Comparison of recommendations in clinical practice guidelines for asthma in children

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Abstract

Background
The objective of this paper was to compare current international guidelines concerning the diagnosis and management of paediatric asthma.

Methods
We systematically searched MEDLINE/PubMed, Cochrane Library, Trip database, EMBASE and the websites of medical societies for Clinical Practice Guidelines (CPGs) on the diagnosis and management of paediatric asthma.
The Agree II tool was used to select high quality guidelines, and recommendations were synthesized to highlight similarities and differences.

Results
The review identified 8 high-quality CPGs, including the international guideline from the Global Initiative for Asthma, as well as national guidelines from the United States of America, Netherlands, United Kingdom, Canada and Australia. Analysis of recommendations revealed consensus on key aspects of diagnosis, such as history-taking and lung function testing, while also highlighting variations in clinical examination, biochemical testing, and technical investigations. Similarly, guidelines converged on the importance of written asthma action plans and reliever therapy with short-acting beta-agonists (SABA), but differed in recommendations for controller therapy, device selection, and treatment goals.

Conclusion
The key recommendations for the diagnosis of paediatric asthma are similar in most clinical practice guidelines. The recommendations for treatment are more diverse concerning the controller and reliever therapy. The dose of ICS and the use of SMART therapy at a specific age are the most relevant differences between the CPGs.

Samenvatting

Achtergrond
Het doel van dit artikel was om de huidige internationale richtlijnen met betrekking tot de diagnose en behandeling van astma bij kinderen te vergelijken.

Methoden
We hebben systematisch gezocht naar klinische richtlijnen over de diagnose en behandeling van pediatrisch astma in MEDLINE/PubMed, Cochrane Library, Trip database, EMBASE en de websites van medische verenigingen.
De Agree II-tool werd gebruikt om richtlijnen van hoge kwaliteit te selecteren en aanbevelingen werden samengevat om overeenkomsten en verschillen te benadrukken.

Resultaten
De recensie identificeerde 8 hoogwaardige CPGs, waaronder de internationale richtlijn van het Global Initiative for Asthma, evenals nationale richtlijnen van de Verenigde Staten van Amerika, Nederland, het Verenigd Koninkrijk, Canada en Australië. Analyse van aanbevelingen bracht consensus aan het licht over belangrijke aspecten van de diagnose, zoals anamnese en longfunctietesten, terwijl ook variaties in klinisch onderzoek, biochemische tests en technisch onderzoek werden benadrukt. Evenzo kwamen richtlijnen samen over het belang van schriftelijke astma-actieplannen en relievertherapie met kortwerkende bèta-agonisten (SABA), maar verschilden ze in aanbevelingen voor controllertherapie, apparaatselectie en behandelingsdoelen.

Conclusie
De belangrijkste aanbevelingen voor de diagnose van astma bij kinderen zijn vergelijkbaar in de meeste richtlijnen voor de klinische praktijk. De aanbevelingen voor de behandeling zijn diverser met betrekking tot de controle- en relievertherapie. De dosis ICS en het gebruik van SMART-therapie op een bepaalde leeftijd zijn de meest relevante verschillen tussen de CPGs.

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Introduction

Asthma is the most prevalent chronic disease among children, and affects between 5 and 10% of children in the European region (1). In Europe, the estimated cost of paediatric asthma is estimated around EUR 3 billion, due to missed school days, restrictions in activities, emergency health care and even death (2).
Asthma is characterized by a chronic airway inflammation with variable expiratory airflow obstruction, causing symptoms such as wheeze, dyspnoea, cough and chest tightness. Whilst 20% of young children have episodes of wheezing, historical asthma guidelines often overlooked the paediatric population (3).

Symptomatic children have a broad differential diagnosis and often a normal physical examination. Objective tests are sometimes difficult to obtain, and there is no gold standard to diagnose asthma (4). These characteristics lead to frequent misdiagnosis. Overdiagnosis can be detrimental as it may subject children to unnecessary treatment and impede the recognition of an alternate diagnosis. Underdiagnosis exposes the child to daily symptoms, exacerbations and airway remodelling.

The aim of this study is to systematically review recommendations for the diagnosis and management of paediatric asthma. By synthesizing diverse recommendations, this research provides primary care physicians with insights into practical strategies for addressing the unique challenges posed by paediatric asthma.

Material and methods

Review scope

The aim of this review was to assess if the recommendations concerning the management and diagnosis of asthma in children differ between published clinical practice guidelines (CPGs).

Search strategy

Two authors searched the medical databases MEDLINE/PubMed, Cochrane Library, Trip database, and EMBASE. The search strategy retained guidelines until July 2022. A Boolean search strategy was jointly designed using available MeSH terms and later adapted to identify relevant studies not indexed by MEDLINE (Table 1). A similar search strategy was used for the other databases.

Table 1: Boolean search strategy

Search strategy	**#1 AND #2 AND #3**
#1	("asthma"[MeSH Terms] OR asthma*[tiab] OR astma*[tiab] OR asthme*[tiab]) OR ("bronchial diseases"[MeSH Terms] OR bronch*[tiab])
#2	("Infant"[Mesh] OR infan*[tiab] OR enfant*[tiab]) OR ("Child"[Mesh] OR child*[tiab]) OR (teen*[tiab] OR newborn*[tiab] OR preschool*[tiab])
#3	"Guideline" [Publication Type] OR "Health policy"[MeSH Terms]

Eligibility criteria

We used the definition of CPGs based on the AGREE II instrument: 'systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances' (5). Only children aged between 0 and 12 years were included. CPGs focussing on the management or diagnosis of asthma were included. Guidelines published in Dutch, French, and English were included. In publications referring to an original guideline, we searched and used only the original and most up-to-date recommendations to simplify the comparison. Guidelines that did not meet these criteria were excluded.

Quality of CPGs

Both authors used the Agree II instrument to assess the quality of the retained CPGs. The guidelines were scored from 0 to 7. Both authors worked independently with periodic comparison and discussion of results. All guidelines that were scored with 7/7 by both authors were included.

Results

Search results

Our initial Boolean search in medical libraries yielded 657 results. The search through the Global Asthma Network (GAN), the Global Initiative for Asthma (GIN), and national medical societies yielded 156 results. These 813 results were screened first on title. All titles that didn't refer directly to asthma were excluded. We subsequently further screened based on abstract and availability of full text. Abstracts that did not mention guidelines for asthma diagnosis or treatment were excluded. The 198 results of this screening were further narrowed down based on the eligibility criteria. This search yielded 29 CPGs (figure 1).

All 29 CPGs were independently rated with the AGREE II tool, as presented in the Appendix. 8 CPGs received the maximum score of 7/7 from both authors: GINA, NHG, FMS, NICE, NIH, SIGN, CTS, and AAH (4,6–13). (table A1)

Cohen's kappa coefficient was used to test the inter-rater reliability between the AGREE II scores of both authors. This analysis requires dichotomous distribution of variables (low or high quality). The authors used an AGREE II score ≥ 4/7 as high quality and < 4/7 as low quality. At this cut-off the Kappa coefficient was 0,72 or a 87% agreement (14).

Content of analysed guidelines

All guidelines discussed diagnosis and management of asthma in children. The NIH focused update 2020 only discussed the management of asthma but referred to the previous ERP3 2007 guideline for some aspects of the diagnosis.

We presented the recommendations from each guideline in 2 sections, one concerning diagnosis, the other concerning the management of asthma. In the recommendations for diagnosis we searched for recommendations about anamnesis, physical examination, biochemical and technical investigations. In the recommendations for management we searched for preventive measures, non-pharmacological measures, the goal of pharmacological intervention, recommendations about inhaler devices, rescue medication, controller medication, the stepwise approach, and dosage of ICS.

Diagnosis

1. <u>Anamnesis</u>

GINA, NHG, FMS, AAH, and NIH recommend questioning about asthma-like symptoms (wheezing, dyspnoea, coughing), symptoms of allergic history, stimuli that trigger asthma (allergic and non-allergic) and smoking status (table 1).

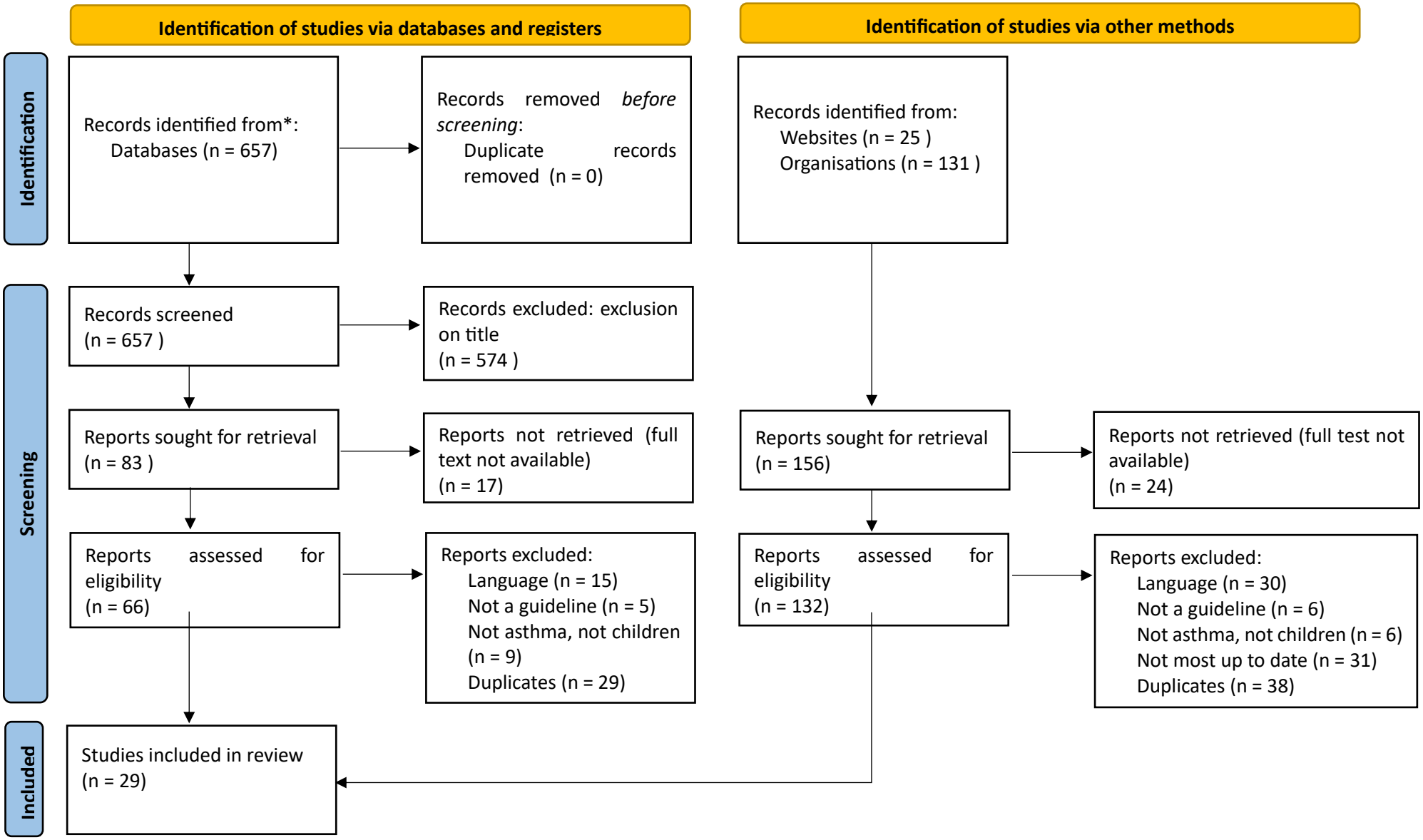


Figure 1: PRISMA flow 2020 diagram

NICE recommends asking about asthma-like symptoms and stimuli that trigger asthma (allergic or non-allergic). CTS and SIGN only recommend questioning about asthma-like symptoms.

2. Physical examination

GINA, NHG, AAH, and NIH recommend a clinical examination involving lung auscultation for possible expiratory wheezing, assessing clinical features of dyspnoea (elevated heart rate, elevated breathing rate, decreased oxygen saturation levels) and activation of accessory muscles during regular breathing. These clinical findings increase the likelihood of asthma but do not rule out the diagnosis if they are not present. Furthermore, GINA, AAH, and NIH recommend a clinical examination for features of allergic rhinitis or the presence of nasal polyposis. Only the AAH recommends an even broader clinical examination including biometrics of the child and assessment of clinical features of atopic skin. The FMS and CTS guidelines do not recommend a clinical examination. The SIGN and NICE guideline only recommend lung auscultation for possible expiratory wheezing.

3. Biochemical examination

GINA, NHG, SIGN , AAH, and NIH recommend a RAST (radioallergosorbent) test only if there is suspicion of an allergic asthma stimulus. This biochemical finding doesn't rule out nor confirms the diagnosis of asthma. According to AAH, SIGN, and NIH, an allergy skin test is an alternative to the RAST test if this test is not conclusive. SIGN is the only guideline that recommends measuring inflammatory biomarkers (blood eosinophilia > 4%). FMS, CTS, and NICE do not recommend any biochemical examination.

4. Technical investigations

4.1 Lung function tests

Lung function tests are recommended by all guidelines. The goal of lung function testing is to objectify variable expiratory airway obstruction. When possible, the diagnosis of asthma is based on characteristic symptoms of asthma in combination with evidence of reversible airway obstruction. Spirometry with bronchodilator reversibility testing is the preferred method to measure reversible obstruction, but other methods such as peak expiratory flow (PEF) measurement or bronchial provocation testing are also proposed in some guidelines.

GINA, NICE, SIGN, and NIH consider that children can undergo spirometry testing from the age of 5. NHG, FMS, AAH, and CTS recommend trying spirometry from the age of 6.

All CPGs recommend assessment of reversible obstructive lung function, preferably with spirometry and bronchodilator reversibility test. A reversibility of 12% is considered to be diagnostic by all guidelines, with no volume changes mentioned. Because of the low sensitivity of spirometry for the diagnosis of asthma, other tests are also recommended as alternative after inconclusive spirometry.

Recommendations about PEF measurements for the diagnosis of asthma vary. NHG, FMS, SIGN, AAH, and NIH don’t recommend PEF measurements for diagnosis. GINA, CTS, and NICE

recommend PEF measurements as an alternative for spirometry or when spirometry is inconclusive. GINA considers that an average diurnal PEF variability >13% demonstrates reversible airflow obstruction. NICE and CTS consider that a 20% increase in PEF after SABA or ICS trial demonstrates reversible airflow obstruction.

Provocation tests are not recommended by NHG and NICE. All other guidelines recommend provocation testing as a useful addition when there is diagnostic uncertainty after spirometry. GINA recommends only exercise challenges for children. The other guidelines recommend one or more of the following provocation tests: methacholine, histamine, mannitol, and exercise challenge tests.

4.2 Chest radiograph

GINA and NIH recommend a chest radiograph when there is diagnostic uncertainty, while AAH recommends a chest radiograph when there are atypical symptoms or localized wheezing. The other guidelines do not recommend a chest radiograph in the diagnostic workup of asthma.

4.3 Fractional Exhaled Nitric Oxide (FeNO)

NICE, SIGN, FMS, and NIH recommend FeNO measurements when there is diagnostic uncertainty after spirometry. Other guidelines do not recommend measuring FeNO.

4.4 Treatment trial

In children unable to perform spirometry or other lung function testing, a therapeutic trial can give the best indication for a diagnosis of asthma. In this case, all guidelines recommend using a treatment trial as a diagnostic tool. NIH recommends an unspecified therapeutic trial in children 1 to 4 years old, with clinical evaluation after 1 month. GINA recommends that under 5 years, low-dose ICS + SABA should be trialled for three months, with clinical improvement supporting the diagnosis of asthma. CTS recommends the same approach but with medium dose ICS + SABA for 3 months, but also recommends giving SABA or even SABA + oral corticosteroids in acute wheezing episodes, with clear improvement after administration also supporting the diagnosis. FMS recommends that under 6 years, high-dose ICS be trialled for three months, with clinical improvement supporting the diagnosis of asthma. NICE recommends trialling medium-dose ICS for 2 months under 5 years, and SIGN recommends an unspecified therapeutic trial under 5 years. AAH and NHG recommend that in children over 12 months, SABA should be administered in acute wheezing episodes, with clinical control after 15 minutes to verify the response.

Table 1: Guidelines for anamnesis.

GINA	NHG	FMS	CTS	NICE	NIH (ERP 3)	SIGN	AAH
Wheezing, dyspnoea, coughing, timing/duration of symptoms, triggers (allergic or non-allergic), smoking status, atopic constitution	Wheezing, dyspnoea, coughing, timing/duration of symptoms, triggers (allergic or non-allergic), smoking status, atopic constitution	Wheezing, dyspnoea, coughing, timing/duration of symptoms, triggers (allergic or non-allergic), smoking status, atopic constitution	Wheezing, dyspnoea, coughing, sputum production	Wheezing, dyspnoea, coughing, variability (daily, seasonal symptoms), triggers (allergic or non-allergic), personal or family history of atopic constitution	Recurrent wheezing, dyspnoea, coughing, triggers (allergic or non-allergic), variability (daily, seasonal symptoms)	Wheezing, dyspnoea, coughing	Wheezing, dyspnoea, coughing, timing/duration of symptoms, triggers (allergic or non-allergic), smoking status, atopic constitution, family history of asthma

Table 2: Guidelines for biochemical examination.

GINA	NHG	FMS	CTS	NICE	NIH (ERP 3)	SIGN	AAH
Not recommended by default in the diagnostic process. RAST test if atopy/an allergic trigger is suspected.	Not recommended by default in the diagnostic process. RAST test if an allergic trigger is suspected. Screening of food allergens is not recommended.	Not recommended	Not recommended	Not recommended	Not recommended by default in the diagnostic process. RAST test or allergy skin test if an allergic trigger is suspected. Role of inflammatory biomarkers (eosinophilia) is being investigated.	Positive allergy skin tests, a positive RAST test or blood eosinophilia > 4% increases the probability of asthma.	Not recommended by default in the diagnostic process. RAST test or allergy skin test if an allergic trigger is suspected.

Table 3: Guidelines for clinical examination.

GINA	NHG	FMS	CTS	NICE	NIH (ERP 3)	SIGN	AAH
Lung auscultation: expiratory wheezing or silent chest are features of asthma. Clinical features of dyspnoea: elevated breathing and heart rate, use of accessory respiratory muscles Inspection of nasal region: features of allergic rhinitis or polyposis. However normal clinical examination can't rule out asthma.	Lung auscultation: expiratory wheezing Clinical features of dyspnoea: elevated breathing and heart rate, use of accessory respiratory muscles Decreased saturation rate. However normal clinical examination can't rule out asthma.	Clinical examination had no added value because normal clinical examination can't rule out asthma.	Clinical examination had no added value because normal clinical examination can't rule out asthma.	Lung auscultation: expiratory wheezing. However normal clinical examination can't rule out asthma.	Lung auscultation: expiratory wheezing, hyper expansion of thorax Clinical features of dyspnoea: elevated breathing and heart rate, use of accessory respiratory muscles Inspection of nasal regio: features of allergic rhinitis or polyposis. Inspection of skin: atopic dermatitis These findings increase the probability of asthma. However normal clinical examination can't rule out asthma.	Lung auscultation: expiratory wheezing However normal clinical examination can't rule out asthma	Lung auscultation: expiratory wheezing Clinical features of dyspnoea: elevated breathing and heart rate, use of accessory respiratory muscles, clubbing Inspection of nasal region: features of allergic rhinitis or polyposis Inspection of skin: atopic dermatitis, chest abnormalities, biometrics of the child However normal clinical examination can't rule out asthma.

Table 4: Guidelines for technical investigations.

	GINA	NHG	FMS	CTS	NICE	NIH (ERP 3)	SIGN	AAH
Age when lung function testing can be tried	5 years	6 years	6 years	6 years	5 years	5 years	5 years	6 years
Spirometry	Recommended to demonstrate reversible airflow obstruction of >12%	Recommended to demonstrate reversible airflow obstruction of >12%	Recommended to demonstrate reversible airflow obstruction of >12%	Recommended to demonstrate reversible airflow obstruction of >12%	Recommended to demonstrate reversible airflow obstruction of >12%	Recommended to demonstrate reversible airflow obstruction of >12%	Recommended to demonstrate reversible airflow obstruction of >12%	Recommended to demonstrate reversible airflow obstruction of >12%
Peak expiratory flow	Alternative to spirometry: average diurnal PEF variability >13% demonstrates reversible airflow obstruction	Not recommended	Not recommended	Alternative to spirometry: 20% increase in PEF after bronchodilator or ICS trial demonstrates reversible airflow obstruction	Recommended when there is diagnostic uncertainty and normal spirometry of obstructive spirometry without reversibility. 20% PEF variability demonstrates reversible airflow obstruction	Not recommended for diagnosis, has a place in monitoring.	Not recommended	Not recommended
Provocation tests	Alternative to spirometry to demonstrate reversible airflow obstruction: exercise challenge test	Not recommended	Methacholine, histamine and exercise challenge tests can be used when there is diagnostic uncertainty	Alternative to spirometry to demonstrate reversible airflow obstruction: Methacholine challenge or exercise challenge	Not recommended	Methacholine, histamine, cold air and exercise challenge tests are useful when there is diagnostic uncertainty,	Methacholine and exercise challenge tests are useful when there is diagnostic uncertainty,	Methacholine, mannitol and exercise challenge tests are useful when there is diagnostic uncertainty, but

	with >12% reduction of FEV1			with >10-15% reduction of FEV1		especially to rule out asthma	especially to rule out asthma	only above the age of 8 years
Chest radiograph	When there is diagnostic uncertainty	Not recommended	Not recommended	Not recommended	Not recommended	When there is diagnostic uncertainty	Not recommended	When symptoms are atypical or wheezing is localized
Therapeutic trial	Under 5 years, a 3 months trial with SABA + low-dose ICS with clinical improvement supports asthma diagnosis. Over 5 years, a therapeutic trial is not used as a diagnostic tool.	Upon presentation with expiratory wheeze, a SABA can be administered, with clinical improvement within 15 minutes supporting diagnosis of asthma	Under 6 years, a 3 months trial with high-dose ICS with clinical improvement supports asthma diagnosis.	Under 5 years, clear improvement of acute episode of wheezing after SABA or SABA + oral corticosteroids supports asthma diagnosis. A 3 months trial with medium-dose ICS with clinical improvement supports asthma diagnosis.	Under 5 years, an 8 weeks trial with medium-dose ICS with clinical improvement supports asthma diagnosis.	Not recommended	Under 5 years and in children who cannot perform spirometry, a therapeutic trial with clinical improvement supports asthma diagnosis.	Children over 12 months presenting with expiratory wheeze, a SABA can be administered, with clinical improvement within 15 minutes supporting diagnosis of asthma.

Treatment

1. Prevention and non-pharmacological treatment

All guidelines recommend written asthma action plans for all patients, except the NHG and FMS, that recommend a written asthma action plan only when asthma is difficult to control (table 8).

Allergen exposure control measures are recommended by CTS, NHG, NIH, and AAH guidelines, but only in children whose symptoms are triggered by allergens.

Non-allergic trigger avoidance includes (second-hand) smoking and air pollution. The CTS only recommends avoiding tobacco smoke exposure. The NICE guideline recommends avoiding air pollution. GINA, NHG, NIH, SIGN, and AAH recommend avoiding both triggers, FMS makes no recommendations.

GINA recommends yearly COVID-19 and influenza vaccination in children over 6 years with moderate to severe asthma. The NHG only recommends yearly influenza vaccines for children under ICS therapy. The NIH recommends influenza vaccination in all children over 6 months. The AAH recommends influenza vaccination in children with severe asthma and COVID-19 vaccination in all asthmatic patients.

GINA, NHG, SIGN, and AAH recommend regular exercise and also recommend reaching a healthy weight.

GINA informs that breathing exercises can alleviate asthma symptoms over 6 years, without effect on lung function. Breathing exercises are recommended by NHG in children when dysfunctional breathing is suspected.

2. Controller therapy

Controller therapy can be initiated when the diagnosis of asthma is confirmed, or sometimes suspected. All guidelines make a difference between children younger than 5 or 6 years and older children, and suggest treating children above 11 or 12 years just like adults. Every guideline uses a stepped approach for asthma treatment, here we only report the preferred treatment options but most guidelines also include alternative treatment options for every step.

All guidelines suggest stepping down controller therapy after 2 to 6 months of good asthma control.

2.1 Children aged 0-5/6 years

In young children, all guidelines recommend SABA as needed (PRN) as a first step, except NIH and GINA which add a short course of ICS during respiratory tract infections (RTI) (table 5). When stepping up to daily controller medication, all guidelines except NHG and FMS recommend starting with daily low doses of ICS. These 2 guidelines recommend starting with a high dose of ICS, with the option to step down to the lowest effective dose if the patient responds to the starting dose.

The next step is a choice between adding an LTRA (recommended by NICE, SIGN, AAH) or giving a higher dose of daily ICS (GINA, CTS, FMS, NIH). The NHG recommends referral to a specialist when the starting high dose ICS is insufficient.

Most guidelines recommend referral to a specialist when medium daily doses of ICS are insufficient. The FMS, addressed to specialists, recommends amping up the ICS dosage until daily quadruple high dose ICS in combination with LTRA and a LABA (equivalent to 1600 µg/d budesonide dry powder inhaler). The NIH, addressed to all medical practitioners, steps up to high doses of daily ICS and LABA and gives oral corticosteroids as a last step.

Table 5: Stepwise management of asthma in children aged 0/1-4/6 years: preferred starting controller medication.

Guidelines	**GINA**	**FMS**	**NHG**	**CTS**	**NICE**	**SIGN**	**AAH**	**NIH**
Step 1	SABA + ICS course during RTI	SABA PRN	SABA PRN	SABA PRN	SABA PRN	SABA PRN	SABA PRN	SABA + ICS course during RTI
Step 2	Low dose ICS	ICS high dose	ICS high dose	Low dose ICS	Low dose ICS	Low dose ICS	Low dose ICS	Low dose ICS
Step 3	Double low dose ICS	Double ICS high dose	Specialist referral	Medium dose ICS	Low dose ICS + LTRA	Low dose ICS + LTRA	Low dose ICS + LTRA	Medium dose ICS
Step 4	Specialist referral	Triple ICS high dose		Specialist referral	Specialist referral	Medium dose ICS	Specialist referral	Medium dose ICS-LABA
Step 5	N/A	Quadruple ICS high dose +- LABA +- LTRA				Specialist referral		High dose ICS-LABA
Step 6								High dose ICS-LABA + oral corticosteroids

2.2 Children aged 5/6-11/12 years

In older children, all guidelines recommend starting with a SABA PRN. When stepping up to daily controller medication, all guidelines except the NHG and FMS recommend starting with daily low doses of ICS (see dosage table). Both Dutch guidelines recommend starting with a high dose of ICS, with the option to step down to the lowest effective dose if the patient responds to the starting dose.

The next preferred step varies widely. The GINA and SIGN recommend associating daily ICS-LABA, the CTS recommends a medium dose ICS, the AAH recommends a high dose ICS and the FMS recommends a double high dose ICS. NICE recommends associating low dose ICS with LTRA, and the NIH recommends ICS-formoterol in a MART approach. The NHG recommends referral.

Follow-up steps are summarized in table 6.

Table 6: Stepwise management of asthma in children aged 5/6-11/12 years: preferred starting controller medication.

Guidelines	**GINA**	**FMS**	**NHG**	**CTS**	**NICE**	**SIGN**	**AAH**	**NIH**
Step 1	SABA PRN	SABA PRN	SABA PRN	SABA PRN	SABA PRN	SABA PRN	SABA PRN	SABA PRN
Step 2	Low dose ICS	High dose ICS	High dose ICS	Low dose ICS	Low dose ICS	Low dose ICS	Low dose ICS	Low dose ICS
Step 3	Low dose ICS-LABA	Double high dose ICS	Specialist referral	Medium dose ICS	Low dose ICS + LTRA	Low dose ICS-LABA	High dose ICS	MART low dose ICS-Formoterol
Step 4	Medium dose ICS-LABA	Triple high dose ICS		Medium dose ICS-LABA	Low dose ICS-LABA	Medium dose ICS		MART medium dose ICS-formoterol
Step 5	Specialist referral	Quadruple ICS high dose +- LABA +- LTRA		Specialist referral	MART low dose ICS-Formoterol	Specialist referral		High dose ICS-LABA
Step 6					MART medium dose ICS-formoterol			High dose ICS-LABA + oral corticosteroids

3. Reliever therapy

All guidelines recommend SABA as needed as reliever therapy for children of all ages. The GINA gives the option of single maintenance and reliever therapy (SMART) with ICS-formoterol starting from the age of 5 years. NIH also recommends SMART for children 4 years and older with moderate to severe asthma

4. Dose of ICS

Table 7 represents the ICS dosage defined by low, medium, and high for each guideline.

5. Devices

5.1 Infants and toddlers

For children aged 0 to 3 years, GINA, NHG, FMS, and CTS recommend a pressurized metered-dose inhaler (pMDI) together with a valved spacer with a face mask. AAH and NIH recommend a pMDI plus valved spacer and face mask for children aged 0 to 5 years. SIGN states that for children aged 0 to 5 years, there is insufficient data to draw recommendations for specific devices. A nebulizer is reserved for the minority of children unable to use a spacer device effectively according to the GINA guidelines.

Table 7: Recommended dosages of ICS.

		Low daily dose (µg/day)			**Medium daily dose (µg/day)**			**High daily dose (µg/day)**		
Drug	Guideline	Child 0-5 years	Child 6-11 years	Child ≥ 12 years	Child 0-5 years	Child 6-11 years	Child ≥ 12 years	Child 0-5 years	Child 6-11 years	Child ≥ 12 years
BDP pMDI	GINA	50-100	100-200	200-500	NA	200-400	500-1000	NA	>400	>1000
	NHG – FMS	50-200			NA			400		
	NICE	100-200			200-400			400-800		
	CTS	100	100-200		200	200-400		NA	>400	>500
	AAH	100-200			NA			200-400		
	SIGN	100			200			400		
	NIH	NA	80-160	80-240	NA	160-320	240-480	NA	>320	>480
Budesonide DPI	GINA	NA*	100-200	200-400	NA	200-400	400-800	NA	>400	>800
	NHG – FMS	100-200			NA			400		
	NICE	100-200			200-400			400-800		
	CTS	NA	<400		NA	400-800		NA	>800	
	AAH	200-400			NA			400-800		
	SIGN	100			200			400		
	NIH	NA	200-400	200-600	NA	400-800	600-1200	NA	>800	>1200
Fluticason proprionate pMDI	GINA	50	50-100	100-250	NA	100-200	250-500	NA	>200	>500
	NHG – FMS	100-200			NA			250		
	NICE	100			100-200			200-400		
	CTS	<200			200-250	200-400	250-500	NA	>400	>500
	AAH	100-200			NA			200-500		
	SIGN	50			100			250		
	NIH	175		250	175-350		250-450	>350		>450

*exception: dry powder cannot be used by children below 5 years of age, however budesonide nebulizer is recommended at a dose of 500µg/d

5.2 Preschoolers

GINA recommends a pMDI plus a valved spacer with a mouthpiece for children aged 4 to 5 years. The Dutch and Canadian guidelines recommend this combination with a mouthpiece for children aged 4 to 7 years of age. The NIH states that a pMDI or a dry powder inhaler (DPI) is equally effective for children above the age of 5 years.

5.3 Older children and teenagers

GINA encourages the healthcare provider to prescribe the most appropriate inhaler device based on patient characteristics (skills, cost, availability) for children above the age of 6 years. Both Dutch guidelines narrow the options to a DPI or an auto inhaler for children above the age of 7 years. CTS and SIGN recommend a DPI or a pMDI with a mouthpiece for children above 6 years, and for children older than 12 years state there is no difference in effectiveness between a pMDI with or without a valved spacer or a DPI. AAH recommends for children above 6 years of age the pMDI plus valved spacer as the first option but states that options such as an auto inhaler or a DPI are equally effective.

The optimal number of breaths to empty a valved spacer completely is generally 5-10 breaths according to the GINA guideline. The NICE guideline does not have a specific recommendation about devices.

6. Treatment goal

All the guidelines state that the ultimate goals are to achieve the best possible asthma control, to reduce the risk of exacerbations and to reduce the risk of side effects of the pharmaceutical treatments.

6.1 Asthma control

The common criteria for good asthma control according to all the guidelines are: symptoms ≤ two times per week, reliever needed ≤ two times per week, no symptoms during sleep, no restrictions of daily activities (working, exercise, school etc). NHG, FMS, SIGN, and CTS consider a normal spirometry (no bronchodilator reversibility, good FEV1 compared to the personal best (≥ 90%) also to be a criterion for good control. NHG, FMS, and SIGN also consider the absence of exacerbations a criterion for good control. CTS states that the absence of a severe exacerbation (no steroid need, no need for hospitalization) and a PEF variability < 10-15% are also criteria for good asthma control. GINA, SIGN, and NIH refer to a set of questionnaires to determine the level of control: children ACT, PAQLQ, ACQ etc.

6.2 Risk of exacerbation

All guidelines state that the presence of certain risk factors can increase the risk of an exacerbation. The common risk factors according to all the guidelines are: a history of severe exacerbation, overuse of SABA reliever (> two prescriptions of 200-dose puff per year), comorbidities (obesity, age, active smoker, hypertension, etc..), low level of asthma control, exposure to triggers. GINA has three other specific risk factors: a spirometry with low FEV1 (or < 60% of the predicted value), the presence of high blood eosinophils and elevated FeNO (in

patients with allergic asthma taking ICS). SIGN and CTS also mention that not meeting all criteria for good control is a risk factor for exacerbation.

Table 8: Non-pharmacological measures.

Recommendation		GINA	NHG	FMS	CTS	NICE	NIH	SIGN	AAH
Prevention and non-pharmacological treatment	Asthma action plan	Recommended for all patients	Recommended for difficult to control asthma	Recommended for difficult to control asthma	Recommended for all patients	Recommended for all patients	Recommended for all patients	Recommended for all patients	Recommended for all patients
	Allergic exposure control	Not recommended	Recommend avoidance of animal, pollen or house dust mites allergens in sensitized children	/	Recommend multi-component allergen avoidance in patients with symptoms triggered by allergens.	/	Recommend multi-component allergen avoidance in patients with symptoms triggered by allergens.	Not recommended	Recommend multi-component allergen avoidance in patients with symptoms triggered by allergens.
	Trigger avoidance	Recommend avoidance of tobacco smoke exposure and air pollution	Recommend avoidance of tobacco smoke exposure and air pollution	/	Recommend avoidance of tobacco smoke exposure	Recommend avoidance of air pollution	Recommend avoidance of tobacco smoke exposure and air pollution	Recommend avoidance of tobacco smoke exposure and air pollution	Recommend avoidance of tobacco smoke exposure and air pollution
	Vaccination	Recommend yearly influenza and COVID-19 vaccination in moderate to severe asthma in children over 6 years.	Recommend yearly influenza vaccination for children under ICS therapy	/	/	/	Recommend yearly influenza vaccination in children over 6 months.	/	Recommend yearly influenza vaccination in severe asthma, and yearly COVID-19 vaccination for all asthmatic patients
	Breathing exercises	In children over 6 years,	Recommend breathing	Recommend breathing	/	/	Not recommended	/	/

		breathing exercises can relieve symptoms of asthma with no effect on lung function.	exercises when there is a suspicion of dysfunctional breathing	exercises when there is a suspicion of dysfunctional breathing					
	Exercise	Recommend regular exercise	Recommend regular exercise	/	/	/	/	Recommend regular exercise	Recommend regular exercise
	Weight loss	Recommend a healthy weight	Recommend a healthy weight	/	/	/	/	Recommend a healthy weight	Recommend a healthy weight
Device		• 0-3 years: pMDI + valved spacer + face mask • 4-5 years: pMDI + valved spacer + mouthpiece • >6 years: choice depends on	• 0-3 years: pMDI + valved spacer + face mask • 4-7 years: pMDI + valved spacer + mouthpiece • >7 years: DPI or autohaler or pMDI + valved spacer + mouthpiece		• 0-3 years: pMDI + valved spacer + face mask • 4-6 years: pMDI + valved spacer + mouthpiece • >6 years: DPI or pMDI + valved spacer +	No strict recommendation, choice depends on the patient's skills.	No strict recommendation, choice depends on the patient's skills. *ERP 3 guideline:* *0-5 years: pMDI + valved spacer* *>5 years: pMDI (with or without valved spacer) or DPI*	• 0-5 years: no recommendation, no evidence of preferred device • 5-12 years: DPI or pMDI + valved spacer • >12 years: DPI or pMDI (with or without valved spacer)	• 0-5years: pMDI + valved spacer + face mask • >6 years: 1st choice pMDI + valved spacer, other options: DPI or autohaler

	patient's skills		mouthpiece • >12 years: DPI or pMDI (with or without valved spacer)				
Treatment goal	Good control, low risk exacerbation and mortality, normal participation (school, work, hobby's etc.), minimal side effects medication						

Table 9: Criteria for asthma control

Guideline	**GINA**	**NHG**	**FMS**	**CTS**	**NICE**	**NIH**	**SIGN**	**AAH**
Common criteria good asthma control	• symptoms ≤ 2 times a week • no symptoms while sleeping			• need for SABA (reliever) ≤ 2 times a week • no limitation of activities (school, hobby, work)				
Secondary criteria	/	• Normal spirometry	• Normal spirometry (no reversibility/ ≥ 90% FEV1 with respect to personal best • No exacerbation	• Normal spirometry (no reversibility/ ≥ 90% FEV1 with respect to personal best • No serious exacerbation (no CS need nor hospitalisation) • PEF diurnal variability < 10-15%	/	/	• Normal spirometry (no reversibility/ ≥ 90% FEV1 with respect to personal best • No exacerbation	/

Table 10: Risk factors for exacerbation

Guideline	GINA	NHG	FMS	CTS	NICE	NIH	SIGN	AAH
Common risk factors for exacerbation	• history of serious exacerbation (CS need or hospitalisation) • Overuse of SABA reliever (> 2 prescriptions 200doses each year)				• Comorbidities (obesity, GERD, rhinosinusitis etc.) • smoking – trigger exposure			
Secondary criteria	• spirometry low FEV1 (< 60% op predicted value) • type 2 inflammatory markers • elevated FeNO (in patients with allergic asthma taking ICS)	/	/	not meeting all criteria for good control	/	/	not meeting all criteria for good control	/

Discussion

This qualitative review yielded a large amount of recommendations for the diagnosis and treatment of asthma in children, from 8 different CPGs. Most of the guidelines are addressed to all healthcare workers and mainly concern adult asthma, with subsections on paediatric asthma. Therefore, the recommendations poorly address the specificity of primary care for wheezing children.

The diagnosis of asthma is complex due to symptoms varying in time and intensity, different phenotypes, and overlap with allergic conditions. Evidence-based CPGs are essential to prevent unnecessary treatment and misdiagnosis, particularly in the vulnerable paediatric population.

There is consensus that physicians should ask about asthma-like symptoms, and most guidelines recommend asking about any allergic history and asthma triggers when taking the child's history. Two guidelines only recommend assessing asthma-like symptoms. The definition of asthma indeed only mentions respiratory symptoms and variable airway obstruction, and allergic or non-allergic triggers are only present in some phenotypes.

Not all guidelines recommend a clinical examination and those that do also disagree on its extensiveness. This is because of the low sensitivity and specificity of clinical signs in the diagnosis of asthma. All guidelines agree that a normal physical examination cannot rule out asthma. Nevertheless, physical examination is essential to assess if another diagnosis is more likely or if comorbidities are present.

Most guidelines recommend a RAST test or skin patch test if an allergic trigger is suspected, but 3 guidelines don't advise any biochemical tests. SIGN is the only one recommending measuring blood eosinophils during diagnosis to assess an atopic constitution. These differences highlight that biochemical exams aren't used for diagnosis but can reveal allergic conditions often present in asthma.

All guidelines agree that lung function testing is necessary to confirm reversible airway obstruction, a core feature of asthma. General advice is to start lung function testing around 5 or 6 years. All guidelines consider spirometry with bronchodilator reversibility to be the first choice. 3 guidelines offer PEF as an alternative lung function test. When there is a normal spirometry, guidelines recommend provocation tests or referral to a specialist for further diagnosis.
The coexistence of different lung function tests highlights the main challenge in asthma diagnosis because airway obstruction fluctuates over time and one normal spirometry cannot rule out asthma. Performing spirometry during a symptomatic episode or repeating spirometry can raise the sensitivity. Daily PEF measurements or PEF during a symptomatic episode can be useful when spirometry is unavailable.

For children under 5 years of age, when lung function tests aren't feasible, all guidelines suggest a treatment trial if history and physical examination suggest asthma. Most CPGs recommend trying controller medication for 2 or 3 months, with improvement in symptoms

and clinical condition raising the likelihood of asthma. Some also suggest providing reliever medication during a symptomatic episode and assessing any improvement after 15 minutes.

Lastly, only 3 guidelines recommend chest radiographs when there is diagnostic uncertainty because chest radiographs are used to exclude other pathologies but not to demonstrate asthma.

The characteristics of primary care make it ideally suited to treat asthmatic patients. Primary care aligns with the variable nature of asthma severity, ensuring prompt intervention and ongoing adjustment of treatment plans. The long-term follow-up also facilitates patient education and empowerment. Additionally, the same physician can treat relevant comorbidities to improve quality of life and can implement relevant secondary prevention strategies like vaccination and smoking cessation advice.

One notable finding is the consensus among guidelines regarding the importance of written asthma action plans. All guidelines recommend providing a tailored written plan to all patients, except the Dutch guidelines that reserve them for difficult-to-control asthma. While all guidelines advocate for general trigger avoidance, only 4 guidelines recommend avoiding aeroallergens. This consensus reflects that patient empowerment can reduce doctor visits and improve quality of life. Differences in recommendations on allergen avoidance arise because of the labour-intensive implementation and individually variable effect. The different national strategies on vaccination are reflected in the national guidelines, with systematically different advice.

The consensus concerning the use of SABA as reliever therapy demonstrates its pivotal role in symptom management and excellent historical safety record. However, the GINA and NIH introduced SMART protocols as a second option in children above 5 years of age. This option mirrors the recent changes in adult asthma and follows the growing evidence supporting SMART protocols in children. Future research will elucidate its place in the treatment of younger children.

The stepped approach to controller therapy is fundamental in asthma management. All guidelines recommend ICS as the cornerstone of daily therapy. The Dutch guidelines are the only that recommend starting with a high ICS dosage in every patient, while other guidelines recommend starting treatment based on clinical judgment of severity. Notably, age stratification guides treatment decisions, with a more cautious approach for children under 5 or 6 years old. In these younger children, guidelines avoid associating LABA and are quicker to recommend specialist referral. In older children, the association of LABA is reserved for moderate to severe cases. This age-based differentiation reflects the uncertainty of asthma diagnosis in young children, where symptomatology is less distinct and the effectiveness of LABA is still unproven.

The place of LTRA is also variable, sometimes considered a last resort association on top of ICS and LABA, sometimes as a possible association with ICS for moderate asthma, and sometimes not recommended at all.

The choice of device for administering medication depends on the age of the child. There is consensus that for children under 5-7 years, a pMDI with a valved spacer and face mask or mouthpiece is recommended. Nebulizers are never recommended as a first choice. In children above 7 years, the evidence is lacking and the choice depends on patient factors.

To decide when to step up or step down treatment, clinicians need to assess asthma control and risk of exacerbations. For asthma control, 4 criteria are recommended by all guidelines: symptoms ≤ 2 times a week, use of reliever ≤ 2 times a week, no symptoms while sleeping, and no limitation of activities. Some guidelines add secondary parameters such as spirometry, presence of exacerbations or PEF variability. The following risk factors increase the chance of exacerbations: a history of severe exacerbation, overuse of SABA, presence of comorbidities, trigger exposure, and smoking. Spirometric values, the presence of inflammatory biomarkers, and an elevated FeNO are also proposed by a minority of guidelines.

The study discussed in this paper presents a comprehensive analysis of various CPGs concerning the diagnosis and management of asthma in children, and has several strengths and limitations. Strengths include its systematic approach to literature search and selection, utilizing established tools like the AGREE II instrument for assessing guideline quality. The inclusion of a wide range of guidelines spanning different regions and specialties enhances the comprehensiveness of the findings. The detailed comparison of recommendations across guidelines provides valuable insights into the current landscape of paediatric asthma care. However, several limitations need acknowledgment. The search strategy might have missed relevant guidelines despite efforts to utilize multiple databases and comprehensive search terms. Additionally, the inclusion criteria limited the scope to guidelines published in Dutch, French, and English, potentially excluding information from guidelines in other languages. Furthermore, the quality assessment of guidelines using the AGREE II instrument, while providing a structured approach, is inherently subjective and might introduce bias. Moreover, the discussion lacks consideration of contextual factors such as healthcare system differences and resource availability, which can significantly influence guideline applicability and implementation. Finally, while the paper provides a comprehensive overview of existing guidelines, it does not consider updates or revisions beyond July 2022, potentially overlooking recent advancements in asthma management. Addressing these limitations could enhance the robustness and applicability of the study findings.

Conclusion

In this study, the recommendations of 8 CPGs were compared to identify relevant differences and similarities in the diagnosis and management of asthma in children. These recommendations cover various aspects of asthma care including anamnesis, physical examination, biochemical and technical investigations, preventive and non-pharmacological measures, choice of controller and reliever medication, dosage of ICS, choice of inhaler device, and treatment goals. This synthesis of recommendations reveals the essence of paediatric asthma care and will allow primary care physicians to optimise their daily practice.

From a medical viewpoint the GINA guideline provides the most evidence-based and detailed recommendations. However, national guidelines take the local implementation and operation of the healthcare system more into account. For general practitioners we believe that the knowledge of different guidelines improves patient-centred care.

References

1. The Global Asthma Report 2022 [Internet]. [cited 2024 Apr 30]. Available from: http://globalasthmareport.org/burden/burden.php

2. van den Akker-van Marle ME, Bruil J, Detmar SB. Evaluation of cost of disease: assessing the burden to society of asthma in children in the European Union. Allergy. 2005 Feb;60(2):140–9.

3. Cope SF, Ungar WJ, Glazier RH. International Differences in Asthma Guidelines for Children. Int Arch Allergy Immunol. 2009;148(4):265–78.

4. Global Initiative for Asthma - GINA [Internet]. [cited 2022 Oct 6]. 2022 GINA Main Report. Available from: https://ginasthma.org/gina-reports/

5. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. Can Med Assoc J. 2010 Dec 14;182(18):E839–42.

6. Astma bij kinderen | NHG-Richtlijnen [Internet]. [cited 2022 Oct 6]. Available from: https://richtlijnen.nhg.org/standaarden/astma-bij-kinderen

7. Duiverman EJ, Jöbsis Q, van Essen-Zandvliet EE, van Aalderen WM, de Jongste JC, Sectie Kinderlongziekten van de Nederlandse Vereniging voor Kindergeneeskunde. [Guideline 'Treating asthma in children' for pediatric pulmonologists (2nd revised edition). I. Diagnosis and prevention]. Ned Tijdschr Geneeskd. 2003 Sep 27;147(39):1905–8.

8. Overview | Asthma: diagnosis, monitoring and chronic asthma management | Guidance | NICE [Internet]. NICE; [cited 2022 Oct 6]. Available from: https://www.nice.org.uk/guidance/ng80

9. Cloutier MM, Teach SJ, Lemanske RF, Blake KV. The 2020 Focused Updates to the NIH Asthma Management Guidelines: Key Points for Pediatricians. Pediatrics. 2021 Jun;147(6):e2021050286.

10. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. J Allergy Clin Immunol. 2007 Nov;120(5 Suppl):S94-138.

11. British Thoracic Society, Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. Thorax. 2014 Nov;69 Suppl 1:1–192.

12. Yang CL, Hicks EA, Mitchell P, Reisman J, Podgers D, Hayward KM, et al. Canadian Thoracic Society 2021 Guideline update: Diagnosis and management of asthma in preschoolers, children and adults. Can J Respir Crit Care Sleep Med. 2021 Nov 2;5(6):348–61.

13. Australian Asthma Handbook [Internet]. [cited 2022 Oct 6]. Available from: https://www.asthmahandbook.org.au/

14. McHugh ML. Interrater reliability: the kappa statistic. Biochem Medica. 2012 Oct 15;22(3):276–82.

15. McNamara D, Asher I, Davies C, Demetriou T, Fleming T, Harwood M, et al. Asthma And Respiratory Foundation NZ New Zealand Child Asthma Guidelines: a quick reference guide. :26.

16. Borges W, Burns D, Sarinho E, Guedes H, Pitchon R, Anderson MIP, et al. Asthma in childhood: drug therapy. Rev Assoc Médica Bras. 2011 Aug;57:369–76.

17. Masekela R, Jeevanathrum A, Kling S, Gray TC, Morrison J, Vanker A, et al. Asthma treatment in children: A pragmatic approach. S Afr Med J. 2018 Jul 25;108(8):612–8.

18. Pizzichini MMM, Carvalho-Pinto RM de, Cançado JED, Rubin, Cerci Neto A, Cardoso AP, et al. 2020 Brazilian Thoracic Association recommendations for the management of asthma. J Bras Pneumol [Internet]. 2020 Mar 2 [cited 2022 Oct 6];46. Available from: http://www.scielo.br/j/jbpneu/a/jbyyhBv98bWq3WksvBqnDBn/?lang=en

19. Management Guidelines [Internet]. [cited 2024 Apr 30]. Available from: http://globalasthmanetwork.org/advocacy/guidelines.php

20. Gaillard EA, Kuehni CE, Turner S, Goutaki M, Holden KA, de Jong CCM, et al. European Respiratory Society clinical practice guidelines for the diagnosis of asthma in children aged 5-16 years. Eur Respir J. 2021 Oct;58(5):2004173.

21. López-Viña A, Agüero-Balbín R, Aller-Alvarez JL, Bazús-González T, Cosio BG, García-Cosio FB, et al. [Guidelines for the diagnosis and management of difficult-to-control asthma]. Arch Bronconeumol. 2005 Sep;41(9):513–23.

22. van der Molen T, Østrem A, Stallberg B, Østergaard MS, Singh RB. International Primary Care Respiratory Group (IPCRG) Guidelines: management of asthma. Prim Care Respir J J Gen Pract Airw Group. 2006 Feb;15(1):35–47.

23. Arakawa H, Adachi Y, Ebisawa M, Fujisawa T, Committee for Japanese Pediatric Guideline for Childhood Asthma, Japanese Society of Pediatric Allergy and Clinical Immunology, et al. Japanese guidelines for childhood asthma 2020. Allergol Int Off J Jpn Soc Allergol. 2020 Jul;69(3):314–30.

24. Ducharme FM, Dell SD, Radhakrishnan D, Grad RM, Watson WT, Yang CL, et al. Le diagnostic et la prise en charge de l'asthme chez les enfants d'âge préscolaire : document de principes de la Société canadienne de thoracologie et de la Société canadienne de pédiatrie. Paediatr Child Health. 2015 Oct 5;20(7):362–71.

25. Deschildre A, Abou-Taam R, Drummond D, Giovannini-Chami L, Labouret G, Lejeune S, et al. Mise à jour des recommandations (2021) pour la prise en charge et le suivi des patients asthmatiques adolescents (de 12 ans et plus) sous l'égide de la Société de pneumologie de langue française (SPLF) et de la Société pédiatrique de pneumologie et allergologie (SP2A). Version longue. Rev Mal Respir. 2022 Feb 1;39(2):e1–31.

26. Organization WH. Prevention and control of noncommunicable diseases: guidelines for primary health care in low resource settings [Internet]. World Health Organization; 2012 [cited 2024 Apr 30]. Available from: https://iris.who.int/handle/10665/76173

27. Marguet C. Prise en charge de la crise d'asthme de l'enfant (nourrisson inclus). Rev Mal Respir. 2007 Apr;24(4):427–39.

28. FitzGerald JM, Lemiere C, Lougheed MD, Ducharme FM, Dell SD, Ramsey C, et al. Recognition and management of severe asthma: A Canadian Thoracic Society position statement. Can J Respir Crit Care Sleep Med. 2017 Oct 2;1(4):199–221.

29. Larenas Linnemann DES, Del Río Navarro BE, Luna Pech JA, Romero Lombard J, Villaverde Rosas J, Cano Salas MC, et al. Recommendations for the prevention and diagnosis of asthma in children: Evidence from international guidelines adapted for Mexico. Allergol Immunopathol (Madr). 2018 Jun;46(3):291–303.

30. Al-Moamary MS, Alhaider SA, Alangari AA, Ghobain MOA, Zeitouni MO, Idrees MM, et al. The Saudi Initiative for Asthma - 2019 Update: Guidelines for the diagnosis and management of asthma in adults and children. Ann Thorac Med. 2019 Jan 1;14(1):3.

31. Masekela R, Risenga SM, Kitchin OP, White DA, Davis G, Goussard P, et al. The diagnosis of asthma in children: An evidence-based approach to a common clinical dilemma. S Afr Med J. 2018 Jun 26;108(7):540.

Appendix

Table A.1: AGREE II scores by both authors

Guideline title	Publication or latest update	Source - country of origin	Agree II score	
			Author 1	Author 2
New Zealand Child Asthma Guidelines(15)	2020	Respiratory foundation New Zealand	3/7	3/7
Asthma in childhood: drug therapy(16)	2011	Brazilian Society of paediatrics - Brazil	3/7	5/7
Asthma management guideline 2020 focussed update (9)	2020	NIH - United States	7/7	7/7
Asthma treatment in children: a pragmatic approach (17)	2018	SAMJ - South Africa	4/7	4/7
Asthma: diagnosis, monitoring and chronic asthma management(8)	2021	NICE – United Kingdom	7/7	7/7
Asthma bij kinderen(6)	2022	NHG – Netherlands	7/7	7/7
Asthma bij kinderen(7)	2021	Federatie medische specialisaten – Netherlands	7/7	7/7
Australian Asthma Handbook(13)	2022	National Asthma Council – Australia	7/7	7/7
Brazilian Thoracic Association: recommendations for the management of asthma(18)	2020	Brazilian Thoracic Association – Brazil	3/7	2/7
Canadian Thoracic Society 2021: guideline update: diagnosis and management of asthma in preschoolers, children and adults(12)	2021	Canadian Thoracic Society – Canada	7/7	7/7
Clinical practice guideline for the management of childhood asthma (19)	2014	Malaysian Thoracic Society – Malaysia	1/7	2/7
European Respiratory Society: clinical practice guidelines for the diagnosis and management of asthma (20)	2021	European Respiratory Society – Europe	5/7	7/7
GINA guideline 2022 report (4)	2022	GINA	7/7	7/7
Guideline for asthma management in Nigeria (19)	2017	Nigeria Thoracic Society - Nigeria	4/7	2/7
Guidelines for the diagnosis and management of difficult to control asthma (21)	2005	Spanish Respiratory Society of Pulmonology and Thoracic Surgery – Spain	2/7	2/7
International Primary Care Respiratory Group (IPCRG)	2006	International Primary Care Respiratory Group	3/7	2/7

Guidelines: management of asthma (22)				
Japanese guideline for childhood asthma (23)	2020	Japanese Society of Pediatric Allergy and Clinical Immunology – Japan	4/7	5/7
Le diagnostic et la prise en charge de l'asthme chez les enfants d'âge préscolaire (24)	2015	Canadian Pediatric Society – Canada	3/7	3/7
Malawi Standard Treatment Guidelines (MSTG) (19)	2015	Ministry of Health Malawi	1/7	1/7
Mise à jour des recommandations (2021) pour la prise en charge et le suivi des patients asthmatiques adolescents(25)	2021	la Société de pneumologie de langue franc¸aise (SPLF) et de la Société pédiatrique de pneumologie et allergologie	5/7	5/7
Palestinian guidelines for diagnosis and management of bronchial asthma (19)	2003	Ministry of Health Palestina	4/7	2/7
Prevention and control of noncommunicable diseases: guidelines for primary health care in low resource settings (26)	2012	WHO	5/7	7/7
Prise en charge de la crise d asthme de l' enfant: Recommandations pour la pratique Clinique (27)	2007	Groupe de Recherche sur les Avancées en PneumoPédiatrie (GRAPP) – France	3/7	3/7
Recognition and management of severe asthma: a Canadian Thoracic Society statement (28)	2017	Canadian Thoracic Society – Canada	6/7	7/7
Recommendations for the prevention and diagnosis of asthma in children: evidence from international guidelines adapted for Mexico (29)	2017	Sociedad Espanola de Inmunologıa Clinica,Alergologıa y Asma Pediatrica - Mexico	4/7	4/7
Guide sur le diagnostic er la prise en charge de l'asthme de l'enfant (19)	2010	Société Algérienne de Pédiatrie – Algeria	2/7	3/7
SIGN 158: British guideline on the management of asthma (11)	2019	British Thoracic Society – United Kingdom	7/7	7/7
Saudi Initiative for Asthma: guidelines for the diagnosis and management of asthma in adults and children (30)	2019	SINA/Saudi Thoracic Society – Saudia Arabia	4/7	4/7
The diagnosis of asthma in children: An evidence based approach to a common clinical dilemma (31)	2018	South African Childhood Asthma Working Group – South Africa	4/7	3/7