

Hypoadrenalism Stakeholder subgroup 1 discussion
Date: 05/01/22 Time: 10am – 1pm

**University of Newcastle, Royal Pharmaceutical Society, Sheffield Children’s NHS Trust,
Society for Endocrinology, Alex The Leukodystrophy Charity, CAH Support Group**

<p>Guideline Title</p> <p>Hypoadrenalism: acute and long-term management</p> <p>Adrenal insufficiency is the more usual term. - NHSE/I and in the related NICE guidance. Should Hypoadrenalism be changed to Adrenal insufficiency?</p>	<p>The group preferred the term adrenal insufficiency, as this is the term commonly used in clinical practice and is the term used in literature..</p>
<p>3.1 Population: 3.1.1 Groups that will be covered:</p> <ul style="list-style-type: none"> Babies, children, young people and adults with suspected and diagnosed hypoadrenalism. <p>Specific consideration will be given to babies and children.</p>	<p>Is the population appropriate?</p> <ul style="list-style-type: none"> Are there any specific subgroups that have not been mentioned? <p>No changes to the subgroups mentioned in the draft scope.</p> <p>Specific consideration for babies and children</p> <p>The group agreed this is appropriate, especially for neonates and younger children, as they require different consideration to adults. The group was aware that Adrenal insufficiency is over-diagnosed in babies. The group noted that some babies are started on steroids because of a diagnostic test that doesn’t have robust evidence. They thought that clinically this is a difficult population, and noted that CH and congenital and genetic are different from other groups with adrenal insufficiency. The group discussed and agreed that this population should remain within the scope rather than warranting their own guideline. The management principles are the same for acute and emergency management. The difficulty is in making the diagnosis. It was thought that there is need to give consideration to children with developmental disabilities because steroid replacement can be more challenging. It was noted that there can be challenges with compliance. It was suggested that this matter be added to equalities section along with elderly patients in care homes in terms of access to additional steroid medication.</p> <p>The group noted that evidence for children may need to be extrapolated from evidence for adults. Additionally, for CAH the evidence base is also small, especially for older adults.</p>
<p>3.3.1 Key clinical issues that will be covered:</p>	<p>These are the key areas of clinical management that we propose covering in the guideline. Do you think this is appropriate, acknowledging we must prioritise areas for inclusion?</p>

<p>1 Information and support</p> <ul style="list-style-type: none"> • for people with suspected and diagnosed hypoadrenalism (and their families and carers) <p>2 Initial identification and referral for further investigation of suspected hypoadrenalism</p> <p>3 Managing hypoadrenalism</p> <ul style="list-style-type: none"> • Adrenal crisis <ul style="list-style-type: none"> ○ identification of adrenal crisis ○ emergency management • Pharmacological treatment of primary adrenal insufficiency, and secondary and tertiary adrenal insufficiency • Management of intercurrent illness and periods of stress: <ul style="list-style-type: none"> ○ physiological stressors, including minor (for example colds) and major illnesses (for example, severe infection, cardiac events) ○ planned and emergency invasive procedures ○ intrapartum care ○ psychological stressors <p>4 Ongoing care and monitoring</p> <ul style="list-style-type: none"> • The frequency and content of monitoring of hypoadrenalism 	<p>Information and support</p> <ul style="list-style-type: none"> - To include information and support for prevention of adrenal crisis and for emergency care of adrenal crisis - Information on steroids ? <p>The stakeholder group agreed with these.</p> <p>Initial identification and referral for further investigation of suspected hypoadrenalism</p> <ul style="list-style-type: none"> - Risk factors, signs and symptoms - What tests if any should be done before referral for diagnosis ? <p>The group thought it was difficult to draw a distinction between suspecting and diagnosing hypoadrenalism. They also thought a better definition is needed of who to suspect. They noted that it is also unclear where the cut off is, and when some with 'suspected' hypoadrenalism becomes a patient who requires an investigation.</p> <p>The group noted the absence of diagnosis in the scope and thought this created a gap in the guidance. They discussed the large population that could be considered as being at risk of adrenal insufficiency due to very common symptoms (e.g., tiredness, abdominal pain). They pointed out that the scope would address trying to identify who is at risk and then management, so wanted to know why diagnosis was excluded. However, they didn't think there was uncertainty about how to diagnose adrenal insufficiency, although they noted that there was a need for consistent advice once diagnosis has been made.</p> <p>Primary care and when to refer</p> <p>The group thought that primary care clinicians do not currently have access to advice about screening, and it would be helpful to have advice on when to refer to consultants. One stakeholder suggested that the guideline could reduce unnecessary referrals, as in her experience many referrals are not adrenal insufficiency. The potential cost impact of this was noted.</p> <p>Diagnosis in relation to emergency situations would be helpful. However, it was noted that if diagnosis is made by specialists then this may not need to be covered in the guideline.</p>
<p>3.3.2 Key clinical issues that will not be covered:</p> <p>1 Adrenal fatigue</p> <p>2 Diagnosis of hypoadrenalism</p>	<p>Are there tests that should be identified before referral to an endocrinologist?</p> <p>It was thought that clinical judgement and the availability of resources locally would have an impact here, and the group stressed caution related to the length of time people who potentially have adrenal failure are asked to wait for tests, as this could be lethal. The variation of practice was mentioned here as well, in some areas, patients can be seen quickly by specialist but not all areas currently have the capacity to deliver this level of service.</p>

<p>3 Diagnosis, management and monitoring of underlying medical conditions that causes hypoadrenalism</p> <p>4 Steroid weaning</p>	<p>It was thought that in addition to screening for cortisol levels, the timing of the test is important, and the appropriateness of testing. The group thought it important to reduce unnecessary testing, as this sometimes leads to unnecessary patient anxiety. The group mentioned the importance of prioritising people for investigation and referral.</p> <p>To summarise, the group noted that it would be helpful to give non specialist settings: (e.g., in A&E / GPs) advice about what red flags they should be aware of related to hypoadrenalism and what should prompt referral and urgent referral. It was thought that identifying the red flags could include testing of cortisol levels.</p> <p>Managing hypoadrenalism Not just pharmacological also medical care , so questions are around strategies and not just pharmacological treatment.</p> <p>The strategies discussed by the group would ideally address:</p> <ul style="list-style-type: none"> • Prescribing issue: Patients experience challenges with getting repeat prescriptions from GP, as tablets are prescribed for a 28-day period, but if they experience difficult days that require a double dose, they may run out sooner. • Provision of emergency prescription. • Patient education: enabling the person to practice self-management. • Supporting people so they understand and are able to take the lowest possible dose that can help them to avoid side effects while also avoiding adrenal crisis. • Transition: ensuring we equip young people so they understand how to access repeat prescriptions and offer clarity on what their emergency regime should be. • Possible provision of emergency kits at home and school, particularly for children. • The group noted that there is currently no controversy about what is prescribed. Hydrocortisone is preferred and prednisolone is easier for patients to take. However, there are some very new drugs available on the market. <p>Physiological stressors and invasive procedures Agreed with these. The group suggested that the following be considered:</p> <ul style="list-style-type: none"> • dental procedures as they are often overlooked. • immunisations and radiological investigations (children get general anaesthetics for MRI, uncertainty about whether steroids should be increased int this scenario) <p>Intrapartum care – can we cover by cross referring to another NICE guideline. The group offered no suggestions on this item.</p> <p>Psychological stressors</p>
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Differing views on this item, it was viewed as both controversial and uncontroversial by group members. The group thought it would be helpful to explore and understand the risk of psychological stressors for people living with adrenal insufficiency. The example of a bed-ridden young person, dealing with hypoadrenalism (after an exam) was mentioned. When considering exercise, it was noted that a common query is whether the advice given to people with hypoadrenalism is to take more steroids when exercising

Ongoing care and monitoring

The group agreed this should be included

The key issues mentioned during discussions included:

- Deprescribing during the delivery of End-of-life care
- Weaning and stopping prescriptions during paediatric care.
- Availability of clinical review of hypoadrenalism for neonates after a few months with a plan to retest and stop steroids
- Review steroid dose and timing and potential complications in:
 - a. Adults with other conditions and considerations, for example: osteoporosis, diabetes, weight management
 - b. Older people with Type 1 diabetes. Clinicians need to know if screening should be done and how.
 - c. Younger patients.
 - d. Older patients with pernicious anaemia and autoimmune disease.
- Permanent or transient causes of hypoadrenalism was mentioned. It was discussed whether these should be considered separate issues as repeat testing might be different. It was noted that transient causes are usually due to adrenal suppression from steroids
- Education of the person with hypoadrenalism and their family.
- Access to multi-disciplinary team that includes endocrinology nurses.
- Comorbidity was mentioned as a major issue for all age groups.
- Fertility and reproduction may affect the choice of steroid used for treatment.
- The group considered what information should be provided for the person with hypoadrenalism at diagnosis: contact for specialist nurse, electronic alert, steroid alert cards for the family, the use of wristbands and other ways to increase awareness.
- The group noted that people with adrenal insufficiency are entitled to free prescriptions, however, GPs are not always aware of this (suggested that this be added to the information and support section).
- Flu vaccination was mentioned as an issue, and it was noted that this sometimes gets missed.

Key clinical issues that will not be covered:

Adrenal fatigue – not included as seen as something that is not tangible, it would be hard to include

	<p>One group member noted that their practice signposts patients to an information sheet on this. It was thought that this isn't recognised from a clinical perspective, and it would be ok to not include this on the guideline.</p> <p>Diagnosis of hypoadrenalism Diagnosis, management and monitoring of underlying medical conditions that causes hypoadrenalism Steroid weaning</p> <p>The group thought this issue links to deprescribing, and that clarification is needed on if this is in relation to steroid weaning in cases where they are prescribed for causes other than hypoadrenalism.</p> <p>The group thought it would be helpful to distinguish between replacement steroid vs. anti-inflammatory steroids</p> <p>The group was aware of other rare conditions (e.g., ALD) where 'not adrenal insufficient' should not always be assumed to be 'autoimmune'. They thought this could be addressed in the section of the scope on identification. These people could be identified there if appropriate.</p>
Further Questions:	
1. Are there any critical clinical issues that have been missed from the Scope that will make a difference to patient care?	
Priority areas identified: The management of adrenal insufficiency in paediatrics was flagged, it was thought that the management of Adrenal crisis for adults is accepted and fairly straightforward.	
2. Are there any areas currently in the Scope that are irrelevant and should be deleted?	
No	
3. Are there areas of diverse or unsafe practice or uncertainty that require address?	
<p>There was thought to be diverse practice related to the following:</p> <ul style="list-style-type: none"> • How care is delivered across the service and the level of specialism available in different services. • The availability and access to endocrine specialist nurses. • Stakeholders noted that rheumatologists would not have access to endocrine nursing service • It was noted that some Addison disease patients are managed at district hospitals • It was thought that most other adrenal insufficiency patients gravitate towards tertiary centre • Addison's patients under primary care, however, are usually managed in smaller hospitals or could be managed by local DGH doctors. • Some patients express the feeling that they have not been managed properly • Paediatric patients would usually be referred to tertiary services at some point • If people diagnosed with adrenal insufficiency can't access specialist centres, communication from specialist is important (for example, providing information about the availability of new treatments) • For children with severe asthma, muscular dystrophy, other rheumatic or inflammatory conditions taking long term steroids, it was suggested that the scope should cover this group and aim to provide the same education and alert systems and sick day plans available to other patients. This is assuming they fit into a standard tertiary group. • Variation in practice was noted in the use of long-term steroids for all ages, it was thought that this was an area of care generally not done very well 	

- It was thought that what would help with variation in practice was a possible review of the definition of tertiary group, if this group was defined as *those who qualify for a steroid card* it was thought that it could help.

4. Which area of the scope is likely to have the most marked or biggest health implications for patients?

No comments.

5. Which practices will have the most marked/**biggest cost** implications for the NHS?

The following was mentioned for consideration:

- GPs can be concerned about cost of medication weighed against cost of admission for an adrenal crisis
- Unnecessary referrals to specialist that can quickly be identified as not having adrenal insufficiency (often occurs with infants)
- Prednisolone vs hydrocortisone. Specifically, short vs. long term costs of using prednisolone (this drug is cheaper but is associated with long term complications)

6. Are there any **new practices** that might **save the NHS money** compared to existing practice?

The following recent changes and new pharmacological treatments were highlighted:

- New compounds now available, including a new twice daily sustained release preparation
- New neonatal formulations marketed by Diurnal:
 - Alkindi (specifically for children)
 - Efmody – twice daily formulation
- Some trusts have changed to prednisolone as this is cheaper than hydrocortisone which is controversial – data to suggest it leads to longer term complications

7. If you had to delete (or de prioritise) two areas from the Scope what would they be?

No comments.

8. As a group, if you had to rank the issues in the Scope in order of importance what would be your areas be?

No comments.

9. What are the top 5 outcomes?

(scope currently has:

- Mortality
- Health related quality of life
- Complications of hypoadrenalism
- Fatigue ?
- Adequacy of replacement steroid doses (how is this measured?)
- Adrenal crisis
- Complications of adrenal crisis
- Treatment related adverse events

No changes from group.

<p>10. Any comments on guideline committee membership?</p> <ol style="list-style-type: none"> 1. Patient Member (x2 minimum) 2. General practitioner x1 3. Endocrine Clinical Nurse Specialist (adult and paediatric) - request for one of each 4. 5. Consultant Endocrinologist x1 6. Consultant Emergency medicine physician x1 7. Consultant Endocrinologist Paediatrician x1 – may need 2 due to variation in practice, need different perspectives 8. General Paediatrician consultant x1 9. Pharmacist x2 community and secondary care – add paediatric pharmacist <p><u>Other/Cooptees:</u></p> <ul style="list-style-type: none"> - Prehospital practitioner /paramedic - Obstetrician - Anaesthetist - Dentist - General medical consultant x1 with an interest in adrenal insufficiency/non specialist 	<p>Additional suggestions from stakeholders included:</p> <ul style="list-style-type: none"> • A clinician that carries out steroid work – e.g., rheumatologist • Eating disorder psychiatrist. It was thought that this would be helpful for appropriately identifying patients who are referred via eating disorder services • Physician who works with CFS patients. It was thought that this would be helpful for appropriately identifying patients referred via CFS route.
<p>11. Are there any areas that you think should be included for the purposes of the quality standard? Are there any service delivery or service configuration issues that you think are important?</p>	
<p>No comment from group.</p>	
<p>12. Other issues raised during subgroup discussion for noting:</p>	
<ul style="list-style-type: none"> • Mental health considerations • Anxiety related to having an adrenal crisis in an unfamiliar situation – limiting their lifestyles, for example limiting travel. • Dosing: it was thought that this will be covered under pharmacological treatment, which is included in the scope • Variation of practice: particularly in the area of paediatrics. Suggested that two paediatric endocrinologists may be needed on the constituency as there is such variation. • The use of Mineralocorticoids mentioned: it was thought that this is often done badly outside of tertiary setting • The use of infusion pumps in paediatrics was mentioned: evidence considered unclear. 	
<p>EIA discussion – refer to document</p>	
<p>The group considered the following and made no additions:</p> <ul style="list-style-type: none"> • People with learning disabilities, People in residential care and People with English as a second language. 	

