Guidelines for Management of Attention-Deficit Hyperactivity Disorder in Adults

Aims
These guidelines aim to provide a structure for assessing and treating ADHD in adults, and aim to be compatible with NICE Guidelines (2008)\(^1\).

Background
ADHD is a highly heritable (~0.76\(^2\)) neurodevelopmental disorder with its onset in childhood, and persistence into adulthood in approximately 43% of cases\(^3\), with impairment persisting in a greater proportion, giving a prevalence for the disorder in adults of 2.5\(^4\)-4.4%\(^5\). The core symptom triad of Inattention, Hyperactivity, and Impulsivity\(^6\), leads to a variety of functional impairments including in employment, education and relationships\(^7\).

Assessment (See Figure 1)
Patients may be referred to adult services with a diagnosis of ADHD as a transition from child services, or may be referred for a diagnostic assessment. In either case a full assessment is required, including: the level of impairment persisting; physical and psychiatric co-morbidities; tolerance of previous medications; and physical examination. Adults referred for diagnosis require a more detailed assessment, including a full developmental history, normally from a collateral informant. DSM-IV-TR\(^6\) or ICD-10\(^7\) criteria are used, but DSM-IV-TR is often favoured, as the ICD-10 diagnosis of Hyperkinetic Disorder only identifies a severe subtype of DSM-IV-TR ADHD\(^1\). New diagnoses of ADHD must be based on evidence that the diagnosis had its onset in childhood, with some of the symptoms continuing into adulthood. School reports and childhood educational psychology assessments can be useful. Rating scales – for example the Barkley Symptom Scales\(^8\), and the Wender Utah Rating Scale\(^9\) – may assist assessment. The ASRS\(^10\) is a screening tool that can be useful in monitoring treatment response. Formal structured interviews (e.g. CAADID) and Neuropsychological testing are not required routinely to make the diagnosis\(^11\).

Comorbidity
Adults with ADHD have higher rates of comorbid depression, anxiety, substance abuse/dependence, and conduct disorder\(^12\). In addition, ADHD is associated with poorer prognosis in Bipolar Affective Disorder\(^13\) and can be a frequent comorbidity in Autism Spectrum Disorders, and Tic Disorders\(^14\). Comorbidities should be assessed and treated as normal. Some SSRIs can be used with stimulants or Atomoxetine for treatment of depression / anxiety.

Methylphenidate is contra-indicated in patients with a history of severe depression, anorexia, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia and psychopathic/borderline personality disorder.\(^15\) Use in these conditions is a matter of clinical judgement. Clinicians without significant experience may wish to take further advice. Care is required when using atomoxetine in patients with a previous history of psychosis.

For Treatment Options See Figures 1-6
Methylphenidate and atomoxetine are not licensed for adults newly diagnosed with ADHD and dosage information is based on NICE guidance.

Initiation takes place in Secondary Care and for GP prescribing follow the OBMH ADHD guidance on the intranet\(^16\).

Special Circumstances

Epilepsy - Titrate all stimulant or non-stimulant medications more slowly, and use with caution. If seizures exacerbated, or de novo seizures occur, stop treatment, and consider consulting a tertiary specialist. Atomoxetine is possibly higher risk than methylphenidate.\(^17\)\(^\text{A}\)

• Tic Disorders – Titration should be slow. Atomoxetine may be better in patients with Tic disorders\(^1\).

• Hyperthyroidism - Listed as contraindication to Methylphenidate and Dexamphetamine\(^18\).

• Risk of Angle Closure Glaucoma – Contraindication to stimulants and Atomoxetine\(^17\),\(^18\),\(^B\)

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\(^{\text{A}}\) Dexamfetamine is likely to reduce the convulsive threshold; caution is therefore advised in patients with epilepsy. However, there are case reports where amphetamines have been used to increase phenytoin or phenobarbital serum levels in an attempt to increase their antiepileptic action.\(^19\)

\(^{\text{B}}\) In patients with narrow angle glaucoma, atomoxetine may be higher risk than methylphenidate or dexamphetamine. Amphetamines and methylphenidate may cause a transient rise in intraocular pressure which is not associated with closure of the angle.\(^17\)
Some Major Interactions (see BNF\textsuperscript{18} or electronic data sheet compendium for individual products)\textsuperscript{5}

- **Atomoxetine:** MAOIs/RIMAs (Potentially life-threatening\textsuperscript{11}); Noradrenergic drugs (some antidepressants); high dose Salbutamol; QT prolonging drugs, drugs lowering seizure threshold; Methadone/Tramadol. Dose adjustment and slower titration of atomoxetine may be necessary in those patients who are also taking CYP2D6 inhibitor drugs (e.g. fluoxetine, paroxetine).
- **Stimulants:** MAOIs/RIMAs (Potentially life-threatening\textsuperscript{11}); coumarins; antiepileptics; possibly Clonidine.

**Other Treatments (not Recommended)**

Some patients may be taking stimulants not licensed in the UK, for example Adderall XR (mixed amphetamine salts). In general these medications should be switched to an alternative stimulant.

Whilst NICE accepts (in certain circumstances) the use of Bupropion, Clonidine, Modafinil and Imipramine in children in tertiary services, they are not recommended for ADHD in adults. There is some evidence for using Bupropion in adults, but NICE was concerned about its side effects\textsuperscript{1}. There is little evidence to support the efficacy and safety of combining Atomoxetine and stimulants\textsuperscript{11}.

**Diversion and Substance Abuse**

16-29\% of students with stimulant prescriptions will be asked to give, sell or trade their medication in their lifetime\textsuperscript{20}. There is no evidence that childhood stimulant treatment increases risk of adult stimulant abuse. There is insufficient evidence to indicate that treatment of ADHD reduces comorbid substance misuse. Illicit substances, especially stimulant-type drugs can interact with prescribed stimulants\textsuperscript{14}.

\textsuperscript{5} www.medicines.org.uk/emc/
**Figure 1: Assessment**

### Symptoms Suggest ADHD
- ≥6/9 Symptoms of Inattention, or
- ≥6/9 Symptoms of Hyperactivity / Impulsivity

**Consider Alternative Diagnoses**

#### Age of Onset
- Diagnosis usually requires onset of symptoms before age 7, but NICE recognises onset before age 12 as appropriate in some cases.

#### Exclusion Criteria
- NICE accepts diagnosis in those with Pervasive Developmental Disorder or General Learning Disability

#### Impairment in Adult ADHD
- Occupational
- Dangerous Driving
- Activities of Daily Living
- Relationships
- Childcare

#### Cardiovascular Disorders
- There have been reports of sudden death in adults receiving medication for ADHD. In children an association between sudden death on amphetamines (methylphenidate and dexamphetamine) and structural cardiac abnormalities has been implied. Severe hypertension, structural cardiac abnormalities, and cardiovascular disease (including arrhythmias) are contraindications to stimulants and cautions against atomoxetine.

#### Substance Misuse
- Significant substance misuse should be treated before ADHD, though ongoing use of alcohol or cannabis does not prevent treatment.

#### Medication Indicated as First Line Treatment
(See Figure 2)

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**Consider Psychosocial Treatment as Alternative to Medication**

**Medication Indicated as First Line Treatment**

**Ongoing Cardiovascular Problems**

**Medical/Family History any Cardiovascular Disease**

**Current Severe Substance Misuse or Severe Mental Illness**

**Patient Wants Medication**

**ECG Normal**

**Full Medical/Psychiatric History & Appropriate Physical Examination**

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**Medication Indicated as First Line Treatment**

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**Medication Indicated as First Line Treatment**
**Oxford Health NHS Foundation Trust**

**Figure 2: Medical Treatment Algorithm**

**Immediate Release Methylphenidate (Ritalin®, Medikinet®, Equasym)**

**Patient Advice:**
- Inform about loss of appetite, insomnia, and rarely psychosis. Give information leaflets about medicine and diagnosis.

**Baseline Tests:**
- Physical: Weight, BP and Heart Rate and bloods for LFTs
- ECG if medical/family history of serious cardiac disease, or indicated by physical examination

**Prescribing Immediate Release (IR):**
- Week 1: 5mg b.d. or t.d.s.
- Week 2: 10mg b.d. or t.d.s
- Titrate dose against side effects & symptoms - maintenance dose may be 80-100mg daily. Usually b.d. or t.d.s., but can be q.d.s normally last dose should be 4 hrs before bedtime.

**Assess ongoing effectiveness including using Ratings Scales, for example ASRS10, after at least 6 weeks.**

**If treatment to continue enter monitoring protocol (see Figure 5)**

**Modified Release Methylphenidate (Concerta XL®, Equasym XL®, Medikinet XL®)**

**Patient Advice:**
- Inform about loss of appetite, insomnia, and rarely psychosis. Give information leaflets about medicine and diagnosis.

**Baseline Tests:**
- Physical: Weight, BP and Heart Rate and bloods for LFTs
- ECG if medical/family history of serious cardiac disease, or indicated by physical examination

**Prescribing Modified Release (MR):**
- Week 1: 10mg (Equasym or Medikinet); 18mg (Concerta) o.m.
- Titrate weekly against side effects and symptoms: Max 100mg / day (Equasym or Medikinet) or 72mg (Concerta)1

**Assess ongoing effectiveness including using Ratings Scales, for example ASRS10, after at least 6 weeks.**

**If treatment to continue enter monitoring protocol (see Figure 5)**

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**Atomoxetine (second line treatment)**

**Patient Advice:**
- Inform about very rare severe hepatotoxicity (4 cases in >4 million patients, post marketing analysis11), and associated symptoms.
- If <30 years old warn of risk of increased suicide behaviours
- Though possibly preferable to stimulants in patients with a history of psychosis, Atomoxetine can worsen psychosis. A history of psychosis is a caution in Atomoxetine.

**Baseline Tests**
- Physical: Weight, BP and Heart Rate and bloods for LFTs
- ECG if medical/family history of serious cardiac disease, or indicated by physical examination

**Prescribe Atomoxetine:**
If >70kg:
- Week 1: 40mg daily
- Week 2: 60mg daily
- Week 3: 80mg daily
If <70kg:
- Week 1: 0.5mg/kg/day
- Week 2: 1.2mg/kg/day
(tables available – 10mg, 18mg, 25mg, 40mg, 60mg, 80mg.)

Usually single daily dose, but can be divided b.d.
Figure 3: Medical Treatment Algorithm – Treatment Failure

Treatment with Methylphenidate Failed

- Incomplete Response
  - No Response on Reasonable Dose
  - Ensure dose maximised
  - Consider increasing number of doses
  - For any other dosage options seek advice from clinician with appropriate experience.

Consider Atomoxetine

- If Response Remains Sub-Optimal
  - Reconsider Methylphenidate

Treatment with Atomoxetine Failed

- Incomplete Response
  - No Response on Reasonable Dose
  - Ensure dose maximised

Consider Methylphenidate

- If Response Remains Sub-Optimal

Treatment Failures Despite Adequate Trials of Methylphenidate and Atomoxetine

- Discuss Options with Patient
  - Immediate Release Dexamphetamine
    - Week 1: 5mg b.d.
    - Titrate to Symptoms over 4-6 weeks
    - Max 60mg / day
    - Usually b.d. or t.d.s., but can be q.d.s.
  - Patient Wants Trial of Dexamphetamine
    - If Partial Response to Medication
      - Consider Adding Formal Psychosocial Treatment
    - If No Response to Medication
      - Consider Switching to Formal Psychosocial Treatment
  - Patient Wants Psychosocial Treatment

Figure 4: Managing Side Effects

Stimulants:
- Insomnia – Consider reducing number of doses and taking last dose earlier. IR formulation may be better. Insomnia can be a symptom of ADHD, and sometimes stimulants can improve sleep.
- Psychotic Symptoms – Withdraw medication, assess and treat psychosis, consider Atomoxetine
- Tics – Reduce dose; assess pros and cons of treatment; consider Atomoxetine as alternative.

Atomoxetine:
- Signs of Liver Failure – Withdraw drug. Seek urgent medical advice.

Stimulants or Non-Stimulants:
- Resting Tachycardia, Arrhythmia, Systolic BP >95th Percentile or Clinically Significant Increase – discuss with appropriate physician. Perform ECG. Evidence in youths treated with Methylphenidate suggests that in general its effects on BP & Pulse, though extant, are probably not clinically significant.
- Loss of Appetite / Weight - Take medication during/after food. Add calorific snacks. Larger evening meal.
Figure 5: Monitoring Protocol on Treatment:

Check for Side-Effects (6 weeks after initiation or dose changes, then every 6 months):
- **Atomoxetine** – Suicidal thoughts, insomnia, constipation, dizziness, dry mouth, loss of appetite, nausea, jaundice, dark urine. Also sexual dysfunction should be specifically enquired about.
- **Stimulants** – Anxiety, irritability, dry mouth, insomnia, loss of appetite, nausea. Also, psychotic symptoms.

Physical Monitoring (All Treatments):
- **Weight** – 3 months and 6 months after initiation, then every 6 months
- **Blood Pressure and Heart Rate** – 3 monthly or following a dose increase
- **Blood Tests and ECG** – Not required routinely

Clinical Effectiveness
- This should be reviewed yearly. Need for social, psychological and occupational support should be assessed.

OBMH Shared Care Protocols:
- NICE supports the devolution of monitoring and prescribing to primary care, following initiation and stabilisation, under local shared care protocols
- OBMH has ADHD shared care agreements with Oxfordshire PCT and Buckinghamshire PCTs for 'the treatment of children and adolescents and continued prescribing in patients transferred to adult services'. Currently the agreement does not cover newly prescribed adult patients
- The protocols allow for prescribing and monitoring to be devolved to Primary Care, with the agreement of the GP involved, when:
  - The patient’s condition is stable
  - The dose of Methylphenidate/Atomoxetine is stable
  - There is an annual review of treatment with yearly drug-free trial to assess benefits of treatment
- NICE recognises that if there have been periods without treatment information from this can form part of decisions to continue treatment – the MHRA drug safety update Jan 2010 indicates that patients on methylphenidate should have a yearly drug-free period
- Under current shared care agreements specialists remain responsible for reviewing the patient regularly at least every 6 -12 months, though it is recognised that this may be a telephone review. An annual evaluation of the benefit of treatment is required. In addition specialists remain responsible for ensuring blood pressure, pulse and weight measurements occur.

Figure 6: Psychosocial Management

**Targets for Psychosocial Intervention**
- Psychoeducation
- Self-Esteem
- Learning Adaptive Thinking Skills
- Patient-Specific Issues:
  - Anger Management
  - Communication
  - Procrastination

Skills:
- Attention
- Organisation
- Planning

NICE Recommendations: CBT for ADHD
- NICE states: ‘for adults with ADHD, drug treatment should be the first-line treatment unless the person would prefer a psychological approach’.
- Where functional impairment persists after medical treatment CBT (group CBT first-line) should be considered.
- CBT should also be considered where the patient does not want medication, or where their residual functional impairment is mild enough to be managed by CBT alone.
References


6. DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders, American Psychiatric Association


16. OBMH (2010) Oxfordshire & Buckinghamshire PCTs ADHD Shared Care Arrangements


18. BNF (British National Formulary)


Further Resources
- Milton Keynes, Oxfordshire, Buckinghamshire, Berkshire East and Berkshire West (MOBB) Priorities Forum Policy Statement 177
- www.addiss.co.uk