence has to be regarded as a shared agreement between the patient (or their families in this case) and the clinician, these data might reflect an underlying poor alliance in the decision-making process that needs to be addressed.

Treatment adherence has been related to a good outcome, even when the treatment used is placebo.[35] It has also been shown that patients' core beliefs have a direct impact on their illness management, which is probably explained by treatment adherence as an intermediate step in this association. In addition, positive attitudes and treatment adherence might be correlated with other protective factors, all of them interacting together for a better outcome. Similarly, attitudes of young people toward their condition and its treatment are likely to influence the outcome. Greater improvement and reduced severity of symptoms have been shown when patients adequately adhere to medication regimens.[36] **Some of this improvement may come about because less severely affected families find it easier to comply. Generally, there is a trend for better adherence to be associated with better outcome in medical trials, even when the 'treatment' is only a placebo.**

Factors related to treatment adherence have been traditionally divided into patient-related, medication-related and environmental factors (Figure 1).[32]

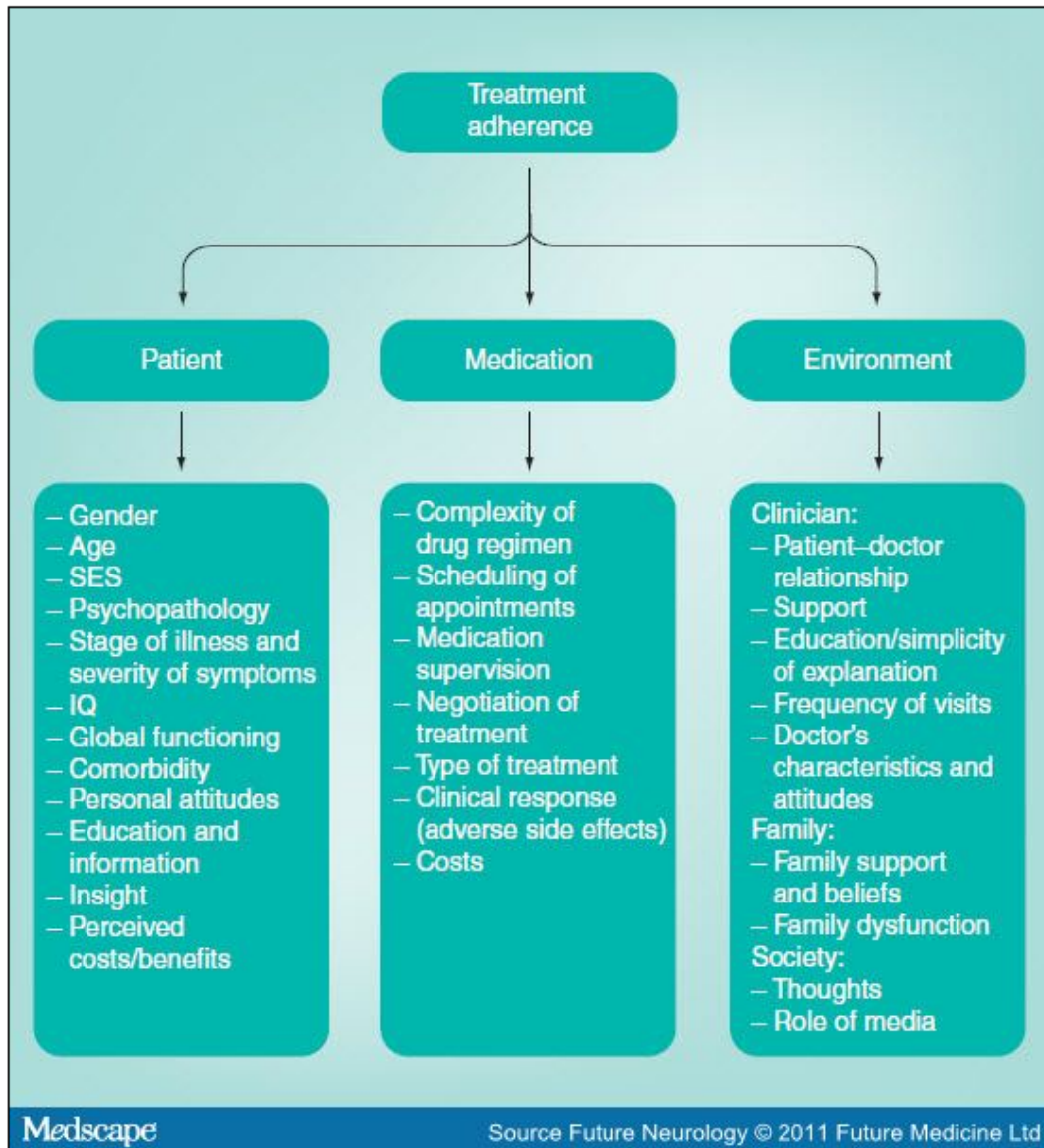


Figure 1.

Factors Related to Treatment Adherence.

It is very important to distinguish ‘nonintentional nonadherence’, when the patient fails to take the medication as a result of forgetting or misunderstanding instructions about the drug schedule, from ‘intentional nonadherence’, when the patient makes a specific decision not to take the prescribed medication.[37] The first situation is very likely to happen as ADHD itself is associated with forgetfulness and difficulties with sticking to daily routines. However, very little is known about the ‘intentional’ or specific attitudes and the reasons for nonadherence in children and adolescents with ADHD. These attitudes seem to be conditioned by a number of different components, including personal, family and environmental factors (Box 3).

Box 3. Factors Associated with Treatment Nonadherence in Children and Adolescents with Attention Deficit–hyperactivity Disorder.

Medscape

Child's factors

- Male gender
- Low IQ
- Old age
- Poor socioeconomic status
- ADHD-related factors:
 - Greater severity of symptoms
 - More distractibility
 - Lower self-control
- Comorbidity:
 - More anxiety and emotional problems
 - Presence of conduct problems

Treatment-related factors

- Multiple daily dosing
- Social stigma
- Concerns about long-term safety
- Individual attitudes (disliking medications)

Environmental and family factors

- Family dysfunction and psychopathology
- Parental age and low IQ in parents
- Parents' personalities
- Negative parental attitudes towards treatment
- Inadequate treatment supervision
- Poorer clinical response
- More side effects

ADHD: Attention deficit–hyperactivity disorder;
IQ: Intelligence quotient.

Source Future Neurology © 2011 Future Medicine Ltd

Attitudes and perceptions toward treatments are potentially influenced by the role of families and the diffuse environment in which the young adult grows up. For instance, a family member can regard the psychiatric symptoms as more behaviorally based and thus refuse the medical treatment regimen. Conversely, some families may consider medication to be of crucial importance and then disregard the role of behavioral approaches.

Parenting a child with ADHD might be especially difficult, since these children require more involvement, understanding and greater levels of patience. When a parent has undiagnosed ADHD in addition to the child, there can often be significant dysfunction within the family. A parent with untreated ADHD will certainly have a very difficult time following treatment recommendations for the child, creating routines and structure at home, being consistent with their child and implementing and following through with behavioral or psychoeducational programs.[38]

Encouraging Adherence to Treatments: the Role of Education

When trying to disentangle the specific factors associated with attitudes towards treatment in adolescents with ADHD, three main components emerge: concerns about the disorder and different treatments; insight into the illness and the need of medical treatment; and the patient–doctor relationship [Ferrin M *et al.*, Manuscript

Submitted]. Importantly, these three factors are intimately correlated, susceptible to modification and shaped by knowledge, and thus an adequate transmission of information may have a decisive impact on the attitudinal factors toward treatments (Figure 2).

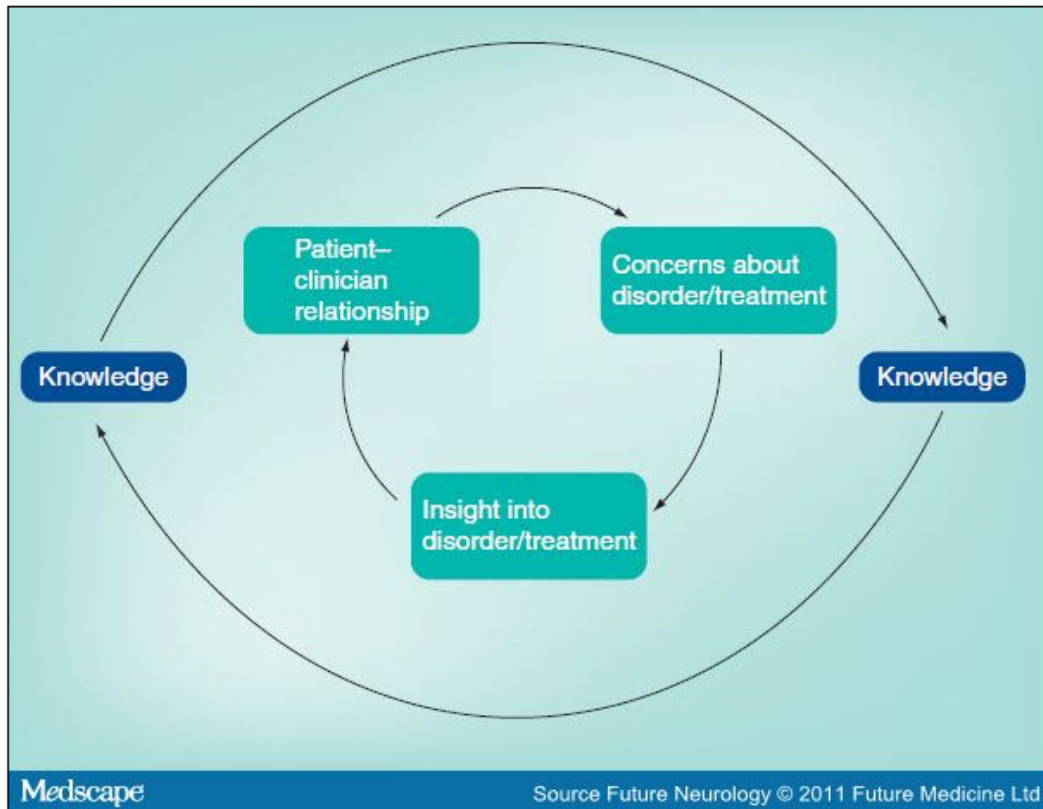


Figure 2.

Attitudes Towards Treatment in Attention Deficit–hyperactivity Disorder and the Role of Knowledge.

General methods for transmitting information might include books and texts, and internet resources. At this level, media (especially the internet) have emerged as powerful sources of information and opinion regarding psychiatric disorders and the impact of treatment. Internet social networks, including Twitter and Facebook, can be used as effective tools for transmitting information and attitudes.[4] However, some media suggest that parents are deficient in their ability if they fall back on medication and encourage them to bring up their children without drugs. The clinician should know the potential impact of the media both for improving positive attitudes and for creating false beliefs and expectations.[4]

Educational programs for families and children and adolescents also need to be regarded as different and specific tools for providing information to these families; these programs are not based on cognitive or cognitive–behavioral approaches or parent management training, but more specifically “for informing patients and their relatives about the illness and its treatment, facilitating both understanding and personal handling of the illness and supporting those afflicted in coping with the disorder”.[39] An excellent example of what is considered to be a structured psychoeducation program for mental health has been developed by Colom and Vieta;[40] this program has shown efficacy in reducing core symptoms and the frequency of relapse while improving treatment adherence. Although no meta-

analysis regarding the efficacy of these interventions in ADHD has been carried out[41] (the literature regarding this specific topic is particularly scarce in ADHD), some studies have demonstrated the potential of these programs to reduce symptoms, improve quality of life and improve parents' knowledge and treatment adherence.[8,9,41–43] These types of interventions are probably underutilized in ADHD and in psychiatry generally.

According to the evidence, a number of characteristics need to be met for psychoeducational interventions to be effective (Box 4).[39,40] Transmission of information must be clear and given according to the specific family's or young person's level of understanding. It must also be multidirectional and include not only families but also the young person and their broader environment. Schools are good targets and need to be considered as a bidirectional source for communicating with families and young people to increase their knowledge, and for the teachers as a way of improving recognition and management of the disorder. Education should also be regarded as an active, ongoing process in which attitudes are constantly shaped and modified by information (Box 4).

Box 4. Main Characteristics of a Good Psychoeducation Program.

- Systematic, structured and based on previous evidence-based programs
- Culturally adapted for the specific population
- Mainly informative (about disorders and its treatment)
- Didactic, encouraging participants' discussion and participation
- Delivered in groups (8–10 people)
- Weekly sessions, lasting for a period of 4–16 weeks
- Main therapist (usually plus co-therapists) included
- Including material and internet resources
- Allowing families and participants to get the 'expert role' on that topic

Medscape

Source Future Neurology © 2011 Future Medicine Ltd

The importance of these educational programs for families would stem from their power to enhance a positive therapeutic alliance between the patient and their clinician and also to disentangle disagreement or controversial points that might have emerged from media or different general resources.[39–41] This would imply that when a decision to medicate is contemplated, a careful and detailed explanation is needed, and the decision itself should only be made after a responsive discussion involving the clinician, the family and the young adult. Eventually, educational programs for families could help make families and young people active agents in the decision-making process, thereby enhancing therapeutic adherence.

Longer-term Aspects of Medication

It has not yet been possible to mount rigorously controlled and randomized trials over the period of several years for which medication is usually recommended. The MTA study has reported observational follow-up studies for several years after the end of the 14-month trial.[44] There was rather little difference in outcome that could be attributed to the treatment of the initial trial. This negative result has been widely reported in the media, sometimes with the misleading suggestion that medication has been shown to be ineffective in the longer term. As a result, many children and their families have become more reluctant than before to take medicine and have felt confused about how long treatment should be continued for.

Conclusions from the MTA follow-up studies are actually quite hard to draw.[45,46] The end of the 14-month trial was also the end of randomization; after that point, subjects selected their own treatment. This self-selection makes it probable that people will select the best treatment for them. The subsequent outcome – with all groups showing fewer symptoms than before the treatment started – is in keeping with this formulation, rather than with the rather gloomy notion that nothing works. It is also possible that the beneficial effects of the intensive treatment in the three active arms of the trial waned once the subjects reverted to usual treatment. In either case, there is no reason to regard the pharmacotherapy of ADHD as short term only. It makes better sense to encourage subjects to find and adopt the regime that best suits them, accepting that there is a considerable range of individual responsiveness.[44,46]

A database from general practice in the UK has shown a rapid fall-off in the use of prescribed medication for ADHD once the young person reaches the age of 16 years.[47,48] This may apply in other countries as well. There are several reasons for this: the worst is that many adult services are not able or willing to prescribe. This calls for educational and administrative action, which is being implemented in the wake of the NICE report in the UK. There are also individual reasons for early termination of treatment, which may coexist in the same person.

First, there may be real doubt (as previously considered) about the value of pharmacotherapy in the long term. In the absence of clear scientific knowledge, the best response to this is individual trial. People receiving treatment should have periodic withdrawals from the drug (probably every year or so) to determine whether they still have a need for the treatment.

Second, adolescence brings a sharp need for autonomy. If children have been coerced into taking medication or have seen it as a means of satisfying others' needs rather than their own, they are likely to rebel against it when they can choose. Such an attitude calls for prevention by encouraging the children to become expert in their condition and its treatment, to appraise the good and the bad effects of medication and make rational decisions about the balance for them. A qualitative enquiry by Singh and Waldman indicates that many children can do just that.[49] When a negative attitude has developed, it will usually be best to encourage the teenager to experiment with taking or not taking the medication, noting the effects on themselves and how others treat them, and discussing with their physician and with other people they trust.

Third, some individuals may simply have found the regime irksome and tedious. It is worth spending time to understand what the problems are. Single daily dosage with a long-acting medication can reduce both forgetting and stigma. Reminders and 'buddy systems' can help overcome forgetfulness. Adverse effects such as sleep and appetite change can often be dealt with symptomatically or by a change of dose or medication.[2]

Fourth, a worrying change in some adolescents is a feeling of nihilism or despair about their condition and its impact. ADHD is indeed a chronic condition, it does hold people back from achieving their goals and it does give rise to a good deal of social rejection. Depressive affect needs to be recognized and treated. A goal of education and counseling is to help young people to set and achieve realistic goals for themselves and to recognize their successes in combating the disorder.

Fifth, adverse effects may outweigh any benefits for some individuals.[50] The most

common serious effects are blood pressure rising over the 95th percentile and reduced growth velocity, and both of these must be monitored regularly. Short of physical hazard, however, the unpleasantness of 'minor' effects such as headache, insomnia and stomach upsets may deter young people from continuing with treatment. Symptomatic relief is very often possible with measures such as diet change and sleep hygiene[2] and, if not, change of dose or preparation will often relieve the problem. First, however, the problem must be detected. This will need both a systematic checklist of possible symptoms and an open-ended enquiry regarding any other problems encountered. Some potential difficulties (e.g., sexual dysfunction) will not be on most checklists; in addition, problems that are unrelated to medication will not be on the checklist, but could be attributed to the medication if they are not recognized and explained. For an existing side effect symptoms checklist that the clinician could access and use, we suggest the list by Hill and Taylor.[7]

Some people may experience subtler adverse effects. They may have a crisis of authenticity: "Is the 'real me' the way I am with medication and without ADHD or is ADHD part of the 'real me' and therefore to be valued?" This does not have a glib answer; it calls for responsive discussion so that the young person can decide their actions in the light of their values. The practical value of the medication may be valued in whatever way one resolves the theoretical question. Throughout this article, we have tried to emphasize the need to help young people and their families towards a mature understanding of pharmacotherapy so that they may become not merely passive adherents to treatment, but intelligent consumers.

Conclusion

Medication is a valuable means of treatment for children and adults with ADHD, and raises several issues for children and caregivers. This article reviews how families can be helped by existing evidence to make decisions about the choice of initial treatment, to distinguish core ADHD features from coexisting psychopathology and to maintain adherence to chosen treatments. The value of psychoeducation for young people and families is stressed, in helping them towards expert understanding and good individual choices.

Future Perspective

The choice of intervention may in future be informed by genomic testing and by the impact of medication on neuroimaging measures. At present, methylphenidate remains the most widely used medication and its operation is so swift that prediction of response by DNA testing is scarcely necessary. However, we can expect to see a wider range of medicines coming into use, and it may well become desirable to have a clearer means of determining the first choice of therapy. Genomic testing has the potential for determining both pharmacokinetic properties (and therefore the dosage regimes likely to be most efficient) and the receptor characteristics that may indicate which drug is likely to have the most suitable neurochemical profile. Furthermore, in cases that are refractory to psychological or pharmacological intervention, it may well be useful to use functional neuroimaging to characterize whether the expected brain changes are taking place.

These technological advances may increase the confidence with which patients and families use treatment. More immediately, we can hope that clinical development will close the gap between good psychoeducational practice as outlined in this article and routine practice as it now exists in many parts of the world.

References

- Taylor E: Developing ADHD. *J. Child Psychol. Psychiatry* 50,126–132 (2009).
- Taylor E, Dopfner M, Sergeant J *et al.*: European clinical guidelines for hyperkinetic disorder – first upgrade. *Eur. Child Adolesc. Psychiatry* 13(Suppl. 1),17–30 (2004).
- Banaschewski T, Coghill D, Santosh P *et al.*: Long-acting medications for the hyperkinetic disorders. A systematic review and European treatment guideline. *Eur. Child Adolesc. Psychiatry* 15(8),476–495 (2006).
- National Institute for Health and Clinical Excellence (NICE): *Attention Deficit Hyperactivity Disorder. Diagnosis and Management of ADHD in Children, Young People and Adults*. The British Psychological Society and The Royal College of Psychiatrists, UK (2009). •• Current UK guidelines for the diagnosis and treatment approaches in children, adolescents and adults with attention deficit–hyperactivity disorder (ADHD).
- Pelham WE, Fabiano GA: Evidence-based psychosocial treatments for attention-deficit/hyperactivity disorder. *J. Clin. Child. Adolesc. Psychol.* 37(1),184–214 (2008).
- Swanson JM, Kraemer HC, Hinshaw SP *et al.*: Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. *J. Am. Acad. Child Adolesc. Psychiatry* 40(2),168–179 (2001).
- Hill P, Taylor E: An auditable protocol for treating attention deficit/hyperactivity disorder. *Arch. Dis. Child.* 84(5),404–409 (2001).
- The MTA Cooperative Group: Multimodal Treatment Study of Children with ADHD. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch. Gen. Psychiatry* 56(12),1073–1086 (1999). •• Along with⁹, this was one of the first studies that compared the benefits of medication, psychological approaches and both psychological plus pharmacological interventions with community treatment in a cohort of children and adolescents with ADHD. First results are described here after a 14-month follow-up.
- The MTA Cooperative Group: Moderators and mediators of treatment response for children with attention-deficit/hyperactivity disorder. *Arch. Gen. Psychiatry* 56(12),1088–1066 (1999). •• Along with⁸, this was one of the first studies that compared the benefits of medication, psychological approaches and both psychological plus pharmacological interventions with community treatment in a cohort of children and adolescents with ADHD. First results are described here after a 14-month follow-up.
- Bernard S, Turk J: *Developing Mental Health Services for Children and Adolescents with Learning Disabilities. A Toolkit for Clinicians*. The Royal College of Psychiatrists Publication, UK (2009).
- Barkley RA: Predicting the response of hyperkinetic children to stimulant drugs: a review. *J. Abnorm. Child Psychol.* 4(4),327–348 (1976).
- Taylor E, Schachar R, Thorley G, Wieselberg HM, Everitt B, Rutter M: Which boys respond to stimulant medication? A controlled trial of methylphenidate in boys with disruptive behaviour. *Psychol. Med.* 17(1),121–143 (1987).
- Santosh PJ, Taylor E, Swanson J *et al.*: Refining the diagnoses of inattention and overactivity syndromes: a reanalysis of the multimodal treatment study of attention deficit hyperactivity disorder (ADHD) based on ICD-10 criteria for hyperkinetic disorder. *Clin. Neurosci. Res.* 5,307–314 (2005).
- Brown TE: *ADHD Comorbidities: Handbook for ADHD Complications in Children and Adults*. American Psychiatric Publishing, Washington, DC, USA (2009).
- Vance A, Arduca Y, Sanders M, Karamitsios M, Hall N, Hetrick S: ADHD, combined type, dysthymic disorder and anxiety disorders: differential patterns of neurodevelopmental deficits. *Psychiatry Res.* 143,213–222 (2006).
- Buitelaar JK, Van der Gaag RJ, Swaab-Barneveld H, Kuiper M: Prediction of clinical response to methylphenidate in children with attention-deficit hyperactivity disorder. *J. Am. Acad. Child Adolesc. Psychiatry* 34(8),1025–1032 (1995).
- Maughan B, Rowe R, Messer J, Goodman R, Meltzer H: Conduct disorder and oppositional defiant disorder in a national sample: developmental epidemiology. *J. Child Psychol. Psychiatry* 45(3),609–621 (2004).
- Taylor E: Comorbidity in neurodevelopmental disorders: the case of attention-deficit–hyperactivity-disorders. In: *Comorbidities in Developmental Disorders: Clinics in Developmental Medicine No. 187*. Bax M, Gillberg C (Eds). MacKeith Press, UK, 60–74 (2010).
- Taylor E: Managing bipolar disorders in children and adolescents. *Nat. Rev. Neurol.* 5(9),484–491 (2009).
- Wilens TE, Faraone SV, Biederman J, Gunawardene S: Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics* 111(1),179–185 (2003).
- Molina BS, Brooke SG, Flory K *et al.*: Delinquent behavior and emerging substance use in the MTA at 36 months: prevalence, course, and treatment effects. *J. Am. Acad. Child Adol. Psychiatry* 46(8),1028–1040 (2007).
- Stahl SM: Mechanism of action of stimulants in attention-deficit/hyperactivity disorder. *J. Clin. Psychiatry* 71(1),12–13 (2010).

- Rutter M: *Rutter's Child and Adolescent Psychiatry. (5th Edition)*. Wiley-Blackwell, UK (2008).
- Garnock-Jones KP, Keating GM: Atomoxetine: a review of its use in attention-deficit hyperactivity disorder in children and adolescents. *Paediatr. Drugs* 11(3),203–226 (2009).
- Dew RE, Kollins SH: Lisdexamfetamine dimesylate: a new option in stimulant treatment for ADHD. *Expert Opin. Pharmacother.* 11(17),2907–2913 (2010).
- Rabiner DL, Anastopoulos AD, Costello EJ, Hoyle RH, Swartzwelder HS: Predictors of nonmedical ADHD medication use by college students. *J. Atten. Disord.* 13,640–648 (2010).
- Hess US, Whalen SP, Sandoval LM, Lynch G, Gall CM: Ampakines reduce methamphetamine-driven rotation and activate neocortex in a regionally selective fashion. *Neuroscience* 121(2),509–521 (2003).
- Tourette's Syndrome Study Group: Treatment of ADHD in children with tics: a randomized controlled trial. *Neurology* 58(4),527–536 (2002).
- Bloch MH, Panza KE, Landeros-Weisenberger A, Leckman JF: Meta-analysis: treatment of attention-deficit/hyperactivity disorder in children with comorbid tic disorders. *J. Am. Acad. Child Adolesc. Psychiatry* 48(9),884–893 (2009).
- Faraone SV, Glatt SJ: A comparison of the efficacy of medications for adult attention-deficit/hyperactivity disorder using meta-analysis of effect sizes. *J. Clin. Psychiatry* 71(6),754–763 (2010).
- Harpur RA, Thompson M, Daley D, Abikoff H, Sonuga-Barke EJ: The attention-deficit/hyperactivity disorder medication-related attitudes of patients and their parents. *J. Child. Adolesc. Psychopharmacol.* 18(5),461–467 (2008).
- Buckley P: *Adherence to Mental Health Treatment*. Oxford University Press, NY, USA (2009).
 - Recent book of treatment adherence in psychiatry. An excellent place to start for an overview of treatment adherence on mental health.
- Charach A, Ickowicz A, Schachar R: Stimulant treatment over five years: adherence, effectiveness, and adverse effects. *J. Am. Acad. Child Adolesc. Psychiatry* 43(5),559–567 (2004).
- Thiruchelvam D, Charach A, Schachar RJ: Moderators and mediators of long-term adherence to stimulant treatment in children with ADHD. *J. Am. Acad. Child Adolesc. Psychiatry* 40(8),922–928 (2001).
- Osterberg L, Blaschke T: Adherence to medication. *N. Engl. J. Med.* 353(5),487–497 (2005).
 - Seminal article on treatment adherence and its potential benefits for outcome.
- Safren SA, Duran P, Yovel I, Perlman CA, Sprich S: Medication adherence in psychopharmacologically treated adults with ADHD. *J. Atten. Disord.* 10(3),257–260 (2007).
- Atkins L, Fallowfield L: Intentional and non-intentional non-adherence to medication amongst breast cancer patients. *Eur. J. Cancer* 42(14),2271–2276 (2006).
- Barkley RA, Brown TE: Unrecognized attention-deficit/hyperactivity disorder in adults presenting with other psychiatric disorders. *CNS Spectr.* 13(11),977–984 (2008).
- Bauml J, Frobose T, Kraemer S, Rentrop M, Pitschel-Walz G: Psychoeducation: a basic psychotherapeutic intervention for patients with schizophrenia and their families. *Schizophr. Bull.* 32(Suppl. 1),S1–S9 (2006).
- Colom F, Vieta E: *Psychoeducation Manual for Bipolar Disorder*. Cambridge University Press, UK (2006). •Excellent book that shows the details of a structured psychoeducational intervention program for patients with bipolar disorder, which has been shown to be of benefit in successive controlled trial studies.
- Montoya A, Colom F, Ferrin M: Is psychoeducation for children and adolescents with ADHD efficacious? A systematic literature review. *Eur. Psychiatry* (2011) (In press).
- Svanborg P, Thernlund G, Gustafsson PA, Hagglof B, Poole L, Kadesjo B: Efficacy and safety of atomoxetine as add-on to psychoeducation in the treatment of attention deficit/hyperactivity disorder: a randomized, double-blind, placebo-controlled study in stimulant-naive Swedish children and adolescents. *Eur. Child Adolesc. Psychiatry* 18(4),240–249 (2009).
- Ferrin M, Ruiz-Veguilla M, Centeno-Collado MS, Salcedo-Collado MD, Moreno-Granados JM, Ramirez-Gonzalez AI: Evaluation of a psycho-education program for families with ADHD children and adolescents in a randomized controlled trial. Presented at: *19th World Congress of the International Association for Child and Adolescent Psychiatry and Allied Professions*. Beijing, China, 2–6 June 2010.
- Molina BS, Hinshaw SP, Swanson JM *et al.*: The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *J. Am. Acad. Child Adolesc. Psychiatry* 48(5),484–500 (2009).
- Banaschewski T, Buitelaar J, Coghill DR *et al.*: The MTA at 8. *J. Am. Acad. Child Adolesc. Psychiatry* 48(11),1120–1121 (2009).
- Hazell PL: 8-year follow-up of the MTA sample. *J. Am. Acad. Child Adolesc. Psychiatry* 48(5),461–462 (2009).
- McCarthy S, Asherson P, Coghill D *et al.*: Attention-deficit hyperactivity disorder: treatment discontinuation in adolescents and young adults. *Br. J. Psychiatry* 194(3),273–277 (2009).
- Wong IC, Asherson P, Bilbow A *et al.*: Cessation of attention deficit hyperactivity disorder drugs in the young (CADDY) – a pharmacoepidemiological and qualitative study. *Health Technol. Assess.* 13(50),III–IV, IX–XI, 1–120 (2009).

- Singh AL, Waldman ID: The etiology of associations between negative emotionality and childhood externalizing disorders. *J. Abnorm. Psychol.* 119(2),376–388 (2010).
- Graham J, Coghill D: Adverse effects of pharmacotherapies for attention-deficit hyperactivity disorder: epidemiology, prevention and management. *CNS Drugs* 22(3),213–237 (2008).
- Levy F: Synaptic gating and ADHD: a biological theory of comorbid ADHD and anxiety. *Neuropsychopharmacology* 29,1589–1596 (2004).
- Biederman J, Ball SW, Monuteaux MC *et al.*: New insights into the comorbidity between ADHD and major depression in adolescent and young adult females. *J. Am. Acad. Child Adolesc. Psychiatry* 47(4),426–434 (2008).
- Willcutt EG, Betjemann RS, McGrath LM *et al.*: Etiology and neuropsychology of comorbidity between RD and ADHD: the case for multiple-deficit models. *Cortex* 46(10),1345–1361 (2010).
- Goldstein S, Schwabach AJ: The comorbidity of pervasive developmental disorder and attention deficit hyperactivity disorder: results of a retrospective chart review. *J. Autism Dev. Disord.* 34(3),329–339 (2004).
- Wilens TE: The nature of the relationship between attention-deficit/hyperactivity disorder and substance use. *J. Clin. Psychiatry* 68(Suppl. 11),4–8 (2007).

Papers of special note have been highlighted as:

- of interest
- of considerable interest