



Medication management and electrocardiogram screening in children with attention deficit hyperactivity disorder



Original Article

Cite this article: Pentony M, Ali Z, Moore K, McNicholas F, and James A (2024) Medication management and electrocardiogram screening in children with attention deficit hyperactivity disorder. *Cardiology in the Young* **34**: 2080–2085. doi: [10.1017/S1047951124025320](https://doi.org/10.1017/S1047951124025320)

Received: 17 August 2023
Revised: 14 March 2024
Accepted: 8 May 2024
First published online: 13 September 2024

Keywords:
attention deficit hyperactivity disorder;
electrocardiogram; screening; medication

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Abstract

Background: To quantify the proportion of referrals sent to Crumlin Cardiology Department for cardiac screening prior to commencement or modifying attention deficit hyperactivity disorder medication and assess the number detected with a clinically significant abnormality. **Methods:** A prospective audit was performed over a 6-month period, from November 2021 to April 2022 inclusive. Referrals sent via outpatient department triage letters, electrocardiogram dept. email, and walk-in electrocardiogram service were screened for those pertaining to commencing or modifying medication for children with attention deficit hyperactivity disorder. Each referral was coded against National Institute for Health and Care Excellence guidelines to determine the degree of clinical details given. Reported abnormalities, recommended management, and correspondence were recorded. **Results:** Ninety-one referrals were received during the 6-month audit period. More than half lacked a clinical indication for referral (53/91, 58.2%), with fewer than one third (26/91, 28.5%) meeting National Institute for Health and Care Excellence criteria for referral for cardiology. Eighty (80/91) referrals had clinical outcomes available for review (missing outpatient department information and age outside of service range accounted for eleven referrals with unavailable clinical outcomes). Of the eighty clinically reviewed referrals, seventy-two (72/80, 90%) were reported as normal with no cardiology follow up required. Eight referrals (8/80, 10%) were reviewed in the Cardiology Outpatient Department prior to commencement or modifying attention deficit hyperactivity disorder medication. Of these, only one (1/80 1%) had a clinically significant abnormality which was a potential contraindication to attention deficit hyperactivity disorder medication use, and this referral was appropriate as per National Institute for Health and Care Excellence guidelines. **Conclusion:** Routine screening prior to attention deficit hyperactivity disorder medication prescription in the absence of clinical indications (as per National Institute for Health and Care Excellence) contributed to delays in medication initiation among young people with attention deficit hyperactivity disorder. Unnecessary referrals have resource implications for cardiology clinical team. Improved adherence to National Institute for Health and Care Excellence guidelines would provide benefits for patients and clinicians.

Pharmacological treatment for children with attention deficit hyperactivity disorder includes approved stimulant medications (eg. Methylphenidate) and non-stimulant options (eg. Atomoxetine, Guanfacine) and has a robust evidence base improving long-term outcomes.¹ Previous concerns regarding the cardiovascular safety profile of such agents have been reported, raising the question of the need for cardiac investigations prior to commencing medical therapy.^{2–4} Subsequent international best practice guidelines state that there is no evidence of increased risk of sudden cardiac death compared to children not receiving stimulant medication and most children do not require referral.^{5–7} However, electrocardiogram screening/cardiology opinion prior to commencing these medications is recommended in specific circumstances.^{5,8} Arguments against routine electrocardiogram screening include unfavourable cost-effectiveness for finite healthcare resources, spurious or inconclusive findings, and delay in medical treatment.^{9–11} Child and Adolescent Mental Health Services provide specialist mental health treatment for young people with attention deficit hyperactivity disorder in the Republic of Ireland.

The Department of Paediatric Cardiology in Children's Health Ireland at Crumlin is the tertiary paediatric cardiology unit and receives referrals from across the Republic of Ireland. As part of this, there are currently three pathways for review. The first option is via a paediatric electrocardiogram review email service, which allows for a formal interpretation on of electrocardiograms by a member of the paediatric cardiology team. These queries come from

healthcare professionals in the Republic of Ireland, and many relate to atypical or ambiguous electrocardiogram recordings. More recently, many of these referrals relate to pre-medication screening for young people with attention deficit hyperactivity disorder.

The second referral pathway involves a service whereby General Practitioners or local Child and Adolescent Mental Health Services teams can send a patient in for a walk-in appointment for an electrocardiogram. These electrocardiograms are then reported by a paediatric cardiology trainee on the Cardiology Team and the results posted or faxed back to the referring clinician.

The third referral pathway involves cardiac review in the Cardiology Outpatient Department. Such referrals come from colleagues across the Republic of Ireland, and typically follow on from clinical findings and concerns. Routine referrals to Cardiology outpatient Department may be waiting up to 2 years for an appointment to see a Paediatric Cardiology Consultant in our institution and therefore, in the absence of significant cardiac pathology, this can lead to suboptimal delay in other treatment.

Aim

This audit aimed to:

- i. Quantify the number of referrals sent to Crumlin Cardiology Department for cardiac screening prior to commencement or modification of attention deficit hyperactivity disorder medication.
- ii. Quantify the proportion of those referred with clinically indicated relevant personal or family history and/or physical findings.
- iii. Quantify the number of electrocardiograms conducted among young people with attention deficit hyperactivity disorder, which detected a clinically significant abnormality.

Methods

Referrals sent via outpatient department triage letter, electrocardiogram departmental email (ecg.review@olchc.ie), and walk-in electrocardiogram service were examined to identify referrals for screening of children prior to commencing or modifying attention deficit hyperactivity disorder medication, including both stimulant and non-stimulant medications.

A prospective audit was performed over a 6-month period, from November 2021 to April 2022 inclusive.

Data were obtained on all referrals sent to Crumlin Cardiology Department and source of each referral eg. General Practitioner, Consultant Paediatrician, Child and Adolescent Mental Health Services team, or alternative healthcare setting established. Those sent for screening prior to commencement of attention deficit hyperactivity disorder medication were identified, and any relevant clinical indication for electrocardiogram screening was noted, such as personal or family history or based on physical examination. Each referral was coded against National Institute for Health and Care Excellence clinical guidelines reflecting the extent of clinical details given, and whether these concerns met criteria for cardiology referral (8, see Supplementary Table S1). National Institute for Health and Care Excellence guidelines are evidence-based recommendations for health and care in England and Wales.¹²

Each referral was coded against the guideline to determine the degree of clinical details given, and whether these concerns met criteria for referral. A record of any prior electrocardiogram and

interpretation was also documented. Finally, reported abnormalities, recommended management, and correspondence were recorded. A study proforma was created for the purpose of this audit, and data were subsequently entered into Excel for analysis.

Results

Ninety-one referrals were received via the electrocardiogram review email, Cardiology Outpatient Department triage system and walk-in electrocardiogram service seeking an opinion on the safety of commencing or modifying medication for children with attention deficit hyperactivity disorder over the time period 1st November 2021–30th April 2022. The age range of referral was 6 to 17 years old, with the median age of referral being 12 years of age. Forty-seven of these referrals (47/91, 51.6%) were reviewed via electrocardiogram review email and thirty referrals (30/91, 32.9%) were received by the walk-in electrocardiogram service. Fourteen referrals (14/91, 15.4%) were sent to the Cardiology Outpatients Department. Referrals were triaged and either replied to via letter or an outpatient department was arranged by consultant cardiologist.

Referrals were sent from various locations across the country, with the majority of referrals from local Child and Adolescent Mental Health Services (71/91, 78%). Thirteen (13/91, 14.3%) requests came from consultant paediatricians and seven (7/91, 7.7%) from General Practitioners (Fig. 1). All General Practitioner's referrals were following a request for an electrocardiogram made by a Child and Adolescent Mental Health Services team.

Most referrals were sent with an electrocardiogram performed (57/91, 62.5%), but of these, only 16 (16/57, 28.1%) had documentation suggesting they were interpreted by the referring clinician. Physical examination of the cardiovascular system was documented in 13/91 (14.3%) referrals made to the cardiology department. Documentation of obtaining family history was present in 23/91 (25.3%) of all referrals. The indications for referrals are summarised in Table 1 below.

There was no indication for referral, other than a request for cardiac screening prior to commencing attention deficit hyperactivity disorder medication in 53/91 (58.2%) of the total referrals. Documentation of a concern regarding personal history or clinical symptoms was mentioned in 9/91 (9.9%) cases. These included a concern regarding clinical symptoms prior to starting or modifying attention deficit hyperactivity disorder medications including chest pain, dizzy spells and palpitations in five cases (5/9), high blood pressure on medication in two cases (2/9), personal history of cardiac disease (background of pulmonary stenosis) in one case (1/9), and a referral concerning "lips go blue" in one case (1/9). There was a referral made including concern regarding family history of cardiac disease in eleven cases (11/91, 12.1%). There was a referral made based on concern regarding a physical examination finding in four cases, (4/91, 4.4%) of all patients. Physical examination abnormalities included a murmur detected (1/4), tachycardia (1/4), high blood pressure (1/4), and low blood pressure (1/4). Reason for referral linked to an abnormality in an electrocardiogram finding applied in 14 cases 14/91 (15.3%). Five of these (35.7%) relied on the automated print out, and there was no clinical interpretation of the electrocardiogram by a healthcare professional in these instances beyond the printed machine interpretation.

Twenty four, 24/91 (26.4%) referrals referenced personal history or clinical symptoms, physical examination, or family history. Of these, the majority (16/24, 66.6%) were appropriate as per the National Institute for Health and Care Excellence

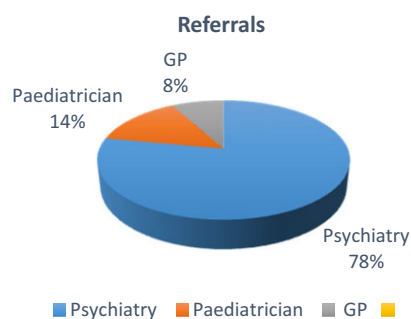


Figure 1. Electrocardiogram referral sources.

guidelines for cardiac screening prior to commencement of attention deficit hyperactivity disorder medications. The eight referrals (8/24, 33.3%) which did not meet National Institute for Health and Care Excellence criteria included nonspecific reference to a family history of cardiac problems/issues in four cases (4/8). The other referral reasons in this category which did not meet National Institute for Health and Care Excellence criteria included “maternal hypertension” (1/8), “history of MI in mother’s family” (1/8), first degree relative with CHD (1/8), and “grandfather with irregular heart beat” (1/8).

Physical examination of the cardiovascular system was not documented in the majority of referrals 78/91 (85.7%). Others provided limited physical examination findings including heart rate and blood pressure. Documentation of obtaining family history was not obtained in 68/91, (74.7%) of all referrals reviewed.

Fewer than one third, twenty six (26/91, 28.5%) of referrals met National Institute for Health and Care Excellence criteria for referral for cardiology opinion, including concern regarding clinical symptoms and personal or family history of cardiac disease.

Outcomes

Of the 91 referrals sent to the cardiology department, 80 had clinically reviewed outcomes (80/91, 88%). Outcome findings in 11 referrals (11/91, 12.1%) were not available. Four referrals received (4/91) were not reviewed as they were outside of service age range of sixteen years. Seven outpatient department referrals (7/91) had unknown outcomes as there was no outpatient appointment information available in six cases (6/7) and one referral (1/7) did not attend their appointment twice and was not given a further appointment.

Seventy-two patients (72/80, 88.9%) were reported as having normal electrocardiograms with no cardiology follow up required. Eight patients (8/80, 10%) were seen in the Cardiology Outpatient Department and have a documented outcome available (Table 2). Four electrocardiograms were seen following abnormalities detected via the electrocardiogram review email. Two of these electrocardiograms were with incidental findings: (i) borderline left ventricular hypertrophy and deep q waves and (ii) right bundle branch block in V1 and a murmur, requiring further cardiology review, but neither were considered to contra-indicate attention deficit hyperactivity disorder medication commencement. Two cases warranted a Cardiology Outpatient Department prior to commencing medication included; one due to premature ventricular contractions and the other referencing an abnormality, not specified. Following review, neither patient had contraindication to commencing attention deficit hyperactivity disorder medication.

Four referrals were made via the outpatient department referral system, and of these one had a clinically significant finding of high blood pressure. The remaining three referrals had normal cardiac assessments and no cardiac contraindications to attention deficit hyperactivity disorder medications.

Only one (1/80, 1.2%) referral identified a clinically significant finding, which contraindicated attention deficit hyperactivity disorder medications.

Referral response times

Out of the total number of referrals with clinical outcomes available for review (80), the electrocardiogram email review service responded to the majority (41/42) within 5 days. One referral (1/42) was an outlier and responded to 15 days after date received. Out of eight clinically reviewed referrals sent in via the Cardiology Outpatient Department, patients were offered outpatient appointments ranging from two months (1/8), seven months (1/8), 10 months (1/8), and 11 months (1/8) after date of triage. Four of these outpatient department referrals (4/8) received letters dictated from the cardiology consultant informing team not to defer commencing medications. Referral response time from the electrocardiogram walk-in service (30/80) was unavailable for audit collection.

Discussion

This 6-month audit reveals that only one patient out of 91 referred for cardiac screening pre-attention deficit hyperactivity disorder medication use had a clinically significant abnormality resulting in a recommendation to desist attention deficit hyperactivity disorder medication use.

Cardiovascular safety profile of medications for attention deficit hyperactivity disorder has been widely discussed and investigated. In 2005, concern arose in Canada following international case reports of 20 sudden deaths in patients taking Adderall XR, of which 14 cases were in the paediatric age group.¹³ Health Canada responded by immediately withdrawing the medication from the market, causing widespread concern amongst physicians and patient groups alike. This decision was later reversed; however, anxiety surrounding the cardiovascular safety profile of these medications remained. In 2008, the American Heart Association released a statement recommending routine electrocardiogram screening as a reasonable routine baseline investigation in addition to the existing recommendations of clinical and physical examination findings.¹⁴ Minor increases in diastolic blood pressure and heart rate are observed with methylphenidate and amphetamines, but evidence is mounting that statistically significant increases in QTc intervals (heart-rate corrected QT interval), or severe cardiovascular events have not been seen.^{15,16} Most recent best practice international guidelines recommend against the routine use of electrocardiogram in the absence of cardiovascular risk factors in clinical history or physical examination.^{7,8}

It is recommended that all children who are due to commence medication for attention deficit hyperactivity disorder have a primary assessment in the first instance including documentation of a personal and family history pertinent to cardiac disease and accompanied by a physical examination, which includes careful cardiac assessment.^{6,8} The results of this audit noted an absence of evidence of cardiovascular physical examination or family history in the majority of referrals. It is unclear in these circumstances whether these findings are due to a lack of documentation in the

Table 1. Clinical indications for referral

Clinical Indication for referral	Total Referrals N = 91	Email N = 47 (47/91, 51.6%)	Walk in ECG N = 30 (32.9%)	OPD N = 14 (15.4%)	Referred categorised as Appropriate as per NICE Guidelines?
1. No clinical indication	N = 53 (53/91, 58.2%)	N = 30 (30/47, 63.8%)	N = 21 (21/30, 70%)	N = 2 (2/14, 14.3%)	All screening requests do not meet criteria for referral
2. Personal history or clinical symptoms	N = 9 (9/91, 9.9%)	N = 2 (2/47, 4.3%)	N = 3 (3/30, 10%)	N = 4 (4/14, 28.6%)	All met criteria for cardiology referral
3. Concern regarding family history	N = 11 (11/91, 12.1%)	N = 1 (1/47, 2.1%)	N = 6 (6/30, 20%)	N = 4 (4/14, 28.6%)	27.3% met criteria for referral (inappropriate included “family history of MI”, “hypertension” and “cardiac problems in the family”)
4. Concern on physical examination	N = 4 (4/91, 4.4%)	N = 2 (2/47, 4.3%)	N = 0 (0/30, 0%)	N = 2 (2/14, 14.3%)	All met criteria for cardiology referral
5. Concern for ECG abnormality	N = 14 (14/91, 15.3%)	N = 12 (12/47, 25.5%)	N = 0 (0/30, 0%)	N = 2 (2/14, 14.3%)	64.3% met criteria for referral. 5 were not appropriate as these were machine reading abnormalities and not interpreted beyond the automatic print out - all these ECGs were normal when reviewed by cardiology team)

Table 2. Cardiology outpatient outcomes

Reason for referral	OPD	OPD outcome	CI to ADHD medications?
1. PVC's on ECG	OPD 3 months	Likely incidental finding. Normal exam.	No
2. Abnormal ECG	OPD 1 month	Normal cardiac assessment.	No
3. Borderline LVH	No OPD made	No OPD made on system	No (Written in follow up)
4. Concern re family history SCD	OPD 2 months time	ASD on echocardiogram. Follow up OPD 2 months time.	No
5. RBBB in V1	OPD referral made	OPD information not available	No (Written in follow up letter)
6. Brother with pulmonary hypertension	OPD 11 months	Normal cardiac assessment	No
7. Chest pain and palpitations	OPD 7 months	Normal cardiac assessment	No
8. Palpitations on medications	OPD 10 months time	High blood pressures	Yes

referral, or whether these children did not undergo physical and history assessment in the first instance. Given the majority of referrals in our audit were from Child and Adolescent Mental Health Services teams (71/91, 78%), this brings into question the role of the psychiatrist in physical examination of their patients, especially among young people with attention deficit hyperactivity disorder. Greenstone and colleagues studied psychiatrists' attitudes to their role in managing their patients' physical health working in the UK and found that 78% of those surveyed felt that their clinical examination skills had deteriorated since working in psychiatry, and almost half (47%) reported that confidence in detecting abnormal clinical signs was low.¹⁷ The absence of physical examination documentation suggests that there may be a role for further training in physical examination and clinical history skills in order to improve confidence and quality of assessment. There may be an improvement in psychiatrist confidence levels with more focus on physical health with time. The College of Psychiatrists of Ireland training curriculum for basic and higher

specialist training now outlines core learning outcomes for trainees in relation to physical healthcare. A recent small study (n = 33) in 2021 examined the perceived confidence levels amongst psychiatrists (both consultant and trainee level) from one geographical region in Republic of Ireland regarding their physical health competencies, with items drawn from the College of Psychiatrists of Ireland core curriculum. The majority reported moderate to extreme confidence in the cardio-vascular system (57–58%), higher than other systems.¹⁸

In the absence of risk factors for cardiac disease and sudden death, routine electrocardiogram screening or routine cardiology subspecialty referrals including echocardiography is not recommended.⁶ Over half of referrals received, 58.2% related to “screening” electrocardiogram's prior to commencement of attention deficit hyperactivity disorder medication, but in the absence of clinical concern regarding cardiac history or physical findings. The high referral rate for screening electrocardiogram's is understandable, given the historical concerns regarding cardiovascular safety profile,

and the American Heart Association's previous advice regarding electrocardiogram being a reasonable investigation to undertake as part of medication prescribing.¹⁴ It is evident that some healthcare professionals involved in prescribing medication for attention deficit hyperactivity disorder still err on the side of caution with referral for cardiology opinion. The creation of an easy proforma approved by both Cardiology and Psychiatry teams in order to reduce the unnecessary extra investigation of screening electrocardiogram or cardiology opinion in the absence of a clinical or physical examination risk factor is important.^{7,8}

Four of the clinically reviewed electrocardiograms (5%) had abnormalities that required a cardiology opinion in outpatient department. This was in keeping with the observed incidence of 6.4% (24/372) in Thomas's retrospective study.¹¹ Similar to the study by Thomas *et al.*, incidental findings such as ventricular hypertrophy were seen in one of the four abnormal electrocardiograms in our audit. Outpatient department referrals are a significant burden on Children's Health Ireland resources, as each child is seen by several staff including administration, outpatient department nurse, electrocardiogram and echocardiogram technicians, cardiology registrar, and consultant. This group of patients may be waiting up to 2 years for an appointment to see a Paediatric Cardiology Consultant and therefore, in the absence of significant cardiac pathology, can lead to suboptimal delay in other treatment. It is inevitable that the disclosure of incidental electrocardiogram findings can cause considerable additional stress to families, especially considering the lengthy waiting period to be reviewed by a paediatric cardiologist. It is imperative that these incidental findings should not delay the treatment of children who require medical treatment of attention deficit hyperactivity disorder.

With the application of best practice guidelines, there is a potential to reduce the number of non-clinically indicated routine electrocardiogram's performed on children prior to commencing attention deficit hyperactivity disorder medication. This should lead to reducing the number of "false positive" contra-indications based on electrocardiogram findings and other spurious findings requiring referrals for tertiary cardiology review.

While the electrocardiogram email review service yielded a very prompt reply service (46/47 were replied to within 5 days, 98%), there was a considerable delay in cardiology opinion with regards to the outpatients' referrals with some appointments given at 11 months past the referral date. More careful referral including relevant personal, family, or physical examination findings may improve waiting times for these outpatient department referrals. These delays in accessing cardiac opinion are replicated elsewhere with ultimately spurious findings on electrocardiogram leading to a delay in appropriate medical treatment for children with attention deficit hyperactivity disorder.¹¹

The creation of a national guideline for healthcare professionals who work with children with attention deficit hyperactivity disorder including Child and Adolescent Mental Health Services, paediatricians, and General Practitioners is warranted. This guideline is in keeping with current best practice recommendations including careful physical examination and documentation of cardiac history and family history (Supplementary Table S2). Unnecessary screening electrocardiograms and routine cardiology outpatient referrals prior to commencement of attention deficit hyperactivity disorder medications may be avoided, and indications for tertiary subspecialist cardiology opinion will be clearly outlined. The authors hope that implementation of this guideline

will reduce unnecessary delays to treatment for children with attention deficit hyperactivity disorder and plan to pilot and evaluate the guideline's impact on referral rates to our centre.

Limitations of audit

The lack of any specific coding system to classify outpatient department referrals as screening for attention deficit hyperactivity disorder medication may have limited detection of all cases. Equally, the audit was not able to quantify the number of pre-screening electrocardiograms conducted outside of our institution.

This audit is also limited by the small study size covering 6 months in total; however, the careful use of standardised method to code referrals, and the creation of a referral checklist, should facilitate a subsequent audit cycle to be completed.

Conclusions

Routine screening prior to attention deficit hyperactivity disorder medication prescription in the absence of clinical indications (as per National Institute for Health and Care Excellence guidelines, 8) contributed to delays in medication initiation for young people with attention deficit hyperactivity disorder and resource implications for cardiology clinical team. Improved adherence to National Institute for Health and Care Excellence guidelines with respect to cardiovascular health would provide benefits for patients and clinicians.

Careful documentation of pertinent personal and family history, combined with physical examination, is recommended as best practice as part of the primary assessment of children due to commencing stimulant medication. The use of a standardised referrer's checklist should avoid unnecessary delays to appropriate care and will be subject to further audit going forward.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S1047951124025320>.

Acknowledgements. None.

Financial support. None.

Competing interests. None.

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