National Institute for Health and Care Excellence

Final

Adrenal insufficiency: identification and management

Evidence review A: Information, support and decision making

NICE guideline NG243

Evidence reviews underpinning recommendations 1.1.1 to 1.1.9 in the NICE guideline

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Final

These evidence reviews were developed by NICE

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Contents

1. Information, support and decision making

1.1. Review questions

- 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)?
- What information and support do people diagnosed with adrenal insufficiency need for the prevention and emergency care of an adrenal crisis?

1.1.1. Introduction

Information and Support

Adrenal insufficiency is a rare, potentially life-threatening condition that requires taking daily life-essential glucocorticoid hormone replacement, and for primary adrenal insufficiency, mineralocorticoid hormone replacement. The treatment, need for care and outcomes for adrenal insufficiency depend partly on the underlying condition. There is a large amount of self-care involved so patients can manage day-to-day life and maintain a good quality of life. There are no national standards that health care professionals adhere to.

In current practice, there is variation in the content and level of information and support provided to patients with adrenal insufficiency. Some patients have access to specialist services and clinical nurse specialists who provide patient support and education, patient support groups also provide information, but this support is not available to all.

This evidence review seeks to identify effective and adequate information and support strategies for this population, so they are aware of necessary self-care strategies, meeting individual needs and preferences in order to reduce unnecessary harm to this patient population.

Information and support for the prevention and emergency care of an adrenal crisis

Adrenal crisis is a life-threatening medical emergency whereby people do not have adequate cortisol levels. It can occur at diagnosis of adrenal insufficiency, if patients do not take their medication, have an intercurrent illness or physiological stress such as sepsis, injury or surgery and do not have appropriate increases of glucocorticoid medication either orally or if very unwell parenterally.

Patients, families, and carers need to understand how to increase daily doses of glucocorticoids if they are unwell, and how to prevent adrenal crises by self-administration of intramuscular hydrocortisone.

This evidence review seeks to identify effective and adequate information and support strategies for this population to support patients to self-manage adrenal insufficiency and prevent adrenal crises.

1.1.2. Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Objective	To explore perceptions and experiences of people with adrenal insufficiency, their families, and carers in order to determine their information and support needs for routine and emergency management of their health.
Population and setting	People with adrenal insufficiency (primary, secondary, or tertiary) or who are suspected of having adrenal insufficiency (and their families and carers). The following population stratification will be applied where possible: • Adults (aged ≥16 years). • Young people (>12-16 years). • Children aged ≥1 up to 12 years. • Infants and children <1 year.
Context	Adrenal insufficiency may have a considerable effect on daily living and may lead to adrenal crisis if not identified and treated. Information and support may be important to inform routine management of adrenal insufficiency and prevention and management of adrenal crisis.
Review strategy	Synthesis of qualitative research. Results presented in narrative/table format. Quality of the evidence will be assessed by a GRADE CERQual approach for each review finding.

1.1.3. Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4. Qualitative evidence

1.1.4.1. Included studies

Seven qualitative studies were included in the review[1-4, 6-8] these are summarised in Table 2 below. Key findings from these studies are summarised in the qualitative evidence summary below (Table 3). See also the study selection flow chart in Appendix C, study evidence tables in Appendix D, and excluded studies lists in Appendix F.

As sufficient qualitative evidence was identified, all studies that included only quantitative data from surveys and questionnaires were excluded. Studies could be stratified into those investigating information and support needs for adults with adrenal insufficiency[4, 6, 8] and those investigating information and support needs for children and young people (age range 3 months-18 years across the three studies) and their carers[1-3, 7]

The studies of children and young people and their carers all focussed on children diagnosed with congenital adrenal hyperplasia (CAH). Studies by Fleming et al (2017)[3], Boyse et al (2014)[1] and Simpson et al (2018)[7]interviewed parents of children with CAH. Carroll (2018)[2] interviewed children with CAH and their caregivers (defined as an adult family member on whom children depend, to meet their emotional, behavioural, physical, and medical needs).

Three studies[1-3] focussed on children and young people with CAH and their caregivers were from the USA and one was from the UK[7]. All three studies[4, 6, 8] focussed on adults with adrenal insufficiency were from Europe, with one[6] from England.

The themes developed within each study commonly addressed either review question 1.1 only, or addressed review questions 1.1 and 1.2, but with a focus on the prevention of

adrenal crisis rather than emergency management. Accordingly, and partly due to the small number of studies available, interpretations and explanations from the original studies were synthesised to gain insight into themes present across the body of evidence as a whole. The main concepts found in each individual study which were relevant to either or both of our review questions were drawn together to inform understanding of overarching themes i.e., these synthesised overarching themes were developed with reference to both research questions (1.1 and 1.2) together.

The resulting synthesised theme was then considered in relation to its relevance to each research question and labelled accordingly. If a synthesised theme was developed that only included data from studies on adults, this theme was labelled as adults only. If a synthesised theme was developed that only included data from studies on children and young people with CAH and their carers, this theme was labelled as children and young people only.

1.1.4.2. Excluded studies

For details of excluded studies, please see Appendix F

1.1.5. Summary of studies included in the qualitative evidence.

Table 2: Summary of studies included in the evidence review.

Study	Design	Population	Research aim	Comments
Boyse et al (2014)[1]	Individual, semi-structured telephone interviews with conventional content analysis	Parents of children with CAH n=6; (2 male/4 female) from 4 families Age of child 5-11 years USA	To characterize early parent caregiver experiences and needs in CAH, with a focus on contextual factors that can be modulated through education and support, delivered by health care providers or via the newborn screening system.	Parents asked to recall experiences of their first child born with CAH 5-11 years ago. 3/4 families experienced the birth of a subsequent CAH-affected child which may have affected recollections of the first affected child.
Carroll (2018)[2]	Mixed methods study including semi-structured telephone interviews with children and caregivers. Descriptive content analysis using a hermeneutical, phenomenological framework	Female children who had been diagnosed with CAH and one of their caregivers. n=20 children Age range 7-18 years n=20 caregivers Median age 45 years, age range 29-62 USA	What themes on health-related quality of life (HRQOL) and factors that may contribute to the HRQOL of children with CAH emerged during interviews among: a. children with CAH? b. caregivers of children with CAH?	Demographic characteristics were only presented for the full sample of 25 child-caregiver dyads that completed the quantitative element of study rather than the 20 that participated in the interviews. Participants partially recruited via CARES support organisation.
Fleming et al (2017)[3]	Mixed methods study including semi-structured telephone interviews. Thematic analysis, based on Family Management Style Framework theoretical framework.	Parents of children with CAH n= 16 from 9 families (n=7 mother/father dyads, n= 2 single mothers). Age of parents not reported. Age of children range 2-15 years. USA	To describe circumstances surrounding adrenal crisis events in children with CAH; to explore parents' perceptions of the consequences of having a child with a life-threatening condition; and to examine a relationship between parents' perceived management ability and the impact CAH has on the family.	Participants recruited via invitations sent to members of CARES support organisation.

Study	Design	Population	Research aim	Comments
Malstram et al (2018)[4]	Qualitative study with photovoice methods (series of 6 focus group sessions over 7 weeks with use of participants' photographs to facilitate discussion). Analysis by photovoice methods and thematic analysis	Adults with autoimmune Addison's Disease (AAD) n=5 Age range 40-77 years Sweden	What aspects in everyday life with AAD are important? What possibilities and challenges do persons with AAD experience in everyday life?	Participants were taking part in an ongoing self-management education program for people with AI. Potential participants who had not yet attended the self-management education, were excluded.
Shepherd et al (2017)[6]	Mixed methods study including face-to-face semi-structured interviews with thematic content analysis.	Adult patients with primary adrenal insufficiency (PAI). n=10 Mean age of 47 years (age range 21 to 63 years) England	To explore if patients with PAI have sufficient knowledge and understanding of the condition; knowledge of how and when to adjust steroid replacement during acute illness or stressful event; and been provided with the required information.	Participants, predominantly female (n=8). Interviewer known to participants.
Simpson et al (2018)[7]	Mixed methods study including qualitative face-to-face semi-structured interviews with thematic content analysis.	Parents (n=20) of children with CAH n=17; (8 male/9 female) Age of child 3 months-10 years UK	To capture the experiences of parents of children with AI/CAH including their views on psychosocial impact of living with and managing the condition	Most participants were recruited via a support organisation. Parents whose children were aged over six were asked to focus on their earlier experiences (retrospective).
Van der Meij (2016)[8]	Mixed methods study including semi-structured telephone interviews. Conventional content analysis.	Adult patients with primary and secondary AI who received the same glucocorticoid stress management education. Patients with CAH, tertiary adrenal insufficiency and transient adrenal insufficiency excluded.	To identify the reasons of patients' insufficient knowledge (of adjusting the dose of glucocorticoids in special circumstances) and to determine their care needs from patients' perspectives.	Semi-structured interview participants had been assessed as having inadequate knowledge of how to deal with stressful situations in the quantitative element of the study (52% of the recruited sample). All participants had experienced the same glucocorticoid stress management education programme.

Study	Design	Population	Research aim	Comments
		n= 43 Mean age = 54.1 years (SD 13.5). Netherlands		

See Appendix D for full evidence tables.

1.1.6. Summary of the qualitative evidence

Table 3: Review findings

Main findings	Statement of finding
1) Improve awareness that stressful situations require increased dose of hydrocortisone [adults only][4, 6, 8] (Quality assessment – Low)	Need improvement in awareness that stressful situations require increased dose of hydrocortisone; requires an individualised approach to self-management [Adults only]
2) Desire for more information and education[1-4, 6, 8] (Quality assessment – Low)	Desire for more information and education on: symptoms, medicine management and administration; adverse effects (or not) of hydrocortisone; preparation for adrenal crisis; decision-making in everyday life and a survival guide.
3) Information and support to be available throughout journey of AI[1-4, 6, 8] (Quality assessment – Moderate)	Requirements for information and support to be available throughout journey of AI, especially at diagnosis but then repeated regularly (e.g., demonstration of hydrocortisone injections) and taking into account changes in life stage.
4) Value of social support[1, 2, 4, 6] (Quality assessment – Moderate)	Value of social support (from family, friends, and peer-support groups)
5) How to communicate requirements of managing AI to child's extended caregivers [Children and young adults with CAH only][2, 3] (Quality assessment – Low)	Desire for information and support in how to communicate the requirements of managing AI to others in child's life [Children and young adults with CAH only]
6) Inadequate knowledge of AI by HCPs[2-4, 6, 7] (Quality assessment – Moderate)	Experienced inadequate knowledge of AI by HCPs and dissatisfied with the support and advice they provide.

See Appendix E for full GRADE-CERQual tables.

1.1.6.1. Narrative summary of review findings

Review finding 1: Improve awareness that stressful situations require increased doses of hydrocortisone [Adults only]

This finding is derived from the three studies[4, 6, 8] that are based on adults with adrenal insufficiency. Participants in each study referred to the need for adjustment of medication (hydrocortisone) according to stressful situations, and so self-care was described as complex and demanding. A clear theme identified by van der Meij et al (2016)[8] was unawareness about the need for adjusting hydrocortisone in stressful situations, in study participants with inadequate knowledge of AI post-completion of a stress-management education programme. This review finding also captures findings from Malstram et al (2018)[4] and Shepherd et al (2017)[6] that highlight the need for an individualised approach to self-management, particularly around assessing potentially stressful situations. The study by Malstram et al (2018)[4] provided rich data that described how 'fine tuning' was needed in everyday life; this was described as a very individual process, for example, considering how different individuals perceive a situation as stressful or not. Therefore, self-management techniques around adjustments in medication also need to be tailored to the individual.

Explanation of quality assessment:

This finding is substantially driven by findings from van der Meij et al (2016)[8], which has moderate concerns related to methodological limitations. These limitations are due to a discrepancy in the reporting of the number of interviews, and the way in which the study was restricted to participants who had inadequate AI knowledge following an education

programme. This information gap may therefore be a reflection of a single education programme, rather than reflecting views of a wider group of adults with adrenal insufficiency. Methodological limitations in two studies[4, 6] were minor and mostly related to recruitment strategies. There were minor concerns about coherence, due to some participants in the study by Shepherd et al (2017)[6] describing a good understanding of the need to adjust medication. There were no concerns about relevance or adequacy. Overall assessment of confidence was low due to concerns about methodological limitations and coherence.

Review finding 2: Desire for more information and education

A clear finding across all six included studies[1-4, 6, 8] is a desire for more information and education on adrenal insufficiency by participants and is relevant to children, young adults and adults. Participants in studies by Carroll (2018)[2] and Shepherd et al (2017)[6] express a need for more information but the exact nature of that information is not expanded upon. Other studies' participants indicate they would like more information on symptoms[4] medicine management and administration[1, 4]; adverse effects (or not) of hydrocortisone[8]; preparation for adrenal crisis[3]; decision-making in everyday life[4]; and a 'survival guide'[1]. Although the overarching desire for more information is consistent across studies, the exact nature of the information participants would like varies, though this does mostly relate to medication and prevention of adrenal crisis.

Explanation of quality assessment:

The six studies exhibited a range of methodological limitations, which were overall rated moderate. Three studies[2, 4, 6] had minor concerns about recruitment strategies/relationship with researcher; two studies[3, 8] had moderate concerns about discrepancies in number of interviews/rigour of analysis; one study[1] had severe concerns about similar issues plus additional concerns about ethical approval and clarity of data collection. There was moderate concern about coherence due to the variation in topics of information desired across studies. There was minor concern about adequacy due to the lack of richness of data on each of the specific topics to be covered in information. There were no concerns about relevance. Overall assessment of confidence was low due to concerns about methodological limitations, coherence and adequacy.

Review finding 3: Information and support to be available throughout journey of AI

This review finding draws upon evidence from all six studies[1-4, 6, 8] and is relevant to children, young adults and adults. All studies support an overarching theme that information and support should be available to people with adrenal insufficiency from diagnosis, continuing throughout long-term management and adapting appropriately to relevant life stages. A specific need to repeat the demonstration of an emergency injection of hydrocortisone was highlighted by participants in the study by Fleming et al (2017)[3]; similarly, van der Meij et al (2016)[8] highlighted that participants wanted a repetition of educational programmes on AI, which may be linked to other themes identified around forgetting medication and misconceptions.

Two studies[1, 4] reported findings that present participant views on their changing requirements for information throughout the journey of AI from diagnosis to long-term management. Although information needs are most intensive at diagnosis, participants in these studies explained that they would like information to continue after diagnosis and throughout their journey of adrenal insufficiency, including details on information related to financial matters for example. This is further supported by findings from Shepherd et al (2017)[6] that describe the change in psychological states experienced from diagnosis through to the later stages of having adrenal insufficiency. Care-givers interviewed in studies by Carroll et al (2018)[2] and Fleming et al (2017)[3] described how they were concerned about the management of adrenal insufficiency as their child progresses to adolescence as they would have less control over their child's treatment regimen and response to crises as they enter young adulthood. Further, concerns around growth and fertility may become more common worries around this age.

Explanation of quality assessment:

The six studies exhibited a range of methodological limitations, which were overall moderate. Three studies[2, 4, 6] had minor concerns about recruitment strategies/relationship with researcher; two studies[3, 8] had moderate concerns about discrepancies in the number of interviews/rigour of analysis; one study[1] had severe concerns about similar issues plus additional concerns about ethical approval and clarity of data collection. Although there is sufficient evidence to support the requirement for information throughout the lifetime with adrenal insufficiency, data is less rich on the need for repeated demonstrations of injections of transition into adolescence. This is reflected in minor concerns about adequacy. There were no concerns about coherence or relevance. Overall assessment of confidence was moderate due to concerns about methodological limitations and adequacy.

Review finding 4: Value of social support.

This review finding draws upon evidence from four studies and is relevant to children and young adults (two studies[1, 2]) and adults (two studies[4, 6]). All four studies refer to the role of social support for people with adrenal insufficiency. The ability to be able to connect with others in a specific support group for people with adrenal insufficiency is described by Malstrom et al (2018)[4] (adults) and Boyse et al (2014)[1] (children). The ability to discuss shared experiences and offer reassurance and support to each other were features of such peer support that were viewed positively. Participants in the study by Shepherd et al (2017)[6] and Carroll (2018)[2] spoke more generally about social support offered by other routes, including support from family and friends. Participants in the study by Shepherd et al (2017)[6] spoke mostly about the importance of support from family, particularly if seeking urgent medical attention (as they would be knowledgeable about AI) and viewed this as the most important source of support. Participants in the Carroll (2018)[2] study described both the importance of support from family and friends but also a desire for more access to specific peer-support groups for children with AI and their caregivers.

Explanation of quality assessment:

Of the four studies supporting this review finding, three[2, 4, 6] had minor concerns about methodological limitations due to recruitment strategies/relationship with the researcher, and one study[1] had more severe concerns due to similar issues plus additional concerns about ethical approval and clarity of data collection/analysis. Overall assessment of confidence was moderate due to concerns about these methodological limitations.

Review finding 5: How to communicate requirements of managing AI to child's caregivers [Children and young adults with CAH only]

This review finding draws upon findings from two studies[2, 3] relevant only to children and young people with CAH. Fleming et al (2017)[3] interviewed parents of children and young people with CAH and Carroll (2018)[2] interviewed both children with CAH and their caregivers (separately). Parents in both studies described the need for educating several extended caregivers in their child's life, such as school healthcare teams, sports coaches, babysitters, and extended family, about AI. There were difficulties in not knowing how much information on adrenal insufficiency to share with extended caregivers (for example talking to babysitters about the injection or instructing sports coaches about signs and management of adrenal crisis). Caregivers in the Carroll (2018) study[2] specifically wanted "a way to explain it [CAH] to others". Several caregivers in this study commented that they wanted a universal language about CAH to communicate with their child and their extended caregivers. Participants in the Fleming et al (2017) study[3] explained that conversations with extended caregivers often had to be repeated several times e.g., school nurse and day-care provider.

Explanation of quality assessment:

The two studies[2, 3] that support this finding have minor concerns about methodological limitations due to recruitment strategies/relationship with the researcher and additional concerns in the study by Fleming et al (2017)[3] due to analytic approach. There were minor

concerns about relevance due to one study[2] focussing on female children only. There were moderate concerns about adequacy as this finding is supported by data from only two studies. There were no concerns about coherence. Overall assessment of confidence was low due to concerns about adequacy, relevance, and methodological limitations.

Review finding 6: Inadequate knowledge of AI by HCPs

This review finding draws upon evidence from five studies and is relevant to children and young adults (three studies[2, 3, 7]) and adults (two studies[4, 6]). Overall these study findings show that participants have experienced inadequate knowledge of AI by HCPs[4], and would like them to be better informed on the condition[2]. The rich data from Malstrom et al (2018)[4] explains that participants feel forced to 'become the expert' on AI because of the inadequate knowledge of HCPs. Children and young adults interviewed in the study by Carroll (2018)[2] specifically wanted HCPs to be better informed on growth and fertility. Participants in two further studies[3, 6], expressed general dissatisfaction with the support and advice HCPs provide on AI. In one study[7], parents faced challenges associated with clinicians' low awareness of CAH and some struggled to convince them of the significance of their child's symptoms to obtain a diagnosis.

Explanation of quality assessment:

In terms of methodological limitations, four studies[2, 4, 6, 7] had minor issues due to recruitment strategies and/or relationships with the researcher, and one study[3] with an additional concern about the analytic approach. There were no concerns regarding coherence and adequacy. There were moderate concerns about relevance, due to potential indirectness to the review questions; participants' comments are about the information and knowledge that healthcare professionals hold rather than information and support that people with AI would like to receive. Overall assessment of confidence was moderate due to concerns about relevance and methodological limitations.

1.1.7. Economic evidence

The committee agreed that health economic studies would not be relevant to this review question, and so were not sought.

1.2. The committee's discussion and interpretation of the evidence

1.2.1. The quality of the evidence

This review looked at the information and support needs of people with adrenal insufficiency, and their families or carers by analysis of views, opinions and experiences reported. Information from qualitative studies was summarised into six different themes. Themes were derived from the evidence identified and were not prespecified by the committee. Four synthesised themes were derived from evidence from adults, children and young people with CAH and their parents/carers. One synthesised theme was derived from evidence from adults with adrenal insufficiency. One synthesised theme was derived from evidence from children with CAH and their parents/carers. Overall, three synthesised themes were relevant to research question 1.1 (routine management of adrenal insufficiency), and three synthesised themes were relevant to both research questions 1.1 and 1.2 covering routine management of adrenal insufficiency and prevention and emergency care of adrenal crisis.

In line with GRADE CERQual, confidence in the evidence base informing the review ranged from low to moderate. Confidence in the evidence for 3 out of 6 themes was moderate; confidence for 3 out of 6 themes was low. The primary reasons for downgrading review findings were due to methodological limitations in the contributing studies. These commonly included the relationship between the researcher and the participants not having been

explored, concerns about recruitment strategies and discrepancies in reporting (for example in a number of interviews conducted). Further concerns about the lack of clarity of data collection methods, data analysis and ethical approval procedures were noted for some findings. Evidence was occasionally downgraded due to concerns about coherence, with participants within or across studies expressing variation in views about their information and support needs; adequacy, when insufficient data was available; and relevance, when the context was not directly relevant to the review question.

Overall, the committee commented that the amount of evidence presented in the evidence review was limited, and it did not cover all aspects of the review questions. For routine management of adrenal insufficiency, information and support needs when exercising, travelling, working non-standard hours or taking part in religious observances such as fasting, were not addressed by the studies included in the review. The information and support needs of people with adrenal insufficiency during emergency care of adrenal crisis were also not addressed in the evidence review. Overall, the evidence available focussed on general aspects of routine management and support for the prevention of adrenal crises.

1.2.2. Findings identified in the evidence synthesis.

The evidence review supported the requirement for people with suspected or diagnosed adrenal insufficiency, and their families and carers, to be provided with information and support for routine management of adrenal insufficiency and prevention of adrenal crisis. This is supported by review finding *2) Desire for more information and education*. In terms of the specific content of information and support, the evidence base was limited with only a few examples cited across studies. The Committee discussed that information and support is highly variable and that some people find it difficult to access accurate and reliable information. This was further supported by lay members' experience of the condition. Therefore, consensus recommendations on the specific content that should be included when providing information and support were made. This content is detailed in recommendations describing the information and support needs of people with adrenal insufficiency at the time of diagnosis. In line with review findings *1) Improve awareness that stressful situations require an increased dose of hydrocortisone* and *2) Desire for more information and education,* the evidence review supports the need for information on support in understanding symptoms; when to administer additional corticosteroids beyond usual doses; and how to administer corticosteroids in an emergency situation. The committee agreed these were important components to include because they enabled self-management of the condition in both routine and emergency situations, and when to seek clinical advice. The committee stressed how important it was that people know from the time of their diagnosis how to obtain emergency steroid cards and set up medical alerts to help keep them safe and prevent adrenal crisis. People with adrenal insufficiency should be fully confident and in self-management and any additional requirements for treatment as non-specialist are not always aware of how to manage the condition. This also includes managing medication supplies when travelling and when to adjust dosing due to increases in temperature, or the need to adjust timing of dosages when travelling though time-zones, or if fasting or doing shiftwork.

The committee identified further action needed to support people with adrenal crisis at the time of diagnosis. These actions were informed by aspects of the evidence review such as preparing for an adrenal crisis, and how to administer emergency injections of hydrocortisone, and supplemented by a discussion of clinical practice and experiences of the condition as described by committee members.

In line with review finding *4) Value of social support*, the committee agreed it is important to signpost people with adrenal insufficiency to peer-support groups and charities that support people with adrenal insufficiency. Also, in line with this finding about the value of social support from personal networks, the committee agreed it is important for healthcare teams to explore with people their preferences for disclosing their diagnosis and treatment with family, friends and their employers or educational institutions. This is with a view to ensuring access

to appropriate support in their local surroundings and ensuring that people they spend time with can recognise, and where appropriate, have access to the person's management plan to provide support if signs of an adrenal crisis appear.

The evidence review highlighted the need for information and support to be provided to people with adrenal insufficiency, not only at diagnosis but throughout their journey with the condition. This is reflected in review finding 3) *Information and support to be available throughout the journey of adrenal insufficiency.* This finding was consistent with the views of the committee and reflected in recommendations on ongoing information, which specifies the need to review information and support needs regularly. In line with the evidence base reviewed, it is important that the approach taken includes consideration of the needs of children as they mature and transition to adulthood. The Committee also presented views that life events might trigger a review, for example, starting a family or going to university.

For people who are in education, it is necessary to provide parents or carers with a management plan so they can choose whether to share it with the education provider when discussing the needs of their child. This was raised as a specific point by the committee and is informed by review findings *5) How to communicate requirements of managing AI to child's extended caregivers and 4) Value of social support.* The committee agreed *to make a* recommendation based on expertise from clinical practice, lay members' experiences of the condition, and the evidence review. They also agreed the guideline on Transition from children's to adults services for young people provided generic recommendations that reflect best practice and were applicable to children and young people with adrenal insufficiency to ensure health and social care needs continue to be met and decided to cross-refer to this.

The committee highlighted that not all people with adrenal insufficiency have the capability to self-manage their condition alone. For example, the committee felt that recommendations needed to be appropriate for people with disabilities, cognitive decline and learning difficulties. They agreed to refer to the NICE guideline on decision-making and mental capacity which provides guidance on the assessment of mental capacity to make decisions at a particular time and 'in best interests' decision-making for individuals who are assessed as lacking the capacity to make a particular decision.

The committee agreed the information and support recommendations for people with adrenal insufficiency will help to improve the quality and consistency of care for the affected population. They will help promote awareness of the condition and its risks, resolve uncertainties regarding treatment and provide emotional and practical support to help individuals cope with the condition's psychological and social aspects.

The Committee noted that several recommendations in existing NICE guidelines were relevant to the provision of support and information for people with adrenal insufficiency. Therefore, the Committee agreed that signposting readers to NICE's guidelines on patient experience in adult NHS services, Babies, children and young people's experiences of healthcare, Shared decision making, and Medicines Adherence was appropriate.

The committee also noted the statutory guidance for governing bodies in supporting children and young people with medical conditions at school and the Royal College of Nursing guidance on meeting health needs in educational settings. Committee members agreed both provided helpful information for health professionals and non-health staff on key legislation and policy as well as general principles to support access to education.

Overall, the committee agreed that despite the limitations in the available evidence, the themes reported in the evidence directly aligned with the committee's knowledge and experience of NHS based practice and was strongly supported by the experience of the lay members' experience. Therefore, they were confident in making strong recommendations based on these findings and supplemented any gaps in the evidence base with their consensus opinion and clinical expertise.

1.2.3. Cost-effectiveness and resource use

Cost-effectiveness evidence was not sought as this was a qualitative review. The recommendations provide guidance on the information and support that people with adrenal insufficiency should be provided at the time of diagnosis and throughout their treatment pathway. The recommendations made by the committee are reflective of best practice.

The committee acknowledged that the information and support provided to people with adrenal insufficiency in current practice is generally in line with the recommendations made for this review question. However, in instances where best practice is not being observed in clinical practice, the additional cost to the NHS for implementing these recommendations is likely to be minimal as the recommendations are concerned with the provision of information. The committee acknowledged that in some instances it is possible a small amount of additional health care professional time may be required to provide this additional information. However, the committee concluded that this cost would be marginal and therefore this review question would not result in a significant resource impact.

1.2.4. Recommendations supported by this evidence review.

This evidence review supports recommendations 1.1.1 to 1.1.9.

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Appendices

Appendix A Review protocols

A.1 Draft review protocol for information and support for routine management of adrenal insufficiency

ID	Field	Content
1.	Review title	Information and support for routine management
2.	Review question	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?
3.	Objective	To explore perceptions and experiences of people with adrenal insufficiency, their families and carers in order to determine their information and support needs for routine and emergency management of their health.
4.	Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos • PsychINFO • CINAHL

		Searches will be restricted by: • Date limitations – none • English language studies • Human studies The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5.	Condition or domain being studied	Adrenal insufficiency
6.	Population	Inclusion: People with adrenal insufficiency (primary, secondary or tertiary) or who are suspected of having adrenal insufficiency (and their families and carers The following population stratification will be applied, where possible: • Adults (aged ≥16 years) • Young people (>12-16 years) • Children aged ≥1 up to 12 years • Infants and children <1 Exclusion: None specified
7.	Phenomena of interest	Views, opinions and experiences of people with adrenal insufficiency and/or their families and carers regarding information, education and support they find most helpful in routine and emergency management of their health.
8.	Comparator	Not applicable

9.	Types of study to be included	Qualitative interview and focus group studies (including studies using grounded theory, phenomenology or other appropriate qualitative approaches, including survey data or other types of questionnaires only if they provide analysis from open-ended questions). Quantitative data from surveys and questionnaires will only be considered if insufficient qualitative evidence is identified. This will be decided in discussion with the guideline committee.
10.	Other exclusion criteria	Non-English language studies Quantitative studies (i.e., closed questionnaire surveys) Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	-

12.	Primary outcomes (critical outcomes)	Themes will be derived from the evidence identified for this review and are not pre-specified. They may include:
		• how to ensure an adequate supply of medicines
		• advice on what to do in certain situations such as:
		  ○ when exercising e.g., competitive recreational and activities with risk of injury
		  ○ travelling e.g., across time zones, extremes of climates
		  ○ working non-standard hours
		  ○ taking part in religious observances such as fasting
		• how to prevent an adrenal crisis
		• emergency care of adrenal crisis
		• content in particular for transition to adult services
		• pregnancy
		• educational information for schools including medicines administration and injections
		• illness and physiological stress (e.g. sick-day rules)

13.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.

		The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Additional qualitative studies will be added to the review until themes within the analysis become saturated, i.e., studies will only be included if they contribute towards the development of existing themes or to the development of new themes. The point at which data saturation is reached will be noted within the review. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately. • a sample of the data extractions. • correct methods are used to synthesise data. • a sample of the risk of bias assessments. Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.	
14.	Risk of bias (quality) assessment	Risk of bias will be assessed using the Critical Appraisal Skills Programme (CASP) qualitative checklist, as described in Developing NICE guidelines: the manual.	
15.	Strategy for data synthesis	The synthesis of qualitative data will follow a thematic analysis approach. Information will be synthesised into main review findings. Results will be presented in a detailed narrative and in table format with summary statements of main review findings. GRADE CERQual will be used to synthesise the qualitative data and assess the certainty of evidence for each review finding.	
16.	Analysis of sub-groups	None	
17.	Type and method of review	☐	Intervention
		☐	Diagnostic
		☐	Prognostic

		☒	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
18.	Language	English	
19.	Country	England	
20.	Anticipated or actual start date	June 2022	
21.	Anticipated completion date	April 2024	
22.	Stage of review at time of this submission	Review stage	Started / Completed
		Preliminary searches	☐ / ☐
		Piloting of the study selection process	☐ / ☐
		Formal screening of search results against eligibility criteria	☐ / ☐
		Data extraction	☐ / ☐
		Risk of bias (quality) assessment	☐ / ☐
		Data analysis	☐ / ☐
23.	Named contact	5a. Named contact Guideline Development Team NGC 5b Named contact e-mail Hypoadrenalism@nice.org.uk 5e Organisational affiliation of the review	

		National Institute for Health and Care Excellence (NICE)
24.	Review team members	Sharon Swain [Guideline lead] Saoussen Ftouh [Senior systematic reviewer] Meena Tafazzoli [Systematic reviewer] Alexandra Bannon [Health economist] Stephen Deed [Information specialist]
25.	Funding sources/sponsor	Development of this systematic review is being funded by NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10237.
28.	Other registration details	-
29.	Reference/URL for published protocol	-
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts

		• issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
31.	Keywords	Hypoadrenalism, adrenal insufficiency, congenital adrenal hyperplasia, patient, carer, views, information, education, support	
32.	Details of existing review of same topic by same authors	-	
33.	Current review status	☐	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
34.	Additional information	-	
35.	Details of final publication	www.nice.org.uk	

Appendix B Literature and search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[5]

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches for patient views were run in Medline (OVID), Embase (OVID), CINAHL Current Nursing and Allied Health Literature (EBSCO) and PsycINFO (OVID). Search filters were applied to the search where appropriate.

Table 4: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 July 2022	Qualitative studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 July 2022	Qualitative studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
PsycINFO (OVID)	Inception – 22 July 2022	Qualitative studies Exclusions (animal studies, letters, case reports) Human English language
Current Nursing and Allied Health Literature (CINAHL) (EBSCO)	Inception – 22 July 2022	Exclusions (Medline records) Human English Language

Medline (Ovid) search terms

1.	exp Adrenal Insufficiency/
2.	Adrenal Hyperplasia, Congenital/
3.	(addison* disease or addisonian*).ti,ab,kf.
4.	((adrenal* or adrenocort* or adreno cort*) adj3 (insufficien* or inadequa* or deficien* or suppress* or hypofunction* or disorder* or underactiv* or dysfunction* or abnormal* or problem* or crisis or crises or dysgenesis or destruction or destroy* or hyperplasia or

	hypoplasia or failure* or fails or failed or fatigue or inhibit* or damage* or disruption*)).ti,ab,kf.
5.	((cortisol or aldosterone or adrenocorticotrop* or adreno corticotrop* or ACTH or corticotropi* releas* or corticotrophi* releas* or corticoliberin or CRH) adj3 (insufficien* or inadequa* or deficien* or suppress* or reduc* or decreas* or descend* or diminish* or lack* or less or lessen* or low or lower* or limited)).ti,ab,kf.
6.	(hypoadrenal* or hypo adrenal* or hypoadrenocorticism or hypo adrenocorticism or adrenoleukodystrophy or adreno leukodystrophy or adrenomyeloneuropathy or adreno myeloneuropathy or hypoaldosteronism or hypo aldosteronism).ti,ab,kf.
7.	((adrenogenital or adreno genital) adj (syndrome or disorder*)).ti,ab,kf.
8.	((haemorrhag* or hemorrhag* or bleed*) adj3 adrenal*).ti,ab,kf.
9.	(Bronze Schilder* Disease or Melanodermic Leukodystrophy or Schilder-Addison* Complex or Siemerling-Creutzfeldt* Disease).ti,ab,kf.
10.	((Allgrove or 3A or TripleA or AAA) adj syndrome).ti,ab,kf.
11.	(CAH or X-ALD).ti,ab.
12.	(Waterhouse-Friderichsen* syndrome or antiphospholipid syndrome).ti,ab,kf.
13.	Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy.ti,ab,kf.
14.	or/1-13
15.	letter/
16.	editorial/
17.	news/
18.	exp historical article/
19.	Anecdotes as Topic/
20.	comment/
21.	case report/
22.	(letter or comment*).ti.
23.	or/15-22
24.	randomized controlled trial/ or random*.ti,ab.
25.	23 not 24
26.	animals/ not humans/
27.	exp Animals, Laboratory/
28.	exp Animal Experimentation/
29.	exp Models, Animal/
30.	exp Rodentia/
31.	(rat or rats or mouse or mice or rodent*).ti.
32.	or/25-31
33.	14 not 32
34.	limit 33 to English language
35.	exp Patients/ or exp Family/ or Caregivers/
36.	Consumer Health Information/ or Needs Assessment/ or Patient Education as Topic/ or Patient Education Handout/ or Health Communication/ or Information Dissemination/
37.	((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) adj3 (information* or advice or advis* or need* or requirement* or support* or access* or service* or educat* or learn* or teach* or train*)).ti,ab,kf.
38.	((information* or educat*) adj3 (need* or requirement* or support* or seek* or access* or disseminat* or barrier* or service*)).ti,ab,kf.
39.	(support* adj3 (need* or requirement* or assess* or seek* or access* or barrier* or service*)).ti,ab,kf.

40.	"Patient Acceptance of Health Care"/ or exp Patient Satisfaction/
41.	((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) adj3 (belief* or attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or experience* or opinion* or preference* or feedback*)).ti,ab,kf.
42.	or/35-41
43.	34 and 42
44.	Qualitative research/ or Narration/ or exp Interviews as Topic/ or exp "Surveys and Questionnaires"/ or Health care surveys/
45.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
46.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
47.	or/44-46
48.	43 and 47

Embase (Ovid) search terms

1.	exp Adrenal cortex insufficiency/
2.	Congenital adrenal hyperplasia/
3.	(addison* disease or addisonian*).ti,ab,kf.
4.	((adrenal* or adrenocort* or adreno cort*) adj3 (insufficien* or inadequa* or deficien* or suppress* or hypofunction* or disorder* or underactiv* or dysfunction* or abnormal* or problem* or crisis or crises or dysgenesis or destruction or destroy* or hyperplasia or hypoplasia or failure* or fails or failed or fatigue or inhibit* or damage* or disruption*)).ti,ab,kf.
5.	((cortisol or aldosterone or adrenocorticotrop* or adreno corticotrop* or ACTH or corticotropi* releas* or corticotrophi* releas* or corticoliberin or CRH) adj3 (insufficien* or inadequa* or deficien* or suppress* or reduc* or decreas* or descend* or diminish* or lack* or less or lessen* or low or lower* or limited)).ti,ab,kf.
6.	(hypoadrenal* or hypo adrenal* or hypoadrenocorticism or hypo adrenocorticism or adrenoleukodystrophy or adreno leukodystrophy or adrenomyeloneuropathy or adreno myeloneuropathy or hypoaldosteronism or hypo aldosteronism).ti,ab,kf.
7.	((adrenogenital or adreno genital) adj (syndrome or disorder*)).ti,ab,kf.
8.	((haemorrhag* or hemorrhag* or bleed*) adj3 adrenal*).ti,ab,kf.
9.	(Bronze Schilder* Disease or Melanodermic Leukodystrophy or Schilder-Addison* Complex or Siemerling-Creutzfeldt* Disease).ti,ab,kf.
10.	((Allgrove or 3A or TripleA or AAA) adj syndrome).ti,ab,kf.
11.	(CAH or X-ALD).ti,ab.
12.	(Waterhouse-Friderichsen* syndrome or antiphospholipid syndrome).ti,ab,kf.
13.	Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy.ti,ab,kf.
14.	or/1-13
15.	letter.pt. or letter/
16.	note.pt.
17.	editorial.pt.
18.	case report/ or case study/
19.	(letter or comment*).ti.

20.	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
21.	or/15-20
22.	randomized controlled trial/ or random*.ti,ab.
23.	21 not 22
24.	animal/ not human/
25.	nonhuman/
26.	exp Animal Experiment/
27.	exp Experimental Animal/
28.	animal model/
29.	exp Rodent/
30.	(rat or rats or mouse or mice or rodent*).ti.
31.	or/23-30
32.	14 not 31
33.	limit 32 to English language
34.	patient/ or family/ or caregivers/
35.	consumer health information/ or needs assessment/ or communication barrier/ or patient education/ or medical information/ or information dissemination/
36.	((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) adj3 (information* or advice or advis* or need* or requirement* or support* or access* or service* or educat* or learn* or teach* or train*)).ti,ab,kf.
37.	((information* or educat*) adj3 (need* or requirement* or support* or seek* or access* or disseminat* or barrier* or service*)).ti,ab,kf.
38.	(support* adj3 (need* or requirement* or assess* or seek* or access* or barrier* or service*)).ti,ab,kf.
39.	patient preference/ or patient satisfaction/ or consumer attitude/ or patient attitude/
40.	((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) adj3 (belief* or attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or experience* or opinion* or preference* or feedback*)).ti,ab,kf.
41.	or/34-40
42.	33 and 41
43.	health survey/ or exp questionnaire/ or exp interview/ or qualitative research/ or narrative/
44.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
45.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
46.	or/43-45
47.	42 and 46

PsycINFO (OVID) search terms

1.	exp Adrenal Gland Disorders/

2.	(addison* disease or addisonian*).ti,ab,id.
3.	((adrenal* or adrenocort* or adreno cort*) adj3 (insufficien* or inadequa* or deficien* or suppress* or hypofunction* or disorder* or underactiv* or dysfunction* or abnormal* or problem* or crisis or crises or dysgenesis or destruction or destroy* or hyperplasia or hypoplasia or failure* or fails or failed or fatigue or inhibit* or damage* or disruption*)).ti,ab,id.
4.	((cortisol or aldosterone or adrenocorticotrop* or adreno corticotrop* or ACTH or corticotropi* releas* or corticotrophi* releas* or corticoliberin or CRH) adj3 (insufficien* or inadequa* or deficien* or suppress* or reduc* or decreas* or descend* or diminish* or lack* or less or lessen* or low or lower* or limited)).ti,ab,id.
5.	(hypoadrenal* or hypo adrenal* or hypoadrenocorticism or hypo adrenocorticism or adrenoleukodystrophy or adreno leukodystrophy or adrenomyeloneuropathy or adreno myeloneuropathy or hypoaldosteronism or hypo aldosteronism).ti,ab,id.
6.	((adrenogenital or adreno genital) adj (syndrome or disorder*)).ti,ab,id.
7.	((haemorrhag* or hemorrhag* or bleed*) adj3 adrenal*).ti,ab,id.
8.	(Bronze Schilder* Disease or Melanodermic Leukodystrophy or Schilder-Addison* Complex or Siemerling-Creutzfeldt* Disease).ti,ab,id.
9.	((Allgrove or 3A or TripleA or AAA) adj syndrome).ti,ab,id.
10.	(CAH or X-ALD).ti,ab.
11.	(Waterhouse-Friderichsen* syndrome or antiphospholipid syndrome).ti,ab,id.
12.	Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy.ti,ab,id.
13.	or/1-12
14.	Letter/
15.	Case report/
16.	exp Rodents/
17.	or/14-16
18.	13 not 17
19.	limit 18 to English language
20.	exp Patients/ or Family/ or exp Caregivers/
21.	Health Information/ or exp Needs Assessment/ or Client Education/ or Communication barriers/
22.	((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) adj3 (information* or advice or advis* or need* or requirement* or support* or access* or service* or educat* or learn* or teach* or train*)).ti,ab.
23.	((information* or educat*) adj3 (need* or requirement* or support* or seek* or access* or disseminat* or barrier* or service*)).ti,ab.
24.	(support* adj3 (need* or requirement* or assess* or seek* or access* or barrier* or service*)).ti,ab.
25.	Client Satisfaction/ or Client Attitudes/
26.	((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) adj3 (belief* or attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or experience* or opinion* or preference* or feedback*)).ti,ab.
27.	or/20-26
28.	qualitative methods/ or exp interviews/ or exp questionnaires/

29.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
30.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
31.	or/28-30
32.	19 and 27
33.	19 and 31
34.	32 or 33

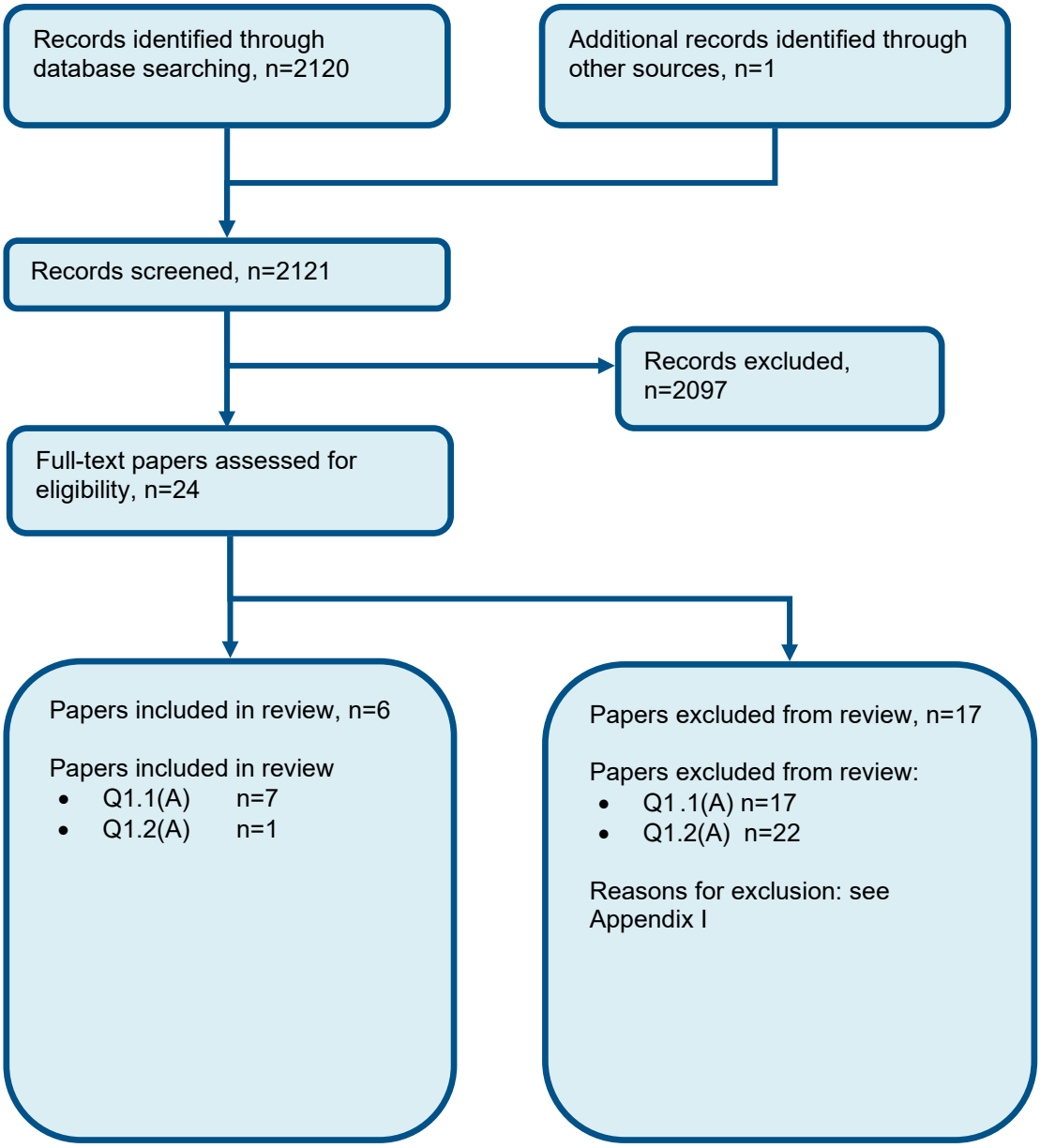
CINAHL (EBSCO) search terms

S1.	(MH "Adrenal Insufficiency+")
S2.	(MH "Adrenal Hyperplasia, Congenital")
S3.	TI ((addison* disease or addisonian*)) OR AB ((addison* disease or addisonian*))
S4.	TI (((adrenal* or adrenocort* or adreno cort*) AND (insufficien* or inadequa* or deficien* or suppress* or hypofunction* or disorder* or underactiv* or dysfunction* or abnormal* or problem* or crisis or crises or dysgenesis or destruction or destroy* or hyperplasia or hypoplasia or failure* or fails or failed or fatigue or inhibit* or damage* or disruption*))) OR AB (((adrenal* or adrenocort* or adreno cort*) AND (insufficien* or inadequa* or deficien* or suppress* or hypofunction* or disorder* or underactiv* or dysfunction* or abnormal* or problem* or crisis or crises or dysgenesis or destruction or destroy* or hyperplasia or hypoplasia or failure* or fails or failed or fatigue or inhibit* or damage* or disruption*)))
S5.	TI (((cortisol or aldosterone or adrenocorticotrop* or adreno corticotrop* or ACTH or corticotropi* releas* or corticotrophi* releas* or corticoliberin or CRH) AND (insufficien* or inadequa* or deficien* or suppress* or reduc* or decreas* or descend* or diminish* or lack* or less or lessen* or low or lower* or limited))) OR AB (((cortisol or aldosterone or adrenocorticotrop* or adreno corticotrop* or ACTH or corticotropi* releas* or corticotrophi* releas* or corticoliberin or CRH) AND (insufficien* or inadequa* or deficien* or suppress* or reduc* or decreas* or descend* or diminish* or lack* or less or lessen* or low or lower* or limited)))
S6.	TI ((hypoadrenal* or hypo adrenal* or hypoadrenocorticism or hypo adrenocorticism or adrenoleukodystrophy or adreno leukodystrophy or adrenomyeloneuropathy or adreno myeloneuropathy or hypoaldosteronism or hypo aldosteronism)) OR AB ((hypoadrenal* or hypo adrenal* or hypoadrenocorticism or hypo adrenocorticism or adrenoleukodystrophy or adreno leukodystrophy or adrenomyeloneuropathy or adreno myeloneuropathy or hypoaldosteronism or hypo aldosteronism))
S7.	TI (((adrenogenital or adreno genital) AND (syndrome or disorder*))) OR AB (((adrenogenital or adreno genital) AND (syndrome or disorder*)))
S8.	TI (((haemorrhag* or hemorrhag* or bleed*) AND adrenal*)) OR AB (((haemorrhag* or hemorrhag* or bleed*) AND adrenal*))
S9.	TI ((Bronze Schilder* Disease or Melanodermic Leukodystrophy or Schilder-Addison* Complex or Siemerling-Creutzfeldt* Disease)) OR AB ((Bronze Schilder* Disease or Melanodermic Leukodystrophy or Schilder-Addison* Complex or Siemerling-Creutzfeldt* Disease))
S10.	TI (((Allgrove or 3A or TripleA or AAA) AND syndrome)) OR AB (((Allgrove or 3A or TripleA or AAA) AND syndrome))
S11.	TI ((CAH or X-ALD)) OR AB ((CAH or X-ALD))
S12.	TI ((Waterhouse-Friderichsen* syndrome or antiphospholipid syndrome)) OR AB ((Waterhouse-Friderichsen* syndrome or antiphospholipid syndrome))
S13.	TI Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy OR AB Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy

S14.	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13
S15.	(MH Patients+) OR (MH Family+) OR (MH Caregivers)
S16.	(MH "Consumer Health Information") OR (MH "Needs Assessment") OR (MH "Patient Education as Topic") OR (MH "Patient Education Handout") OR (MH "Health Communication") OR (MH "Information Dissemination")
S17.	TI (((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) AND (information* or advice or advis* or need* or requirement* or support* or access* or service* or educat* or learn* or teach* or train*))) OR AB (((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) AND (information* or advice or advis* or need* or requirement* or support* or access* or service* or educat* or learn* or teach* or train*)))
S18.	TI (((information* or educat*) AND (need* or requirement* or support* or seek* or access* or disseminat* or barrier* or service*))) OR AB (((information* or educat*) AND (need* or requirement* or support* or seek* or access* or disseminat* or barrier* or service*)))
S19.	TI ((support* AND (need* or requirement* or assess* or seek* or access* or barrier* or service*))) OR AB ((support* AND (need* or requirement* or assess* or seek* or access* or barrier* or service*)))
S20.	(MH "Patient Satisfaction+")
S21.	TI (((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) AND (belief* or attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or experience* or opinion* or preference* or feedback*))) OR AB (((patient* or inpatient* or outpatient* or carer* or client* or user* or customer* or consumer* or caregiver* or care giver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or relative* or sibling* or sister* or brother* or grandparent* or grandfather* or grandmother*) AND (belief* or attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or experience* or opinion* or preference* or feedback*)))
S22.	S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21
S23.	S14 AND S22

Appendix C Qualitative evidence study selection

Figure 1: Flow chart of qualitative study selection for the review of information and support for routine management of adrenal insufficiency



Appendix D Qualitative evidence

Study	van der Meij et al (2016)[8]
Aim	1. to assess the knowledge of adjusting the dose of glucocorticoids in special circumstances in patients with adrenal insufficiency who had previously been educated on this topic. 2. to identify the reasons of their insufficient knowledge and to determine their care needs from patients' perspectives'.
Population	186 adult patients (>18 years) with AI from patient records who received the same glucocorticoid stress management education between August 2009 and October 2011. Patients with congenital adrenal hyperplasia (n = 18), tertiary adrenal insufficiency (n = 11), transient adrenal insufficiency (n = 16), impaired cognition (n = 16) and insufficient control of Dutch language (n = 6) were excluded from this study. Remaining 119 patients received a letter in which consent was asked to call them by telephone to receive information about the study. Of these 119 patients, 83 agreed to participate in the study. Participants received a structured telephone interview to test their knowledge using hypothetical situations of physical and mental stress. Forty-three (51.8%) of the 83 patients who previously received education had insufficient knowledge about how to act during stressful situations and were interviewed using a semi-structured interview. Characteristics of qualitative participants: n= 43; male n=23 (53.5%), female n=20 (46.5%). Mean age was 54.1 years (SD 13.5). 9 (20.9%) had primary AI and 34 (79.1%) secondary AI. The median disease duration was 4 years (range: 0.5–44 years).
Setting	Outpatient clinic of the department of endocrinology at the University Medical Center Utrecht (Netherlands)
Study design	Qualitative and quantitative study
Methods and analysis	Semi-structured telephone interview to elicit the underlying reasons from patients' perspective for their lack of knowledge. All qualitative interviews started with two opening questions: 'What do you think is the reason that, despite education, your knowledge is insufficient on how to act during stress?' and 'What are your needs in order to act adequately in future during physical and emotional stress?' Based on the answers, in-depth questions were posed to generate causes and care needs. In the last part of the interview, participants were asked their opinion on possible improvements in care. Conventional content analysis conducted. This involved reading transcripts of interviews. The first six text sections (meaningful paragraphs) of the 36 interviews were separately coded by two researchers. The initial codes were compared and did not differ between the two researchers. Subsequently, all texts were coded. In the next phase, the concepts were pooled and brought under broader categories. These categories were discussed by both researchers and a third researcher and led to consensus on the definitive categories. These categories were used to organize and group codes into meaningful clusters/ relevant topics, related to the research question.
Findings	4 categories identified regarding reasons for inadequate knowledge about how to act in stress situations:
	Unawareness: Unawareness about the need for adjusting hydrocortisone in stressful situation, or understanding that stress leads to a increased demand for cortisol

Study	van der Meij et al (2016)[8]
	Coping with the disease: Participants were not consciously engaged with their disease and/or had a relaxed attitude to AI so became careless and reluctant to increase dose of hydrocortisone or seek medical advice.
	Misconceptions: fear of adverse effects of too much hydrocortisone; reluctance to act on stressful situations unless on advice of doctor; apathy about missing doses of hydrocortisone.
	Forgetting: simply forgotten information from educational programme or insufficient experience of stressful situations.
	Care needs identified in 5 main categories:
	Repetition: education programme should be repeated with variance in preferred format (- repeat educational consultation (n=29); group education (n=26); internet-based education (n=24); yearly reminder (n=27)
	Mnemonic: participants would like a mnemonic to help with decision-making in stressful situation
	Reassurance: require reassurance that increasing hydrocortisone will create no harm
	Learning from experience: can only learn how to deal with stress once I have experienced it
	Optimise social support: social environment related to self-management
Funding	No specific grant from any funding agency in the public, commercial or not-for-profit sector.
Limitations and applicability of evidence	Note discrepancy in reporting of number of interviews used in qualitative analysis (36 mentioned in data analysis, abstract and demographic information in results give information on 43 participants in the semi-structured interview). Analysis looks superficial, rather than a clear in-depth development of themes. Applicability – note these participants had been assessed as having inadequate knowledge of how to deal with stressful situations – 48% of the recruited sample were assessed to have adequate knowledge. Likely to reflect the knowledge gaps resulting from one specific educational programme. Reported categories relevant to RQ 1.1 in terms of overall aims of information and support (but not specifics on various situations of stress) and the format in which this might be usefully delivered.

Study	Boyse et al (2014)[1]
Aim	To characterize early parent caregiver experiences and needs in CAH, with a focus on contextual factors that can be modulated through education and support delivered by health care providers or via the newborn screening system.
Population	Parents of children with CAH recruited from a larger study to pilot web-based materials for parents of newborns identified by newborn screening (NBS). Invitation letter sent out. At the time of enrolment, two of the four families also had an older child with CAH. The first affected child (two girls, ages 5 and 6 and two boys, ages 8 and 11) was the focus of the current study.

Study	Boyse et al (2014)[1]
	Characteristics: n=6; male n=2, female n=4 from 4 families.; age not reported. White/non-Hispanic n=5, Asian/pacific islander n=1. Education: high school n=1; some college n=2; college graduate n=2; graduate degree n=1. Employed/self-employed n=5, FT parent/caregiver n=1.
Setting	Parents of children with CAH recruited from a larger study to pilot web-based materials for parents of newborns identified by newborn screening (NBS) in United States.
Study design	Qualitative study Parents were asked to reflect on time after birth of their first child (retrospective)
Methods and analysis	Individual, semi-structured telephone interviews lasted 45–90 minutes; parents were asked how they learned about CAH and its management, including contextual factors in the process. They were also asked to comment on how they feel their needs could have been better met during that time. Interviews were audio-recorded, transcribed, and coded. Conventional content analysis was used to produce a description of parents' experiences organised by theme. Data analysis consisted of identifying significant statements and then developing “clusters of meaning” or themes. Coding categories were developed inductively and were derived directly from the raw data. Two coders, the interviewer, and the transcriber, independently read the transcripts, noted important statements that emerged on repeated readings, and assigned preliminary codes. In subsequent readings, each independently consolidated and refined the coding scheme, and categorized codes to form meaningful clusters. Coding schemes were then compared and contrasted, referencing the transcripts to inform joint decisions about how to reconcile minor differences. Inter-rater agreement was high with no substantive discrepancies, and consensus on the initial coding scheme was easily reached. The coders then employed the resulting coding scheme to independently code the transcripts. Subsequent meetings resulted in agreement on coding for all six interview transcripts.
Findings	
	Three themes identified:
	Communicating health information: experienced difficulties in way info way communicated to them when child first diagnosed (incomprehensible medical jargon). Parents did self-directed searching for supplementary information but received no information on evaluating appropriate healthcare information.
	Unmet needs: Easy to digest basic, factual, information wanted at first diagnosis, including how to give medication at home, a ‘survival guide’ and referral to trustworthy information. Desire for more information over time e.g., on financial matters, paying for care. A need for reassurance also expressed. Lack of true ‘medical home’ i.e., endocrinologist/primary care/themselves are central coordinators of care. Parents of girls viewed genital surgery as a necessity rather than a decision point in care of the child.

Study	Boyse et al (2014)[1]
	Social support: Although some practical and emotional support received from family and friends, there was a strong sense of value of peer support from other parents of other children with CAH. Congenital Adrenal Hyperplasia Research Education and Support (CARES) Foundation viewed as an important resource for information and support, specifically for a way to connect with similar others.
Funding	The Michigan Department of Community Health and the Eunice Kennedy Shriver National Institute of Child Health & Human Development
Limitations and applicability of evidence	Note this study reports experiences from a small sample of 4 families, recalling experiences of 5-11 years ago. For three of the four families, the birth of a subsequent CAH-affected child prior to the interview poses the risk of confounding recollections of the first affected child. Findings only applicable to parents of infants diagnosed with CAH during newborn screening, not other forms of AI or other route to diagnoses of CAH. Methods scant of detail on use of topic guide, and some lack of clarity in analysis methods.

Study	Malstram et al (2018)[4]
Aim	What aspects in everyday life with AAD are important? What possibilities and challenges do persons with AAD experience in everyday life?
Population	Purposive sampling of patients from the Department of Endocrinology, Metabolism and Diabetes at Karolinska University Hospital (Sweden), who were taking part in an ongoing self-management education program for persons with adrenal insufficiency during the period of September-December 2015. Invitations to all with primary adrenal insufficiency (Addison's disease) over age 18 years and able to communicate in Swedish. Exclusion criteria: having been diagnosed with adrenal insufficiency other than the primary kind and having one or more concomitant conditions with severe physiological or psychological symptoms. Characteristics: n=5 with AAD; n= 3 male, n= female 2; age range 40-77 years, lived with AAD 1-57 years; n=3 employed, n=2 retired. n=5 Swedish; n= 4 had family, n=1 no family.
Setting	Outpatients from the Department of Endocrinology, Metabolism and Diabetes at Karolinska University Hospital (Sweden), who were taking part in an ongoing self-management education program for persons with adrenal insufficiency during the period of September-December 2015.
Study design	Qualitative study using photovoice methods

Study	Malstram et al (2018)[4]
Methods and analysis	This photovoice method had 3 stages: generation of data had three overall stages: identifying themes for weekly discussions, taking photos each week, selecting photographs, sharing and contextualizing stories, and identifying central issues and them. The group met for 6 sessions over 7 weeks. After a first orientation session, the group reached consensus in wanting weekly 2-hour sessions, with each member sending 3–5 photographs by email to the first author one day before each session. Each subsequent session started with a review of the previous week followed by a show and tell of the members' photographs. Researchers facilitated the PVM sessions. In this way, the members of the PVG generated data both visually and verbally from individual and group reflections as well as joint discussions. The sessions were audio-recorded and transcribed, and the first author wrote reflective field notes after each session. Analysis by photovoice methods and thematic analysis. A software package was utilized to reduce the raw information and to code, organize, and sort the data. Data linked to the aim of the study were assigned codenames, and then codes with similar meanings were merged and preliminary themes were created. The first and last authors then compared and integrated the themes from the thematic analysis and the PVG analysis. All members from the PVG also volunteered, on several occasions, to read and validate the final findings and gave comments that the authors incorporated to the final scientific presentation. The thematic analysis of text material from the PVG sessions helped to illustrate themes with stories in combination with photos. Although no new themes were identified, the researchers see the analysis as strengthened by working both inductively and deductively. This allowed for a building on concepts and theories with an occupational perspective, to understand everyday life with AAD.
Findings	Five themes were identified:
	Individual and fine tuning in everyday life: Everyday symptoms such as physical and mental fatigue have to be regularly addressed through fine tuning of the person's individual medicine intake, activity- and stress levels. Fine tuning in everyday life was also described as being very individual – stressors are individual and so are the required adjustments in everyday life. Fine-tuning and self-care (eg time to rest, thinking preventively, being observant and cautious, avoiding stress and infections) are needed to avoid risk of adrenal crisis.
	It is not how it was: Majority described everyday life with AAD as complex, involving negotiations and feelings of insecurity regarding the everyday management of the disease. Several aspects could act as barriers to wellbeing, including increased sensitivity to stress and infections, reduced strength and energy, difficulty recovering after strain, and an increased need for rest due to both physical and mental fatigue – dual view of the disease, often invisible. They perceived that they reacted to and were made unwell by a much wider range of influences than described by their healthcare providers. They also thought the recommendations regarding their medicine management were limited and difficult to implement. Although many recommendations were the same for all persons with AAD, the group argued that their needs were unique. members' experiences did not match the information they had received from their healthcare providers.
	The power of knowledge and support: Requirement for equal and adequate knowledge and information. Group-members said that the little knowledge and information that did exist was not always equal, adequate, or accessible to either of them as persons with AAD or people in their surroundings. They argued that in order for them to make informed decisions they needed accurate knowledge about symptoms, medicine management, and everyday life. Lack of opportunity for self-management education and support regarding AAD

Study	Malstram et al (2018)[4]
	was a big barrier in everyday life. They desired extended information and support, regardless of how long they had had the disease; it was especially important at the beginning, so one would know what to expect from life with the disease. Sharing experiences with others in the same situation was helpful. They also expressed that being part of the group was valuable both for knowledge and support. Participants saw support from the healthcare system and their surroundings as a facilitator for their wellbeing. Being able to ask questions of experts and having people in their close environment who had knowledge about the disease were important to feel safe. Reluctance to being open about disease – related to a general lack of societal knowledge about what it's like to manage and live with AAD.
	Becoming the expert in an uncertain context. Lack of healthcare team and societal awareness of AI means that people with AI are forced to become their own experts. Their knowledge was based on lived experiences rather than standardised recommendations from healthcare providers. Everyday lives consisted of continuous individual assessments and negotiations, which included weighing information and knowledge against their symptoms and learning the skills they needed to cope. Uneven and inadequate knowledge about the disease had often been experienced, particularly in contexts such as emergency care, primary care, and other specialist care (even in different endocrinology departments) – leads to confusion and mixed messages
	Finding balance and paving new ways: Many had adapted to having AAD be adapting e.g., work assignments or hours (requirements for this is individually based depending on their perceived everyday stress and ability to cope with stress). Other adaptations include incorporating time for recouperation between activities and leading a calmer life. Meaningful and engaging activities gave the group-members energy, recuperation, and a sense of being well rather than ill. Extended planning and sticking to routines regarding sleep, nutrition, and exercise were central to maintaining wellbeing. If their routines failed and their disease worsened, this could greatly disrupt their wellbeing and balance because their focus then had to shift to extended selfcare.
Funding	Swedish Society for Medical Research.
Limitations and applicability of evidence	Features of analysis, including member checking, use of reflective field notes, and use of participants to corroborate thematic analysis, suggest a thorough approach to qualitative analysis. Sample was small. The way the participants were approached meant that those who had not yet attended the self-management education for AAD were excluded. As were those who did not experience the disease as challenging and therefore chose not to be included. This may have affected the results of the study. It is not therefore possible to discuss whether other persons with either AAD or other kinds of adrenal insufficiencies would experience the same barriers and challenges in everyday life as this particular sample.

Study	Simpson 2018[7]
Aim	1. capture the experiences of parents of young children with AI/CAH including their views on psychosocial impact of living with and managing the condition and 2. further explore the emerging themes and related issues with larger numbers of parents through an online survey.
Population	A purposive sample of 20 parents (14 mothers and 6 fathers) of 17 children (nine female and eight male). All were based in the UK and were recruited via the Living with CAH support group. Recruitment material (an advert and information sheet) was disseminated to potential participants via newsletters, members' news alerts and websites, inviting parents to contact the research team. The majority of parents had children aged 6 or younger at the time of the interview (range: 3 months-10 years). Three parents with children over the age of 6 took part and were asked to focus on their experiences during the child's first 6 years of life.
Setting	The majority of the interviews took place in the family's home (UK).
Study design	Mixed methods study (qualitative and quantitative) qualitative semi-structured interviews followed by an online survey
Methods and analysis	Semi-structured qualitative interviews were conducted with parents in the UK. The interviews encouraged parents to disclose a full and rich account of their experiences as well as allowing the researcher to maintain a focus and guide the interview, rather than dictate its direction. Interview questions were open ('tell me about…') and designed to gain a better understanding of parents' experiences and the psychosocial impact of AI/CAH, from diagnosis to the present. Interviews typically lasted 1 hour. The interview topic guide, informed by findings from the initial literature review, included diagnosis, treatment, impact, information and support and hopes and concerns for the future. Parents whose children were aged over six were asked to focus on their earlier experiences (i.e. their child's first 6 years of life). Interviews took place between September and December 2014. A small number of the interviews were conducted with both parents present, although typically just one parent chose to take part. Interviews were transcribed verbatim by a professional transcribing company and transcripts were read and checked for accuracy. The transcripts were then analysed thematically by a member of the research team with the support of assisted qualitative data analysis software, NVivo 8. The coding structure developed over time, as data were coded under both anticipated themes (such as those identified in the literature and those included in the topic guide) and new emergent themes. Following the initial steps in the analysis process, in order to clarify the main topics under each overarching theme, all of the coded data were exported to theme-specific files and a further round of analysis was conducted. A second member of the research team checked the coding structure and the data coded against it. Research team members met regularly throughout the data collection and analysis stages of the study to discuss and clarify emerging themes. Findings were also discussed with a wide range of stakeholders including parents and professionals of different disciplines (via project steering group meetings and conferences), providing the opportunity to consider a variety of insights and interpretations.
Findings	Diagnosis: Parents faced challenges associated with clinicians' low awareness of CAH and some struggled to convince general healthcare professionals (e.g. general practitioners and health visitors) of the significance of their child's symptoms; they had to 'fight'

Study	Simpson 2018[7]
	for a diagnosis. There were differences between professionals and hospitals particularly in relation to awareness of the condition. There were also inadequacies in the way that the diagnosis (or potential diagnosis) was given to families with some children only being diagnosed as a result of them going into adrenal crisis.
	Treating and managing the condition: Four sub-themes emerged- 1) Medicating correctly: Parents found that there was a large burden associated with having to get the right dose of medication to their child at the right time and frequency. They found it challenging that they not only had to follow routine medication regimes but were also responsible for recognising when to adapt and adjust medication during illness and stress. Preparation of medication was also an issue particularly hydrocortisone. 2) Delegating treatment responsibilities to childcare agencies was difficult. Some parents had to give up work until the child was old enough to join nursery or school in order to delay or manage the transition of care to others. 3) Disruption to family life due to frequent medical appointments and the time they may require which also impact on siblings and the affected child's school life. 4) Adapting to new routines as parents adjust to their new caring roles especially after leaving the supportive environment of the hospital with their newborn babies.
	Thinking about the future: Parents reported feeling worried about their child's future and had concerns about the possible long-term effects of the condition and medication. They worried about whether the child would grow and develop normally and had concerns about how their child would cope with medication and surgery. Parents also had concerns about how girls born with ambiguous genitalia when they're older, transition from paediatric to adult health and they did not want their child to grow up feeling different from their peers.
	Practical and emotional support: Parents talked about various sources of practical and emotional support that they found helpful and recognising when their own support needs were not being met. They valued the support beyond that of the supervising doctors such as support from psychologists and specialist nurses and being able to connect with other families through support groups. However, parents did face unmet needs for practical and emotional support for example due to lack of knowledge of the condition amongst local health teams.
Funding	The study was initially funded as part of the TAIN project (www.tain-project.org). The TAIN project was funded by the Seventh Framework Programme (CORDIS FP7) of the European Commission, HEALTH. Further funding for the study was provided as a Research Agreement between Genetic Alliance UK and Diurnal Ltd.
Limitations and applicability of evidence	Most participants were recruited via support organisations which may bias the results. Potential for recall bias as parents of children over 6 years were asked to describe their experience in the first 6 years of their child's life.

Study	Shepherd et al (2017)[6]
Aim	To explore if patients with PAI have sufficient knowledge and understanding of the condition; knowledge of how and when to adjust steroid replacement during acute illness or stressful event; and been provided with the required information.
Population	Adult patients with primary adrenal insufficiency (PAI). Planned to recruit 15 participants, data saturation achieved after 10 interviews. Characteristics: n= 10; n=2 male and n=8 female. Mean age of 47 years (age range 21 to 63 years). Median duration of PAI of 19 years (range 3–46 years). All were White Europeans. n=7 previous hospital admission due to adrenal crisis.
Setting	Two hospitals in a single tertiary NHS Trust, England
Study design	Mixed methods study including qualitative semi-structured interviews and review of participants' healthcare records.
Methods and analysis	Pragmatic purposive sampling was used to approach participants from waiting area of endocrine clinic. Those interested in taking part contacted researcher at a later date. Inclusion criteria: participants 18 years old or over, English speaking and with an established diagnosis of PAI based on endocrinologist diagnosis, and usually administers their own medication. The lead author (an endocrine specialist nurse at the centre) was known to the patients. Individual face-to-face, semi structured interviews and review of participant's health care records were carried out. Interviews lasted up to 60 min and were conducted at a location of the participant's choice. A conversational interview technique was utilised with the aid of a semi structured interview guide, which was developed from key themes in the literature and from the clinical researchers' experience in the field. This interview guide allowed flexibility to accommodate new topics and concepts introduced by the participants. Data analysis was a thematic content analysis: a stepped process of identifying themes and categories that 'emerge from the data'. Interview data was reconfirmed with participants to determine accuracy of understanding and allow them to add further data. Field notes were maintained regarding setting and participant and an auditable decision trail was maintained by documenting raw data and data gathered was peer reviewed by academic supervisors.
Findings	Four categories were identified:
	Addison's disease and hydrocortisone replacement: Participants identified signs and symptoms of PAI prior to diagnosis. All the respondents described the length of time to diagnosis as a problem, receiving many differential diagnoses, despite seeking medical attention on several occasions prior to diagnosis. Participants described the unwanted effect of medication, particularly bone health.
	Stress and corticosteroids: Good understanding of the need to adjust medication. Medication intake was bound to a prescribed rigid treatment regimen which required rather complex and demanding self-care. Reliance on HCPs as the expert and relied on them for advice and extra medication (even if they were incorrect). Two participants had an emergency hydrocortisone injection kit. All participants wore emergency identification (steroid card/medical ID jewellery).
	Patient compliance/adherence: There was a noticeable difference in the quality and quantity of education provided to participants on pre and post diagnosis from healthcare professionals. Several respondents felt they were given insufficient knowledge and advice and

Study	Shepherd et al (2017)[6]
	indicated that they would have liked to have received more information. Three support systems; family, healthcare professionals and voluntary were identified as important to, and relied upon by, the participants. Family provided substantial support when it came to the management of the participants' condition and when seeking a diagnosis. E.g., relied on assertiveness of family during intercurrent illnesses. This was related to the administration of emergency treatment when seeking urgent medical attention. Mixed response to HCP support – some felt had important rapport, others felt did not receive HCP support. Support from voluntary self-help groups was not always seen as a priority by participants.
	Transition: The psychological progression involved in adapting to change, from pre diagnosis to their present situation going through a process of 'reeling' (a finale to a recognizable existence at time of diagnosis), 'dealing' (a static stage during which time they reported feeling overwhelmed and isolated, self-absorption to try to reclaim themselves) and 'healing' (acceptance of the diagnosis and adaptation, feeling of becoming normal again)
Funding	No funding was sought for the study.
Limitations and applicability of evidence	The small sample was predominantly female, so applicability of findings to males limited. Notable that the interviewer was known to the participants; so, this lack of independency could have impacted on interviewee responses.

Study	Fleming et al (2017)[3]
Aim	To describe circumstances surrounding adrenal crisis events in children with CAH; to explore parents' perceptions of the consequences of having a child with a life-threatening condition; and to examine a relationship between parents' perceived management ability and the impact CAH has on the family.
Population	The purposive intent of the interview sample was to achieve maximum variation in terms of both the demographic profile of families (e.g., parents of boys and girls, families having children of varying ages, families from different geographic areas of the USA, etc.) and their experiences managing adrenal crisis events. Parents reporting both high and low impact of the condition on their family as well as management ability (as identified in the questionnaire stage of the study) were included. Characteristics: n= 16 parents of children with CAH; n= 7 male/n=9 female from 9 families (n=7 mother/father dyads = 2 single mothers); age of parents not reported. Age of children range 2-15 years, sample reported to be 'heterogeneous in nature when examining demographic variables such as family income, age of the child, and where in the USA they resided'. The majority of participants were Caucasian.
Setting	Parents of children with CAH identified by Congenital Adrenal Hyperplasia Research Education and Support (CARES) Foundation, a support organisation in the US.

Study	Fleming et al (2017)[3]
Study design	Mixed methods study including semi-structured interviews. Semi-structured interviews were conducted to elicit more detailed descriptions of parents' experiences in managing CAH-related crises and their perceptions of how the consequences of living with the threat of crisis influenced their child's and their family's life.
Methods and analysis	Parents were recruited through CARES Foundation (CARES), a non-profit organization, based in New Jersey, which provides support to families having a child with CAH. To be included in the study, the parent needed to be over the age of 18, English speaking, and have a child between the ages of birth and 18 years diagnosed with classic, salt-wasting CAH and free from any other complex health conditions. A parent was defined as a person who lived in the same household with the child and had the responsibility of caring for the child and managing the child's CAH, even if the parent was not the biological mother or father. Recruitment for the study consisted of an "Invitation to Participate" letter that CARES emailed to its members who had previously expressed an interest in participating in the research. Semi-structured telephone interview using an interview guide (with each parent participating separately). Topics for the interview guide focused on parents' description of their crises management experiences and their perceived competence and ability to manage the condition based on the three components of the Family Management Style Framework (FMSF). Qualitative data collection took place after online survey data collection (in a sub-sample of participants of phase 1) and continued until common themes repeatedly emerged to the point of saturation. All interviews were coded using a combination of a start list of codes based on the FMSF and the online measures and codes inductively derived from interview data. The analysis of interview data first focused on developing a thematic summary of each parent's interview, then completion of narrative family case summaries of each interview. In families where both parents participated, the analysis addressed the extent to which parents had a shared or discrepant thematic profile to look for varying patterns of family management. Additionally, comparisons were made across all parents' thematic summaries and across all families to provide a greater understanding of the nature and range of perceived consequences, for a variety of families, of having a child with CAH.
Findings	
	Definition of the situation: Certain aspects of their child's CAH management were going very well such as administering daily medication, their child's current height and weight, and their child's performances in school. Differences in families of children with CAH Vs other families identified due to extra attention child with CAH required (e.g. not allowing non-family members to babysit). When asked what the most important information was to relay to parents having a child just diagnosed with the condition, the majority of parents responded that being prepared to manage an adrenal crisis event was paramount. Parents within same dyad 'on the same page' and condition becomes easier to manage over time (especially once age 5 as by then child could communicate how they were feeling physically and emotionally. Adrenal crisis events were described as inherently stressful, and parents stated that knowing that their child could die if their response was not effective was both overwhelming and terrifying. Over time, parents developed a daily routine for condition management that they viewed as manageable. However, during illness and adrenal crisis, there were management challenges, and during these times, the parental view of the condition and the child would temporarily change.

Study	Fleming et al (2017)[3]
	Management behaviour: Parents described daily management of CAH as relatively straightforward, consisting of giving their child oral steroids two to three times a day, sometimes in a highly structured routine that could not be compromised. Discussed making a conscious choice to treat their child normally and not unnecessarily restrict activities because of the condition.
	Perceived consequences: Parents described how efforts to incorporate CAH management as part of the usual family routine were successful; however, unpredictable, acute illnesses and the possibility of adrenal crisis could dramatically disrupt that routine. Parents also expressed concerns for their child's health and wellbeing regarding puberty/adolescence as well as their anticipation that they would have less control over the treatment regimen and response to crises as the child becomes a young adult. Parents stated they felt CAH had minimal impact on the siblings; however, parents noted that siblings did experience distress during adrenal crisis episodes in their child with CAH. for some parents, having a child with CAH resulted in challenging reproductive decisions (e.g., not having further children, opting for prenatal treatment of dexamethasone, use of preimplantation genetic testing. A recurrent theme concerning the perceived consequences for families having a child with CAH was the need for additional or special planning, e.g., family planning, planning for potential adrenal crisis events, and planning for their child's health and safety as they grow into adolescents and young adults.
	Contextual influences on family management: Parents stated that although they were satisfied with the relationships they had with their current paediatric endocrinologists, providers did not offer support to them emotionally and did not refer them to family support groups—local nor national. parents from five families described not being appropriately prepared by their initial providers for adrenal crisis events. Parents stated that their current providers have educated them on how to administer the emergency injection of hydrocortisone; however, the process had been demonstrated only one time by either their paediatric endocrinologists or their staff members (i.e., nurses, physician assistants, medical assistants). Four parents voiced concern that one-time instruction was insufficient in terms of feeling confident in their ability to effectively manage an adrenal crisis. Parents who expressed satisfaction in the interviews regarding how their providers have prepared them to handle adrenal crisis events described being taught how to administer the injection by a nurse or doctor face-to-face. Parents described educating their child's school nurse or day-care provider on CAH and reviewing injection instructions with school nurses on a yearly basis. Overall, favourable experiences with school personnel were reported by processes could be lengthy and repetitive when staff/schools changed.
	Social network: Fear over their child becoming ill while under the care of the babysitter, not knowing how much instruction to give the babysitter regarding the injection (preferred family babysitters). Mixed feelings about extended families – some did not understand the challenges of CAH, others were supportive and helpful. Parents relayed how sports participation was a source of concern and described fears that physical exertion might trigger an adrenal crisis; however, parents also stated that they wanted their children with CAH to participate in sports because of the benefits, both socially and physically, associated with being on a sports team. Parents discussed the importance of instructing coaches about the signs and management of a crisis. Some parents chose to leave their paediatric endocrinologist because of dissatisfaction with their level of knowledge.
Funding	Funded by a National Institute of Nursing Research Grant, an American Nurses Foundation/SNRS Research Grant, and a CARES Foundation Research Grant.

Study	Fleming et al (2017)[3]
Limitations and applicability of evidence	Recruitment via voluntary organisation CARES, so only reflective of views of parents who have opted into additional support from CARES and may be highly motivated to seek information and support. It is also possible that they are more knowledgeable than other parents of children with CAH who have not sought such CARES support. Thematic analysis deductive and strongly based on the FMSF theoretical framework.

Study	Carroll (2018)[2]
Aim	What themes on HRQOL and factors that may contribute to the HRQOL of children with CAH emerged during interviews among: a. children with CAH? b. caregivers of children with CAH?
Population	Recruited via emails to CARES Foundation members and through flyers at children's hospital endocrinology clinics. Inclusion criteria: female child between the age of 7-18 years old at the time of enrolment; child has diagnosis of CAH due to 21-hydroxylase deficiency; caregiver over the age of 18 at the time of enrolment; the ability to read, understand, and speak English; the ability to understand the study and provide consent/assent to participate. 20 child-caregiver dyads participated in the QUAN and QUAL components of the study and five child-caregiver dyads participated only in the QUANT component. The sample included female children (age 7-18) who had been diagnosed with CAH and one of their caregivers. Demographic characteristics were only presented for the full sample of 25 child-care-giver dyads (below) rather than the 20 that participated in the QUAL component of the study only. Characteristics of children: n= 25, all female, median age 11 years (range 7 to 18); 60% classical CAH diagnosis; 40% non-classical CAH diagnosis; ethnicity White (72%), Black or African American (12%) and other (12%). Characteristics of caregivers: n=25, n=23 female, n=2 male; median age 45 years (range 29-62); ethnicity White (76%), Black or African American (12%). Most caregivers had completed at least 2 years of college.
Setting	United States, convenience sample recruited via CARES Foundation and a children's hospital endocrinology clinics.
Study design	Mixed methods study including qualitative
Methods and analysis	Semi-structured telephone interviews conducted with children and their caregiver. The interview guide consisted of 10 broad questions with a subset of questions for each broad category to encourage sharing information in greater details and discourage acquiescence. The first three questions solicited information about communication and disclosure of diagnosis to others such as family members, friends, and other people in the caregiver and child's life. Caregivers were asked about how they talk about CAH with the child, and children were asked how they talked about CAH with their caregiver. The next two questions transitioned into children's and caregivers' perception of the child's health, and the child's experience living with CAH. There was one question that addressed peer relationships and the child's ability to get along with others. The following two questions related to the child's self-esteem and sense of belonging. The next question focused on what was most important to the child and how to improve the lives of children with CAH. The last question summarized what was heard in the interview and asked the participant to validate, confirm, correct, and add to what was

Study	Carroll (2018)[2]
	heard by the interviewer. The interview with each participant lasted approximately 30 to 90 minutes. The interview was audio recorded, and the audio recorder was visible to the investigator, the child, and caregiver. All interviews were transcribed and entered into Nvivo. Descriptive content analysis using a hermeneutical, phenomenological framework was applied to describe children's and their caregiver's perceptions of HRQOL and lived experiences by theme. Data analysis consisted of line-by-line coding of the interview data. Recurring codes from the child and caregiver interviews were aggregated into categories and themes. Trustworthiness was explored through credibility and reliability to demonstrate integrity of the qualitative findings (i.e. subsample of respondent validation procedures were carried out)
Findings	Child theme 1) living with CAH - subcategories of *knowledge about diagnosis; health; limitations; friends; adaptation.* Children get information about diagnosis from their caregiver, including the need to take medication. Children believed they were in good health. Limitations associated with schedule and timing of medications. Friends help with medical management. Adaptation was defined by children's attitudes, perceptions, and acceptance in living with CAH. Varied responses about self-esteem. Many children take the medication themselves.
	Child theme 2) normalcy. Children describe their health identity as normal.
	Child theme 3) disclosure of diagnosis. Often only close family, friends and school personnel would know about the diagnosis. Otherwise, information shared on a need-to-know basis.
	Child theme 4) feelings associated with having CAH. Social stigma, awareness of need to take medication.
	Child theme 5) what should we know. Adolescents have worries and fears that HCPs should know about (eg growth, fertility). Social support from family and friends is important. Desire for lives with CAH to be improved by de-stigmatising and to feel normal.
	Caregiver theme 1) living with CAH. Living with CAH impacted some aspect of the child's life. Some described it as "challenging", "a bit stressful", "hard", and "embarrassing.". Subcategories of *communication; child's health; child's management of disease; normalcy; and adaptation.* Recounts of communicating with child about their CAH matter-of-factly, age variable. Several commented on the need for universal language to communicate with not only the child, but with other individuals in their life. Caregivers overall felt children were healthy but some concerns re weight gain and getting sick more often. Over time, child learns to take their medicine on their own and becomes more involved at medical appointments. Caregiver treats childlike normal. Caregivers viewed adaptation as a process that involved learning how to adjust and accept the situation. Adaptive methods of dealing with CAH were exhibited in the child's attitude, behaviour, and ability to connect and engage in social activities with others. Sports, being physically fit, family, friends, and accomplishments were all things caregivers believed influenced self-esteem and fostered adaptation. Weight gain, wanting to "fit in", and "wanting the attention and approval of their siblings" were associated with negative self-esteem.
	Caregiver theme 2) feelings of the caregiver. At diagnosis, feeling anxious and overwhelmed. Moving to concerned, fearful, cautious, and protective over time. Fears and concerns about genital surgery outcomes. Fear that if child gets sick, injection not given in time. Feel alone as no one to talk to about issues.

Study	Carroll (2018)[2]
	Caregiver theme 3) disclosure. No problems in caregiver disclosing information to child (truthful, honest and willing to answer and share as much information as the child needed). Hesitancy disclosing CAH outside close family (term AI preferred over CAH).
	Caregiver theme 4) what we should know. Caregivers found it challenging to identify what the child worries or fears with regards to CAH. Social support from friends and family was most important to the child. They believed that being able to connect and interact within that social network without fear of being stigmatized was essential to the child's life. Strong desire that HCPs are better informed/educated on AI. Frustration about many negative experiences with healthcare providers.
	Caregiver theme 5) improvements. Education, social acceptance, research, camps, financial support, and support groups were thought to improve children's lives. As previously mentioned, caregivers were frustrated about the lack of education between health care providers so more education for providers was listed at the top for improvement e.g., understanding that CAH can be life threatening. Caregivers also believed that there should be more education for themselves and "a way to explain it [CAH] to others." Social support in the form of support groups for children, caregivers, and families was believed to also improve the lives of children. Several caregivers mentioned that more support is needed for children themselves and more understanding for the parents (huge responsibility to hold alone).
Funding	Beta Theta-at-Large chapter of Sigma Theta Tau International Honor Society of Nursing, the University of Tennessee Health Science Center College of Nursing, and the Cares Foundation of New York
Limitations and applicability of evidence	Note the main focus of the study was on quality of life. Only small aspects of the final themes refer to information and support. No major concerns regarding methods of data collection and/or analysis, though the demographic characteristics of the qualitative sample only were not reported. Limitation due to no reporting of the 20 child-caregiver dyads who took part in the qualitative part of study only. Demographics of 25 child-caregiver dyads who took part in qual and quant parts only available.

Appendix E GRADE-CERQual tables

E.1 Qualitative evidence summary

Table 5: Summary of evidence

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Theme 1: Improve awareness that stressful situations require increased dose of hydrocortisone [adults only] [4, 6, 8]					
3	Semi-structured interviews (2 studies) and a photovoice method study (1 study)	Need improvement in awareness that stressful situations require increased dose of hydrocortisone; requires an individualised approach to self-management [Adults only]	Limitations	Moderate concerns about methodological limitations [a]	LOW
			Coherence	Moderate concerns about coherence [b]	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) One study[8] with moderate issues due to discrepancy in reporting of number of interviews, and limited to only patients 'with inadequate AI knowledge' post stress-management education programme, and two studies[4, 6] with minor issues due to recruitment strategies.
(b) Moderate concerns about coherence due to some participants in one study[6] describing good understanding of the need to adjust medication.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Theme 2: Desire for more information and education[1-4, 6, 8]					
6	Semi-structured interviews (5 studies) and a photovoice method study (1 study)	Desire for more information and education on: medicine management and administration; adverse effects (or not) of hydrocortisone; preparation for adrenal crisis; decision-making in everyday life.	Limitations	Moderate concerns about methodological limitations [a]	LOW
			Coherence	Moderate concerns about coherence [b]	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy [c]	

(a) Moderate concerns about methodologic limitations due to minor concerns in 3 studies[2, 4, 6] about recruitment strategies/relationship with researcher, moderate concerns in 2 studies[3, 8] about discrepancies in number of interviews/rigour of analysis and severe concerns in one study[1] about similar issues but with additional concerns about ethical approval and clarity of data collection.
(b) Moderate concerns about coherence. The requirement for more information is consistent across all studies, but the examples of what that information should cover, does vary across studies.
(c) Minor concerns about adequacy. Sufficient data to support the requirement for more information, but data is less rich on the specific topics to be covered in the information.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Theme 3: Information and support to be available throughout journey of AI[1-4, 6, 8]					
6	Semi-structured interviews	Requirements for information and support to be available throughout journey of AI, especially at diagnosis but then repeated regularly (eg demonstration of hydrocortisone injections) and taking into account changes in life stage	Limitations	Moderate concerns about methodological limitations [a]	MODERATE

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	(5 studies) and a photovoice method study (1 study)		Coherence	No about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

(a) Moderate concerns about methodologic limitations due to minor concerns in 3 studies[2, 4, 6] about recruitment strategies/relationship with researcher, moderate concerns in 2 studies [3, 8] about discrepancies in number of interviews/rigour of analysis and severe concerns in one study[1] about similar issues but with additional concerns about ethical approval and clarity of data collection).

(b) Minor concerns about adequacy. Sufficient data to support the requirement for more information throughout lifetime with AI, but data is less rich on examples about repeated demonstrations of injections demonstrations or transition into adolescence.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Theme 4: Value of social support[1, 2, 4, 6]					
4	Semi-structured interviews (3 studies) and a photovoice method study (1 study)	Value of social support (from family, friends and peer-support groups)	Limitations	Moderate concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
			Adequacy	No concerns about adequacy	

(a) Moderate concerns about methodologic limitations due to minor concerns in 3 studies[2, 4, 6] about recruitment strategies/relationship with researcher; and severe concerns in one study[1] about similar issues but with additional concerns about ethical approval and clarity of data collection/analysis.

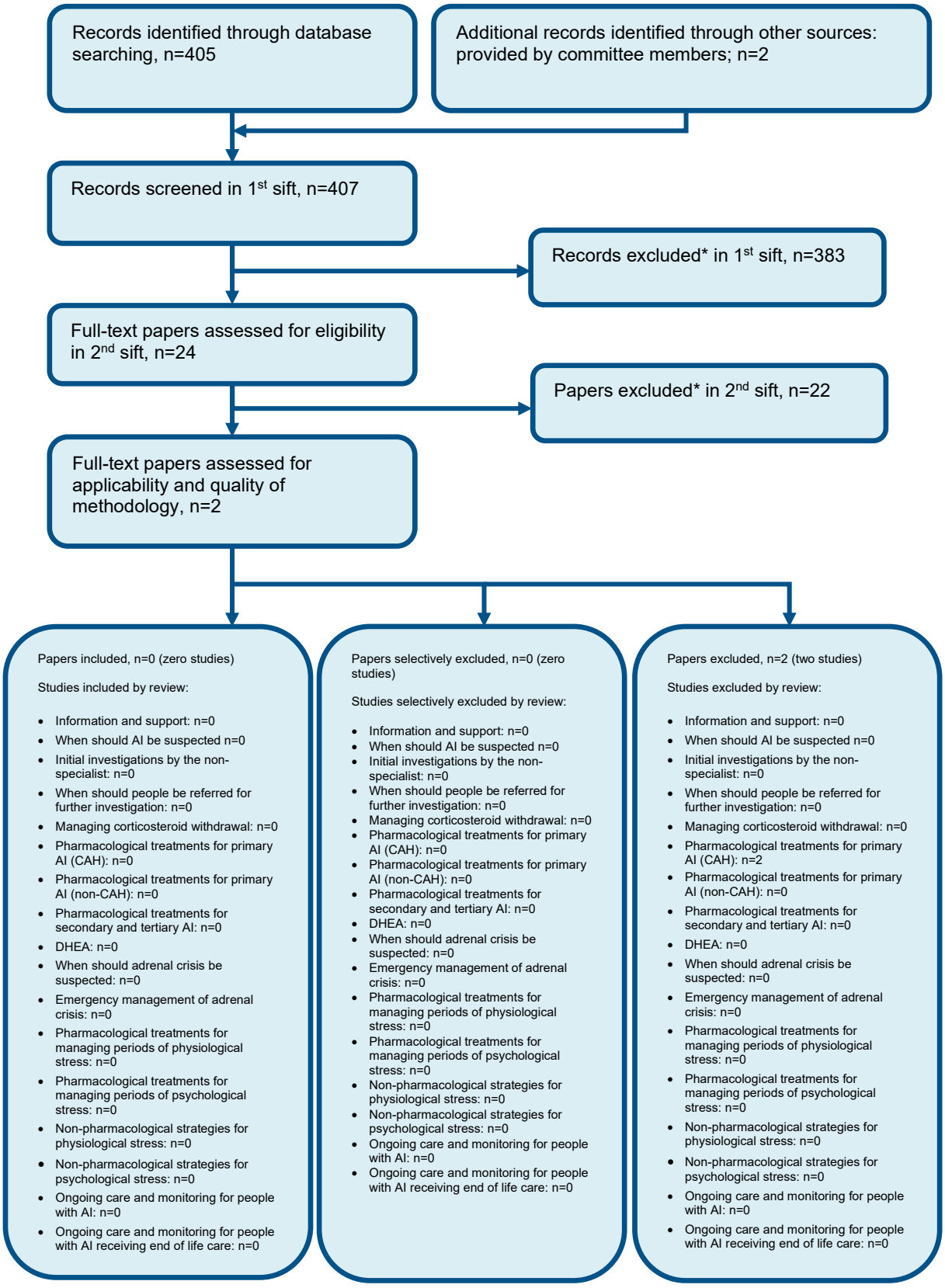
Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Theme 5: How to communicate requirements of managing AI to child's extended caregivers [Children and young adults with CAH only][2, 3]					
2	Semi-structured interviews (2 studies)	Desire for information and support in how to communicate the requirements of managing AI to others in child's life [Children and young adults with CAH only]	Limitations	Minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	Moderate concerns about adequacy [c]	

(a) Minor concerns about methodological limitations due to minor concerns in 2 studies[2, 3] about recruitment strategies/relationship with researcher and additional concerns in one study[3] due to analytic approach.
(b) Minor concerns about relevance due to one study[2] on female children only.
(c) Moderate concerns about sufficiency of data from only 2 studies.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Theme 6: Inadequate knowledge of AI by HCPs[2-4, 6]					
5	Semi-structured interviews (4 studies) and a photovoice method study (1 study)	Experienced inadequate knowledge of AI by HCPs and dissatisfied with the support and advice they provide.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Moderate concerns about relevance [b]	
			Adequacy	No concerns about adequacy	

(a) Four studies[2, 4, 6, 7] with minor issues due to recruitment strategies and/or relationship with researcher, and one study with an additional concern about analytic approach.
(b) Concerns about directness to the review questions, as participants comments are about the information and knowledge that healthcare professionals hold rather than information and support that people with AI would like to receive.

Appendix F Economic evidence study selection



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix G Economic evidence tables

None.

Appendix H Health economic model

No original economic modelling was undertaken for this review question.

Appendix I Excluded studies.

I.1 Clinical studies

Table 6: Studies excluded from the qualitative review.

Study	Reason for exclusion
Bharadwaj, M., Tyagi, V., Dabas, A. et al. (2021) Quality of life and disease perceptions in caregivers of children with Congenital Adrenal Hyperplasia. Medical Journal Armed Forces India	- Data not reported in an extractable format or a format that can be analysed - Study design not relevant to this review protocol *Quantitative study about QoL of care givers not information and support*
Bouziane, Toumader, Belmahi, Nadia, Salhi, Houda et al. (2020) Knowledge and attitude of patients with adrenal insufficiency. Annals of African medicine 19(4): 252-257	- Study design not relevant to this review protocol *Quantitative survey study, with closed questions assessing knowledge and skills relevant to AI.*
Burger-Stritt, Stephanie, Eff, Annemarie, Quinkler, Marcus et al. (2020) Standardised patient education in adrenal insufficiency: a prospective multi-centre evaluation. European journal of endocrinology 183(2): 119-127	- Study design not relevant to this review protocol *Quantitative questionnaire study pre and post education programme*
Burger-Stritt, Stephanie, Kardonski, Pavel, Pulzer, Alina et al. (2018) Management of adrenal emergencies in educated patients with adrenal insufficiency-A prospective study. Clinical endocrinology 89(1): 22-29	- Study design not relevant to this review protocol *Quantitative questionnaire study evaluating management of adrenal crisis prospectively.*
Carroll, Lacretia, Graff, Carolyn, Wicks, Mona et al. (2020) Living with an invisible illness: A qualitative study exploring the lived experiences of female children with congenital adrenal hyperplasia. Quality of Life Research: An International Journal of Quality-of-Life Aspects of Treatment, Care & Rehabilitation 29(3): 673-681	- Secondary publication of an included study that does not provide any additional relevant information *Secondary publication from Carroll (2018 thesis). Combines analysis of children and caregivers, where thesis presents these separately. Thesis included as this is closer fit to requirements of the protocol.*
Carroll, Lacretia, Graff, Carolyn, Wicks, Mona et al. (2021) Health-Related Quality of Life of Children with Congenital Adrenal Hyperplasia: A Mixed Methods Study. Journal of pediatric nursing 58: 88-94	- Secondary publication of an included study that does not provide any additional relevant information *Secondary publication from Carroll (2018 thesis). Combines analysis of children and caregivers, where thesis presents these separately. Thesis included as this is closer fit to requirements of the protocol.*
Chapman, S C E, Llahana, S, Carroll, P et al. (2016) Glucocorticoid therapy for adrenal insufficiency: nonadherence, concerns, and dissatisfaction with information. Clinical endocrinology 84(5): 664-71	- Study design not relevant to this review protocol *Quantitative study including a survey study satisfaction with information about glucocorticoids.*

Study	Reason for exclusion
de Bray, Anne, Tomas, Jon, Gittoes, Neil et al. (2020) Management of endocrine conditions at the end of life. British journal of hospital medicine (London, England: 2005) 81(5): 1-9	- Review article but not a systematic review - Study design not relevant to this review protocol *Review article about endocrine treatments for people at end of life (including those with AI).*
Godbout, Ariane, Tejedor, Isabelle, Malivoir, Sabine et al. (2012) Transition from pediatric to adult healthcare: assessment of specific needs of patients with chronic endocrine conditions. Hormone research in paediatrics 78(4): 247-55	- Study design not relevant to this review protocol *Quantitative questionnaire study about transition for multiple endocrinopathies.*
Kampmeyer, Daniela, Haas, Christian Stefan, Moenig, Heiner et al. (2017) Self-management in adrenal insufficiency - towards a better understanding. Endocrine journal 64(4): 379-385	- Study design not relevant to this review protocol *Quantitative survey study of people with AI regarding patient knowledge of their disease.*
Makaya, Taffy, Gilbert, Jennifer, Ryan, Fiona et al. (2018) Adrenal insufficiency, steroid sick-day rules and the paediatric endocrine nurse. Nursing children and young people 30(2): 26-31	- Study design not relevant to this review protocol *Quantitative questionnaire study about knowledge of sick-day rules.*
Repping-Wuts, H.J.W.J., Stikkelbroeck, N.M.M.L., Noordzij, A. et al. (2013) A glucocorticoid education group meeting: An effective strategy for improving self-management to prevent adrenal crisis. European Journal of Endocrinology 169(1): 17-22	- Study design not relevant to this review protocol *Quantitative study about self-management outcomes post information/education intervention.*
Singarayan, Vasantha, David, Anita, Ayyar, Vageesh et al. (2020) Study to assess the knowledge of caretakers regarding corticosteroid therapy in children with congenital adrenal hyperplasia - 21 hydroxylase deficiency. Journal of family medicine and primary care 9(6): 2814-2817	- Data not reported in an extractable format or a format that can be analysed - Study design not relevant to this review protocol *Quantitative questionnaire study about 'knowledge about GC therapy.*
van Eck, Judith P, Gobbens, Robbert J, Beukers, Joke et al. (2016) Much to be desired in self-management of patients with adrenal insufficiency. International journal of nursing practice 22(1): 61-9	- Study design not relevant to this review protocol *Quantitative survey study about self-reported quality of self-management.*
Vidmar, Alaina P, Weber, Jonathan F, Monzavi, Roshanak et al. (2018) Improved medical-alert ID ownership and utilization in youth with congenital adrenal hyperplasia following a parent educational intervention. Journal of pediatric endocrinology & metabolism: JPEM 31(2): 213-219	- Study design not relevant to this review protocol *Quantitative survey study pre-post an educational intervention on medical alert ID products.*
White, Katherine G (2019) A retrospective analysis of adrenal crisis in steroid-dependent	- Data not reported in an extractable format or a format that can be analysed

Study	Reason for exclusion
patients: causes, frequency and outcomes. BMC endocrine disorders 19(1): 129	- Study design not relevant to this review protocol *Quantitative questionnaire study focused on the circumstances of experienced adrenal crisis.*
Yeoh, Phillip, Czuber-Dochan, Wladyslawa, Aylwin, Simon et al. (2022) Lived experience of people with adrenocortical carcinoma and associated adrenal insufficiency. Endocrinology, diabetes & metabolism 5(4): e341	- Population not relevant to this review protocol - Systematic review used as source of primary studies *Population group potentially not in protocol - AI associated with adrenocortical carcinoma.* *Systematic review of quantitative studies*

I.2 Health Economic studies

None.