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# Pediatric Respirology and Critical Care Medicine

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# Pediatric Respirology and Critical Care Medicine

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# Pediatric Respirology and Critical Care Medicine

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## Contents

# Pediatric Respiratory Morbidity in Asia: Harnessing Diversity for Better Outcomes

Pediatric respiratory morbidity arises from a wide variety of problems that may be congenital, infective, or allergic in nature, occurring either independently or as part of systemic diseases. These conditions range from simple to complex and life-threatening. Because of this diversity, the burden—both morbidity and mortality—attributable to respiratory diseases in children varies widely not only between countries but also within countries. These variations stem from differences between urban and rural populations, socio-economic disparities, and unequal access to healthcare. The current issue touches upon three different aspects of pediatric respiratory disease in equally diverse settings.

Shen *et al*.[1] have shared their experience in controlling fatal severe asthma among Chinese children. Fatal asthma can result from multiple factors, including individual risk factors affecting disease severity, access to care, quality of care provided, and the availability of appropriate medications and guidance for their use. Interventions to prevent asthma-related mortality in children therefore require a multipronged strategy. The paper discusses and shares experiences in effectively reducing asthma mortality through various health-system-level interventions. It outlines the role of a national action plan focused on asthma control in vulnerable child populations and documents the evolution of national guidance as global and local evidence changed. The authors also highlight the establishment of specialised asthma clinics at different levels of healthcare to support guideline implementation and emphasise the essential role of trained health staff in running these centres. The impact of training on quality of care is brought into focus, along with the long-term sustainability of these efforts through regular certification and plaque-recognition programs. Finally, the paper raises valid concerns regarding the need to identify children at high risk of severe or fatal attacks, proposing alternative strategies since many deaths occur at home or before reaching a health facility. These insights are relevant to other nations and offer a broad framework that can be adapted or adopted to reduce asthma-related mortality in children across diverse settings.

Ng *et al*.'s[2] retrospective study on vitamin D and zinc status among children hospitalised in Hong Kong SAR documents deficiencies in these micronutrients, which play important roles in preventing respiratory diseases. Only 24% of children showed adequate levels of both nutrients, while about 25.6% had combined deficiency or insufficiency. Such local data is important as the global prevalence of low vitamin D varies according to latitude, skin pigmentation, sun exposure, cultural practices, and diet. Many LMIC populations have a high prevalence of low 25(OH)D levels in infants and adolescents. Zinc deficiency is similarly common in low-resource settings where diets are cereal-based, animal-protein intake is low, and diarrhoeal disease burden is high. Soil zinc depletion and food-processing techniques further reduce dietary zinc bioavailability. High-risk groups for these deficiencies include exclusively breastfed infants without supplementation, preterm infants, children with malabsorption (such as cystic fibrosis, celiac disease, or inflammatory bowel disease), those with chronic liver or renal disease, children with limited sunlight exposure, obese children (due to vitamin D sequestration), and children with recurrent infections.

Serum 25-hydroxyvitamin D [25(OH)D] is the accepted marker of vitamin D status; however, acute illness and inflammation can alter circulating levels. Variability in vitamin D–binding protein levels and assay methods also influences interpretation. Similarly, serum/plasma zinc has high biological variability and is reduced by inflammation, fasting status, and time of day. These factors must be considered when interpreting these results.

Large, methodologically robust meta-analyses and individual participant data (IPD) analyses exist for both nutrients, although results vary depending on outcome measured, population characteristics, dosing regimen, and baseline status. Numerous randomized controlled trials have evaluated vitamin D supplementation for preventing acute respiratory infections (ARIs). Earlier pooled analyses showed modest reductions in ARI risk, particularly among individuals who were vitamin D-deficient at baseline and when supplements were administered daily or weekly rather than as large bolus doses.[3] More recent and larger meta-analyses—including IPD analyses—report more nuanced or null overall effects when newer trials are included.[4,5] Evidence for benefit in reducing asthma exacerbations exists in some trials but is not consistently reproduced across all studies.[6] Factors contributing to these mixed results include heterogeneity in baseline vitamin D status, differences in dosing regimens, age distributions, and outcome definitions.

For zinc, evidence of benefit in conditions other than acute diarrhoea is mixed. Some trials and meta-analyses show shorter hospital stays or faster clinical recovery with zinc supplementation, especially in populations with prevalent baseline deficiency; however, other analyses report no consistent benefit across all settings.[7-9] Trials combining zinc with vitamin A or other micronutrients have also produced mixed findings; synergistic effects are biologically plausible but not consistently demonstrated. Targeted supplementation—treating documented deficiency—shows more consistent benefit than routine high-dose supplementation in unselected populations. For pneumonia and other severe respiratory diseases, the evidence for vitamin D or zinc as adjunct therapies is mixed and appears to depend on baseline nutritional status, age, geography, and dosing schedules. The study by Ng *et al*.[2] adds to understanding of deficiency prevalence in the Hong Kong SAR population.

Huang *et al*.[10] have shared their experience with flexible fiberoptic pediatric bronchoscopy (FFB) based on a chart review of 155 children from a centre in southern Taiwan. The article highlights the indications and utility of the procedure across different age groups. They document the role of FFB in evaluating airway abnormalities in infants presenting with noisy breathing, and their findings align with many other published studies. However, variations in diagnostic yield across studies do exist, partly because upper airway disease and stridor may be primarily evaluated by ENT specialists in some centres.

Hope this diverse mix of the articles in this issue have something for our equally diverse readership.

May you ring in the New Year with Happy reading!

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## Conflicts of interest

There are no conflicts of interest.

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Original Article

# Vitamin D and Zinc Deficiency in a Pediatric Population: A Retrospective Study

**Daniel Kwok-Keung Ng[1], Roman Shing-Cheung Ho[2], Angel Yee-Man Wong[3], Shuk-Yu Leung[4]**

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## Abstract

**Background:** Vitamin D and zinc are essential micronutrients with critical roles in immune regulation, bone health, and cellular function. Unfortunately, deficiencies in both nutrients are prevalent globally, particularly among pediatric populations. **Methods:** This retrospective study investigated the prevalence of vitamin D and zinc deficiencies in the pediatric population managed in either out-patient or in-patient setting in one private hospital in Hong Kong and to assess the association between these deficiencies with respiratory infections and growth parameters. **Results:** A retrospective analysis of 262 pediatric patients (less than 19 years old) revealed a high prevalence of abnormally low vitamin D levels (22.9% deficiency and 41.6% insufficiency) and zinc deficiency (37.0%), with 25.6% exhibiting combined deficiencies. Vitamin D and zinc levels were positively correlated ($r = 0.24$, $P < 0.001$). Combined deficiencies were associated with an increased risk of pneumonia (odds ratios 4.5, 95% confidence interval 1.8–11.2, $P = 0.001$). Unfortunately, the deficiencies could not be predicted from anthropometric growth indicators such as weight, height, or body mass index percentile. **Conclusions:** Vitamin D insufficiency/deficiency and zinc deficiency are common in pediatric population. Screening for the deficiency of both vitamin D and zinc is indicated for children with pneumonia even in the absence of subnormal growth. Earlier detection and intervention through supplementation or dietary modifications would be beneficial in promoting the health of this otherwise healthy pediatric population and potentially reduce pneumonia recurrence.

**Keywords:** Children, Chinese, deficiency, pneumonia, vitamin D, zinc

## Introduction

Vitamin D and zinc are essential nutrients with broad physiological roles, including immune regulation, bone health, and cellular functions.[1] Vitamin D plays a critical role in calcium metabolism and immune modulation, while zinc is vital for enzyme function, deoxyribonucleic acid (DNA) synthesis, and immune defense.[2,3] Recent research underscored the common occurrence of vitamin D and zinc deficiencies, particularly among pediatric populations. These deficiencies are especially concerning during the critical stages of childhood and adolescence, as they exacerbate immune system dysfunction, contribute to bone demineralization, and hinder normal growth and development.[4-6] Children with both deficiencies often present with increased rates of respiratory diseases, such as pneumonia or asthma.[7-10] Despite this, the co-occurrence of these deficiencies is often under-recognized in clinical practice, leading to missed opportunities for earlier intervention and treatment.

Vitamin D is synthesized in the skin on exposure to sunlight or obtained through dietary sources. It undergoes two hydroxylation reactions in the liver and kidneys to form its active metabolite, 1, 25-dihydroxyvitamin D, which is responsible for regulating calcium and

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phosphate absorption in the intestines.[11] In addition to its significance in sustaining bone health, vitamin D plays a pivotal role in regulating the immune system by stimulating the production of antimicrobial peptides and enhancing the activity of immune cells, thereby aiding the gut microbiome and safeguarding the lungs against infections.[12] Zinc, on the other hand, is crucial for a wide range of enzymatic processes, including DNA replication, protein synthesis, and cell division.[3] In addition, zinc deficiency during growth phases can contribute to growth faltering, as evidenced by a review identifying a link between inadequate dietary zinc and stunting in children under 4 years old. [13] Zinc is also integral to immune function, supporting the development and activity of immune cells, particularly T-cells, B-cells, and natural killer cells. Zinc deficiency can impair the immune system's ability to fend off infections and can disrupt the integrity of epithelial barriers, which are vital for preventing pathogen invasion.[14-16]

The global prevalence of vitamin D deficiency was estimated to affect up to 1 billion people, with a large proportion of these cases found in children. Moreover, vitamin D insufficiency may be found in nearly 50% of the population.[17,18] In Southeast Asia, the prevalence of vitamin D deficiency ranges from 6% to over 70%, depending on the population studied.[19] Concerning Hong Kong, Chan *et al.*[20] revealed that 33.5% of healthy 3-month-old infants had vitamin D deficiency. For children under 6 years, Guo *et al.*[21] found that 10.8% are estimated to have vitamin D deficiency, while for ages 6–11 years, Zhang *et al.*[22] published regional data with a prevalence of up to 40.3%. Cheung *et al.*[23] showed that adolescents in Hong Kong exhibited the highest prevalence, with 64.7% of 12–16-year-old having deficient vitamin D levels. Similarly, zinc deficiency affects approximately 17% of the global population, with higher rates among children in low-income countries.[24] Data specifically focusing on the population in Hong Kong regarding zinc deficiency are limited. Nevertheless, Lu *et al*.[6] reported that approximately 9.62% of children 6 to 18-years-old in China had zinc deficiency. Within this population, zinc deficiency was found to be more prevalent in younger children (6–11 years) compared to older children (12–18-years), with a prevalence of 10.44% and 8.85%, respectively.[6]

The coexistence of vitamin D and zinc deficiencies has even more significant compounded effects on health, especially in vulnerable populations like children.[4,24] Both nutrients are essential for immune function, bone health, and growth, and deficiencies in either can exacerbate immune dysfunction, making individuals more susceptible to infections.[12,14,18,25] In children, these deficiencies are associated with growth delays, increased risk of respiratory infections, and impaired bone development.[8-10,26] Studies showed that they influenced each other's function. Zinc, for instance, is essential for the proper functioning of vitamin D receptors and plays a critical role in the transcriptional regulation of vitamin D-dependent genes.[27,28] Conversely, vitamin D supports zinc homeostasis by regulating zinc transporter proteins, such as ZnT10, to maintain adequate cellular zinc levels.[29]

The primary objective of this study was to evaluate the prevalence of vitamin D insufficiency/deficiency and zinc deficiency among the pediatric population in Hong Kong, while exploring their associations with respiratory infections and growth parameters and assess potential correlations between vitamin D and zinc levels with anthropometric growth indicators, including weight, height, and body mass index (BMI) percentiles.

## Materials and Methods

### Study population

This was a retrospective cross-sectional study analyzing data from a sample of 262 pediatric patients, including both in-patients and out-patients, under 19 years old collected from the pediatric clinic at Hong Kong Sanatorium and Hospital, a private general hospital in Hong Kong Special Administrative Region, China. The study period was from January 2023 to December 2024. The study was approved by the Hong Kong Sanatorium and Hospital Medical Group Research Committee (RC 2025-24).

### Data collection

Serum levels of vitamin D (measured as 25-hydroxyvitamin D) and zinc were collected through routine blood tests. Vitamin D insufficiency was defined as serum levels 50–75 nmol/L, while vitamin D deficiency as serum levels <50 nmol/L. Zinc deficiency was defined as serum zinc levels <10 μmol/L. In addition, gender, age, and available anthropometric data, including weight, height, and BMI percentiles, were collected for each patient along with diagnoses leading to medical consultation of respiratory conditions such as pneumonia, bronchiolitis, and asthma. For the diagnosis of pneumonia, it was based on the presence of symptoms and signs of pneumonia, that is, fever, cough, dyspnea, inspiratory crackles, percussion dullness, and chest X-ray changes with or without elevated C-reactive protein and procalcitonin. All the diagnoses were made by one of the author's diabetes knowledge, an accredited pediatric respiratory medicine specialist.

### Statistical analysis

The study assessed the prevalence of zinc deficiency, vitamin D insufficiency/deficiency, as well as the coexistence of both deficiencies. In addition, the prevalence of pneumonia was analyzed across various deficiency groups to explore potential associations with these nutrient levels. The relationship between vitamin D/zinc deficiencies and growth indicators, such as weight,

height, or BMI, was also examined. Furthermore, correlation between vitamin D and zinc levels was also investigated.

The normality of data was assessed by the Shapiro–Wilk test. Continuous variables were presented as the mean ± standard deviation. Non-normal variables were reported as median (interquartile range). Categorical variables are summarized as frequencies and percentages. The Chi-square or Fisher's exact tests were used to compare proportions. The receiver-operating characteristic (ROC) curve analysis was used to determine the serum vitamin D level for identifying pneumonia. Logistic regression analysis was used to investigate predictors of pneumonia. Odds ratios (OR) along with 95% confidence interval (CI) were calculated. Pearson's correlation coefficient analysis was used for assessing the association between serum zinc and vitamin D levels. A $P$ value < 0.05 was considered statistically significant. All statistical analyses were performed using IBM Statistical Package for the Social Sciences Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

## Results

A total of 262 children were included for analysis with mean age of 5.6 ± 3.4 years with a male-to-female ratio of 1.9:1. Diagnoses ranged from allergic rhinitis (30.9%), pneumonia (21.0%), bronchiolitis (12.2%), asthma (6.1%), and upper respiratory infection (4.2%) [Table 1].

**Table 1: Demographic data and diagnoses ($n$ = 262)**

| *N* | 262 |
|---|---|
| Age, years (mean ± SD) | 5.6 ± 3.4 |
| Male-to-female ratio | 1.9:1 |
| Diagnoses: | |
| Allergic rhinitis | 81 (31%) |
| Pneumonia | 55 (21%) |
| Bronchiolitis | 32 (12%) |
| Asthma | 16 (6%) |
| URI | 11 (4%) |
| GE | 9 (3%) |
| Sinusitis | 6 (2%) |
| Tonsillitis | 6 (2%) |
| Influenza | 5 (2%) |
| OSAS | 5 (2%) |
| Viremia | 4 (2%) |
| Others | 32 (13%) |

SD = standard deviation, URI = upper respiratory infection, GE = gastroenteritis, OSAS = obstructive sleep apnea syndrome

Of the 262 patients studied, 41.6% (109 patients) had vitamin D insufficiency and 22.9% (60 patients) had vitamin D deficiency. Zinc deficiency was identified in 37.0% (97 patients). Combined vitamin D deficiency/insufficiency and zinc deficiency was identified in 25.6% (67 patients). Single deficiency/insufficiency was identified in 50.0% (131 patients). Only 24.4% (64 patients) exhibited adequate levels of both nutrients.

### Age trends

The prevalence of vitamin D deficiency was found to increase with age, whereas the prevalence of zinc deficiency decreased with age [Table 2].

The observed trend of increasing vitamin D deficiency with age in this study was consistent with the previous research on the general population. Specifically, the prevalence of vitamin D deficiency among southern Chinese under 6 years old is 10.8%,[21] rising to 40.3% in those aged 6–11 years,[22] and reaching 64.7% among Hong Kong Chinese adolescents.[23]

A ROC curve analysis ($n$ = 55) demonstrated that serum vitamin D level had modest predictive value for pneumonia risk, with an AUC = 0.624 (95% CI 0.540–0.707, $P$ = 0.005). This suggested that lower vitamin D levels were associated with a significant, though moderate, increase in pneumonia likelihood.

Logistic regression analysis ($n$ = 262) further identified serum vitamin D and zinc levels as independent risk factors for pneumonia in children, even after adjusting for demographic and anthropometric variables. In univariate analysis, each 1 nmol/L increase in vitamin D was associated with a 2% reduction in pneumonia odds (OR 0.98, 95% CI 0.966–0.993, $P$ = 0.004), while each 1 μmol/L increase in zinc reduced pneumonia odds by 19.2% (OR 0.808, 95% CI 0.706–0.925, $P$ = 0.002). In contrast, growth parameters (height, weight, or BMI) as well as age and gender were not significant predictors of pneumonia risk in this cohort. In multivariable analysis, after adjusting for gender, age, height, weight, and BMI, both vitamin D (OR 0.98 per nmol/L, 95% CI 0.969-0.998, $P$ = 0.022) and zinc (OR 0.83 per μmol/L, 95% CI 0.720–0.956, $P$ = 0.010) remained significant protective factors [Table 3].

**Table 2: Prevalence of subnormal levels of vitamin D and zinc in children of different age groups within the study population**

| | <6 Years old ($n$ = 152) | 6–11 Years old ($n$ = 94) | 12–16 Years old ($n$ = 16) | Total ($n$ = 262) |
|---|---|---|---|---|
| Vitamin D deficiency (%) | 19/152 (12.5%) | 30/94 (31.9%) | 11/16 (68.8%) | 60/262 (22.9%) |
| Vitamin D insufficiency (%) | 63/152 (41.4%) | 41/94 (43.6%) | 5/16 (31.3%) | 109/262 (41.6%) |
| Zinc deficiency (%) | 54/152 (35.5%) | 40/94 (42.6%) | 3/16 (18.8%) | 97/262 (37.0%) |

**Table 3: Logistic regression analysis of risk factors for pneumonia in the study population– Univariate and multivariate models**

| | Univariate analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| **Variables** | **OR** | **95% CI** | ***P* value** | **OR** | **95% CI** | ***P* value** |
| Gender (Female) | 1.821 | 0.993 to 3.339 | 0.053 | | | – |
| Age, years | 1.008 | 0.923 to 1.101 | 0.865 | | | – |
| Height *z*-score | 1.012 | 0.826 to 1.239 | 0.911 | | | – |
| Weight *z*-score | 1.118 | 0.880 to 1.420 | 0.360 | | | – |
| BMI *z*-score | 1.216 | 0.922 to 1.604 | 0.166 | | | – |
| Vitamin D level | 0.980 | 0.966 to 0.993 | 0.004 | 0.983 | 0.969 to 0.998 | 0.022 |
| Zinc level | 0.808 | 0.706 to 0.925 | 0.002 | 0.830 | 0.720 to 0.956 | 0.010 |

OR = odds ratios, CI = confidence interval, BMI = body mass index

**Table 4: Combined vitamin D and zinc deficiency associated with increased pneumonia occurrence (odds ratios 4.5, 95% confidence interval 1.8–11.2, $P = 0.001$)**

| Vitamin D/zinc status | Pneumonia ($n = 27$) | No pneumonia ($n = 136$) | Total ($n = 163$) |
|---|---|---|---|
| Double deficiency (vitamin D < 50 nmol/L and zinc <10 μmoL/L) | 11 | 18 | 29 |
| No deficiency (vitamin D ≥ 50 nmol/L and zinc ≥10 μmol/L) | 16 | 118 | 134 |

Furthermore, children with both vitamin D (<50 nmol/L) and zinc (<10 μmol/L) deficiencies had a more than fourfold increased risk of pneumonia (OR 4.5, 95% CI 1.8–11.2, $P = 0.001$) [Table 4].

A significant positive correlation was observed between serum zinc and vitamin D levels in the studied pediatric cohort ($n = 262$). Pearson correlation analysis yielded a correlation coefficient of $r = 0.244$ with a $P$ value < 0.001, indicating a significant, albeit modest, association between the two micronutrients. These findings supported the notion that deficiencies in these micronutrients frequently coexist, underscoring the importance of concurrent assessment in the pediatric populations.

Analysis of the cohort revealed that the overall prevalence of overweight, obese, and underweight individuals was 24.7% in boys and 13.9% in girls, with boys demonstrating a higher, though not statistically significant ($P = 0.078$) rate of overweight/obesity compared to girls (18.5% vs. 12.5%, $P = 0.333$). These findings were consistent with the previous community studies in Hong Kong, which also reported higher rates of overweight and obesity among boys (23.5% vs. 16.3%).[30]

When examining the relationship between obesity and pneumonia, obese children (BMI > 95th percentile) appeared more likely to develop pneumonia (35.7%) compared to children with normal BMI (20.3%), but this difference did not reach statistical significance ($P = 0.1784$).

**Table 5: Association between vitamin D status and overweight/obesity in the study population**

| Vitamin D status | Overweight/obese ($n = 36$) | Non-overweight/obese ($n = 194$) | Total ($n = 230$) |
|---|---|---|---|
| Vitamin D < 75 nmol/L | 22 (61%) | 128 (66%) | 150 |
| Vitamin D ≥ 75 nmol/L | 14 (39%) | 66 (34%) | 80 |

**Table 6: Association between zinc status and overweight/obesity in the study population**

| Zinc status | Overweight/obese ($n = 36$) | Non-overweight/obese ($n = 194$) | Total ($n = 230$) |
|---|---|---|---|
| Zinc <10 μmol/L | 12 (33%) | 72 (37%) | 84 |
| Zinc ≥10 μmol/L | 24 (67%) | 122 (63%) | 146 |

Further analysis explored the association between overweight/obesity and micronutrient status. No significant correlation was found between BMI z-score and vitamin D levels ($r = 0.017$, $P = 0.799$), and the prevalence of vitamin D deficiency or insufficiency did not differ significantly between overweight/obese and non-overweight/obese groups (OR = 0.81, 95% CI 0.39–1.69, $P = 0.57$). Table 5 Similarly, zinc deficiency was not associated with overweight or obesity (OR = 0.85, 95% CI 0.40–1.80, $P = 0.67$) [Table 6].

These results indicated that, within this population, anthropometric measures such as BMI were not reliable predictors of vitamin D or zinc deficiency. Moreover, while there was a trend toward increased pneumonia risk in obese children, this association was not statistically significant in the current sample. Overall, the data suggested that routine screening for micronutrient deficiencies should not be limited to children with abnormal BMI, and that both normal-weight and overweight/obese children were at risk for suboptimal vitamin D and zinc status.

## Discussion

It was an important to note that while vitamin D insufficiency, defined as <75 nmol/L,[31] has been widely adopted as a clinical threshold in countries such as Poland,[32] Central European nations,[33] USA,[34] and Japan,[35] it is often not recognized as abnormal in other countries, including Hong Kong, although it was shown to be correlated with clinical outcomes.

Jaybhaye *et al.*[36] in fact reported that the prevalence of vitamin D insufficiency was similar in those with or without recurrent respiratory tract infections—defined as experiencing more than six respiratory tract infections per year, including both upper and lower respiratory tract infections—at 25% versus 22%, respectively. In contrast, Hebbar *et al.*[37] reported that the prevalence of vitamin D insufficiency was much higher in asthmatic children than in controls, that is, 62% versus 49% ($P = 0.02$). Similarly, Aydin *et al.*[38] reported that 18% of children with recurrent tonsillitis exhibited vitamin D insufficiency compared to 0% in those without the condition ($P < 0.001$). Reid *et al.*[39] in a study conducted in New Zealand on children undergoing tonsillectomy for conditions such as obstructive sleep apnea syndrome and acute pharyngotonsillitis, reported that 78% had a 25-hydroxyvitamin D deficiency and 15.6% had vitamin D insufficiency. Thus, it was imperative for vitamin D insufficiency to be diagnosed and managed with vitamin D supplement and as importantly a chance to review the diet which might be inadequate as shown in the current study that vitamin D level was correlated with zinc level.

Zinc deficiency was defined as a serum zinc concentration <57 μg/dL (8.7 μmol/L) in the afternoon or <65 μg/dL (9.9 μmol/L) in the morning for preschool children.[40] Serum zinc level shows circadian variations, with the plasma zinc level being highest in the morning and decreasing toward the afternoon, fluctuating in a range from 80 μg/dL to 65 μg/dL, that is, 20% fluctuation over the period of 0700 h to 1400 h.[41] To facilitate consistent comparisons and simplify interpretation, standardizing blood collection to a specific time, preferably in the morning, would allow the use of a single lower limit of normal for diagnosing zinc deficiency. A limitation in the current study was blood samples that were collected at the time of consultation for convenience, which may have overestimated the prevalence of zinc deficiency because the lower limit of normal being at 10 μmol/L, a threshold typically applicable to morning zinc levels, potentially misclassifying some afternoon samples as deficient. Moreover, in the presence of inflammation, serum zinc concentration decreases as zinc is engaged in acute inflammation.[42] The lack of standardization in blood collection timing and consideration of inflammation status can lead to an overestimation of zinc deficiency in the current study.

Although inflammation adjustment may enable more precise estimation of zinc deficiency, it only resulted in very marginal changes in the actual prevalence of zinc deficiency.[43] Furthermore, since the measurement of an aerosol-generating procedure, α-1-acid glycoprotein, was not done in this center, regression correction using the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia approach to assess the degree of inflammation[44] was not feasible for the current study. Future studies could benefit from standardizing blood collection times and incorporating inflammatory biomarkers to enhance the precision of zinc deficiency assessments.

This study demonstrates a high prevalence of both vitamin D insufficiency/deficiency (64.5%) and zinc deficiency (37.0%) among pediatric patients in Hong Kong, with about one-quarter (25.6%) exhibiting concurrent subnormal levels of both micronutrients. Notably, the prevalence of vitamin D deficiency increases with age–rising from 12.5% in children under 6 years, to 31.9% in those aged 6–11, and 68.8% in adolescents–while zinc deficiency showed a decreasing trend with age. These findings mirror patterns reported in the general Chinese pediatric population.[21-23] However, children seeking medical attention demonstrated a markedly higher prevalence of zinc deficiency, with 37.0% of the current study cohort being affected, compared to 9.62% among children aged 6–18-years in the general Chinese population.[6] Importantly, a significant positive correlation was observed between serum vitamin D and zinc levels ($r = 0.244$, $P < 0.001$). This coexistence suggested that vitamin D and zinc may influence each other's metabolism and immune-modulating effects and emphasizes the need for concurrent screening of both micronutrient levels. The current study also found that children with combined vitamin D and zinc deficiencies had more than fourfold increased risk of pneumonia (OR 4.5, 95% CI 1.8–11.2, $P = 0.0012$), and both deficiencies independently predicted higher pneumonia risk after adjusting for confounders. These results underscored the critical role of vitamin D and zinc in immune defense, particularly against respiratory infections.

Despite the high rates of deficiency, there was no significant correlation between vitamin D or zinc status and anthropometric growth parameters such as weight, height, or BMI percentiles in this cohort. Logistic regression analyses confirmed that neither height, weight, nor BMI z-scores were significant predictors of vitamin D or zinc deficiency, reinforcing the inadequacy of relying on physical growth parameters alone to identify at risk children, and supporting the need for routine biochemical screening rather than clinical assessment alone, especially in those with recurrent respiratory infections.

Interestingly, while obesity appeared to increase the likelihood of pneumonia (35.7% in obese children vs.

20.3% in those with normal BMI), this association did not reach statistical significance ($P = 0.1784$) and may warrant further study.

## Recommendations

Given these findings, routine biochemical screening for vitamin D and zinc deficiencies should be implemented in pediatric populations, especially among those presenting with respiratory infections. Early identification and intervention through supplementation or dietary modifications are essential to reduce the risk of respiratory morbidity and to optimize overall health outcomes. Public health initiatives should focus on raising awareness about the importance of vitamin D and zinc in immune function, promote dietary sources rich in these nutrients, and encourage safe sun exposure practices. In addition, clinicians should consider screening for zinc deficiency in children identified with vitamin D deficiency/insufficiency. Finally, further research is needed to clarify the relationship between obesity and pneumonia risk in children, as well as to elucidate the molecular interactions between vitamin D and zinc, to better understand their potential synergistic effects on childhood health.

## Conclusion

This study reveals a high prevalence of suboptimal vitamin D (64.5%) and zinc (37.0%) levels among Hong Kong pediatric population, with 25.6% exhibiting deficiencies in both. Inadequate level in vitamin D and/or zinc is associated with increased risk for pneumonia. The absence of correlation between these deficiencies and growth (weight, height, and BMI) underscores the inadequacy of relying on anthropometric parameters for screening of vitamin D and zinc levels in children. Screening for vitamin D insufficiency/deficiency and zinc deficiency is recommended in children with pneumonia. Early detection enables timely interventions that potentially decrease recurrence of pneumonia.

## Author contributions

Ng performed all. Leung SY did data analysis and manuscript preparation. Ho and Leung SY did literature search, manuscript preparation, editing, and review. Wong was involved in writing up the article.

## Data availability statement

Data were stored in Ng DK computer and available on request.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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Original Article

# Age-Dependent Patterns in Pediatric Flexible Bronchoscopy: A 5-Year Experience from a Tertiary Center in Southern Taiwan

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## Abstract

**Background:** Flexible bronchoscopy (FB) has become an essential diagnostic and therapeutic tool. However, age-dependent variations in clinical indications, bronchoscopic findings, and bronchoalveolar lavage (BAL) yield remain underexplored. **Methods:** We conducted a retrospective chart review of pediatric patients (<18 years) who underwent FB at a tertiary medical center in southern Taiwan between May 2020 and April 2025. Clinical data, bronchoscopic findings, and BAL results were analyzed and stratified by age group. **Results:** A total of 155 pediatric FB procedures were analyzed, including 57 infants, 76 children, and 22 adolescents. The most common indication overall was unexplained stridor or wheezing (38.1%), predominantly among infants (71.9%). In contrast, chronic cough and radiologic abnormalities were more common in older children and adolescents. The most frequent bronchoscopic findings included airway inflammation (47.1%), laryngomalacia (36.1%), and pharyngomalacia (12.9%), with notable age-related differences in distribution. BAL was performed in 75 patients, yielding positive cultures in 38.6% and viral detection in 9.3%. BAL findings contributed to diagnostic clarification in 60.0% and led to therapeutic modifications in 61.3% of cases. *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* were the most commonly isolated pathogens, and anaerobic organisms were identified in 12 patients, often in polymicrobial infections. **Conclusions:** Pediatric FB reveals age-related patterns in clinical presentation and airway pathology. FB, particularly when combined with BAL, offers substantial diagnostic value across pediatric age groups. Early use of FB should be considered in children with persistent or unexplained respiratory symptoms, especially in infants with suspected congenital anomalies or older children with inflammatory airway disease.

**Keywords:** Age-dependent airway pathology, bronchoalveolar lavage, pediatric flexible bronchoscopy

## Introduction

Over the past decade, pediatric flexible bronchoscopy (FB) has become an essential diagnostic and therapeutic tool in pediatric respiratory medicine.[1,2] It is widely used for the evaluation of persistent or complex respiratory symptoms, including chronic cough, stridor, dysphonia, recurrent pneumonia, lobar collapse, and suspected foreign body aspiration.[3,4] By allowing direct visualization of airway anatomy and dynamic changes, bronchoscopy provides critical diagnostic insights that complement clinical and radiographic findings.[5-7]

Pediatric airway diseases exhibit significant age-related variation, largely due to developmental differences in airway anatomy, immune function, and disease susceptibility.[8] Congenital anomalies are more common in infants, while older children more often present with acquired conditions such as airway malacia or post-infectious inflammation.[9] Recognizing these patterns is essential for accurate diagnosis and management. Bronchoalveolar lavage (BAL), commonly performed during bronchoscopy, enables cytological and microbiological analysis of lower-airway samples.[10] BAL plays a key role in diagnosing bacterial bronchitis,

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bronchiectasis, and infections like tuberculosis, viral pneumonia, and fungal disease.[11,12]

In this retrospective chart review (RCR), we analyzed pediatric patients who underwent FB at Kaohsiung Chang Gung Memorial Hospital. The aim of this study was to evaluate the patients' demographic and clinical characteristics, the clinical indications for bronchoscopy, and the bronchoscopic and BAL findings in this population.

## Materials and Methods

This RCR was conducted at Kaohsiung Chang Gung Memorial Hospital, a tertiary referral center in southern Taiwan. We analyzed de-identified medical records of all pediatric patients who underwent FB between May 1, 2020, and April 30, 2025. All patients included in the analysis were minors. Data were anonymized, securely stored on institutional password-protected systems, and accessible only to authorized study personnel. The study protocol was approved by the Institutional Review Board (IRB) of Kaohsiung Chang Gung Memorial Hospital (IRB No. 202501109B0; approved on September 26, 2025). All experiments followed guidelines, with written consent from a parent or guardian for all subjects.

### Patient selection

Eligible participants were children under 18 years of age who underwent FB during hospitalization during the study period. For patients who underwent multiple bronchoscopic procedures during a single admission, only data from the first procedure were included in the analysis.

### Data collection

Clinical data were extracted from electronic medical records and included demographic information (sex, date of birth, age at the time of the procedure, height, weight, and comorbidities), as well as a history of intubation, tracheostomy, or mechanical ventilation. Bronchoscopy variables included procedure date, clinical indication (diagnostic or therapeutic), and whether BAL was performed. BAL was not performed routinely in all FB procedures, but selectively in patients for whom additional microbiologic information was clinically relevant. The main indications for BAL in our cohort included recurrent pneumonia or atelectasis, chronic wet cough, unexplained persistent respiratory symptoms despite prior treatment, radiographic abnormalities, or when occult infection was clinically suspected. Esophagoscopy was selectively performed only when gastroesophageal reflux disease was clinically suspected based on associated symptoms or failure to respond to standard therapy. The diagnosis of reflux esophagitis in this study was based on cases in which esophagoscopy was performed and confirmed.

Clinical presentations, such as cough, stridor, and fever, were recorded. Bronchoscopic findings (e.g., airway inflammation, malacia, structural anomalies, or foreign bodies) and BAL microbiologic results were documented. Changes in clinical diagnosis or treatment attributable to the bronchoscopy or BAL findings were also noted. Airway inflammation was defined based on visual bronchoscopic appearance, including mucosal erythema, edema, and increased secretions. Microscopic cytological confirmation was not routinely required.

During the COVID-19 pandemic, FB was restricted at our institution in accordance with hospital infection-control policies and international guidance on aerosol-generating procedures. Indications were tightened, and most patients underwent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing with nasopharyngeal reverse transcription polymerase chain reaction (RT-PCR); BAL was reserved for selected cases.

### Statistical analysis

Descriptive statistics were used to summarize all study variables. Categorical variables were presented as frequencies and percentages. Continuous variables were reported as means with standard deviations or medians with interquartile range (IQR), depending on their distribution. All statistical analyses were performed using Statistical Package for the Social Sciences software, version 24 (IBM Corp., Armonk, NY, USA).

## Results

A total of 155 pediatric patients underwent FB at our institution, comprising 57 infants (0–1 year, 36.7%), 76 children (1–12 years, 49.0%), and 22 adolescents (12–18 years, 14.1%). The overall median age was 1.83 years (IQR: 0.25–8.5), with a median height of 83.0 cm (IQR: 57.4–130.0) and a median weight of 11.0 kg (IQR: 6.0–28.5). The cohort included 81 males (52.3%) and 74 females (47.7%). The baseline demographic information is shown in Table 1.

The most frequently reported presenting symptom was respiratory distress (68/155, 43.8%), followed by stridor (59/155, 38.0%), cough (44/155, 28.3%), and fever (23/155, 14.8%). Stridor was especially prevalent among infants (42/57, 73.6%), while cough was more commonly observed in children aged 1–12 years (30/76, 39.4%). Fever was reported in 3/57 (5.2%) of infants, 14/76 (18.4%) of children, and 6/22 (27.2%) of adolescents. Cyanosis was present in 10/155 (6.4%) of patients, most commonly in infants and children. Wheezing was documented in 7/155 (4.5%), hemoptysis in 4/155 (2.5%), and failure to thrive in 2/155 (1.2%).

Table 2 presents the distribution of indications. The most common indication for bronchoscopy was unexplained stridor or wheezing, reported in 59 of 155 patients (59/155,

**Table 1: Demographic and clinical characteristics of children undergoing bronchoscopy (*n* = 155)**

| Age group | Total (*n* = 155) | Infants (0–1 year) | Children (1–12 years) | Adolescents (12–18 years) |
|---|---|---|---|---|
| *N* | 155 | 57/155 (36.7%) | 76/155 (49.0%) | 22/155 (14.1%) |
| Age (years), median (IQR) | 1.83 (0.25–8.5) | 0.17 (0.08–0.33) | 3.54 (1.81–8.00) | 14.46 (13.77–15.75) |
| Height (cm), Median (IQR) | 83.0 (57.4–130.0) | 55.0 (50.0160.0) | 81.0 (74.0–85.0) | 161.3 (157.2–163.8) |
| Weight (kg), Median (IQR) | 11.0 (6.0–28.5) | 5.0 (3.3–6.5) | 10.0 (8.9–12.0) | 55.0 (48.0–57.5) |
| Gender, *n* (%) | | | | |
| Male | 81 (52.3%) | | | |
| Female | 74 (47.7%) | | | |
| Symptoms, *n* (%) | | | | |
| Respiratory distress | 68 (43.8%) | 31 (54.3%) | 30 (39.4%) | 7 (31.8%) |
| Stridor | 59 (38.0%) | 42 (73.6%) | 16 (21.0%) | 0 (0.0%) |
| Cough | 44 (28.3%) | 7 (12.2%) | 30 (39.4%) | 7 (31.8%) |
| Fever | 23 (14.8%) | 3 (5.2%) | 14 (18.4%) | 6 (27.2%) |
| Cyanosis | 10 (6.4%) | 4 (7.0%) | 5 (6.5%) | 0 (0.0%) |
| Wheezing | 7 (4.5%) | 1 (1.7%) | 3 (3.9%) | 3 (13.6%) |
| Hemoptysis | 4 (2.5%) | 0 (0.0%) | 2 (2.6%) | 2 (9.0%) |
| Failure to thrive | 2 (1.2%) | 1 (1.7%) | 1 (1.3%) | 0 (0.0%) |

IQR = interquartile range.

Values are expressed as *n* (%), calculated within each age category

**Table 2: Indications for pediatric bronchoscopy by age group (*n* = 155)**

| Indication | Total (*n* = 155) | Infants (*n* = 57) | Children (*n* = 76) | Adolescents (*n* = 22) |
|---|---|---|---|---|
| Unexplained stridor or wheezing | 59 (38.1%) | 41 (71.9%) | 16 (21.0%) | 2 (9.0%) |
| Recurrent pneumonia or atelectasis | 27 (17.5%) | 2 (3.5%) | 19 (25.0%) | 6 (27.2%) |
| Chronic cough | 18 (11.5%) | 1 (1.7%) | 12 (15.7%) | 5 (22.7%) |
| Suspect structural anomalies | 18 (11.5%) | 12 (21.0%) | 6 (7.8%) | 0 (0.0%) |
| Radiographic abnormality | 11 (7.0%) | 1 (1.7%) | 5 (6.5%) | 5 (22.7%) |
| Suspect foreign body aspiration | 10 (6.5%) | 0 (0.0%) | 10 (13.1%) | 0 (0.0%) |
| Hemoptysis | 4 (2.6%) | 0 (0.0%) | 2 (2.6%) | 2 (9.0%) |
| Inhalation injury | 3 (1.9%) | 0 (0.0%) | 1 (1.3%) | 2 (9.0%) |
| Bronchoscopic-assisted intubation | 2 (1.3%) | 0 (0.0%) | 2 (2.6%) | 0 (0.0%) |
| Tracheostomy evaluation | 3 (1.9%) | 0 (0.0%) | 3 (3.9%) | 0 (0.0%) |

Values are expressed as *n* (%), calculated within each age category

38.1%), and was especially prevalent among infants (41/57, 71.9%). Recurrent pneumonia or atelectasis accounted for 27 of 155 cases (27/155, 17.5%), with a higher frequency in children aged 1–12 years (19/76, 25.0%) and adolescents (6/22, 27.2%). Chronic cough was identified in 18 patients (18/155, 11.5%), including 12/76 (15.7%) in children and 5/22 (22.7%) in adolescents. Suspected structural anomalies were also reported in 18 patients (18/155, 11.5%), predominantly among infants (12/57, 21.0%). Radiographic abnormalities prompted bronchoscopy in 11 patients (11/155, 7.0%), while suspected foreign body aspiration was recorded in 10 (10/155, 6.5%), almost exclusively among children aged 1–12 years (10/76, 13.1%). Less frequent indications included hemoptysis (4/155, 2.6%), inhalation injury (3/155, 1.9%), bronchoscopic-assisted intubation (2/155, 1.3%), and tracheostomy evaluation (3/155, 1.9%). Notably, adolescents had a higher proportion of bronchoscopy for radiographic abnormalities (5/22, 22.7%) and chronic cough (5/22, 22.7%) compared to younger groups.

Table 3 summarizes bronchoscopic findings. Bronchoscopic evaluation revealed airway inflammation as the most common finding, observed in 73 of 155 patients (73/155, 47.1%), followed by laryngomalacia in 56 patients (56/155, 36.1%), pharyngomalacia in 20 (20/155, 12.9%), and reflux esophagitis in 17 (17/155, 11.0%). Normal bronchoscopic findings were reported in 12 patients (12/155, 7.7%). Age-specific patterns were evident. Laryngomalacia was predominantly found in infants (40/57, 70.1%), as were pharyngomalacia (12/57, 21.0%) and reflux esophagitis (12/57, 21.0%). In contrast, airway inflammation was more commonly identified in older patients, including 46/76 (60.5%) of children and 16/22 (72.7%) of adolescents. Less frequent findings included tracheomalacia (12/155, 7.7%), vocal fold paralysis (7/155, 4.5%), tracheal bronchus (6/155, 3.9%), and subglottic stenosis (5/155, 3.2%). These structural airway anomalies were distributed across age groups but were slightly more frequent in infants and children. Rare bronchoscopic findings included granulation

**Table 3: Bronchoscopic findings in children undergoing bronchoscopy, stratified by age group ($n$ = 155)**

| Bronchoscope findings | Total ($n$ = 155) | Infants ($n$ = 57) | Children ($n$ = 76) | Adolescents ($n$ = 22) |
|---|---|---|---|---|
| Airway inflammation | 73 (47.1%) | 11 (19.2%) | 46 (60.5%) | 16 (72.7%) |
| Laryngomalacia | 56 (36.1%) | 40 (70.1%) | 16 (21.0%) | 0 (0.0%) |
| Pharyngomalasia | 20 (12.9%) | 12 (21.0%) | 8 (10.5%) | 0 (0.0%) |
| Reflux esophagitis | 17 (11.0%) | 12 (21.0%) | 4 (5.2%) | 1 (4.5%) |
| Normal findings | 12 (7.7%) | 0 (0.0%) | 8 (10.5%) | 4 (18.1%) |
| Tracheomalacia | 12 (7.7%) | 5 (8.7%) | 6 (7.8%) | 1 (4.5%) |
| Vocal fold paralysis | 7 (4.5%) | 2 (3.5%) | 5 (6.5%) | 0 (0.0%) |
| Tracheal bronchus | 6 (3.9%) | 3 (5.2%) | 2 (2.6%) | 1 (4.5%) |
| Subglottic stenosis | 5 (3.2%) | 1 (1.7%) | 4 (5.2%) | 0 (0.0%) |
| Granulation | 4 (2.6%) | 1 (1.7%) | 2 (2.6%) | 1 (4.5%) |
| Tracheal stenosis | 4 (2.6%) | 0 (0.0%) | 3 (3.9%) | 1 (4.5%) |
| Bacterial tracheitis | 3 (1.9%) | 1 (1.7%) | 2 (2.6%) | 0 (0.0%) |
| Pulmonary hemorrhage | 2 (1.3%) | 0 (0.0%) | 1 (1.3%) | 1 (4.5%) |
| Choanal atresia | 2 (1.3%) | 1 (1.7%) | 0 (0.0%) | 1 (4.5%) |
| Adenoid hypertrophy | 2 (1.3%) | 0 (0.0%) | 2 (2.6%) | 0 (0.0%) |
| Vallecular cyst | 2 (1.3%) | 2 (3.5%) | 0 (0.0%) | 0 (0.0%) |
| Foreign body | 2 (1.3%) | 0 (0.0%) | 2 (2.6%) | 0 (0.0%) |
| Vocal cord granulation | 2 (1.3%) | 1 (1.7%) | 0 (0.0%) | 1 (4.5%) |
| Vocal fold nodule | 2 (1.3%) | 0 (0.0%) | 2 (2.6%) | 0 (0.0%) |
| Inhalation injury | 2 (1.3%) | 0 (0.0%) | 1 (1.3%) | 1 (4.5%) |
| Vascular ring | 2 (1.3%) | 2 (1.3%) | 0 (0.0%) | 0 (0.0%) |
| Mucus plug | 1 (0.6%) | 0 (0.0%) | 1 (1.3%) | 0 (0.0%) |
| Cleft palate | 1 (0.6%) | 1 (1.7%) | 0 (0.0%) | 0 (0.0%) |
| Glossoptosis | 1 (0.6%) | 1 (1.7%) | 0 (0.0%) | 0 (0.0%) |
| Oral tumor | 1 (0.6%) | 0 (0.0%) | 1 (1.3%) | 0 (0.0%) |
| Hemangioma | 1 (0.6%) | 1 (1.7%) | 0 (0.0%) | 0 (0.0%) |

Values are expressed as $n$ (%), calculated within each age category

**Table 4: Bronchoalveolar lavage (BAL) findings by indication in children undergoing bronchoscopy ($n$ = 75)**

| Indication for BAL | *N* | Microbiologic yield | Clinical impact |
|---|---|---|---|
| Unexplained stridor or wheezing | 13 | Virus: 1/13 (7.7%), Culture: 7/13 (53.8%) | Dx: 11/13 (84.6%) Tx: 9/13 (69.2%) |
| Recurrent pneumonia or atelectasis | 26 | Virus: 3/26 (11.5%), Culture: 12/26 (46.1%) | Dx: 12/26 (46.2%) Tx: 15/26 (57.7%) |
| Suspect foreign body aspiration | 4 | Virus: 0/4 (0.0%), Culture: 1/4 (25.0%) | Dx: 2/4 (50.0%) Tx: 2/4 (50.0%) |
| Chronic cough | 18 | Virus: 3/18 (16.7%), Culture: 6/18 (33.3%) | Dx: 14/18 (77.8%) Tx: 14/18 (77.8%) |
| Inhalation injury | 1 | Virus: 0/1 (0.0%), Culture: 0/1 (0.0%) | Dx: 0/1 (0.0%) Tx: 0/1 (0.0%) |
| Radiographic abnormality | 9 | Virus: 0/9 (11.1%), Culture: 3/9 (33.3%) | Dx: 3/9 (33.3%) Tx: 3/9 (33.3%) |
| Suspect structural anomalies | 1 | Virus: 0/1 (0.0%), Culture: 0/1 (0.0%) | Dx: 0/1 (0.0%) Tx: 0/1 (0.0%) |
| Hemoptysis | 3 | Virus: 0/3 (0.0%), Culture: 0/3 (0.0%) | Dx: 3/3 (100.0%) Tx: 3/3 (100.0%) |
| Total | 75 | Virus: 7/75 (9.3%), Culture: 29/75 (38.6%) | Dx: 45/75 (60.0%) Tx: 46/75 (61.3%) |

Dx = diagnosis change, Tx = treatment change.

Clinical Impact reflects cases in which BAL findings contributed to a revised diagnosis or change in clinical treatment, as documented in medical records

(4/155, 2.6%), tracheal stenosis (4/155, 2.6%), bacterial tracheitis (3/155, 1.9%), pulmonary hemorrhage (2/155, 1.3%), choanal atresia (2/155, 1.3%), adenoid hypertrophy (2/155, 1.3%), vallecular cyst (2/155, 1.3%), vocal cord granulation (2/155, 1.3%), vocal fold nodule (2/155, 1.3%), inhalation injury (2/155, 1.3%), and vascular ring (2/155, 1.3%). In addition, several findings were observed in only one patient (0.6%), including a mucus plug, cleft palate, glossoptosis, oral tumor, and a hemangioma. Most of these rare conditions were identified in infants or children, with only a few cases noted in adolescents.

Table 4 displays BAL findings. Among the 75 pediatric patients who underwent BAL, the most common indications were recurrent pneumonia or atelectasis ($n$ = 26), chronic cough ($n$ = 18), and unexplained stridor or wheezing ($n$ = 13). Overall, the diagnostic yield of viral isolation testing was relatively low, with viral pathogens detected in seven cases (9.3%), whereas culture positivity was noted in 29 cases (38.6%). Clinical impact varied by indication. BAL results led to a revised diagnosis in 60.0% of cases and a change in treatment in 61.3%.

**Table 5: Identified pathogens from pediatric bronchoscopy specimens**

| Pathogen detection from BAL | Detection method | Category | *N* |
|---|---|---|---|
| *Adenovirus* | Virus isolation | Virus | 3 |
| *Cytomegalovirus* | Virus isolation | Virus | 2 |
| *Human Rhinovirus/Enterovirus* | Multiple PCR | Virus | 2 |
| *Mycoplasma pneumoniae* | Multiple PCR | Atypical Bacteria | 1 |
| *Haemophilus influenza* | Multiple PCR | Bacteria | 1 |
| *Acinetobacter baumannii* | Culture | Bacteria | 1 |
| *Aerobes* | Culture | Bacteria | 2 |
| *Enterobacter cloacae* complex | Culture | Bacteria | 3 |
| *Pseudomonas aeruginosa* | Culture | Bacteria | 7 |
| *Klebsiella pneumoniae* | Culture | Bacteria | 2 |
| *Escherichia coli* | Culture | Bacteria | 1 |
| *Stenotrophomonas maltophilia* | Culture | Bacteria | 2 |
| *Moraxella catarrhalis* | Culture | Bacteria | 2 |
| Methicillin-resistant *Staphylococcus aureus* | Culture | Bacteria | 5 |
| *S. aureus* | Culture | Bacteria | 1 |
| *Proteus mirabilis* | Culture | Bacteria | 1 |
| *Citrobacter koseri* | Culture | Bacteria | 1 |
| *Serratia marcescens* | Culture | Bacteria | 1 |
| *Streptococcus pneumoniae* | Culture | Bacteria | 3 |
| *Actinomyces odontolyticus* | Culture | Anaerobe | 1 |
| *Fusobacterium* sp. | Culture | Anaerobe | 1 |
| *Prevotella* sp. | Culture | Anaerobe | 2 |
| *Prevotella melaninogenica* | Culture | Anaerobe | 4 |
| *Prevotella nanceiensis* | Culture | Anaerobe | 2 |
| *Veillonella* sp. | Culture | Anaerobe | 3 |
| *Veillonella parvula* | Culture | Anaerobe | 1 |
| *Veillonella atypica* | Culture | Anaerobe | 2 |
| *Veillonella dispar* | Culture | Anaerobe | 1 |
| *Parvimonas micra* | Culture | Anaerobe | 1 |
| *Mycobacterium tuberculosis* complex | Culture | Mycobacteria | 1 |

BAL = bronchoalveolar lavage, PCR = polymerase chain reaction

A total of 33 distinct microbial species were identified from BAL specimens [Table 5]. Bacterial pathogens accounted for the majority of isolates. The most frequently detected organisms were *Pseudomonas aeruginosa* (seven cases) and methicillin-resistant *Staphylococcus aureus* ([MRSA], five cases), followed by *Streptococcus pneumoniae* and *Serratia marcescens* (three cases each). A wide range of gram-negative and gram-positive bacteria were also recovered through culture, including *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Stenotrophomonas maltophilia*. In addition to aerobic bacteria, anaerobic organisms were identified in 12 patients and included multiple species of *Veillonella* (e.g., *V. parvula*, *V. atypica*, and *V. dispar*), *Prevotella*, *Fusobacterium*, and *Actinomyces odontolyticus*. These anaerobes were most often part of polymicrobial infections, particularly in children with suspected aspiration or chronic airway conditions. Viral pathogens were detected in a minority of cases: *Adenovirus* in three patients, *Cytomegalovirus* in two, and *Human rhinovirus/enterovirus* in two. These were identified by polymerase chain reaction (PCR) or viral isolation. Atypical and mycobacterial organisms were rare. *Mycoplasma pneumoniae* was detected in one patient via PCR, and *Mycobacterium tuberculosis complex* was isolated from one BAL culture.

## Discussion

This retrospective study analyzed 155 pediatric FB performed at a tertiary medical center in southern Taiwan between 2020 and 2025 to assess clinical indications, bronchoscopic findings, and their impact on decision-making. The results align with international observational data, further supporting the broad utility and clinical value of pediatric bronchoscopy in respiratory disease diagnosis and management.[13,14]

### Clinical indications and age distribution

In our cohort, the most common indication for FB was unexplained stridor or wheezing (38.1%), predominantly observed in infants (71.9%). This highlights the essential role of FB in early airway evaluation during infancy. Similar patterns have been reported internationally. Yavuz

*et al*.[15] identified stridor as the leading indication (26%) in the United Arab Emirates, and Atag *et al*.[16] similarly noted that suspected airway disease was a leading indication for FB in infants within the pediatric intensive care unit, with airway malacia identified in over half of all cases. Thomas *et al*.[17] emphasized the importance of age stratification (≤2 years vs. >2 years) in FB indication analysis.

In contrast, older children (1–12 years) and adolescents (12–18 years) showed more diverse indications, including chronic cough, recurrent pneumonia, and persistent radiologic abnormalities. These findings are consistent with Ferraro *et al*.,[14] who reported that FB was commonly used to evaluate recurrent lower respiratory infections or chronic wet cough (41.6%).

## Bronchoscopic findings by age group

The most common bronchoscopic abnormality in our cohort was airway inflammation (47.1%), followed by laryngomalacia (36.1%) and pharyngomalacia (12.9%). In comparison, Yavuz *et al*.[15] documented tracheomalacia (17%), laryngomalacia (4%), airway inflammation (10%), and mucus plugs (10%).

In our cohort, the prevalence of inflammatory changes increased with age, observed in 60.5% of children and 72.7% of adolescents, suggesting age-related pathophysiologic differences. In contrast, infants (0–1 year) most commonly presented with stridor (73.6%) and respiratory distress (71.9%), with corresponding bronchoscopic findings of laryngomalacia (70.1%) and pharyngomalacia (21.0%). These results are consistent with prior studies by Thomas *et al*.[17] and Midulla *et al*.,[18] which link abnormal breath sounds to underlying congenital airway anomalies.

Based on symptom-based grouping [Supplementary Table 1], distinct diagnostic patterns were observed across clinical presentations. Among the 59 children who underwent FB for unexplained stridor or wheezing, laryngomalacia was the most frequently identified abnormality (44/59, 74.6%). However, other diagnoses were also observed, including vascular ring, hemangioma, tracheomalacia, and vocal fold paralysis. These findings underscore the broad range of underlying causes of pediatric stridor and wheezing, highlighting the value of bronchoscopy in detecting atypical or coexisting airway lesions, particularly in cases with ambiguous clinical features. Dynamic airway abnormalities were especially prevalent in early childhood, reinforcing the diagnostic utility of FB in this age group.[14,19,20] By contrast, older children and adolescents demonstrated greater diagnostic heterogeneity, with airway inflammation being the most frequent finding.[21] These age-dependent differences underscore the importance of FB in evaluating chronic respiratory symptoms and structural airway changes across developmental stages. On the contrary, children who underwent FB for recurrent pneumonia or atelectasis and chronic cough most commonly exhibited airway inflammation (26/27, 96.2%, and 17/18, 94.4%, respectively), suggesting that FB and BAL provide complementary diagnostic information in cases of persistent lower-airway disease. Cases referred for suspected structural anomalies ($n = 18$) demonstrated heterogeneous findings, including laryngomalacia, subglottic stenosis, and reflux-related changes, which frequently guided further multidisciplinary evaluation and management.

## Bronchoalveolar lavage diagnostic yield and clinical impact

In this study, a total of 75 pediatric patients underwent BAL. The bacterial culture positivity rate was 38.6%, while viral pathogens were detected in 9.3% of cases. The most frequently identified bacteria included *P. aeruginosa* ($n = 7$), MRSA ($n = 5$), and *S. pneumoniae* ($n = 3$). In addition to aerobic bacteria, anaerobic organisms such as *Veillonella*, *Prevotella*, and *Fusobacterium* were found in 12 patients, typically as part of polymicrobial infections suggestive of aspiration pneumonia or chronic inflammation. Detected viruses included *adenovirus* ($n = 3$) and *cytomegalovirus* ($n = 2$).

These detection rates are modest compared to international series.[15] This discrepancy may be attributed to differences in disease severity, prior antibiotic exposure, or specimen processing protocols.[22,23] Accurate interpretation of BAL results requires careful differentiation between colonization and true infection, which is often guided by semi-quantitative culture thresholds and inflammatory markers such as total leukocyte counts and neutrophil percentages.[21,24] In addition, recognizing visually evident airway inflammation during FB also assisted infection-control decisions, particularly in distinguishing airway colonization from true infection and avoiding unnecessary antibiotic exposure.

Our findings are comparable to a previous study conducted at our institution by Tsai *et al*.,[23] which reported aerobic and anaerobic culture positivity rates of 42% and 24%, respectively, with 55.3% of culture-positive cases resulting in antibiotic modification.In this study, BAL findings led to changes in clinical diagnosis in 60.0% of cases and therapeutic adjustments in 61.3%. The impact was particularly notable among patients with chronic cough or recurrent pneumonia, with 77.8% experiencing changes in clinical management.

The pathogen spectrum was diverse. In line with previous findings, *P. aeruginosa* and *S. aureus* were detected in 23.7% and 15.8% of BAL-positive cases, respectively.[23] Other studies have highlighted regional variation in pathogen profiles, with *Haemophilus influenzae*, *Moraxella*

*catarrhalis*, and *Streptococcus pyogenes* more commonly found in certain populations.[6,25,26]

Notably, several cases in our cohort showed negative cultures but positive results on multiplex polymerase chain reaction (multiplex PCR) testing, underscoring the potential value of emerging molecular diagnostics such as multiplex PCR in improving pathogen detection, particularly in culture-negative patients.[27,28]

## Clinical implications and future directions

This study reinforces the diagnostic value of FB in evaluating unexplained respiratory symptoms and radiologic abnormalities in pediatric patients. In particular, FB proved useful for identifying dynamic airway abnormalities in infants and inflammatory conditions in older children. The ability to directly visualize airway structures and obtain BAL specimens makes FB a central tool in pediatric respiratory care. Consistent with findings by Daou *et al*.[29] and Thomas *et al*.,[17] FB also facilitates targeted antibiotic selection and referral to subspecialties such as otolaryngology or cardiothoracic surgery.

We recommend early consideration of FB in children presenting with persistent stridor, chronic cough, recurrent pneumonia, or unexplained radiologic findings, especially in cases where structural abnormalities or aspiration risks are suspected. When combined with BAL, FB offers critical diagnostic insights and therapeutic guidance that can influence clinical management.

This study has several limitations. As a single-center retrospective analysis, it is subject to potential selection bias and incomplete data. The pathogen distribution and clinical indications may not be representative of other geographic areas and practice settings. The lack of a control group and long-term follow-up limited the assessment of outcomes such as hospitalization duration, readmission rates, and pulmonary function trajectories. In addition, inter-operator variability in technique and subjective interpretation remain an inherent challenge in observational bronchoscopy studies. In addition, no clinically significant procedure-related adverse events were observed during or within 24 h after FB in this cohort; however, procedure-related adverse events were not systematically documented, and therefore, the incidence of minor transient physiologic changes could not be reliably assessed. The lack of SARS-CoV-2 detection in our BAL samples likely reflects pandemic-related case selection (reduced FB volume and selective BAL indications) and diagnostic pathways that favored nasopharyngeal RT-PCR testing.

Future research should focus on multicenter, prospective studies employing standardized BAL protocols and incorporating advanced diagnostic modalities to improve diagnostic precision. Longitudinal follow-up and randomized controlled trials comparing FB-guided vs. empirical treatment strategies are also warranted to further validate the clinical impact and long-term benefits of pediatric FB.

## Conclusions

In conclusion, this study reaffirms the important role of pediatric FB in diagnosing and managing respiratory diseases. Continued multicenter collaboration, integration of advanced diagnostic techniques, and well-designed prospective studies are essential to further define its clinical utility and optimize outcomes for children with respiratory disorders.

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## Author contributions

Concept and Design: H-RY. Definition of Intellectual Content: H-RY. Literature Search: Y-SH. Clinical Studies: Y-SH. Experimental Studies: Y-SH. Data Acquisition: Y-SH. Data Analysis: Y-SH. Statistical Analysis: Y-SH. Manuscript Preparation: Y-SH. Manuscript Editing: Y-SH and H-RY. Manuscript Review: C-KT, C-MT, C-KN, and H-RY.

## Ethical Policy and Institutional Review Board statement

The study protocol was approved by the Institutional Review Board (IRB) of Kaohsiung Chang Gung Memorial Hospital (IRB No. 202501109B0; approved on September 26, 2025).

## Data availability statement

The data that support the findings of this study were obtained from electronic medical records and clinical evaluations of pediatric patients at Kaohsiung Chang Gung Memorial Hospital. Due to patient privacy and ethical restrictions, the original datasets are not publicly available. De-identified data may be made available from the corresponding author upon reasonable request and with approval from the Institutional Review Board of Kaohsiung Chang Gung Memorial Hospital.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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## Supplementary Information

**Supplementary Table 1: Bronchoscopic findings in children undergoing bronchoscopy**

| Bronchoscope findings | Unexplained stridor or wheezing ($n = 59$) | Recurrent pneumonia/ atelectasis ($n = 27$) | Chronic cough ($n = 18$) | Suspect structural anomalies ($n = 18$) | Radiographic abnormality ($n = 11$) | Suspect foreign body aspiration ($n = 10$) | Hemoptysis ($n = 4$) | Inhalation injury ($n = 3$) | Bronchoscopic-assisted intubation ($n = 2$) | Tracheostomy evaluation ($n = 3$) |
|---|---|---|---|---|---|---|---|---|---|---|
| Airway inflammation | 13 | 26 | 17 | 3 | 8 | 5 | 0 | 1 | 0 | 0 |
| Laryngomalacia | 44 | 2 | 1 | 8 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pharyngomalasia | 14 | 1 | | 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| Reflux esophagitis | 9 | 0 | 1 | 5 | 1 | 0 | 0 | 0 | 0 | 0 |
| Tracheomalacia | 5 | 2 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 1 |
| Vocal fold paralysis | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Subglottic stenosis | 2 | 1 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| Granulation | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Tracheal bronchus | 2 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 |
| Vallecular cyst | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Vascular ring | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Tracheal stenosis | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Bacterial tracheitis | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Choanal atresia | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Vocal cord granulation | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Vocal fold nodule | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Vocal fold paralysis | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 1 |
| Hemangioma | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Foreign body | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 |
| Pulmonary hemorrhage | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| Burn injury | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 |
| Oral tumor | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | |
| Negative finding | 0 | 0 | 1 | 1 | 3 | 3 | 2 | 0 | 0 | 2 |

Review Article

# Prevention of Fatal Pediatric Asthma in China

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## Abstract

Asthma, a prevalent chronic respiratory disease worldwide, imposes a significant disease burden on children. According to the Global Burden of Disease, pediatric asthma mortality in China declined by 92.2% over the past three decades (1990–2019). This progress is mainly attributed to the continuous refinement of diagnostic and treatment guidelines, the promotion of standardized inhalation therapy, the implementation of asthma action plans, and the establishment of standardized asthma clinics for children. By 2020, a total of 1289 standardized pediatric asthma clinics had been established nationwide, including 135 that served as regional demonstration centers. However, the absolute number of pediatric asthma deaths in China remains a cause for concern, with approximately 70 children succumbing to asthma annually in recent years. Eliminating asthma deaths still requires constant vigilance and sustained efforts. The primary challenges currently encountered include the transition of care for adolescents with asthma, the early recognition of anaphylaxis, and the management of airway mucus plugging. Future efforts should identify avoidable risk factors, optimize adolescent transition care, enhance emergency response capabilities among healthcare professionals, standardize airway mucus hypersecretion management, and promote integrated Traditional Chinese and Western medicine to improve asthma control and reduce pediatric asthma mortality.

**Keywords:** Asthma, children, China, death, prevention

## Introduction

Asthma is the most common chronic respiratory disease in children, and its exacerbations and related deaths have imposed a heavy burden on society and families. The prevalence of asthma in Chinese children is on the rise. In 2010, the prevalence of asthma among Chinese children aged 0–14 reached 3.02%, an increase of 50.6% compared to that in 2000.[1,2] Both the Global Initiative for Asthma and the Chinese guidelines for the diagnosis and prevention of pediatric asthma include the goal of minimizing the risk of asthma-related deaths.[3,4] Between 1990 and 2021, the asthma mortality rate among people aged 0–19 worldwide decreased significantly from 1.43 to 0.42 per 100,000 people. Correspondingly, the number of deaths in this age group also decreased dramatically from 32,505 to 11,049.[5] Although the asthma mortality rate is now at a relatively low level, most asthma-related deaths are preventable. The theme of World Asthma Day in 2020 was "enough asthma deaths," which inspired many suggestions such as "zero tolerance for asthma deaths" and "eliminating asthma deaths."[6]

## Asthma Mortality in Chinese Children and Adolescents Aged 0–19 Years

Over the past 30 years, there has been a significant decline in the mortality rate of pediatric asthma in China. The Global Burden of Disease 2019 (2019) indicated that the asthma mortality rate for Chinese children and adolescents was 0.03 per 100,000 population in 2019, representing a significant 92.2% decrease compared to 1990.[7] In 2021, the mortality rate (0.03 per 100,000) ranked 182nd out

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of 192 countries globally and 43rd out of 47 countries in Asia.[5]

More accurate data on asthma deaths among the 0–19 age group is obtained from the Chinese National Mortality Surveillance System. The system consists of 605 monitoring points, covering a population of over 300 million, which is approximately 24.0% of the national population.[8] It registers all death cases occurring within the jurisdiction of each monitoring point. Between 2008 and 2018, the asthma mortality rate for Chinese children and adolescents aged 0–19 fluctuated between 0.023 and 0.046 per 100,000. It peaked at 0.046 per 100,000 in 2009 and 2012, and dropped to 0.023 per 100,000 in 2018, a 42.5% decline from 2008.[9] This reflects a significant downward trend in asthma mortality in China, in line with the global pattern. Compared with other countries, the mortality rate of childhood asthma in China is relatively low. During the same period, the asthma mortality rate for American children aged 0–17 was roughly 10 times higher than that in China.[10]

## Past and Current Efforts to Reduce Pediatric Fatal Asthma

Over the past 30 years, the children's asthma mortality rate in China has significantly declined, largely owing to the relentless efforts of successive generations. These efforts have driven the continuous updates of the Chinese childhood asthma guidelines offering scientific guidance; promoted the widespread use of inhalation therapy as a key treatment method for children's asthma; fully implemented the China Children's Asthma Action Plan (CCAAP); and established of standardized asthma clinics for children to provide a critical guarantee for standardized diagnosis and treatment. With the aforementioned measures, childhood asthma-related deaths decreased from 148 in 2009 to approximately 70 per year between 2015 and 2021 [Figure 1].

### Iterative updates of the Chinese pediatric asthma guidelines

The Chinese pediatric asthma diagnosis and treatment guidelines, updated several times over the past three decades, have become one of the most influential guidelines in China in terms of its long history and wide recognition.[11]

Founded in 1987 by the Chinese Medical Association's Pediatrics Branch Respiratory Group, the Asthma Collaboration Group has been actively involved in the development and refinement of pediatric asthma management guidelines. In 1988, it released diagnostic and classification criteria, setting the stage for future epidemiological surveys.[12] In 1992, the guidelines were revised to include early detection, treatment, and prevention principles, and to promote inhalation therapy.[11] In 1998, further refinements focused on disease stage classification, severity assessment, and treatment plans. In 2003, the revision focused on the diagnosis and treatment of severe asthma exacerbations, updating management of life-threatening asthma.[13] The 2008 revision integrated domestic and international recommendations and evidence-based medicine, making significant changes to diagnosis, assessment, monitoring, and treatment strategies.[14] In 2016, the guideline for the diagnosis and optimal management of asthma in children (2016) was published. It was adapted to Chinese pediatric asthma diagnosis and treatment practices and has been widely recognized and affirmed.[15] In 2020, the guidelines incorporated treatment pathways for difficult-to-treat and severe asthma and detailed the selection of step-wise treatment and the process for treatment de-escalation.[16] In 2023, the current situation and development strategies of diagnosis and treatment of bronchial asthma in children in China (2022) was published, detailing the current status of pediatric asthma management in China, proposed standardized management strategies and future goals, to guide relevant policies and development plans.[11] In 2025, the latest version of the guidelines, along with a patient and public version, was launched. These updates aim to enhance the diagnostic and treatment capabilities, increase awareness of asthma among patients and the public, and improve adherence to standardized diagnosis and treatment.[17,18]

Over the past decade, in addition to the asthma guidelines, multiple guidelines and consensus statements related to pediatric asthma have also been published [shown in Table 1].[11,17-27] Although the guidelines represent the consensus among pediatricians at the theoretical level, their implementation faces multilevel barriers, including access to inhalation therapy, guideline compliance, and public awareness. We must continue efforts to achieve the goal of zero asthma-related deaths.

### Widespread use of inhalation therapy for pediatric asthma in China

Inhalation therapy is a cornerstone of pediatric asthma management, consisting of two distinct categories: maintenance therapy [primarily inhaled corticosteroids] and reliever therapy.[28] It involves the administration of medication in aerosol or dry powder form through the mouth or nose, delivering the drug directly to the airways and lungs. This method enables precise and high-concentration local drug delivery. Importantly, as the medication directly reaches the target organ, it significantly reduces systemic adverse reactions. Asthma inhalation therapy is superior to oral or intravenous administration in terms of both safety and efficacy.

In China, inhalation therapy has been widely applied and promoted as a fundamental approach for pediatric asthma pharmacological treatment. Selecting appropriate inhalation devices is crucial for Chinese

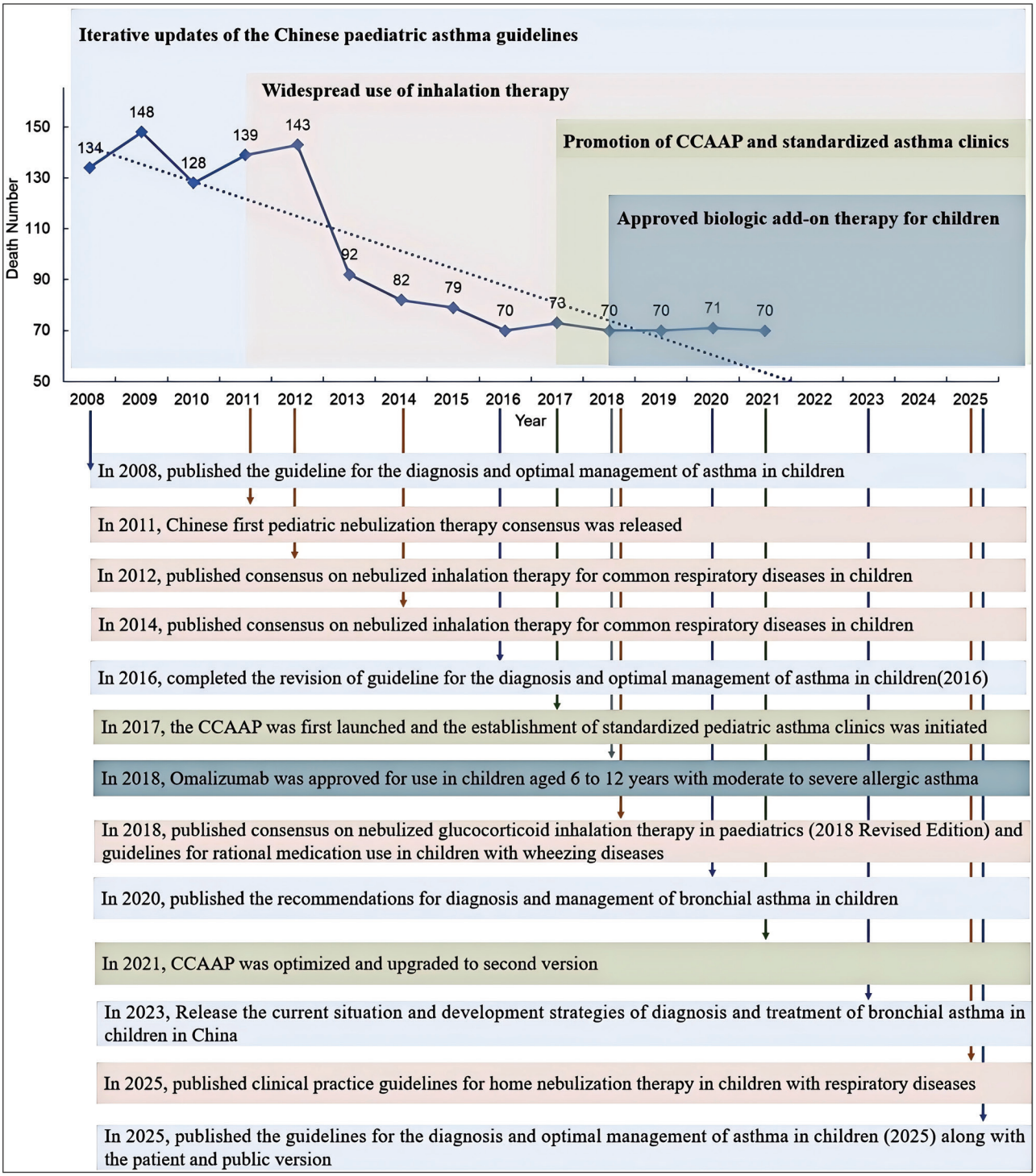


**Figure 1:** Factors and achievements behind the significant decline in pediatric asthma mortality in China. CCAAP = China Children's Asthma Action Plan

doctors in delivering inhalation therapy. Currently, common inhalation devices used in clinical practice include pressurized metered-dose inhalers (pMDIs), pMDIs combined with spacer or one-way valve spacers, dry powder inhalers, and nebulizers. Each of these devices has its own advantages in terms of operating characteristics, drug delivery efficiency, and patient suitability.

The proper use of inhalation devices is vital for asthma control.[29] Even with effective medications provided by healthcare professionals following evidence-based guidelines, many asthma patients still experience exacerbations and persistent symptoms, largely due to improper use of inhalation devices.[30] Using inhalation devices correctly helps achieve the necessary drug levels in the lungs, reduces disease symptoms, prevents worsening

**Table 1: Major guidelines or consensus related to pediatric asthma in the past decade**

| Year | Title |
|---|---|
| 2025 | Guidelines for the diagnosis and optimal management of asthma in children (patient and public version, 2025) |
| 2025 | Guidelines for the diagnosis and optimal management of asthma in children (2025) |
| 2025 | Expert consensus on the standardized construction of pediatric allergy and immunology diagnosis and treatment center/allergy and immunology outpatient department |
| 2025 | Clinical practice guidelines for home nebulization therapy in children with respiratory diseases (2025) |
| 2024 | Expert consensus on pediatric lung diffusing capacity tests |
| 2024 | Chinese expert consensus on thunderstorm asthma in children |
| 2024 | Expert consensus on common issues in clinical application of pediatric lung function testing |
| 2024 | Clinical practice guidelines for the diagnosis and management of children with cough in China (version 2023 for primary care) |
| 2024 | Evidence-based guideline for dust mite allergen immunotherapy in children with allergic asthma (Patient Version) |
| 2024 | Evidence-based guideline for dust mite allergen immunotherapy in children with allergic asthma (Medical Version) |
| 2023 | Current situation and development strategies of diagnosis and treatment of bronchial asthma in children in China (2022) |
| 2023 | Expert consensus on the diagnosis and treatment of chest tightness variant asthma in children |
| 2023 | Clinical practice expert consensus on differential diagnosis and initial management of wheezing in children under 6 years of age |
| 2023 | Expert consensus on diagnosis and management of bronchial asthma comorbidities in children |
| 2023 | Chinese experts' advice on adolescent asthma management and transitional care of adolescents with asthma |
| 2022 | Expert consensus on exercise prescription for asthmatic children in China |
| 2022 | Thirty key issues on exercise prescription for children with asthma in China |
| 2022 | Evidence-based guidelines for food allergy in children in China |
| 2022 | Clinical practice guideline for the rational use of oral H1-antihistamines in children (2022 edition) |
| 2022 | Concerns about children with anaphylaxis in China: Implementing the China Children's Anaphylaxis Emergency Action Plan |
| 2022 | Expert consensus on childhood management of bronchopulmonary dysplasia |
| 2021 | Expert consensus on detection and clinical application of exhaled nitric oxide in children (2021 edition) |
| 2021 | Expert consensus on identification and prevention of adverse reactions of commonly used asthma drugs in children |
| 2021 | Clinical practice guidelines for the diagnosis and management of children with cough in China (version 2021) |
| 2021 | One hundred key issues on the Chinese Children's Asthma Action Plan |
| 2021 | Expert consensus on clinical application of the China Children's Asthma Action Plan. |
| 2021 | Recommendations for the diagnosis and treatment of anaphylaxis in Chinese children |
| 2021 | Expert consensus on the clinical application of Omalizumab in children with allergic asthma |
| 2021 | Chinese expert consensus on clinical practice of allergen test in children (2021 edition) |
| 2020 | Recommendations for diagnosis and management of bronchial asthma in children (2020) |
| 2020 | Expert consensus on the prevention and treatment of asthma in children by integrated traditional Chinese and Western medicine |
| 2020 | Expert Consensus on Rational Use of Antimicrobial Drugs for Common Asthmatic Diseases in Children |
| 2019 | Consensus on diagnosis and management of allergic diseases in children |
| 2019 | Expert consensus on the safe and rational use of aminophylline in children |
| 2018 | Guidelines for rational drug use in children with wheezing disorders |
| 2018 | Expert Consensus on the Application of Inhaled Glucocorticoid Aerosol Therapy in Pediatrics (2018 Revised Edition) |
| 2018 | Expert consensus on vaccination of children with special health status (II)—Bronchial asthma and vaccination |
| 2018 | Expert consensus on mite-specific immunotherapy for allergic airway diseases in children |
| 2018 | Expert Consensus on the Application of H1 Antihistamines in Common Allergic Diseases in Children |
| 2017 | Series guidelines for pediatric pulmonary function |
| 2016 | Clinical application expert consensus on the leukotriene receptor antagonist in common childhood respiratory diseases |
| 2016 | Guideline for the diagnosis and optimal management of asthma in children (2016) |

*This table refers to the current situation and development strategies of diagnosis and treatment of bronchial asthma in children in China, and supplements the information.[11]

of the condition, and improves respiratory function and quality of life.

Pediatric experts in China have issued a series of consensus statements and guidelines to standardize healthcare professionals' education, training, and follow-up assessment of inhalation techniques for children and their parents, providing an operational framework for clinical practice [Figure 2].[20,31-40] In the early stages, nebulization equipment was simple, and the technology was rudimentary. With the optimization of equipment

and the standardization of procedures, nebulization rooms have become widespread in medical institutions, offering a standardized setting for nebulization therapy for acute asthma relapse. The nebulization room (>20 m², accommodating more than 6–10 children) employs zoned segregation. Children with infectious respiratory disease are isolated from others, while noninfectious patients are grouped by condition. Caregiver accompaniment is limited to one per child, and symptomatic individuals are prohibited from entry. Environmental controls require at least twice-daily 30-min ventilation cycles or equivalent air disinfection using air sterilizers or ultraviolet light. Continuous exhaust must be maintained during operation, with increased frequency and extended duration during epidemic seasons. Routine monitoring is mandated to ensure airborne bacteria remain below 4.0 colony-forming unit (CFU)/plate (5-min exposure) and surface bacteria remain below 10.0 CFU/cm².[39] Today, the close integration of nebulization therapy and nebulization rooms has established a popularized and standardized medical model. This has propelled inhalation therapy, with its advantages of targeted drug delivery, high efficiency, and low toxicity, to become an essential component of pediatric acute asthma management.

## Comprehensive promotion of the China Children's Asthma Action Plan

Every asthma patient should have an asthma action plan. In 2017, Chinese pediatric societies and associations jointly launched the first CCAAP management scheme, comprising a written plan and an electronic management platform. The CCAAP adopts the internationally recognized traffic light model, identifies green, yellow, and red zones based on clinical symptoms and peak expiratory flow (PEF) monitoring results, and provides specific recommendations for age-appropriate medications and inhaler devices. In 2018, a survey across 10 tertiary hospitals showed that CCAAP significantly improved knowledge, attitude, and practice questionnaire scores among 173 asthmatic children aged 6–14 years.[41] In 2021, after 4 years of promotion and clinical application, CCAAP was optimized and upgraded to its second version. By December 2024, the electronic CCAAP had managed nearly 47,000 children across 33 provinces and 381 cities nationwide.

The electronic CCAAP is a home-based tool for daily data collection, asthma control assessment, and patient education. It features a dual-portal design for daily use by both patients and doctors, fostering collaborative disease management. The patient portal collects daily PEF data and asthma symptoms from children and automatically recommends medication regimens based on the asthma action plan. Additionally, the patient portal provides educational and management functions, including information on asthma management, pollen forecasts, and extreme weather alerts. Children with asthma can contact their pediatricians via a "one-click consultation" feature, enabling online adjustments to the CCAAP and treatment regimen. Meanwhile, the doctor portal facilitates analysis of PEF values, symptoms, and trigger factors upon entering yellow and red zones, and reviews periodic

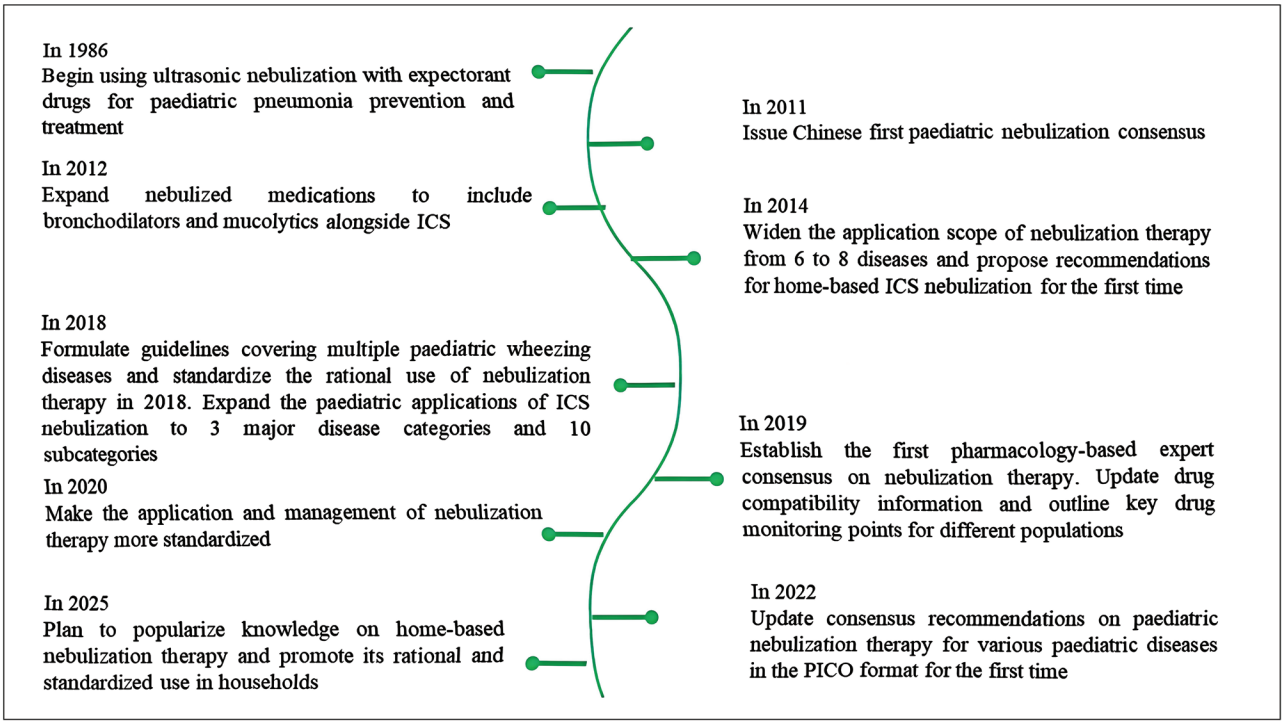


**Figure 2:** The development history of pediatric nebulization therapy in China[20,31-40]

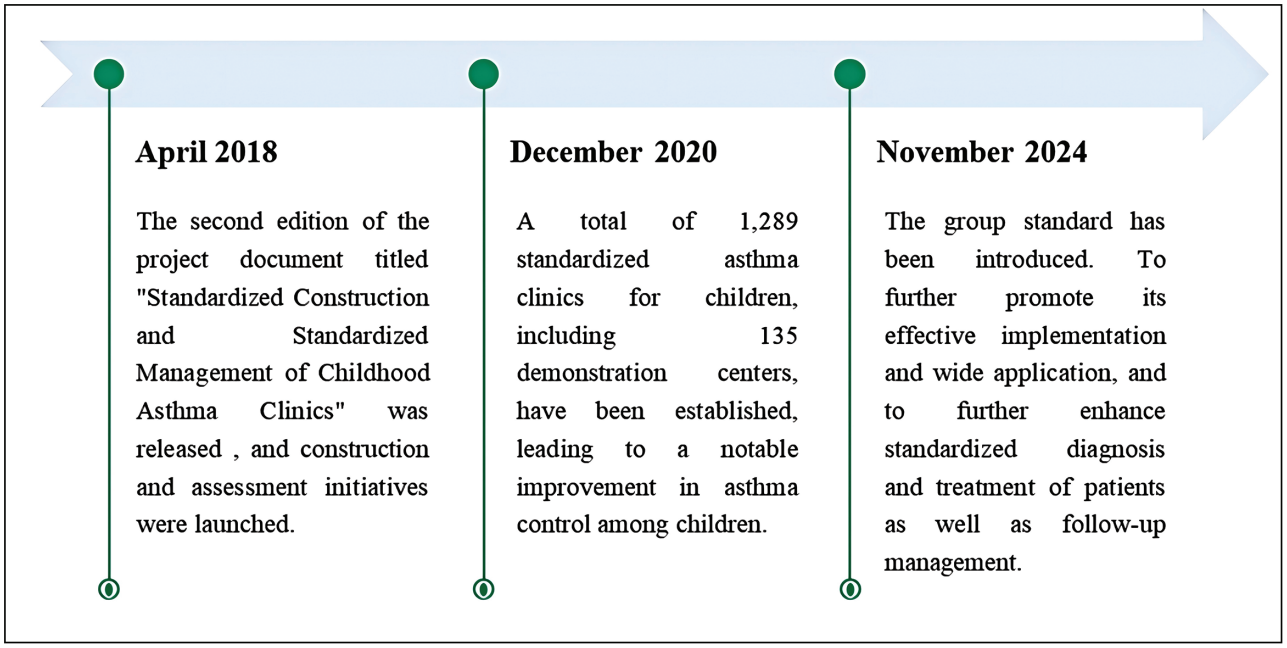


**Figure 3:** Historical evolution of standardized asthma clinics for children

management outcomes, including distribution ratios and frequency. It also features medication adherence analysis, detailed medication logs, and self-management adherence analysis to help pediatricians evaluate implementation effectiveness and identify causes of poor asthma control. From September 2021 to March 2025, over 64,000 online consultations were generated. In 2024, the application standard of CCAAP was released, aiming to enhance children's self-management of asthma and achieve standardized asthma management.

## Standardized asthma clinics for children

The standardized asthma clinics are an integrated platform for standardized comprehensive diagnosis and management, incorporating checkups, evaluation, diagnosis, therapy, and education. It enables early diagnosis, early treatment, and standardized management of pediatric asthma.

The construction of standardized asthma clinics for children in China is continuously evolving and improving [Figure 3]. In 2017, the Chinese standardized asthma clinics for children project was initiated. In 2018, the second edition of the project document standardized the construction and management of childhood asthma clinics, was released, and construction and evaluation work were carried out. By 2020, 1289 standardized asthma clinics for children, including 135 regional demonstration centers, had been established. Fifty-six training sessions had been conducted, training 2560 pediatricians and 650 nurses, covering 2560 hospitals nationwide. Also, 4518 patient education activities had been held, with online publicity reaching 1 million people. On average, the clinics served 1.33 million patients annually, and the asthma control rate among patients who completed the questionnaire reached 84.1%.[42]

In 2024, the official release of the "Standard for the construction of childhood asthma clinic" marked a significant step toward the standardized and scientific management of pediatric asthma. This standard adopted a three-pronged approach, focusing on discipline development, personnel training, and certification and plaque presentation, to enhance pediatric asthma diagnosis and treatment comprehensively.

In terms of discipline development, the standard emphasized the rational planning of treatment areas, precise allocation of nebulization equipment and medications, optimized staffing, and strengthened outpatient follow-up and quality control, all aimed at creating an efficient diagnostic and treatment process.

The personnel training program employed a standardized, integrated theory-practice model for front-line pediatricians, comprising: (1) theoretical instruction on clinic protocols, guidelines, and test interpretation; (2) case-based workshops; (3) hands-on workshops for pulmonary function and FeNO testing (5 test reports per modality); (4) site visits to demonstration clinics; and (5) completion certification following assessment. This curriculum facilitated standardized skill acquisition and promoted clinical readiness through structured competency-based training.

The certification and plaque presentation plan was clearly outlined, with 621 application pilot units to be established in two batches in 2025–the first batch

comprising 314 units and the second batch comprising 307 units. The certification is valid for 2 years. For established standardized pediatric asthma clinics, re-certification will be initiated every 2 years in principle to ensure pediatric patients receive standardized examination, diagnosis, and treatment. Strict certification and plaque presentation procedures motivated various units to actively implement the group standard.

It was worth highlighting that the standard stipulated that at least 80% of children should have a CCAAP. This innovative measure was expected to greatly increase the adoption and utilization rate of CCAAP in pediatric asthma management.

Through process optimization, professional assessment, individualized health education, and real-time disease monitoring, standardized asthma clinics for children effectively improved asthma management awareness and promoted better asthma control. This made them an effective pediatric asthma management approach.

## Management Challenges and Future Perspectives

### Optimizing management of adolescent asthma

We continuously monitored asthma deaths in Chinese children. Using a nationally representative database, we analyzed asthma deaths among Chinese children and adolescents.[43] From 2016 to 2021, 398 deaths were reported, with adolescents accounting for 56.8%. Adolescents had poor medication adherence, with 23.8% having anxiety and 18.8% depression, affecting asthma control. So, Chinese experts' advice on adolescent asthma management and transitional care of adolescents with asthma was made to guide pediatricians and internists in transition care and improve asthma management.[44]

### Paying attention to anaphylaxis

Anaphylaxis is a key trigger for asthma deaths. Childhood asthma deaths often occurred at home (45.0%) or on the way to the hospital (12.0%), underscoring the need for timely medical intervention. Adrenaline is the first-line medication for anaphylaxis, and the prevention of anaphylaxis must be promoted. Adrenaline auto-injectors are routinely prescribed to pediatric patients at risk of anaphylaxis, enabling them or their caregivers to administer immediate emergency treatment before reaching a medical facility, a practice that significantly reduces mortality. Accordingly, the recommendations for the diagnosis and treatment of anaphylaxis in Chinese children and China children's anaphylaxis emergency action plan have been issued to enhance doctors ability to identify and provide emergency care for anaphylaxis.[45,46]

### Managing airway mucus plugging

Fatal asthma attacks were often accompanied by airway mucus plug obstruction. A study analyzed 242 children and adolescents aged 3 and above hospitalized for exacerbation from 2016 to 2021. Of the 151 who had bronchoscopy, 62.9% had mucus plug obstruction.[47] Currently, the consensus on airway hypersecretion management in pediatric asthma is under development. The content covers the management of airway mucus hypersecretion and mucus plugging, emphasizing comprehensive application of measures such as mucus hydration, muco-active drugs, airway clearance techniques, bronchoscopy intervention, oxygen therapy, and respiratory support, and risk factor control, based on standardized anti-asthma treatment.

### Formulating an individualized exercise prescription

Insufficient exercise management was suggested by surveys showing that most middle-school students with asthma (over 80.0%) had low physical activity levels.[48] To address this, a consensus on exercise prescription for asthmatic children in China and 30 key issues on exercise prescription for asthmatic children were released for scientific guidance on exercise.[49,50]

### Integration of Traditional and Western medicine

Traditional Chinese medicine shows potential in pediatric asthma management. Adding Xiao Er Fei Re Qing Granules to standard asthma treatment was shown to effectively promote recovery, particularly in cases where asthma was triggered by respiratory infections.[51] The result of another prospective, multicenter cohort study is in press. Based on this, a clinical guideline for the prevention and treatment of asthma with integrated traditional Chinese and Western medicine has been developed to standardize treatment and improve outcomes.

## Conclusion

Asthma mortality among Chinese children aged 0–19 years has significantly declined over the past 30 years, due to the continuous updating of pediatric asthma guidelines, the widespread adoption of inhalation therapy, the implementation of CCAAP, and the establishment of standardized asthma clinics for children. Other contributing factors encompass enhanced public awareness, targeted caregiver education, and expanded community health promotion initiatives. However, challenges such as the management of adolescent asthma, the response to anaphylaxis, and the treatment of airway mucus plugs still exist. In the future, efforts should focus on enhancing transition care in adolescence, optimizing emergency response systems, and improving the integration of traditional Chinese medicine and Western medicine in treatment strategies, all of which will help further reduce childhood asthma mortality.

### Author contributions

Kunling Shen and Peng Han designed the study. Peng Han performed a literature search, data extraction, and wrote

the manuscript. Pang Han, Yuejie Zheng, Yanmin Bao, and Kunling Shen reviewed the manuscript. All authors approved the final version of the manuscript.

## Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

## Ethical policy and Institutional Review Board statement

This study does not involve ethical approval.


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## Conflicts of interest

There are no conflicts of interest.

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