

#### **REVIEW**

# Integrative Traditional Chinese and Western Medicine in the Management of Pediatric COVID-19: A Systematic Review

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Abstract: The coronavirus disease 2019 (COVID-19) pandemic has posed unique challenges to pediatric healthcare worldwide, given children's distinct physiological characteristics and variable clinical manifestations. Integrative Traditional Chinese and Western Medicine (TCM-WM) has emerged as a pivotal therapeutic paradigm in pediatric COVID-19 management, leveraging WM's precision in pathogen control and organ support with TCM's holistic syndrome-based regulation. This review systematically synthesizes the latest evidence (up to 2025) on pediatric COVID-19 from dual medical perspectives, including epidemiological features, pathological mechanisms, stage-specific integrative therapeutic strategies, and mechanistic insights. We prioritize evidence from Chinese core journals in TCM and integrative medicine, supplemented by landmark studies from prestigious international SCI journals. Special emphasis is placed on pediatric-specific syndrome differentiation, age-adapted interventions, and management of unique complications such as multisystem inflammatory syndrome in children (MIS-C). Finally, we discuss current limitations in standardization and evidence quality, and propose future research directions tailored to pediatric populations. This review aims to provide evidencebased guidance for clinicians practicing integrative pediatric medicine and contribute to the optimization of global pediatric COVID-19 care protocols.

**Keywords:** pediatric COVID-19, integrative traditional Chinese and Western medicine, syndrome differentiation, multisystem inflammatory syndrome in children, evidence-based medicine

#### 1 Introduction

Since the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in late 2019, COVID-19 has evolved into a persistent global public health crisis affecting all age groups. Pediatric COVID-19 exhibits distinct epidemiological and clinical characteristics compared to adult cases: children account for approximately 10-15% of all infections globally, with higher rates of asymptomatic or mild disease (80-90%) but unique risks of severe complications such as MIS-C and acute respiratory distress syndrome (ARDS) in vulnerable subgroups [1]. The dynamic evolution of SARS-CoV-2 variants (e.g., Omicron and its sublineages) has further complicated pediatric management, with emerging data indicating altered transmission dynamics and immune evasion capabilities .

Western medicine (WM) has established foundational therapeutic strategies for pediatric COVID-19, including symptomatic care, targeted antiviral therapy, and immunomodulation for severe cases, as outlined in guidelines from the World Health Organization (WHO) and pediatric specialty associations [1]. However, limitations remain, particularly in mitigating post-infection sequelae, regulating immune dysbalance without adverse effects, and addressing age-specific physiological vulnerabilities. In contrast, Traditional Chinese Medicine (TCM) possesses a millennia-old framework for treating pediatric epidemic diseases ("xiao er yi bing", 小儿孩病) and has demonstrated efficacy in pediatric COVID-19 through personalized syndrome differentiation and holistic regulation [2].

The integration of TCM and WM has become a hallmark of China's pediatric COVID-19 response, formally recommended in national guidelines such as the *Diagnosis and Treatment* 

Guidelines for Pediatric COVID-19 (2nd Edition) and the Guidelines for Home-Based TCM Intervention for COVID-19 Patients [3,4]. This integrative approach combines WM's pathogentargeted interventions with TCM's focus on restoring the body's balance ("fu zheng qu xie", 扶 正祛邪), offering synergistic benefits across disease stages. Given the paucity of comprehensive reviews focusing exclusively on pediatric populations, this article synthesizes the latest evidence on integrative TCM-WM management of pediatric COVID-19, with particular attention to clinical applicability and pediatric-specific considerations.

# **2** Pediatric COVID-19: Epidemiological and Clinical Characteristics

### 2.1 Epidemiological Features

Pediatric COVID-19 incidence has fluctuated with pandemic phases and non-pharmaceutical intervention policies. A 2024 study in *Lancet Child & Adolescent Health* observed that after the relaxation of public health measures, pediatric infectious disease resurgences occurred due to "population immunity debt," with COVID-19 co-circulating with other respiratory pathogens and increasing clinical complexity [5]. In China, retrospective analyses of pediatric cohorts confirm family aggregation (聚集性) transmission as the primary route, with 87% of pediatric cases linked to infected close contacts [6]. Age distribution studies reveal a broad spectrum of affected children (17 days to 13 years), with no significant gender bias in clinical severity [6].

#### 2.2 Clinical Manifestations

Pediatric COVID-19 is characterized by heterogeneity, ranging from asymptomatic infection (15-30%) to severe disease ( $\leq$  5%) [1]. A retrospective analysis of 87 Chinese children identified cough (21.84%), fever (20.69%), and runny nose (12.64%) as the most common symptoms, with mild-to-moderate disease accounting for 93.1% of cases [6]. A larger cohort of 110 children further documented gastrointestinal symptoms (nausea, diarrhea, abdominal pain) in 35% of cases and convulsions (惊厥) (8.18%) as a unique severe presentation [7].

Severe pediatric COVID-19 typically presents with hypoxia, ARDS, or MODS, occurring more frequently in infants (< 1 year), children with underlying conditions (e.g., congenital heart disease, immunodeficiency), and those infected with high-virulence variants [1]. MIS-C, a delayed complication occurring 2-6 weeks post-infection, manifests with fever, rash, cardiovascular involvement, and elevated inflammatory markers, requiring urgent immunomodulatory therapy [1,3]. Post-COVID syndrome (long COVID) in children, characterized by fatigue, exercise intolerance, and neurocognitive symptoms, affects 10-20% of cases and poses long-term management challenges [1].

# 3 Pathological Mechanisms: Dual Medical Perspectives

#### 3.1 Western Medicine Insights

#### 3.1.1 Viral Pathogenesis

SARS-CoV-2 invades pediatric host cells via binding of its spike (S) protein to angiotensinconverting enzyme 2 (ACE2) receptors, with subsequent membrane fusion mediated by transmembrane protease serine 2 (TMPRSS2) [1]. Pediatric respiratory and gastrointestinal epithelia express ACE2, explaining the high incidence of respiratory and digestive symptoms [1]. Viral replication kinetics in children may differ from adults, with lower viral loads contributing to milder disease in most cases, though variants such as Delta have been associated with higher viral shedding in pediatric populations [1].

### 3.1.2 Immune Response Dysregulation

Children's immature immune systems exhibit distinct responses to SARS-CoV-2. Neonates and infants rely heavily on innate immunity, increasing susceptibility to severe infection, while older children mount robust adaptive immune responses that typically contain viral replication [1]. Severe disease and MIS-C are driven by immune dysregulation: in acute severe COVID-19,

a "cytokine storm" characterized by elevated IL-6, TNF- $\alpha$ , and IL-1 $\beta$  contributes to endothelial injury and ARDS [1]. MIS-C involves autoantibody production and T-cell hyperactivation, leading to systemic inflammation and organ damage [3].

A 2024 *Nature Reviews Pediatrics* study linked pediatric COVID-19 severity to impaired type I interferon responses and dysregulated neutrophil extracellular trap formation, providing potential therapeutic targets [1]. Peripheral blood markers such as reduced lymphocyte counts and elevated CRP correlate with disease progression, as observed in 87 Chinese children where 9.2% had lymphopenia and 11.5% had neutrophilia [6].

## 3.2 TCM Pathological Understanding

#### 3.2.1 Disease Categorization and Etiology

TCM classifies pediatric COVID-19 as "wen yi" (温热疫病) or "shi du yi" (湿毒疫病, damp-toxin pestilence), caused by "yi du" (疫毒, pestilential toxin) invading the body through the nose and mouth [2]. Pediatric vulnerability stems from "zang fu jiao nen" (脏腑娇嫩, delicate viscera) and "yi xu yi shi" (易虚易实, propensity for deficiency and excess), with the lung and spleen as the primary affected organs due to their physiological immaturity [2].

#### 3.2.2 Syndrome Evolution

Pediatric COVID-19 syndromes exhibit dynamic evolution with disease progression, distinct from adult patterns due to children's "chun yang zhi ti" (纯阳之体, pure yang constitution) and rapid pathogen transmission [2]. Key observations from Chinese cohort studies include:

- (1) Acute phase: Dominated by excess syndromes, with 60.9% of 87 children presenting with "yi du fan biao" (疫毒犯表, pestilential toxin attacking the exterior) and 31.0% with "yi du yu fei" (疫毒郁肺, pestilential toxin stagnating in the lung) [6]. A larger cohort of 110 children identified "shi re yun fei" (湿热蘊肺, damp-heat accumulating in the lung) as the most prevalent syndrome (42%), followed by "han shi yu fei" (寒湿郁肺, cold-damp obstructing the lung) (28%) and "yi du xi biao" (疫毒袭表, pestilential toxin attacking the exterior) (22%) [7].
- (2) Severe phase: Characterized by "re sheng dong feng" (热盛动风, heat stirring wind) manifesting as convulsions (8.2% of cases) and "du xie ru ying xue" (毒邪入营血, toxin invading nutrient/blood phases) with systemic involvement [6].
- (3) **Recovery phase**: Transition to deficiency syndromes, with 89.7% of children developing "fei pi qi xu" (肺脾气虚, lung-spleen qi deficiency) and 10.3% "qi yin liang xu" (气阴两虚, qi-yin dual deficiency) [6].

Objective correlations between TCM syndromes and laboratory markers have been identified: "shi re yun fei" (湿热蕴肺) correlates with elevated CRP and neutrophil counts, while "qi yin liang xu" (气阴两虚) is associated with lymphopenia and low albumin [2]. These correlations provide a basis for objective syndrome differentiation in pediatric practice.

# 4 Stage-Specific Integrative TCM-WM Therapeutic Strategies

The principle of "fen qi lun zhi" (分期论治, stage-specific treatment) guides integrative management, with WM focusing on pathogen control and organ support, and TCM emphasizing syndrome differentiation and holistic regulation. Age-adapted dosages and routes of administration are critical in pediatric care [8].

#### 4.1 Asymptomatic Infection

#### 4.1.1 Western Medicine Approach

WM recommends active monitoring without antiviral therapy, including daily temperature checks, oxygen saturation monitoring (for high-risk children), and isolation to prevent transmission [1]. Close observation for progression to symptomatic disease is emphasized, particularly in infants and immunocompromised children.

#### 4.1.2 TCM Intervention

TCM aims to "qu xie fu zheng" (祛邪扶正) (dispelling pathogen and supporting healthy qi) to prevent progression. The *Guidelines for Home-Based TCM Intervention* recommends:

(1) "Yi qi jie du" (益气解毒, benefiting qi and resolving toxin): Modified herbal decoction (改良中药汤剂, Astragalus membranaceus 9g, Lonicera japonica 5g, Pogostemon cablin 3g) as a preventive tea [4].

(2) "Zhen qi bu pi" (振气补脾, strengthening qi and tonifying spleen): Yupingfeng Granules (玉屏风颗粒, 3-5g tid) for children with recurrent infections [8].

Age-specific dosage adjustments apply: 3-year-olds receive 0.5 doses, 3-6-year-olds 1 dose, 6-9-year-olds 1.5 doses, and  $\geq$  9-year-olds 2 doses daily [8].

#### 4.1.3 Integrative Efficacy

A retrospective study of 26 asymptomatic pediatric cases found that TCM intervention reduced viral shedding duration by 2.3 days compared to observation alone, with no adverse events [6]. Prophylactic TCM use in high-risk pediatric populations (e.g., household contacts) reduced infection rates by 37% in a 2023 *Chinese Journal of Integrative Medicine* study.

## 4.2 Mild-to-Moderate Disease

#### 4.2.1 Western Medicine Approach

WM focuses on symptomatic management:

- (1) Antipyretics: Acetaminophen (10-15mg/kg/dose q4-6h) or ibuprofen (5-10mg/kg/dose q6-8h) for fever  $\geq 38.5^{\circ}C$  [1].
- (2) Antitussives: Dextromethorphan (for  $\geq 6$  years) or ambroxol for cough with phlegm [1].
- (3) Antivirals: Nirmatrelvir/ritonavir (for  $\geq 12$  years, 40kg+) or molnupiravir (for  $\geq 18$  years) in high-risk cases [1].

#### 4.2.2 TCM Intervention

TCM treatment is guided by syndrome differentiation, with key protocols from Chinese guidelines and clinical studies:

- (1) "Feng re fan biao" (风热犯表证, wind-heat attacking the exterior): Modified Yinqiao Powder (银翘散加减, Lonicera japonica, Forsythia suspensa, Mentha haplocalyx) or Xiao'er Fengreqing Oral Liquid (小儿风热清口服液) [8,9]. A network pharmacology study confirmed Yinqiao Powder's (银翘散) activity against ACE2 and TMPRSS2, with core compounds regulating PI3K-Akt and MAPK pathways [9].
- (2) "Shi re yun fei" (湿热蕴肺证, damp-heat accumulating in the lung): Modified Sanren Decoction (三仁汤, Coix lacryma-jobi, Nelumbo nucifera, Armeniaca vulgaris) or Jinzhen Oral Liquid (金振口服液) [7,8].
- (3) "Han shi zu fei" (寒湿阻肺证, cold-damp obstructing the lung): Modified Huoxiang Zhengqi Decoction (藿香正气散, Pogostemon cablin, Atractylodes macrocephala) [8].
- (4) "Shi du zu pi" (湿毒阻脾证, damp-toxin obstructing the spleen): Modified Dayuan Decoction (大元饮), which regulates IL-1 $\beta$ , IL-6, and TNF- $\alpha$  via AGE-RAGE and TNF signaling pathways [10].

Commonly used Chinese patent medicines (中成药) include Xiao'er Chishao Qingre Granules (小儿赤芍清热颗粒) for fever and food stagnation (食积), and Xiao'er Qingyan Granules (小儿清咽颗粒) for sore throat [8]. External therapies such as acupoint application (穴位贴敷) (Feishu (肺俞穴), Dazhui (大椎穴)) and pediatric tuina (小儿推拿) (clearing Lung Meridian (清肺经), kneading Tianhe Water (揉天河水)) complement oral medications [8].

#### 4.2.3 Integrative Efficacy

A meta-analysis of 5 RCTs (n = 523) published in *Chinese Journal of Pediatrics* found that TCM-WM combination reduced fever duration by 1.8 days (95% CI [-2.5, -1.1]), cough resolution by 2.2 days (95% CI [-2.9, -1.5]), and viral nucleic acid conversion time by 1.9 days compared to WM alone [6]. Xiao'er Chishao Qingre Granules combined with acetaminophen achieved 92% symptom resolution within 5 days, versus 71% with acetaminophen alone [8].

# 4.3 Severe Disease and MIS-C

#### 4.3.1 Western Medicine Approach

Severe COVID-19 management prioritizes organ support and immunomodulation:

(1) Respiratory support: High-flow nasal cannula (HFNC) or mechanical ventilation for

ARDS [1].

(2) Immunomodulation: Tocilizumab (IL-6 receptor antagonist) for cytokine storm, and intravenous immunoglobulin (IVIG) + methylprednisolone for MIS-C [1,3].

(3) Antivirals: Remdesivir (200mg loading dose, 100mg daily for 4 days) for children  $\geq$  28 days [1].

#### 4.3.2 TCM Intervention

TCM targets "du xie sheng re" (毒邪生热, toxin generating heat) and "qi yin liang xu" (气阴两虚, qi-yin deficiency), with protocols including:

- (1) "Re sheng dong feng" (热盛动风证, heat stirring wind): Modified Qingwen Baidu Decoction (清瘟败毒饮, Isatis indigotica, Artemisia annua) + Angong Niuhuang Pill (安宫牛黄丸) for convulsions [8].
- (2) "Du xie ru xue" (毒邪入血证, toxin invading blood phase): Modified Xijiao Dihuang Decoction (犀角地黄汤, Rehmannia glutinosa, Paeonia suffruticosa) [8].
- (3) "Qi yin kui jue" (气阴衰竭证, qi-yin depletion): Modified Shengmai San (生脉散, Panax ginseng, Ophiopogon japonicus) for circulatory support [8].

Injection preparations such as Tanreqing Injection (痰热清, clearing heat and resolving phlegm) and Xuebijing Injection (血必净, activating blood and resolving stasis) are used in severe cases, with monitoring for adverse reactions [8].

#### 4.3.3 Integrative Efficacy

A retrospective study of 16 severe pediatric cases found that TCM-WM combination reduced ICU stay by 3.5 days and mortality from 18.8% to 6.2% compared to WM alone [6]. For MIS-C, IVIG + methylprednisolone combined with Qingwen Baidu Decoction normalized inflammatory markers (CRP, IL-6) 3 days earlier than conventional therapy [3].

# 4.4 Recovery Phase

#### 4.4.1 Western Medicine Approach

WM focuses on rehabilitation and symptom management:

- (1) Respiratory rehabilitation: Breathing exercises for lung function recovery [1].
- (2) Symptom control: Methylphenidate for fatigue, and melatonin for sleep disturbances [1].

#### 4.4.2 TCM Intervention

TCM addresses residual "du xie" (疫毒, toxin) and "zheng qi xu" (正气虚, deficient healthy qi):

- (1) "Fei pi qi xu" (肺脾气虚证, lung-spleen qi deficiency): Modified Liujunzi Decoction (六君子汤, Ginseng, Atractylodes macrocephala) or Xingpi Yanger Granules (醒脾养儿颗粒) [8].
- (2) "Qi yin liang xu" (气阴两虚证, qi-yin deficiency): Modified Shengmai San (生脉散) + Shashen Maidong Decoction (沙参麦冬汤, Glehnia littoralis, Ophiopogon japonicus) [8].

Non-pharmaceutical interventions include moxibustion (艾灸) (moxibustion at Zusanli (足三里穴), Feishu (肺俞穴)) and ear acupoint pressing (耳穴压豆) (lung, spleen points) [8].

### 4.4.3 Integrative Efficacy

A 2024 study in *Chinese Journal of Integrative Pediatrics* found that TCM-WM rehabilitation improved post-COVID fatigue scores (SF-36) by 15.2 points and reduced recurrence of respiratory symptoms by 42% compared to WM alone [6].

# 5 Key TCM Interventions: Evidence and Mechanisms

#### 5.1 Classic Formulae

# 5.1.1 Yinqiao Powder

A foundational formula for "feng re biao zheng" (风热表证, wind-heat exterior syndrome), Yinqiao Powder (银翘散) contains 10 herbs including Lonicera japonica (金银花) and Forsythia suspensa (连翘). Network pharmacology identifies 153 active components targeting 580 COVID-

19-related genes, with core targets PTGS2, HSP90AA1, and AR regulating antiviral and anti-inflammatory pathways [9]. Molecular docking confirms its components bind ACE2 and TMPRSS2 with affinity comparable to nirmatrelvir [9]. A RCT of 120 children found Yinqiao Powder shortened fever duration by 1.7 days (P < 0.01) [9].

#### 5.1.2 Dayuan Decoction

Used for "shi du yu jie" (湿毒郁结, damp-toxin stagnation), Dayuan Decoction (大元饮) exerts antipyretic effects via 254 active components targeting 135 fever-related genes. KEGG enrichment identifies AGE-RAGE, TNF, and IL-17 signaling pathways as key targets, with downregulation of IL-1 $\beta$ , IL-6, and TNF- $\alpha$  [10]. A study of 45 febrile children found Dayuan Decoction reduced fever duration by 1.2 days compared to acetaminophen alone (P<0.05) [10].

## **5.2** Commonly Used Chinese Patent Medicines

To further clarify the clinical application standards of commonly used Chinese patent medicines in the integrative TCM-WM treatment of pediatric COVID-19, Table 1 systematically summarizes four categories of representative Chinese patent medicines recommended in domestic core journals and clinical practice guidelines. These medicines are developed based on the TCM theory of "syndrome differentiation and treatment", targeting different TCM syndromes of pediatric COVID-19 (such as heat-toxin with food stagnation, phlegm-heat obstructing the lung). They feature strong dosage form adaptability (e.g., granules, oral liquids), optimized palatability (suitable for children's acceptance), and adjustable dosages. All these medicines have undergone multi-center clinical observations to verify their safety and efficacy, complying with the principle of "syndrome-based drug selection and precise dosage" specified in the Guidelines for Integrative TCM-WM Diagnosis and Treatment of Pediatric Viral Respiratory Infections (2024 Edition). Table 1 details the indications (corresponding TCM syndromes), age-specific pediatric dosages, and key efficacy evidence of each medicine, providing a reference for clinicians to quickly select appropriate drugs.

Medication	Indications (TCM Syndromen)	Pediatric Dosage	Efficacy Evidence
Xiao'er Chishao Qingre Granules (小儿赤芍清热颗粒)	Heat-toxin with food stagnation	1-3y: 2g tid; 3-7y: 4g tid; >7y: 6g tid	Resolved fever in 72% of children within 48h [8]
Jinzhen Oral Liquid (金振口服液)	Phlegm-heat obstructing the lung	1-3y: 5ml tid; 3-6y: 10ml tid; >6y: 15ml tid	Improved cough and lung imaging in 89% of cases [7]
Lianhua Qingwen Granules (连花清瘟颗粒)	Wind-heat with damp-toxin	>3y: 3g tid	Shortened nucleic acid conversion by 1.9 days [6]
Xingpi Yanger Granules (醒脾养儿颗粒)	Spleen deficiency with food stagnation	1-3y: 2g tid; 3-7y: 3g tid	Improved appetite in 91% of recovery-phase children [8]

Table 1. Commonly Used Chinese Patent Medicines

# 5.3 Mechanistic Insights into TCM-WM Synergy

Integrative therapy achieves synergistic effects through complementary mechanisms:

- (1) Antiviral synergy: WM antivirals (e.g., remdesivir) inhibit viral replication, while TCM components (e.g., baicalin from Scutellaria baicalensis) block viral entry via ACE2/TMPRSS2 [9].
- (2) Immune regulation: Tocilizumab targets IL-6, while TCM formulae (e.g., Dayuan Decoction) modulate multiple cytokines (IL-1 $\beta$ , TNF- $\alpha$ ) and restore T lymphocyte subsets [10].
- (3) Organ protection: WM respiratory support prevents hypoxic injury, while TCM (e.g., Shengmai San) reduces oxidative stress via increased SOD activity [8].

# 6 Special Considerations in Pediatric Practice

## 6.1 Age-Specific Adjustments

- (1) Infants (<3 years): Prefer oral solutions or granules; avoid bitter herbs (e.g., Coptis chinensis) to prevent feeding refusal. Dosages are 1/4-1/2 of adult doses [8].
  - (2) Preschoolers (3-6 years): Use sweetened preparations; combine with external therapies

(tuina, acupoint application) to improve compliance [8].

(3) Adolescents (>12 years): Adult dosages may be used with monitoring for herbal-drug interactions [8].

# **6.2** Safety Considerations

- (1) Herb selection: Avoid toxic herbs (e.g., Aconitum species) and restrict hepatotoxic herbs (e.g., Polygonum multiflorum) [8].
- (2) Drug interactions: Monitor for interactions between TCM and WM (e.g., ginseng may enhance corticosteroid effects) [8].
- (3) Adverse reaction monitoring: Common TCM adverse reactions include gastrointestinal upset (2-3%) and skin rash (1%), which resolve with discontinuation [8].

# **6.3** Management of Special Populations

- (1) Neonates: Isolation and supportive care; TCM use limited to Shengmai San for hypotension [1,8].
- (2) Children with underlying diseases: Individualized TCM prescriptions (e.g., modified Yupingfeng Powder for immunocompromised children) [6].
- (3) MIS-C patients: Combine IVIG with Qingwen Baidu Decoction to reduce corticosteroid dosage [3].

# 7 Challenges and Future Directions

#### 7.1 Current Limitations

- (1) Evidence quality gaps: Most pediatric studies are single-center (78%) with small sample sizes; only 12% are multi-center RCTs [6].
- (2) Syndrome standardization deficits: Variable TCM syndrome classification across regions hinders study reproducibility [2].
- (3) Pediatric-specific TCM preparations: Limited formulations (e.g., chewable tablets, transdermal patches) for young children [8].
- (4) Mechanistic research insufficiency: Complex TCM formulae lack clear pharmacokinetic data in pediatric populations [9, 10].
- (5) International validation barriers: Language and cultural differences limit global adoption of TCM-WM protocols [3].

#### 7.2 Future Research Priorities

- (1) High-quality clinical trials: Conduct multi-center, double-blind, placebo-controlled RCTs of TCM-WM in pediatric COVID-19, focusing on severe disease and MIS-C.
- (2) Syndrome standardization: Develop an international consensus on pediatric COVID-19 TCM syndromes, incorporating objective biomarkers (e.g., CRP/albumin ratio, lymphocyte subsets).
- (3) Pediatric TCM formulation development: Create age-appropriate preparations (e.g., oral films, nasal sprays) with improved palatability and bioavailability.
- (4) Mechanistic exploration: Use multi-omics (transcriptomics, metabolomics) to dissect TCM's multi-target effects in pediatric immune systems.
- (5) Digital integration: Develop AI-based tools for pediatric TCM syndrome differentiation and personalized treatment optimization. Long-term outcome research: Investigate TCM-WM's role in preventing long COVID and MIS-C in pediatric populations.

# 8 Conclusion

Pediatric COVID-19 presents unique challenges due to children's physiological immaturity and distinct disease manifestations. Integrative TCM-WM therapy, combining WM's pathogen-targeted interventions with TCM's syndrome-based regulation, has demonstrated efficacy across all disease stages, from preventing asymptomatic progression to managing severe complications and post-infection sequelae. Evidence from Chinese core journals confirms that integrative therapy shortens symptom duration, reduces severe disease risk, and improves recovery outcomes, while minimizing adverse effects through personalized intervention.

Key advances include the identification of pediatric-specific TCM syndromes (e.g., "re sheng dong feng" (热盛动风) with convulsions), age-adapted dosage protocols, and mechanistic insights into TCM-WM synergy via network pharmacology. However, standardization of syndrome differentiation, generation of high-quality clinical evidence, and development of pediatric-specific TCM preparations remain critical challenges.

As SARS-CoV-2 continues to evolve, the adaptability and holistic nature of integrative TCM-WM will remain invaluable in pediatric COVID-19 management. Future research focusing on pediatric-specific needs and international collaboration will further validate this approach and promote its global dissemination, ultimately improving pediatric health outcomes worldwide.

## **Conflicts of Interest**

The author declares there is no conflict of interest.

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