Supplementary Materials. Development progress

Review of existing guidelines

Practice guideline-related index terms were searched using the following combinations: (hematuria or microhematuria) and "guidelines" and "children." A total of 23 practice guidelines were extracted as a result of the search based on search sources after excluding duplicates. The final selection process of the retrieved literature was conducted by a working committee, as this step required clinical expertise. Literature selection criteria were developed based on the key questions, and the first and second inclusion/exclusion criteria were independently reviewed by two people per article to enhance objectivity. In the first screening, the titles and abstracts of the articles were reviewed. In the second screening, the full texts of the primarily selected articles were reviewed, with reasons for exclusion noted if any articles were excluded. In both phases of the screening process, disagreements between the reviewers were resolved through consensus to finalize the three practice guidelines.

Assessing the quality of the guidelines

The quality of the guidelines selected and deemed to address the key questions after a full-text review was assessed by two people at a time using the AGREE (Appraisal of Guidelines for Research & Evaluation Instrument) II tool. The K-AGREE evaluation form, developed by the Korean Medical Association, was used to reduce interrater variability. In quality evaluation using AGREE, to ensure the reproducibility and clarity of the evaluation results, the basis for assigning scores was described in the evaluation comments section, and the evaluation results of the evaluators were shared so that, if necessary, incorrect evaluation results due to errors or mistakes could be corrected through re-examination (for example, if there was a score difference of four or more points between raters). Evaluation results were derived using a scoring formula for each domain. After the evaluation, practice guidelines with a score of 50 or higher for the "rigor of development" were selected as practice guidelines for recommendations and evidence summaries (Table S1).

Table S1. List of practice guidelines used to develop the recommendation

1	Microhematuria: AUA/SUFU guideline, 2020
2	Hematuria guideline: Dutch Society for Urology, 2010
3	ACR Appropriateness Criteria Hematuria-Child, 2018

ACR, American College of Radiology; AUA, American Urological Association; SUFU, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction.

Selection of key questions

The final recommendations are based on the key questions. The key questions were selected by reviewing existing practice guidelines and selecting clinical issues, reviewing the evidence for each topic, and discussing each topic in the working and development committees to select the key questions for the final five topics. Many clinical experts and methodologists were involved in the selection of key questions and a review of the recommendations and provided their opinions, which were reflected as much as possible. During this process, we conducted a demand survey of external nephrology experts, who were the primary users of practice guidelines, communicated the practice guideline development process through conferences, and solicited input from society members. The key questions were determined by considering the Population, Intervention, Comparator, and Outcome (PICO) factors. The key questions on which the recommendations were based were written in sentence form and finalized by reviewing the feasibility of development.

Preparation of the recommendation comparison tables and assessment of acceptability/applicability

The selected guidelines were reviewed to create a recommendation comparison table for each key question; domestic acceptability and applicability in Korea were evaluated, and the discussions were reflected in the recommendations.

Determine the development method

The principle of these guidelines is based on the adaptation of existing domestic and international guidelines, followed by the addition of the latest research findings. In addition, the "*de novo*" method was selectively reviewed when recommendations could not be found in the existing practice guidelines or when deemed necessary. For adaptive development, we used existing guidelines as the most important source of evidence, added the latest research results, and made systematic changes to adapt the guidelines to the healthcare situation in Korea. However, of the eight key questions selected, only two had guidelines that fit the target population. Therefore, we applied a new creation method.

Search and selection of evidence

The literature search was conducted by searching major domestic and international literature search databases, such as Ovid-MEDLINE, Ovid-EMBASE, KMBASE, and the Cochrane Library, focusing on the keywords of each key question selected by the working group, and supplementing the search results with manual searches. To increase the sensitivity of the search by linking similar key questions using only the P and I of the PICO factors, we systematically organized the search strategy with the help of methodology experts and conducted searches using domestic and international databases to ensure that the final recommendations reflected the domestic situation.

Preparation of an evidence table

The evidence literature for recommendations related to the key questions in this guideline was extracted from selected practice guidelines and organized in a pre-agreed evidence table format. The most recent articles found through additional literature searches were added to finalize the evidence table. All articles included in the evidence tables were subjected to a risk of bias assessment for each study design, and a risk of bias graph was created and summarized using key questions in the "Search and selection of evidence" section of the recommendation (Table S2, Fig. S1).

Table S2. Summary evidence tables

Key question 1

Publisher	Journal and year of publication	Summary
American College of Radiology	*Journal of the American College of Radiology*, 2018	1. Microscopic hematuria without proteinuria: Imaging is usually not necessary at the outset, but ultrasound is considered if microscopic hematuria persists without a clear cause. 2. Microscopic hematuria with proteinuria: Ultrasound is recommended. 3. Asymptomatic gross hematuria: Renal bladder ultrasound is recommended. 4. Suspected nephrolithiasis with painful gross hematuria: Renal bladder ultrasound or non-contrast CT is recommended.
American Urological Association	*The Journal of Urology*, 2013	Renal bladder ultrasound is recommended as the first imaging test in pediatric patients with nephrolithiasis even if the accuracy is low, due to concerns about radiation exposure with CT. Low-dose CT is considered when nephrolithiasis is suspected and not diagnosed on ultrasound.
European Society for Pediatric Radiology	*Pediatric Radiology*, 2009	Ultrasound is recommended as the first imaging test in pediatric patients with hematuria because it is noninvasive and can differentiate most causes. Invasive imaging (CT, cystoscopy) is not recommended as the first imaging test due to the low frequency of tumors in children, unlike in adults.

CT, computed tomography.

Key question 2

No.	First author (year)	Study type	Total (n)	Intervention (n)	Comparison (n)	Study results
1	Trachtman (1984)	Cohort	76	IMH (42)	IMH plus FHx (15) or GHU (19)	The overall prevalence of abnormal renal histology was 56%. (1) Alport syndrome (n = 9), (2) IgAN (n = 8), (3) thinning of the glomerular basement membrane (n = 17), (4) vascular C3 staining (n = 7)
2	Túri (1989)	Cohort	341	Isolated hematuria (226)	Isolated hematuria with symptoms of glomerular disease (47)	In 47 children, a more serious glomerulopathy developed 2–17 years after first the presentation. In all of them, proteinuria was associated with hematuria more than 2 years after onset.
3	Lin (2001)	Cohort	630	IMH (266)	IMH with proteinuria (82)	In IMH, the majority of underlying diseases were IgAN and benign hematuria. In IMH with proteinuria, IgAN and SLE nephritis were the major causes.
4	Bergstein (2005)	Cohort	342	IMH cause undiscovered (274)	IMH cause discovered (68)	Our results indicate that asymptomatic microscopic hematuria in children is rarely associated with a clinically important disease of the urinary tract. No cause was found in the large majority of patients. The most common cause discovered was hypercalciuria (16% of patients) followed by poststreptococcal glomerulonephritis (1%).

5	Lee (2006)	Cohort	461	IMH (289)	IMH with proteinuria (163)	In the group with microscopic hematuria, normal histology was seen in 136 cases (47.1%), thin basement membrane disease in 97 (33.6%) and IgAN in 46 (15.9%). In the group with coexisting proteinuria and microscopic hematuria, as many as 75 children (46.0%) were diagnosed with IgAN, 40 (24.5%) as normal histology, and 30 (18.4%) with thin basement membrane disease. A significantly higher rate of pathological abnormalities was noted in the group with coexisting proteinuria and hematuria compared to the isolated hematuria group.
6	Cho (2013)	Cohort	5,114	IMH (3,724)	IMH with proteinuria (838)	The incidence of GN in each group was 22.88% in IH, 7.61% in IP, 46.90% in CHP, and 69.96% in nephrotic-range proteinuria, respectively. The most common disease in every subgroup was IgAN but accounted for somewhat higher frequencies in the CHP and nephrotic-range proteinuria groups.
7	Zhai (2014)	Cohort	112	IMH (80)	Proteinuria with/without IMH (31)	In IMH urinary abnormality, the only renal biopsy findings were mild lesions in the glomeruli. For proteinuria with or without IMH, IgAN, FSGS, and Alport syndrome were the major causes.
8	Guven (2016)	Cohort	106	IMH (101)	IMH with mild proteinuria (5)	Renal biopsy was performed in all 5 children with IMH and mild proteinuria: 2 patients had hereditary nephropathy and 2 patients had focal segmental glomerulosclerosis. One biopsy specimen revealed nonspecific findings. Renal biopsy was performed in 9 children with IMH: 4 patients had hereditary nephropathy and 5 patients had nonspecific findings.
9	Güngör (2021)	Cohort	136	IMH (107)	IMH with proteinuria (29)	Glomerular hematuria was detected in 32 patients (23.5%), and 22 of those patients (68.75%) had mild proteinuria accompanying asymptomatic microscopic hematuria at baseline and/or follow-up. The most common histopathological diagnosis was IgAN. Glomerular pathologies were found to be significantly more common among the AMHP group compared to IMH (p = 0.00). Patients who developed CKD and hypertension (1.47%) were in the IMH with proteinuria group.

AMHP, asymptomatic microscopic hematuria with proteinuria; CHP, combined hematuria and proteinuria; CKD, chronic kidney disease; FHx, family history; FSGS, focal segmental glomerulosclerosis; GHU, glomerular hematuria; GN, glomerulonephritis; IgAN, immunoglobulin A nephropathy; IH, isolated hematuria; IP, isolated proteinuria; IMH, asymptomatic microscopic hematuria; SLE, systemic lupus erythematosus.

Key question 5

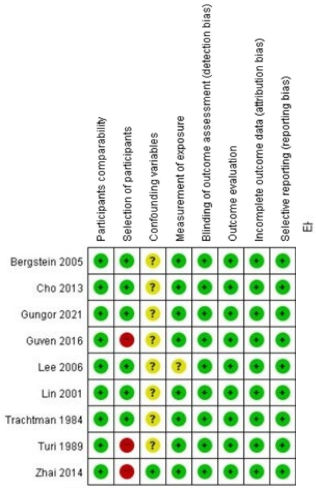
No.	First author (year)	Study type	Total (n)	Intervention (n)	Comparison (n)	Study results
1	Vivante (2011)	Cohort	1,024,875	With hematuria (2,276)	Without hematuria (1,022,599)	Presence of persistent asymptomatic IMH in persons aged 16 through 25 years was associated with a significantly increased risk of treated ESKD for a period of 22 years, although the incidence and absolute risk remained quite low.
2	Túri (1989)	Cohort	341	Isolated hematuria (226)	Isolated hematuria with symptoms of glomerular	In 47 children, a more serious glomerulopathy developed 2–17 years after the first presentation. The percentage of more serious azotemia was 1.7

					disease (47)	(creatinine clearance: 10–50 mL/min/1.73 m^2) and 0.3 (creatinine clearance: <10 mL/min/1.73 m^2). Mortality was 0.58%.
3	Lin (2001)	Cohort	630	After mass screening	Before mass screening	Before mass urinary screening, all RPGN cases progressed to ESKD. In this series, 2 cases (28.5%) were discovered early enough to preserve renal function. Before mass urinary screening, around 50% of FSGS patients progressed to chronic renal insufficiency or ESKD in the 10-year follow-up.
4	Feng (2013)	Cohort	351	IMH (215)	IMH with recurrent macrohematuria and/or proteinuria (136)	During the 2- to 10-year follow-up period, adverse renal events (i.e., development of proteinuria, hypertension, or impaired renal function) were observed in 13/215 patients (6.0%) with IMH and 31/136 patients (22.8%) with IMH with recurrent macrohematuria and/or proteinuria ($\chi^2 = 15.521$, $p < 0.001$).
5	Cho (2013)	Cohort	1,478	IMH (396)	CHP (757) IP (134)	The incidence of glomerulonephritis in each group was 22.88% in IH, 7.61% in IP, 46.90% in CHP, and 69.96% in nephrotic-range proteinuria. The most common disease in every subgroup was IgAN and the disease that showed a higher incidence than other groups was TBMD in the IH group.
6	Kwak (2022)	Cohort	552	IMH (149)	Recurrent GHU (39), CHP (216), IP (100)	The incidence rates of normal renal histopathology according to the indications for biopsy were as follows: recurrent GHU (9/39, 23.1%), IMH (10/149, 6.7%), IP (4/100, 4.0%), CHP (6/216, 2.8%), others (3/22, 13.6%), and total (32/526, 6.1%).

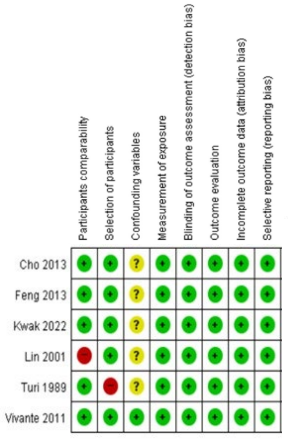
CHP, combined hematuria and proteinuria; ESKD, end-stage kidney disease; FSGS, focal segmental glomerulosclerosis; GHU, gross hematuria; IH, isolated hematuria; IgAN, IgA nephropathy; IMH, asymptomatic microscopic hematuria; IP, isolated proteinuria; RPGN, rapidly progressive glomerulonephritis; TBMD, thin basement membrane disease.

Figure S1. Bias risk assessment.

Key question 2



Key question 5



Assessing the risk of bias

The literature in the evidence tables of existing practice guidelines that assessed the risk of bias was reviewed for compliance with the criteria, and those with acceptable results of risk of bias assessments were adopted. The tools selected for this guideline were utilized for the evaluation in cases where there

were differences in the tools employed among articles in the evidence literature or when the risk of bias was not assessed. The quality assessment of the additional retrieved evidence was conducted by selecting the appropriate tool based on the study design and was independently assessed by two researchers per article, with consensus in case of disagreement; however, if they failed to reach consensus, a third person's opinion was solicited to reach an agreement.

Non-randomized study quality assessment tool: RoBANS 2.0

The risk of bias for non-randomized studies (RoBANS) is a representative tool for assessing the risk of bias in non-randomized studies. RoBANS was developed through the Health Insurance Review and Assessment Service's "Study on the Development of a Quality Assessment Tool for Clinical Research Literature" in 2009 and was revised in 2013 to reflect the latest research trends, such as Cochrane.

Synthesizing evidence

The articles selected from the existing practice guidelines and additional searched articles were categorized by study design, and the necessary items were selected from a list of available materials to extract the relevant contents. Data extraction was conducted according to a predetermined data extraction format (data values reported in tables, etc. were accepted after review); in the case of a comparison of the two intervention methods, a data extraction format with which comparability could be evaluated was considered. Data were extracted from one working group member and reviewed by another. After completing the final evidence table, which included evidence from existing practice guidelines and additional literature, a qualitative description of the extracted data was developed.

Summarization of evidence levels and recommendation grades

The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) methodology was used to assess the level of evidence. Importance was first assessed for each individual outcome, and

then the level of evidence was determined as high, moderate, low, or very low for each individual outcome. The importance of each level of evidence is presented in Table S3.

Table S3. Evidence level and implications of GRADE (Grading of Recommendations Assessment Development and Evaluation)

Level of evidence	Definition
High	You can be very confident that the estimate of the effect is close to the true effect.
Moderate	You can be moderately confident in the estimate of the effect. The estimate of the effect is likely to be close to the actual effect but could be quite different.
Low	There is limited confidence in the estimate of the effect. The actual effect can be quite different from the effect estimate.
Very low	There is little confidence in the estimate of the effect. The actual effect will be quite different from the estimate of the effect.

In the GRADE, the level of evidence is prioritized by study design: high for randomized controlled trials, low for observational studies, and very low for patient group studies. The next step is to consider lowering or raising the level of evidence. For randomized controlled trials, the level of evidence is lowered by one or two levels if any of the following five factors are present: 1) risk of bias, 2) inconsistency (heterogeneity), 3) non-directness, 4) imprecision, or 5) publication bias. For observational studies, the level of evidence can be increased if the following three factors are present: 1) the effect size is large, 2) presence of a dose-response relationship, or 3) confounding variables increase confidence in the effect estimate.

The recommendations were categorized into six levels: strong, conditional, conditional against, strong against, inconclusive, and expert consensus (Table S4). The factors considered in making recommendations included the levels of evidence, benefits and harm, clinical applicability, resources and costs, and values and preferences. Key questions that were not amenable to adaptation and de novo development owing to the paucity of existing research were denoted as recommendations with expert consensus.

Table S4. GRADE (Grading of Recommendations Assessment Development and Evaluation) recommendations and implications

Symbols	Recommendation	Definition
A	Strongly recommended	Strongly recommended in most clinical situations, given the benefits and harms of the treatment, level of evidence, values and preferences, and resources.
B	Conditional recommendations	The use of these treatments may depend on the clinical situation or patient/societal values; thus it is suggested that it is used selectively or conditionally.
C	Conditional against	In some situations or conditions, implementation is not recommended because the harms of the treatment may outweigh the benefits, based on the clinical situation or patient/social value.
D	Strong against	It is not recommended in most clinical situations because the harms of the treatment outweigh the benefits, based on the clinical situation or patient/social value.
I	Inconclusive	It is not possible to decide whether or not to implement an intervention because the level of evidence is too low, the benefit/risk balance is seriously uncertain, or there is too much variation, given the benefits and harms of the treatment, the level of evidence, values and preferences, and resources. This means that the use of a treatment cannot be recommended or opposed; you must defer to the judgment of the clinician.
Expert consensus		Literature for clinical evidence of practice guidelines is lacking, but the use is recommended based on clinical experience and expert consensus, given the benefits and harms of the treatment, level of evidence, values and preferences, and resources.

Formulating recommendations

To improve the degree of clinical implementation of the recommendations, the working group members further reviewed the feasibility of the recommendations, including barriers, facilitators, and suggestions for overcoming them. After drafting the recommendations, they were revised through written reviews via email and conference calls with subject matter experts, and the revised recommendations were subjected to an informal consensus process by the full committee, including a review committee composed of subject matter experts and multiple meetings of the subcommittee (multidisciplinary) with simultaneous or separate participation by all members, followed by a full meeting that resulted in a unanimous consensus among all members. The process did not use formal consensus methods such as voting, but in-depth discussions were held to refine the content and rating of the recommendations. After final approval of the reviewers' review and revision comments, the final recommendation grade was described and finalized by the working group. Eight recommendations are developed for each of the five final categories.

Independent external review

To collect external review opinions before publication of the developed recommendations, separate from the development committee, Korean Society of Pediatric Nephrology, Korean Society of Pediatric Urology, and Korean Society of Nephrology. An external advisory committee composed of clinical and methodology experts expected to be end users of the recommended guidelines was formed. The advisory committee did not prepare recommendations to be included in the clinical practice guideline but served as an external reviewer who consulted at the consensus stage on the derived recommendations. For external review, an expert questionnaire survey was conducted to investigate the degree of consent to the recommendations for each key question. The subject of the survey was an advisory committee (including one methodology expert), and a questionnaire evaluation table was used to respond within the range of 1 point (strongly disagree) to 5 points (strongly agree) to the degree of consent to the recommendation. The external review helped us to harmonize hematuria-related terminology throughout the guideline and to add explanations for some poorly explained abbreviations. We also received feedback that current treatment guidelines for conditions associated with hematuria should be covered in more detail in key question 4, and that further discussion was needed on the usefulness of cystoscopy as a diagnostic test for conditions such as urethral bleeding, nutcracker syndrome, and hemangiomas. Through convergence, we've been able to get feedback and incorporate it into the guidelines.

Update plan for guidelines

In the future, we will continue to derive critical key questions, generate recommendations based on evidence, and update existing recommendations as the evidence changes. The key questions of the evidence-based guidelines will be developed by receiving opinions from patients, related workers, and experts in the clinical field. Because the guidelines produced in the acceptance and adaptation methods are mainly based on research conducted abroad, developing an appropriate recommendation for key questions fitted to the domestic situation based on domestic research results is imperative. The committee will try to promote this in related academic societies and seek cooperation to accumulate data.

We decided to update the latest evidence for the developed recommendation by periodically reviewing new evidence every 5 to 10 years.

Declaration and management of conflicts of interest

All members of the Development Committee provided a conflict-of-interest disclosure before participation and a financial or nonfinancial conflict of interest during the completion of the guidelines. This principle was applied from initiation until the end of development.