NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline scope

Adrenal insufficiency: acute and long-term management

NHS England has asked NICE to develop a guideline on acute and long-term management of hypoadrenalism (adrenal insufficiency).

The guideline will be developed using the methods and processes outlined in developing NICE guidelines: the manual.

1 Why the guideline is needed

Adrenal insufficiency is the inadequate production of corticosteroid hormones by the adrenal glands. Adrenal insufficiency may be:

- primary, that is, because of disease in the adrenal glands themselves (the autoimmune condition Addison's disease is the commonest cause in adults, and congenital adrenal hyperplasia is the commonest cause in children)
- secondary, that is, caused by inadequate adrenocorticotropic hormone production by the pituitary gland (often because of treatment for a pituitary disease, or from pituitary tumours and their treatment)
- tertiary, that is, caused by inadequate corticotrophin releasing hormone production by the hypothalamus (sometimes because of treatment for tumours in the hypothalamus or adjoining structures, or more commonly because of administration of glucocorticoids for more than 4 weeks causing hypothalamic-pituitary-adrenal axis [HPA-axis] suppression). Stopping glucocorticoids may also cause adrenal insufficiency.

Some medicines cause adrenal insufficiency, such as opioids, checkpoint inhibitors (used increasingly for treating cancer), and medicines inhibiting cortisol clearance such as antifungals and antiretrovirals.

Adrenal insufficiency may have a considerable effect on daily living and may lead to adrenal crisis if not identified and treated. Common causes of adrenal crisis in people with adrenal insufficiency are gastrointestinal illness (23%), other infections (25%), surgery (10%) and physiological stress (9%). Adrenal crisis is a medical emergency and can be fatal.

Current practice

The mainstay of adrenal insufficiency management is replacement with glucocorticoids (and mineralocorticoid preparations in primary adrenal insufficiency). These medicines are usually given orally, to maintain a good quality of life and to prevent adrenal crisis. Treatment for adrenal crisis typically includes prompt and appropriate administration of glucocorticoids (hydrocortisone intravenously or intramuscularly) and adequate intravenous fluid hydration with crystalloid.

Care is variable in the UK and small numbers of people die each year from adrenal crisis. Although deaths are rare and avoidable, awareness needs to be raised about the importance of glucocorticoid replacement for people with adrenal insufficiency who are at risk of adrenal crisis. There is an NHS Steroid Emergency Card for people at risk to carry to help ensure prompt, appropriate treatment if they have an adrenal crisis.

Better recognition of people at risk of adrenal insufficiency, and awareness of the acute- and long-term management of adrenal insufficiency, would improve patient care and quality of life, and reduce associated complications. This guideline aims to improve the management of adrenal insufficiency and the quality of life of people with adrenal insufficiency.

2 Who the guideline is for

This guideline is for:

- health and social care practitioners providing NHS-commissioned services, including those working in dental services, school health services and prehospital care
- commissioners of health and social care services

- people using services, their families and carers, and the public.

It may also be relevant for non-NHS healthcare providers of dental services.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive.

Equality considerations

NICE has carried out an equality impact assessment during scoping. The assessment:

- lists equality issues identified, and how they have been addressed
- explains why any groups are excluded from the scope.

The guideline will look at inequalities relating to age, disability, people who are homeless, asylum seekers, refugees, and Gypsy, Roma and Travellers.

3 What the guideline will cover

3.1 Who is the focus?

Groups that will be covered

Babies, children, young people and adults with suspected and diagnosed adrenal insufficiency.

Specific consideration will be given to babies and children.

3.2 Settings

Settings that will be covered

All settings in which NHS-commissioned care is provided.

3.3 Activities, services or aspects of care

Key areas that will be covered

We will look at evidence in the areas listed below when developing the guideline, but it may not be possible to make recommendations in all these areas.

1. Information and support for people with suspected and diagnosed adrenal insufficiency (and their families and carers).
2. Initial identification of people with suspected adrenal insufficiency who may benefit from referral for specialist investigation and care.
3. Prevention of adrenal insufficiency because of corticosteroid withdrawal.
4. Managing adrenal insufficiency:
    - adrenal crisis
        - ⇒ identification of adrenal crisis
        - ⇒ emergency management
    - routine (non-emergency) management
        - ⇒ pharmacological treatment of primary adrenal insufficiency, and secondary and tertiary adrenal insufficiency
    - preventing adrenal crisis during periods of physiological stress:
        - ⇒ minor illnesses (for example, colds) and major illnesses (for example, severe infection, cardiac events)
        - ⇒ planned and emergency invasive procedures
        - ⇒ pregnancy and intrapartum care
    - preventing adrenal crisis during periods of psychological stress.
5. Ongoing care and monitoring, that is, the frequency and content of monitoring of adrenal insufficiency.

Note that guideline recommendations for medicines will normally fall within licensed indications. Exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.

Areas that will not be covered

1. Adrenal fatigue.
2. Diagnosing adrenal insufficiency.
3. Diagnosing, managing and monitoring the underlying medical conditions that cause adrenal insufficiency.

Related NICE guidance

Published

- Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management (2021) NICE guideline NG206
- Type 1 diabetes in adults: diagnosis and management (2021) NICE guideline NG17
- Diabetes (type 1 and type 2) in children and young people: diagnosis and management (2020) NICE guideline NG18
- Intrapartum care for women with existing medical conditions or obstetric complications and their babies (2019) NICE guideline NG121
- Lower urinary tract symptoms in men: management (2015) NICE guideline CG97
- Endoscopic transsphenoidal pituitary adenoma resection (2003). Interventional procedures guidance IPG32

NICE guidance about the experience of people using NHS services

NICE has produced the following guidance on the experience of people using the NHS. This guideline will not include additional recommendations on these topics unless there are specific issues related to adrenal insufficiency:

- Shared decision making (2021) NICE guideline NG197
- Babies, children and young people's experience of healthcare (2021) NICE guideline NG204
- Patient experience in adult NHS services (2021) NICE guideline CG138
- Medicines optimisation (2015) NICE guideline NG5
- Service user experience in adult mental health (2011) NICE guideline CG136

- Medicines adherence (2009) NICE guideline CG76

3.4 Economic aspects

We will take economic aspects into account when making recommendations. We will develop an economic plan that states for each review question (or key area in the scope) whether economic considerations are relevant. If so, we will state whether this is an area that should be prioritised for economic modelling and analysis. We will review the economic evidence and carry out economic analyses, using the NHS and personal social services (PSS) perspective, as appropriate.

3.5 Key issues and draft questions

1. Information and support:
    1.1. What information and support do people with suspected or diagnosed adrenal insufficiency (and their families and carers) need to routinely manage their health (including how to ensure an adequate supply of medicines, advice on what to do in certain situations such as when exercising, travelling, working non-standard hours or taking part in religious observances such as fasting)?
    1.2. What information and support do people diagnosed with adrenal insufficiency need for the prevention and emergency care of an adrenal crisis?
2. Initial identification for referral of people with suspected adrenal insufficiency:
    2.1. When should adrenal insufficiency be suspected (for example, based on risk factors or symptoms)?
    2.2. When should a person who is having exogenous corticosteroids withdrawn be referred for investigation and management of adrenal insufficiency related to HPA-axis suppression?
    2.3. What initial investigations should be done by the non-specialist for people with suspected adrenal insufficiency?
    2.4. When should people with suspected adrenal insufficiency be referred to specialists for further investigation?
3. Preventing adrenal insufficiency because of corticosteroid withdrawal:

3.1. In people at risk of adrenal insufficiency because of prolonged corticosteroid use, what is the best way to manage corticosteroid withdrawal when corticosteroids are no longer needed to control disease activity?

4. Managing adrenal insufficiency:
   4.1. What is the clinical and cost effectiveness of pharmacological treatments for the routine management of primary adrenal insufficiency?
   4.2. What is the clinical and cost effectiveness of pharmacological treatments for the routine management of secondary and tertiary adrenal insufficiency?
   4.3. When should adrenal crisis be suspected?
   4.4. What is the clinical and cost effectiveness of pharmacological treatments for the emergency management of adrenal crisis?
   4.5. What is the clinical and cost effectiveness of pharmacological treatments for managing periods of physiological stress in people with adrenal insufficiency including:
      a) planned and emergency invasive procedures
      b) pregnancy and intrapartum care
      c) intercurrent illness and periods of physiological stress including minor (for example, colds) and major illnesses (for example, severe infection, cardiac events)?
   4.6. What is the clinical and cost effectiveness of pharmacological treatments for managing periods of psychological stress in people with adrenal insufficiency?
   4.7. What is the clinical and cost effectiveness of non-pharmacological strategies to prevent adrenal crisis during periods of intercurrent illness and periods of physiological stress?
   4.8. What is the clinical and cost effectiveness of non-pharmacological strategies to prevent adrenal crisis during periods of psychological stress?
5. Ongoing care and monitoring
   5.1. What ongoing care and monitoring should be offered to people with adrenal insufficiency?

5.2. What ongoing care and monitoring should be offered to people with adrenal insufficiency who are receiving end of life care?

The key issues and draft questions will be used to develop more detailed review questions, which guide the systematic review of the literature.

3.6 Main outcomes

The main outcomes that may be considered when searching for and assessing the evidence are:

- mortality
- health-related quality of life
- complications of adrenal insufficiency
- fatigue
- adrenal crisis
- complications of adrenal crisis
- treatment-related adverse events.

4 Further information

The guideline is expected to be published on 11 April 2024.

You can follow progress of the guideline at: https://www.nice.org.uk/guidance/indevelopment/gid-ng10237.

Our website has information about how NICE guidelines are developed.