UK Kidney Association

The initial management of IgA vasculitis (Henoch Schönlein Purpura) in children and young people

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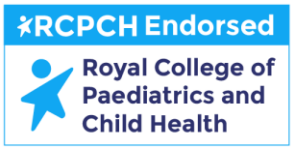
Endorsements

The National Institute for Health and Care Excellence (NICE) has accredited the process used by The UK Kidney Association to produce its Clinical Practice Guidelines. Accreditation is valid until December 2023. More information on accreditation can be viewed at www.nice.org.uk/accreditation



Method used to arrive at a recommendation/Grading the evidence

The guideline was developed under the endorsement of lead organisations (Appendix 1) and followed developmental stages including, forming the multi-speciality IgAV guideline development group (termed the UK IgAV GDG), developing and agreeing the scope, conducting systematic evidence-based literature reviews using pre-defined methodology and working in partnership with relevant stakeholders during a period of formal external consultation (stakeholders listed in Appendix 2). Clinical recommendations were derived from the topic areas and key questions that were identified by the UK IgAV GDG.

The UK IgAV GDG defined the population, intervention, comparator and outcome (termed 'PICO') to identify eligible evidence (Appendix 3). Search concepts were used to identify the relevant population and the disease in question (Appendix 4)[1]. The process of screening and identifying relevant articles was performed according to pre-defined eligibility criteria (Appendix 5) and aligned with the Cochrane Handbook for Systematic reviews of interventions, the RCPCH guideline process manual ('Setting Standards for the Development of Clinical Guidelines in Paediatrics and Child Health, 2020')[2], the UK Kidney Association clinical practice guideline development manual, the 'Appraisals of Guidelines for research and evaluation II' instrument[3] and supported by a knowledge and exchange librarian[4,5]. The identified articles were summarised and presented to the UK IgAV GDG during the development process. The papers were critically appraised for their methodological quality using the Critical Appraisal Skills Programme (CASP) checklists[6]. In cases of uncertainty regarding inclusion of studies, discussion occurred between the two members screening the articles. There were no cases of persisting uncertainty or disagreement where a third member of the UK IgAV GDG was required to assist in decision making. Searching of reference lists was included. No searching of grey literature and no hand searching of conference proceedings or journals took place. Three bibliographic databases were used to identify potential studies (appendix 6) and aligned with those recommended in the Cochrane Handbook for Systematic reviews of interventions[4]. All searches were conducted on 11th March 2022 and were used for a parallel document 'Clinical practice guideline: The management of complications associated with IgA vasculitis (Henoch Schönlein Purpura) in children and young people'. The key questions were split into topic areas (Appendix 7) and written to facilitate the systematic review (Appendix 8). The screening process to identify and select the articles relevant for this guideline is illustrated in the PRISMA diagram (Appendix 9). The literature review yielded 66 studies for inclusion. The members of the working group were presented with evidence

summaries of the literature relevant to each topic area. The working group used the synthesised evidence to form and grade the recommendations using the modified GRADE terminology to reflect the strength of the recommendation and the quality of the supporting evidence. The strength of the recommendation was split into two tiers, grade 1 is a strong recommendation where the benefits outweigh the risks for most patients, and grade 2 is a weaker recommendation where the risks and benefits are more balanced or remain uncertain. The strong (grade 1) recommendations use the wording 'we recommend…' whilst the weaker recommendations (grade 2) will use the wording 'we suggest…'. The quality of evidence is graded using alphabetical domains. Grade A evidence refers to high-quality evidence that is derived from consistent results from randomised controlled trials, or overwhelming evidence of other forms. Grade B is moderate quality evidence from clinical trials that may have some flaws or from other study designs with some strength. Grade C evidence is low-quality evidence from observational studies or trials with serious limitations. Grade D evidence is based on case studies alone or expert opinion. The quality of the evidence could be revised following discussion after review of the synthesised literature.

Conflict of Interest Statement

All authors made declarations of interest in line with the policy in the UK Kidney Association Clinical Practice Guidelines Development Manual. Further details can be obtained on request from The UK Kidney Association.

Contents

Executive Summary 7

Summary of recommendations 8

Quick reference guide 10

List of abbreviations 11

Glossary of terms 12

Background 14

Scope 14

Summary and rationale of recommendations 15

The classification of IgAV in children and young people 15

When to seek specialist advice for a child or young person with IgAV 16

The detection of nephritis in children and young people with IgAV 18

The management of musculoskeletal involvement in children and young people with IgAV 19

Summary of audit measures 20

Summary of research recommendations 20

Lay Summary 21

Lay version of recommendations 21

Lay research recommendations 21

Acknowledgements 22

References 23

Appendix 29

Appendix 1: Lead organisations 29

Appendix 2: Stakeholders 29

Appendix 3: PICO domains 29

Appendix 4: Search concepts 29

Appendix 5: Study eligibility 30

Appendix 6: Bibliographic databases 31

Appendix 7: Topic areas and key questions 31

Appendix 8: Key questions formatted for systematic review 31

Appendix 9: PRISMA diagram of selected studies 32

Appendix 10: The EULAR/PRINTO/PRES 2010 Classification criteria 33

Appendix 11: Definitions of severe clinical signs and symptoms 33

Appendix 12: Summary information poster: outline of methodology 36

Appendix 13: Summary information poster: recommendations 36

Executive Summary

IgA vasculitis (IgAV; also known as Henoch Schönlein Purpura) in children and young people is a common condition that typically presents to general practitioners or emergency physicians during the acute phase of the disease. It is a familiar condition to secondary paediatricians and it may require tertiary paediatric input. Despite its fairly frequent presentation, there are discrepancies in the management of patients and this hinders improvements. Aligning the initial clinical management of IgAV, through the use of nationally agreed best practice recommendations, will hopefully reduce differences in the care patients receive across the UK and improve recognition of features that may warrant more specialist input. The inclusion of a lay translation of the recommendations are designed to empower patients and their families to be involved in the initial management. We offer evidence-based practice guidelines, with research recommendations, covering the recommended initial management of IgAV in children and young people accompanied by suggested audit measures. This document aims to align care and standardise the management of children during the acute phase of the disease and it has been produced in parallel to a complementary document on the best practice guidelines for the complications associated with IgAV in children and young people.

At the time of writing there remains very limited research in this field and the quality of available studies was notably poor. The production and dissemination of these clinical practice recommendations will hopefully facilitate further studies, including well conducted clinical trials, thus strengthening the literature to contribute to evidence-based updates in due course.

Finally, I am enormously grateful to the multi-professional and lay members of the guideline working group for fully supporting this venture whilst providing encouragement and motivation to assist me in leading this project. Their dedicated time and effort in developing this guideline has been much appreciated, especially during an era of ever increasing workloads, and I have no doubt that the group have been united in their desire to rapidly improve outcomes for our children and young people.

Dr. Louise Oni

Chair of the UK IgAV Clinical Practice Guideline Working Group

Summary of recommendations

RECOMMENDATIONS FOR USE IN CHILDREN AND YOUNG PEOPLE UNDER THE AGE OF 18 YEARS WITH IGA VASCULITIS (HENOCH SCHÖNLEIN PURPURA)		
Number	**RECOMMENDATION**	***Grade***
Section 1: CLASSIFICATION OF IGAV IN CLINICALLY SUSPECTED DISEASE		
1.1	*We recommend that professionals follow the EULAR/PRINTO/PRES 2010 classification criteria of IgAV ([7]; appendix 10).*	1B
Section 2: SPECIALIST REFERRAL IN IGAV*		
2.1	*We recommend that specialist advice should be sought for children and young people with IgAV and the following clinical presentations (and symptoms or signs):* • *Severe GI involvement (definition: unremitting abdominal pain, protein losing enteropathy and/or GI bleeding; sub-specialist: paediatric gastroenterology/paediatric rheumatology)* • *Significant nephritis (definition: proteinuria UP: UC ratio of >250mg/mmol, nephrotic syndrome, nephritic syndrome and/or kidney insufficiency; sub-specialist: paediatric nephrology))* • *Central nervous system (CNS) involvement (definition: cerebral vasculitis presenting as neurological symptoms and/or signs; sub-specialist: paediatric neurology/paediatric rheumatology)* • *Pulmonary haemorrhage (definition: pulmonary vasculitis presenting with acute bleeding from the respiratory tract; sub-specialist: paediatric respiratory/paediatric rheumatology).*	1C
2.2	*We suggest that specialist advice should be sought for children and young people with IgAV and the following clinical presentations (and symptoms or signs):* • *Scrotal and / or testicular involvement (definition: orchiditis; sub-specialist: paediatric surgeon/urology)* • *Severe skin manifestations (definition: intense subcutaneous oedema, blistering skin and/or necrotic features; sub-specialist: dermatology/paediatric rheumatology)* • *Severe, unremitting, musculoskeletal involvement (definition: arthropathy that requires hospital admission to assist with symptom management and no signs of improvement; sub-specialist: paediatric rheumatology)*	2D
Section 3: NEPHRITIS SCREENING IN IGAV		
3.1	*We recommend that children and young people should have urinalysis testing performed frequently over a period of 6 months to detect a diagnosis of nephritis (for example weekly screening for the first 4-6 weeks then monthly thereafter).*	1B

3.2	*We <u>suggest</u> that blood pressure assessment should be performed in children and young people with IgAV at diagnosis and if there is evidence of nephritis.*	2C
Section 4: MUSCULOSKELETAL INVOLVEMENT IN IGAV		
4.1	*We <u>recommend</u> appropriate analgesia and rest for musculoskeletal involvement in children and young people with IgAV.*	1C

- We refer readers to the parallel guideline 'The management of complications associated with IgA vasculitis (Henoch Schonlein Purpura) in children and young people'.

Quick reference guide

Section 1: CLASSIFICATION OF IGAV IN CLINICALLY SUSPECTED DISEASE
We recommend professionals follow the EULAR/PRINTO/PRES 2010 classification criteria

Section 2: SPECIALIST REFERRAL IN IGAV
We recommend discussion with a sub-specialist in:
- *Severe, unremitting, GI involvement*
- *Significant nephritis*
- *Central nervous system (CNS) involvement*
- *Pulmonary haemorrhage*

We suggest discussion with a sub-specialist in:
- *Scrotal and / or testicular involvement*
- *Severe skin manifestations*
- *Severe musculoskeletal involvement*

Section 3: NEPHRITIS SCREENING IN IGAV
We recommend urinalysis testing is performed frequently over a period of 6 months.
We suggest blood pressure assessment at diagnosis and to support evaluation of significant nephritis.

Section 4: MUSCULOSKELETAL INVOLVEMENT IN IGAV
We recommend appropriate analgesia and rest for musculoskeletal involvement.

List of abbreviations

ACEi	Angiotensin converting enzyme inhibitor
ACR	American College of Rheumatology
ARB	Angiotensin receptor blocker
CASP	Critical Appraisal Skills Programme
CKD	Chronic Kidney Disease
CNS	Central nervous system
FOB	Faecal Occult Blood
GDG	Guideline Development Group
GI	Gastrointestinal tract
HSP	Henoch Schönlein Purpura
ICD	International Classification of Diseases
IgA	Immunoglobulin A
IgAV	Immunoglobulin A vasculitis
ISKDC	International study of Kidney Disease in Children
IVIG	Intravenous Immunoglobulin
LMWH	Low molecular weight heparin
MMF	Mycophenolate mofetil
MSK	Musculoskeletal
MRI	Magnetic Resonance Imaging
PICO	Population, intervention, control and outcome
PLEX	Plasma exchange
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCPCH	Royal College of Paediatrics and Child Health
RCT	Randomised Controlled Trial
SHARE	Single Hub and Access point for paediatric Rheumatology in Europe
UP: UC	Urine protein:creatinine ratio

Glossary of terms

Term	Definition
Arthritis	Joint swelling and/or functional limitation of movement
Arthralgia	Joint pain
Arthropathy	Arthritis and/or arthralgia
CNS involvement	Cerebral vasculitis presenting as neurological symptoms and/or signs
GI bleeding	Haematochezia, melena, haematemesis and/or occult blood in the stool
GI involvement	GI vasculitis presenting as gastrointestinal symptoms
Haematemesis	Vomiting blood
Haematochezia	The passage of fresh blood often within or alongside stool
Intussusception	Prolapse of one part of intestine into the lumen of the adjoining part causes intestinal obstruction
Melena	Dark black, tarry stools
Nephritis	Kidney inflammation presenting with micro or macroscopic changes in the urine and/or kidney insufficiency
Occult blood	Blood present in the stools that isn't visible to the eye
Orchiditis	Scrotal and/or testicular involvement
Pulmonary haemorrhage	Pulmonary vasculitis presenting with acute bleeding from the respiratory tract
Purpura	A rash of red or purple discoloured spots on the skin that do not blanch on applying pressure
Severe GI involvement	Severe abdominal pain, protein losing enteropathy and/or GI bleeding
Severe GI pain	Bowel angina presenting as abdominal pain that requires hospital admission to assist with symptom management
Severe musculoskeletal involvement	Arthropathy that requires hospital admission to assist with symptom management
Severe skin involvement	Intense subcutaneous oedema, blistering skin and/or necrotic features
Significant nephritis	Heavy proteinuria (equivalent to >2 g/g or urine protein:creatinine ratio of >250mg/mmol), nephrotic syndrome (heavy proteinuria, hypoalbuminaemia <30g/L, oedema), nephritic syndrome (haematuria plus hypertension, impaired kidney function and/or oliguria) and/or kidney insufficiency.

Vasculitis	Inflammation of the blood vessels

Background

This guideline makes recommendations for the initial management of children and young people with Immunoglobulin A vasculitis (IgAV, previously known as Henoch Schönlein Purpura, HSP). This is a small vessel vasculitis and it is the most common form of vasculitis in children, with an incidence of ~20 cases per 100,000 children[8-10] and a median age at presentation of 6 years(9). IgAV usually presents acutely with a purpuric rash that predominates on the lower limbs. It also involves inflammation in the gastrointestinal (GI) tract, musculoskeletal system and/or the kidneys(7). GI tract involvement occurs in up to 72% of patients. GI involvement usually presents with nausea, vomiting and colicky abdominal pain(11). It can involve GI bleeding manifesting as melaena or haematemesis, that can be severe or life threatening(12). GI bleeding has been linked to acute morbidity and the need for a longer hospital admission(13). Intussusception due to GI tract inflammation can occur and testicular inflammation is reported in 14% of male patients[12]. During the acute presentation, up to 90% of patients will have musculoskeletal involvement with arthralgia and arthritis that mainly affects the lower limb joints[12]. This can be painful and debilitating, and it can last several weeks. Kidney involvement, termed IgAV nephritis, is seen in around 40-50% of patients and it is usually asymptomatic and requires screening for at least 6 months after diagnosis to check for signs of evolving nephritis. Most patients have a mild nephritis that self resolves[12,11], with microscopic haematuria and/or low grade proteinuria being a common finding. More significant IgAV nephritis, can present as nephrotic or nephritic syndrome and it is a recognised cause of irreversible chronic kidney disease (CKD) in 1-2% of all children with IgAV[14]. Importantly, IgAV can involve other systems such as the respiratory or neurological systems, although these are very uncommon in children and young people.

There are no current national guidelines to support the best management of this condition and clinical practice varies. The aim of this clinical practice guideline is to reduce unwarranted variation for the initial management of IgAV in children and young people. The complications associated with IgAV, including acute GI complications, are covered within a parallel document.

Scope

The audience for this guideline will be healthcare professionals working in primary, secondary and tertiary healthcare settings in the UK in which IgAV in children and young people will be managed. The population that this guideline relates to is children and young people aged 0-18 years presenting with IgAV.

Summary and rationale of recommendations

The classification of IgAV in children and young people

Number	RECOMMENDATION	*Grade*
Section 1: CLASSIFICATION OF IGAV IN CLINICALLY SUSPECTED DISEASE		
1.1	*We recommend that professionals follow the EULAR/PRINTO/PRES 2010 classification criteria of IgAV ([7]; appendix 10).*	1B

Rationale

One highly relevant study was the development of the EULAR/PRINTO/PRES classification system[7]. This was a multicentre study to derive classification criteria for childhood vasculitides. This was the largest study included in this evidence-synthesis and involved 860 children with IgAV and demonstrated that the EULAR/PRINTO/PRES classification system had excellent sensitivity and specificity in distinguishing the condition from other forms of vasculitis[7]. A further 55 out of the 66 (83%) included studies in the evidence synthesis mentioned how they defined IgAV [15-32,12,33-36,8,37-59,13,60-66]. Of these 18 (18/55; 33%) used the ACR criteria[67] and 17 (17/55; 31%) used the EULAR/PRINTO/PRES classification criteria[7]. Of those that used the ACR criteria, 8 (8/18; 44%) were published before 2010 prior to the EULAR/PRINTO/PRES classification criteria were reported. The evidence included the article produced by the SHARE consortium that used a systematic review of the literature and professional consensus to derive European recommendations for clinical practice and they concluded that the EULAR/PRINTO/PRES classification criteria should be used[46]. The UK IgAV GDG agreed that the evidence supporting the development of the EULAR/PRINTO/PRES classification criteria was of high quality and further studies were unlikely to improve this topic area. Therefore, these criteria were used in the recommendation.

Audit measure

i. The proportion of children and young people with clinically suspected IgAV who have been appropriately classified using the EULAR/PRINTO/PRES 2010 classification criteria (Appendix 10).

When to seek specialist advice for a child or young person with IgAV

Number	RECOMMENDATION	*Grade*
Section 2: SPECIALIST REFERRAL IN IGAV		
2.1	*We recommend that specialist advice should be sought for children and young people with IgAV and the following clinical presentations (and symptoms or signs):* • *Severe GI involvement (definition: unremitting abdominal pain, protein losing enteropathy and/or GI bleeding; sub-specialist: paediatric gastroenterology/paediatric rheumatology)* • *Significant nephritis (definition: proteinuria UP: UC ratio of >250mg/mmol, nephrotic syndrome, nephritic syndrome and/or kidney insufficiency; sub-specialist: paediatric nephrology))* • *Central nervous system (CNS) involvement (definition: cerebral vasculitis presenting as neurological symptoms and/or signs; sub-specialist: paediatric neurology/paediatric rheumatology)* • *Pulmonary haemorrhage (definition: pulmonary vasculitis presenting with acute bleeding from the respiratory tract; sub-specialist: paediatric respiratory/paediatric rheumatology).*	1C
2.2	*We suggest that specialist advice should be sought for children and young people with IgAV and the following clinical presentations (and symptoms or signs):* • *Scrotal and / or testicular involvement (definition: orchiditis; sub-specialist: paediatric surgeon/urology)* • *Severe skin manifestations (definition: intense subcutaneous oedema, blistering skin and/or necrotic features; sub-specialist: dermatology/paediatric rheumatology)* • *Severe, unremitting, musculoskeletal involvement (definition: arthropathy that requires hospital admission to assist with symptom management and no signs of improvement; sub-specialist: paediatric rheumatology)*	2D

Rationale

There were 16 (16/66; 24%) studies that included the indications for hospital admission and/or the need for acute treatment, with the following indications; severe GI involvement (17 studies), severe nephropathy (10 studies), scrotal/testicular involvement (3 studies), skin manifestations (2 studies), musculoskeletal involvement (2 studies), central nervous system involvement (2 studies) and pulmonary haemorrhage (1 study). The definitions used within the literature for each of these clinical signs and symptoms varied and are detailed in Appendix 11 as a reference. The majority of the literature, consisting of mostly observational studies, relating to severe GI or significant nephritis causing acute or long-term complications. CNS involvement and pulmonary haemorrhage were agreed by the UK IgAV GDG to be so rare and so severe that missing these complications could be detrimental to the patient. There was far less evidence to support

detrimental outcomes relating to testicular, skin and musculoskeletal involvement however it was felt important that these symptoms are mentioned as they sometimes require specialist input.

Audit measure

i. The proportion of children and young people with IgAV to receive specialist advice who have severe GI involvement, significant nephritis, CNS involvement and/or pulmonary haemorrhage.

Research recommendation

i. In children and young people with IgA vasculitis, what baseline demographic or clinical parameters predict an increased risk of complications?

The detection of nephritis in children and young people with IgAV

Number	RECOMMENDATION	*Grade*
Section 3: NEPHRITIS SCREENING IN IGAV		
3.1	*We recommend that children and young people should have urinalysis testing performed frequently over a period of 6 months to detect a diagnosis of nephritis (for example weekly screening for the first 4-6 weeks then monthly thereafter).*	1B
3.2	*We suggest that blood pressure assessment should be performed in children and young people with IgAV at diagnosis and if there is evidence of nephritis.*	2C

Rationale

There were no studies directly comparing different clinical tests to aid in the detection of nephritis. A total of 28 out of the 66 (42%) included studies that utilised clinical tests to detect nephritis in an unselected cohort of patients. Of these studies, the following options were used to detect nephritis;

- Urinalysis alone (16 studies); quantified proteinuria and haematuria (4 studies); urinalysis, kidney function and 24 hour proteinuria (3 studies); urinalysis and blood pressure (2 studies); urinalysis and kidney function (1 study); urinalysis, kidney function, urine microscopy (1 study); and kidney function alone (1 study).

Evidence suggested that urinalysis was most commonly used as a minimum test and the UK IgAV GDG supported this as a strong recommendation as it is suitable for all clinical environments. The GDG discussed the use of blood pressure measurements to assist in the detection of nephritis and noted that there were very few studies describing the use of blood pressure measurements for this purpose. Due to the importance of detecting nephritis and its impact on long term kidney outcomes, the group concluded that it was important to include a weak recommendation supporting BP measurement at baseline and in cases with nephritis and highlighted it as a research recommendation.

Audit measures

i. The proportion of children and young people with IgAV who receive urinalysis testing over a period of 6 months to monitor for nephritis.

Research recommendations

i. In children and young people with IgA vasculitis, what is the incidence of hypertension and what are the implications?

The management of musculoskeletal involvement in children and young people with IgAV

Number	RECOMMENDATION	*Grade*
Section 4: MUSCULOSKELETAL INVOLVEMENT IN IGAV		
4.1	*We recommend appropriate analgesia and rest for musculoskeletal involvement in children and young people with IgAV.*	1C

Rationale

There were 8 (8/66; 12% of all studies) studies that addressed musculoskeletal involvement in IgAV. Of the treatments suggested these included;

- Analgesia (2 studies), symptomatic support, analgesia, hydration, bed rest (1 study), bed rest (1 study) and prednisolone (1 study that found it was not statistically significant at reducing the duration of musculoskeletal symptoms).

The UK IgAV GDG agreed that there are very rarely consequences from musculoskeletal involvement. Given this finding and that there was one study reporting no benefit from the use of prednisolone, the use of simple analgesia or symptomatic support seemed appropriate as a recommendation. This also aligned with the recommendations produced by the SHARE consortium.

Audit measure

i. The proportion of children and young people with IgAV who receive analgesia and rest for musculoskeletal involvement

Summary of audit measures

The audit measures align with the strong recommendations (strength grade 1) suggested in this clinical practice guideline. A summary of the audit measures are as follows;

i. The proportion of children and young people with clinically suspected IgAV who have been appropriately classified using the EULAR/PRINTO/PRES 2010 classification criteria (Appendix 10).
ii. The proportion of children and young people with IgAV to receive specialist advice who have severe GI involvement, significant nephritis, CNS involvement and/or pulmonary haemorrhage.
iii. The proportion of children and young people with IgAV who receive urinalysis testing over a period of 6 months to monitor for nephritis.
iv. The proportion of children and young people with IgAV who receive analgesia and rest for musculoskeletal involvement

Summary of research recommendations

The research recommendations covered within this best practice guideline are summarised as follows;

i. In children and young people with IgA vasculitis, what baseline demographic or clinical parameters predict an increased risk of complications?
ii. In children and young people with IgA vasculitis, what are the rates of hypertension and what are the implications?

Lay Summary

The condition called immunoglobulin A vasculitis (known as IgAV) was previously called Henoch Schönlein Purpura. It is a condition where the immune system becomes overactive after a normal childhood illness. It causes a purplish-red rash that is usually on the legs. It can also cause tummy aches, sore joints and kidney problems. The only way to find out about the kidney problems is to test the urine. About half of the children with IgAV will have inflamed kidneys when the urine is tested. The kidneys can get inflamed even after the rash has gone. The condition is more common in primary school aged children, but it can come on at any age. In most children it lasts a few weeks and then it goes away forever. A few children will get long term problems that are usually due to the kidney problems. The aim of this work was to make a guide for how to look after children when they first get IgAV.

This guideline has been made by a group of specialists in the UK and it includes parents with experience of IgAV. Other associations also helped. They made a working group called the UK IgAV GDG. The group started by deciding on the most important questions for children with IgAV. They checked the medical studies reported over the past 20 years. Using the medical studies and group discussion, the group made recommendations. These are written below. A poster is shown in Appendix 12 that shows how they did the work and a poster in Appendix 13 shows the recommendations.

Lay version of recommendations

The best practice recommendations are;

1. In children and young people with IgAV, the diagnosis should use set criteria (called the 'EULAR/PRINTO/PRES 2010 classification criteria'; Appendix 10).
2. Children and young people with IgAV should have specialist advice if they have bad gut problems, bad kidney problems, brain involvement or bleeding in the lungs.
3. In children and young people with IgAV, who have involvement of their testicles, bad skin problems and/or bad joint problems may need input from a specialist.
4. In children and young people with IgAV, a urine test should be done for 6 months to check for kidney problems. This could be weekly checks at first then move to monthly checks.
5. In children and young people with IgAV, blood pressure checks should be done at diagnosis and if the urine tests suggest the kidneys may be inflamed.
6. In children and young people with IgAV who have sore or swollen joints should be given medicines for pain and rest.

Lay research recommendations

The research recommendations are;

i. In children and young people with IgA vasculitis, are there any ways to predict who may get complications?
ii. In children and young people with IgA vasculitis, how many children get high blood pressure and what does this mean?

Acknowledgements

This document has been externally reviewed by key stake holders and during an open consultation process according to the instructions described in the UKKA Clinical Practice Guidelines Development Policy Manual. We would like to acknowledge everyone who has supported this process.

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Appendix

Appendix 1: Lead organisations

Name
British Association of Paediatric Nephrology (BAPN)
UK Kidney Association (UKKA)
Royal College of Paediatrics and Child Health (RCPCH)

Appendix 2: Stakeholders

Name
British society of Paediatric gastroenterology, hepatology and nutrition (BSPGHAN)
British Society of Rheumatology (BSR)
Association of Paediatric Emergency Medicine APEM
Royal College of Emergency Medicine RCEM
Paediatric Emergency Medicine research collaborative for the UK and Ireland (PERUKI)
British Society of Paediatric radiology BSPR
Vasculitis UK

Appendix 3: PICO domains

Population	Intervention	Comparison	Outcome
Children and young people (aged <18 years) with a confirmed diagnosis of IgAV	Classification tools Clinical signs and symptoms Kidney tests Therapeutics	Any intervention compared with any other or no intervention	Diagnosis Complications Duration of symptoms Severity of symptoms

Appendix 4: Search concepts

Search number	Search terms

1	pediatric
2	paediatric
3	child*
4	Adolescen*
5	**1 OR 2 OR 3 OR 4**
6	immunoglobulin A vasculitis
7	IgA vasculitis
8	IgAV
9	Henoch schönlein purpura
10	HSP

Appendix 5: Study eligibility

Criteria	Inclusion	Exclusion
Publication date	Papers published between 2002 to 2022	Papers published prior to 2002
Research type	Primary research	Secondary research
Study type	Meta-analysis Systematic reviews Randomised controlled trials (RCT) If no RCT available to consider; Cohort studies Case series >5 patients Case control studies	Case reports Editorials Comments Annotations Letters Commentaries Books and book chapters Updated systematic reviews by same methodology eg Cochrane (most recent version will be included) Non-traditional therapies (eg: Chinese medicines) and surgical intervention
Publication and study status	Published Completed	Unpublished Ongoing

Language	English	Non-English
Text availability	Full text available	Full text unavailable

Appendix 6: Bibliographic databases

Bibliographic databases	Access uniform resource locator (URL)
MEDLINE	https://www.nlm.nih.gov/medline
EMBASE	https://www.embase.com
Cochrane central register of controlled trials (CENTRAL)	https://www.cochranelibrary.com/central

Appendix 7: Topic areas and key questions

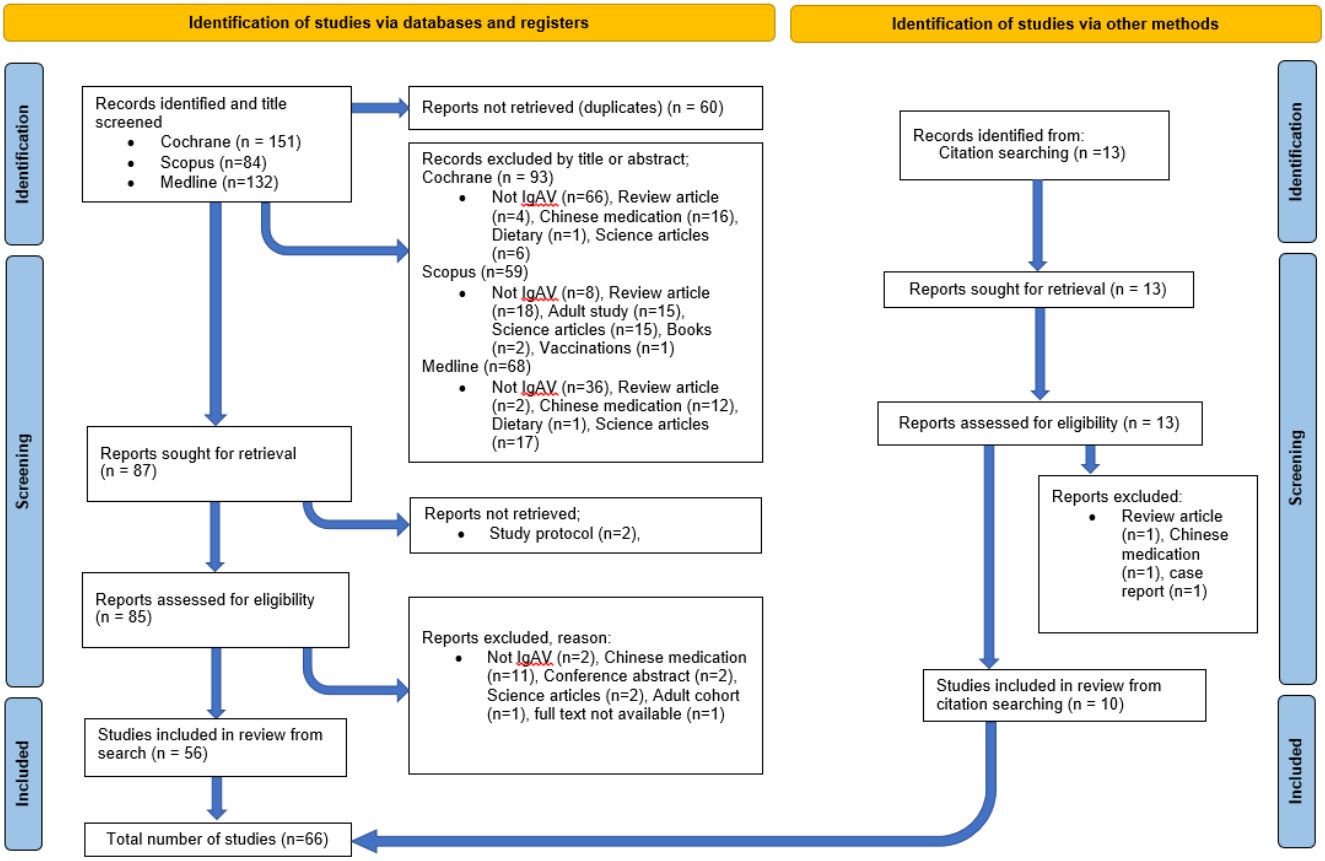
Topic area	Key questions
Classification of IgAV	How do professionals classify IgAV in children and young people?
Outcome of initial assessment in IgAV	What are the clinical indicators in children and young people presenting with IgAV that should prompt consideration of referral or discussion with a specialist?
Nephritis screening in IgAV	In children and young people with IgAV, what are the best tests to indicate the presence of nephritis?
Treatment of initial presentation of IgAV	In children and young people with IgAV, what are the indicators for treating musculoskeletal involvement? In children and young people with IgAV, what are the indicators for treating gastrointestinal involvement?

Appendix 8: Key questions formatted for systematic review

1) In children and young people with IgAV under the age of 18 years, do classification tools allow professionals to classify IgAV to support diagnosis?

2) In children and young people with IgAV under the age of 18 years, are there clinical signs and symptoms that indicate complications that require a referral to a specialist?
3) In children and young people with IgAV under the age of 18 years, what are the best clinical tests to detect a diagnosis of nephritis?
4) In children and young people with IgAV under the age of 18 years, what clinical signs and symptoms would indicate a need for intervention for musculoskeletal involvement that would reduce the duration and/or severity of symptoms?
5) In children and young people with IgAV under the age of 18 years, what clinical signs and symptoms would indicate a need for intervention for gastrointestinal involvement that would reduce the duration and/or severity of symptoms?

Appendix 9: PRISMA diagram of selected studies



Appendix 10: The EULAR/PRINTO/PRES 2010 Classification criteria

Criterion	Glossary	Sensitivity, specificity (%)	Area under the curve (%)
Purpura (mandatory)	Purpura (commonly palpable and in crops) or petechiae, with lower limb predominance (not related to thrombocytopenia).	89, 86	87.5
1. Abdominal pain	Diffuse abdominal colicky pain with acute onset assessed by history and physical examination. May include intussusception and gastrointestinal bleeding.	61, 64	62.5
2. Histopathology	Typically leucocytoclastic vasculitis with predominant IgA deposit or proliferative glomerulonephritis with predominant IgA deposit.	93, 89	91.1
3. Arthritis or arthralgias	Arthritis of acute onset defined as joint swelling or joint pain with limitation on motion. Arthralgia of acute onset defined as joint pain without joint swelling or limitation on motion.	78, 42	59.9
4. Renal involvement	Proteinuria >0.3 g/24 hr or >30 mmmol/mg of urine albumin/creatinine ratio on a spot morning sample. Haematuria or red blood cell casts: >5 red blood cells/high power field or red blood cells cases in the urinary sediment or ≥2+ on dipstick	33, 70	51.4
HSP EULAR/PRINTO/PRES classification definition	Purpura or petechiae (mandatory) with lower limb predominance and at least one of the four above criteria.	100, 87	93.5

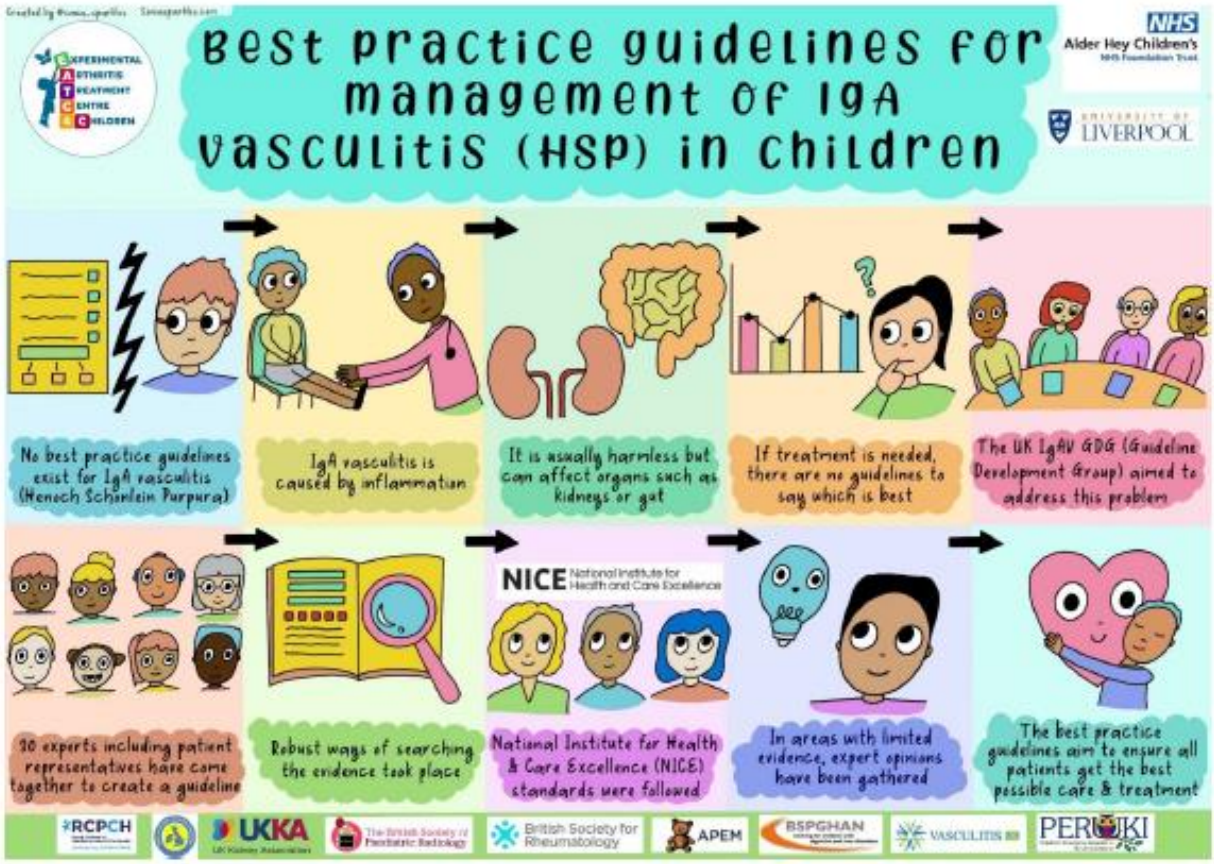
Appendix 11: Definitions of severe clinical signs and symptoms

Clinical parameter	Definitions used with the included literature
Severe GI involvement	Severe abdominal pain and/or GI bleeding
	Severe colicky abdominal pain, bowel oedema in ultrasonography or overt GI bleeding
	Gross gastrointestinal bleeding
	Bowel angina abdominal pain, worse after meals or bowel ischemia including bloody diarrhoea, GI bleeding, melaena, hematochezia or positive occult blood in stool

	Bowel angina (diffuse abdominal pain), GI bleeding (melena, hematochezia, or positive stool test), nausea and vomiting
	Bowel angina (diffuse abdominal pain), GI bleeding (melena, hematochezia, or positive stool test), nausea and vomiting
	Severe protein-losing enteropathy in the form of abdominal pain, oedema and low serum albumin
	GIS bleeding and/or intussusception
	Abdominal pain: requiring radiological examination to exclude intussusception or appendicitis, confirmation of intussusception, complications requiring surgical or endoscopic intervention, gross hematochezia
	Abdominal pain, vomiting, or GIS bleeding. GI bleeding was defined as hematochezia, melena, or hematemesis and/ or the presence of occult blood in stool
	Severe abdominal pain and/or rectal bleeding if intussusception had been excluded
	Severe bowel angina meaning the child couldn't tolerate meals
	Poor oral intake due to GI symptoms
	GIS involvement was defined as stomach ache and/or FOB positivity and presence of melena, hematemesis, hematochezia, or invagination
	Acute diffuse abdominal pain, intussusception, and GI bleeding
Severe nephritis	Nephrotic syndrome (defined as plasma albumin level 25g/L and either 1g of proteinuria/d per m^2 of body surface area in children or >3.5g of proteinuria/d in adults, with or without the presence of oedema) or acute nephritic syndrome (defined as hematuria with at least 2 of the following features hypertension, elevated plasma urea or creatinine serum levels, and oliguria)
	Severe kidney dysfunction as hematuria along with considerable proteinuria (>1 g/m^2/d) and/or increased urea and creatinine with an abnormal kidney biopsy findings
	Nephrotic syndrome with proteinuria >40mg/m^2 body surface/hour or >50mg/kg/day or >2g/day proteinuria with albumin <25g/L and/or acute nephritic syndrome (hypertension, raised urea or creatinine or oliguria)
	Nephrotic syndrome (plasma albumin <25g/L and 1g/day/m^2 proteinuria with or without oedema) or acute nephritic syndrome (haematuria with at least 2 of; hypertension, elevated plasma urea/creatinine, oliguria
	Any of the following findings: (1) hematuria (> 5 red blood cells/high power field), (2) red blood cell casts in urinary sediment, (3) proteinuria > 4 mg/m2/h urine protein, (4) hypertension (systolic and/or diastolic blood pressures ≥ 95th percentile for gender, age, and height on ≥ 3 occasions), (5) nephrotic proteinuria (> 40 mg/m2/h), and (6) kidney insufficiency
	Kidney involvement was defined as: 1) hematuria-5 red blood cells at high power light microscopy; 2) proteinuria-urine protein:creatinine (UP/UCr) ＞0.5 in children under 2 years of age, UP/UCr ＞0.2 in children over 2 years of age; 3) simultaneously meeting the criteria for 1) and 2); and 4) proteinuria over 40 mg/m^2
	Kidney involvement was defined as hematuria (>5 red blood cells per high-power microscopic field) and/or proteinuria (protein concentration in spot urine ≥30mg/dL or spot urine protein/creatinine ratio >0.5 in children <2 years of age and > 0.2 in children ≥ 2 years of age).
	A urine protein/creatinine ratio >2 was defined as nephrotic-range proteinuria

	Kidney involvement was defined as microscopic (presence of ≥5 erythrocytes in the centrifuged urine at 40x) or macroscopic hematuria and/or proteinuria (presence of protein >4 mg/m^2/hour or protein/creatinine >0.2 in 24-h urine) and/or impairment in kidney function
Scrotal/testicular involvement	Scrotum swelling with incidental hemorrhage of the testicles
	Orchiditis
	Testicular sensitivity or scrotal oedema
Skin manifestations	Persisting skin lesions
	Intense subcutaneous oedema
Musculoskeletal involvement	No specific definitions for severe involvement. Definitions used were arthritis and/or arthralgia (2 studies), IgAV associated arthropathy, well defined arthralgia or synovitis, joint swelling and/or limitation of movement, severe or worsening arthralgia, joint swelling and/or functional limitation of joint.
Central nervous system involvement	Convulsion and infarction on MRI was considered as central nervous system (CNS) involvement
	The finding of cerebral vasculitis
Pulmonary haemorrhage	No specific definitions

Appendix 12: Summary information poster: outline of methodology



Appendix 13: Summary information poster: recommendations