




## Access to medicines for children in China

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**ABSTRACT**

Access to essential medicines for children is a big challenge, particularly in low-income and middle-income countries. In China, the average availability of essential medicines for children is 1.6%–46.5%. The availability of generics was generally higher than original brands in public hospitals and the prices of generics were relatively lower and more reasonable (generics: availability, 27.3%–46.5%, prices, 0.52–4.28 times the international reference prices; original brands: 1.6%–33.0%, 2.59–11.38 times the international reference prices). In terms of affordability of medicines for children, generics were more affordable than original brands and tablets/capsules were more affordable than injections. Most commonly used anti-infective medicines (such as amoxicillin capsule, azithromycin tablet, cefuroxime tablet) and antipyretics (such as ibuprofen suspension) were relatively affordable. Six commonly used medicines in paediatrics, including amoxicillin/clavulanic acid, beclomethasone, cefazolin, ceftazidime, ceftriaxone, cyclosporine were unaffordable. Since August 2011, China has successively issued several policies to ensure the accessibility of medicines for children, covering research and development, production, procurement and prices of medicines. The accessibility of medicines for children has been partially improved, but still needs continuous improvement.

**INTRODUCTION**

Access to medicines is essential for children's health. In 2019, the WHO reported that about 5.2 million children under 5 years old died from preventable or treatable diseases worldwide. Most of these diseases could be avoided by timely and rational medication.<sup>1,2</sup> Low-income and middle-income countries with limited resources accounted for the top 10 countries with the most deaths, and China ranked the sixth with 132 000 deaths of children under the age of 5 (mortality rate 7.8‰).<sup>1,2</sup> The leading causes of death in children under 5 years old in China are congenital malformations, deformations or chromosomal abnormalities, injury and poisoning, pneumonia and sepsis.<sup>3</sup> Timely preventive or therapeutic interventions, including appropriate antibiotics and oral rehydration solution, might eliminate the deaths of young children due to diarrhoea and prevent nearly

**KEY MESSAGES**

- ⇒ Access to essential medicines for children is a big challenge, particularly in low-income and middle-income countries, including China.
- ⇒ From 2012 to 2021, the average availability of essential medicines for children was 1.6%–46.5% in China. The availability and affordability of generics were generally higher than original brands, such as anti-infective medicines and antipyretics.
- ⇒ To decrease prices and improve the availability and affordability of medicines for children, China has formulated and implemented a series of policies and measures covering the development, production, procurement, rational use of medicines. This has had some positive effects.
- ⇒ To further improve access to medicines for children in China, medicines for neoplastic disease and chronic diseases (including rare diseases), the revision and improvement of relevant medical insurance policies and the establishment of the 'National Essential Medicines List for Children' should be given more attention.
- ⇒ In China, the accessibility of medicines for children has partially improved, but still needs continuous improvement to meet the needs of children for medicines.

two-thirds of the deaths caused by childhood pneumonia.<sup>4,5</sup>

Access to medicines for children is a major global health issue continuously receiving widespread attention. In 2016, the 69th World Health Assembly adopted a resolution 'Promoting Innovation and Access to High-quality, Safe, Effective and Affordable Medicines for Children' proposed by the Chinese representative. Moreover, the WHO called on member states to achieve healthcare equity through universal health coverage and ensure all children can access essential healthcare services without overburdened finance.<sup>2</sup> Further improving the access, coverage and quality of essential healthcare services for children, including essential medicines, has become an important goal in all countries. In May 2003, the WHO and the International Health Action Organization jointly developed a standardised method named



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**Table 1** Availability of medicines for children in China

Study ID	Time	Area	No of medicines	Medicines availability			
				Public hospitals		Private pharmacies	
				OBs	LPGs	OBs	LPGs
Chen <i>et al</i> 2022 <sup>8</sup>	2021	Sichuan Province, China	30	9.7%	46.5%	/	/
Wang <i>et al</i> 2020 <sup>44</sup>	2019	Weifang City, Shandong Province, China	20	15.8%	44.8%	30.3%	36.7%
Dai <i>et al</i> 2020 <sup>45</sup>	2017	China	42	33.0%	32.0%	/	/
Wei <i>et al</i> 2019 <sup>46</sup>	2016	China	49	1.8%	29.5%	/	/
Wei <i>et al</i> 2019 <sup>46</sup>	2012	China	49	1.6%	40.0%	/	/
Sun <i>et al</i> 2018 <sup>47</sup>	2017	Jiangsu Province, China	40	7.5%	34.2%	8.9%	29.4%
Wang <i>et al</i> 2014 <sup>48</sup>	2012	Shaanxi Province, China	28	10.8%	27.3%	11.9%	20.6%

Note: Availability: the proportion(%) of public hospitals or private pharmacies that could provide medicines. LPGs, lowest price generics; OBs, original brands.

'measuring medicine prices, availability, affordability and price components', which measured the accessibility of medicines from three dimensions: availability, price and affordability.<sup>6</sup> Researchers or relevant government departments can use it to investigate the availability and affordability of medicines for children. This data allow government departments to formulate and improve relevant measures or policies to ensure access to medicines for children.

### ACCESS TO MEDICINES FOR CHILDREN IN CHINA

We have studied accessibility of medicines for children both globally and in China.<sup>7,8</sup> From 2012 to 2021, the average availability of essential medicines for children in China was 1.6%–46.5%. The availability of generics was generally higher than original brands in public hospitals (generics: 27.3%–46.5%, original brands: 1.6%–33.0%) (table 1).<sup>7,8</sup> Availability in private pharmacies showed a similar picture (20.6%–36.7% generics vs 8.9%–30.3% original brands). The differences between the studies were greatest for original brands. Differences in the availability of generic medicines may reflect differences in the list of medicines investigated in individual studies. They may also reflect actual differences in availability in different institutions or provinces. The reasons for the low availability of medicines for children might be related to the low market share of medicines for children, resulting in pharmaceutical companies lacking development and production motivation.<sup>9</sup>

In terms of price, generics for children were relatively less expensive. The prices of original brands were much higher than generics, which were generally more than five times the international reference prices. (original brands: 2.59–11.38 times the international reference prices, generics: 0.52–4.28 times the international reference prices).

Affordability was generally assessed by comparing the daily wage of lowest-paid unskilled government workers

and medicines expenses in the standard treatment of childhood diseases (a full course of therapy for acute diseases or a 30 days supply of medicines for chronic diseases).<sup>5</sup> Medicines were considered affordable if the medicines cost less than the daily wage. Around 90.8% (59/65) of surveyed medicines were considered affordable (generics or original brands cost less than the daily wage). Generics were more affordable than original brands and most generics were considered affordable. Most commonly used anti-infective medicines (such as amoxicillin capsule, azithromycin tablet, cefuroxime tablet) and antipyretics (such as ibuprofen suspension) were relatively affordable. In addition, tablets/capsules were more affordable than injections. And tablets/capsules of most essential medicines for children were considered affordable. Six commonly used medicines in paediatrics, including amoxicillin/clavulanic acid (200 mg/28.5 mg, suspension), beclomethasone (50 µg/dose, 200 dose, inhaler), cefazolin (1 g, injection), ceftazidime (1 g, injection), ceftriaxone (250 mg, injection), cyclosporine (25 mg, tablet/capsule), were unaffordable. (tables 2–4)

### CHINESE STRATEGIES FOR IMPROVING ACCESS TO MEDICINES FOR CHILDREN AND THEIR EFFECTS

#### Encourage the research and development of medicines for children, and speed up the review and approval of medicines for children

In response to the insufficient development and production of medicines for children, in August 2011 and January 2012, the State Council of China respectively issued the 'China Children's Development Programme Outline (2011–2020)',<sup>10</sup> and the '12th Five-Year Plan' for 'National Drug Safety',<sup>11</sup> putting forward the main goals and strategic measures of children development in four aspects—child health, education, legal protection and the environment. These plans encouraged the development and production of medicines for children.

**Table 2** Affordability of medicines for children in China

Study ID	Time	Area	Public hospitals						Private pharmacies							
			OBs			LPGs			OBs			LPGs				
			Affordable medicines (N)	Survey medicines (N)	Affordable medicines (%)	Affordable medicines (N)	Survey medicines (N)	Affordable medicines (%)	Affordable medicines (N)	Survey medicines (N)	Affordable medicines (%)	Affordable medicines (N)	Survey medicines (N)	Affordable medicines (%)		
Chen <i>et al</i> 2022 <sup>8</sup>	2021	Sichuan Province, China	/	/	/	4	7	57%	/	/	/	/	/	/	/	/
Wang <i>et al</i> 2020 <sup>44</sup>	2019	Weifang City, Shandong Province, China	2	4	50%	8	9	89%	4	7	57%	7	7	100%	7	100%
Dai <i>et al</i> 2020 <sup>45</sup>	2017	China	2	5	40%	4	5	80%	/	/	/	/	/	/	/	/
Wei <i>et al</i> 2019 <sup>46</sup>	2016	China	2	8	25%	40	42	95%	/	/	/	/	/	/	/	/
Wei <i>et al</i> 2019 <sup>46</sup>	2012	China	1	9	11%	38	42	90%	/	/	/	/	/	/	/	/
Sun <i>et al</i> 2018 <sup>47</sup>	2017	Jiangsu Province, China	6	8	75%	7	8	88%	5	7	71%	6	7	86%	7	86%
Wang <i>et al</i> 2014 <sup>48</sup>	2012	Shaanxi Province, China	2	3	67%	14	14	100%	2	2	100%	12	12	100%	12	100%

Note: Affordable medicines are medicines that cost less than the daily wage for a course of treatment. LPGs, lowest price generics; OBs, original brands.

**Table 3** Affordable medicines for children in China

Medicines name	Strength	Dosage form
Acetaminophen	500 mg	Tablet
Albendazole	200 mg	Tablet
Aminophylline	0.1 g	Injection
Aminophylline	25 mg/mL	Injection
Amitriptyline	0.025 g	NR
Amlodipine	0.005 g	NR
Amoxicillin	250 mg	Tablet/capsule
Amoxicillin+clavulanic acid	0.375 g	NR
Amoxicillin+clavulanic acid	1.0 g	NR
Amoxicillin+clavulanic acid	125 mg+31.25 mg/5 mL	Suspension
Amoxicillin+clavulanic acid	250 mg+125 mg	Tablet
Aspirin	0.3 g	Tablet
Aspirin	100 mg	Tablet
Atenolol	0.05 g	NR
Azithromycin	250 mg	Tablet/capsule
Benzylpenicillin	1 million IU	Injection
Calamine	100 mL	Lotion
Captopril	0.025 g	NR
Carbamazepine	100 mg	Tablet
Ceftriaxone	1 g	Injection
Cefuroxime	250 mg	Tablet/Capsule
Cefuroxime	750 mg	Injection
Cephalexin	0.25 g	NR
Chloramphenicol	250 mg	Tablet
Chlorpheniramine	4 mg	Tablet
Ciprofloxacin	0.25 g	NR
Clarithromycin	0.25 g	NR
Diazepam	5 mg/mL	Injection
Enalapril	0.005 g	NR
Enalapril	0.01 g	NR
Erythromycin	0.25 g	NR
Fluconazole	0.2 g/100 mL	Injection
Fluconazole	50 mg	Capsule
Ibuprofen	200 mg	Tablet
Ibuprofen	100 mg/5 mL	Suspension
Ibuprofen	2 g/100 mL	Suspension
Isoniazid	100 mg	Tablet
Isosorbide Nitrate	0.005 g	NR
Levothyroxine	50 µg	Tablet
Loratadine	10 mg	Tablet/capsule
Metformin	500 mg	Tablet/Capsule
Metronidazole	0.2 g	NR
Morphine	10 mg	Tablet
Nifedipine	0.01 g	NR
Omeprazole	10 mg	Tablet
Omeprazole	0.02 g	NR

Continued

**Table 3** Continued

Medicines name	Strength	Dosage form
Oral rehydration solution	500 mL	Oral solution
Paracetamol	500 mg	Tablet
Phenobarbital	30 mg	Tablet
Phenobarbital	100 mg/mL	Injection
Phenytoin	50 mg	Tablet
phenytoin sodium	0.1 g	NR
Procaine penicillin	600 mg	Injection
Ranitidine	0.15 g	NR
Salbutamol	100 µg/dose	Inhaler
Simvastatin	0.02 g	NR
Sodium valproate	200 mg	Tablet/capsule
Vitamin A	25 000 IU	Capsule
Vitamin B <sub>6</sub>	50 mg/mL	Injection
NR, not reported.		

From 2016 to 2019, China has released a series of policies, which stated that relevant government departments would give priority review and approval to the medicine for children and provide policy support of ‘timely guidance, immediate review, accelerated approval, encouraging production, priority procurement’ from research and development to approval and sales.<sup>12–16</sup> Now, a ‘green channel’ for children’s medicines has been established, which speeds up the review and approval of medicines for children, especially for those marketed abroad and urgently needed clinically.<sup>12 17</sup>

In recent years, rare diseases in children have attracted more and more attention. The Chinese government has issued special policies for rare disease medicines development. First, national fiscal and taxation policy support it.<sup>18</sup> In February 2019, the Policy on the Value-added Tax of rare disease medicines was issued, in which providing tax incentives for pharmaceutical companies to encourage the development of rare disease medicines, and reducing the costs of rare disease medicines for patients. Second, the rapid review and approval system for medicines and medical devices for rare disease has been introduced. A green channel for a rapid review on rare disease medicines has been established, and the

**Table 4** Unaffordable medicines for children in China

Medicines name	Strength	Dosage form
Amoxicillin+clavulanic acid	200 mg: 28.5 mg	Suspension
Beclomethasone	50 µg/dose, 200 dose	Inhaler
Cefazolin	1 g	Injection
Ceftazidime	1 g	Injection
Ceftriaxone	250 mg	Injection
Cyclosporine	25 mg	Tablet/capsule

review time limit for rare disease medicines approval to enter the green channel is 130 workdays. Additionally, technical guidance for the development of rare disease medicines has been produced. In June 2022, the Center for Drug Evaluation of the National Medical Products Administration (NFDA) issued the ‘Technical Guidelines for Clinical Research and Development of rare disease medicines’. This is the first technical guidelines for rare diseases in China, which provides scientific study frameworks and advice for rational and efficient rare disease medicines development.<sup>19</sup>

Benefiting from these support policies, significant progress has been made in the development and production of medicines for children. From 2014 to 2019, more than 9000 medicines for children were approved in China, including 2118 medicines (23.2%) whose medicine package inserts only included indications and usage for children. Before 2014, of the more than 3 500 medicines, only about 60 were dedicated to children, accounting for less than 2%.<sup>20</sup> The formulations of medicines for children have also been enriched and the number of formulations such as granules and oral solutions suitable for children has increased significantly. The number of newly approved granules and oral liquid preparations were 1319 and 952.<sup>21</sup> The Chinese NFDA reported that a total of 26 medicines dedicated to children were approved in 2020, an increase of 36.8% compared with 2019. This growth would continue through July 2021.<sup>22</sup> Fourteen other medicines dedicated to children have been approved for marketing, and dozens dedicated to children or for adding children’s indications or usage were under review, of which 22 have been included in the priority review and approval list.<sup>22</sup>

### Encourage clinical trials of medicines for children

In recent years, China focused on strengthening the management of clinical trials on children’s medication, promoting the establishment of clinical trial platforms and research teams, and improving enrolment of children. The NFDA has issued guidelines for conducting clinical trials of medicines in the paediatric population.<sup>23 24</sup> Relevant departments are actively exploring the establishment of management policies which included: ‘providing clinical trial data and medication information when applying for new drugs in children’, ‘For productions already on the market, the pharmaceutical companies are required to timely supplement and update clinical data in children’.<sup>17</sup>

### Ensure the supply of medicines for children

To avoid out of stock of medicines for children, China emphasises the need to ‘strengthen the monitoring of the supply and use of medicines for children, provide price and purchasing assistance policy for clinically necessary medicines that are in short supply, and arouse the enthusiasm of pharmaceutical companies for production and distribution; for medicines with less clinical need, carry out fixed-point

production and storage to ensure supply’. Moreover, China is establishing an early warning mechanism for ensuring the supply of medicines that are not always available, which is helpful to timely obtain the real-time situation of drug production, actively coordinate and solve the outstanding problems and difficulties existing in pharmaceutical companies, and improve the continuous supply capacity.<sup>25</sup>

### Promote the procurement of medicines for children, including essential medicines

For improving the availability of medicines for children in medical institutions, the ‘Announcement on Further Strengthening the Procurement and Use of Medicines for Children in Medical Institutions’<sup>26</sup> was issued in September 2015. This pointed out that all regions should attach great importance to the procurement and use of medicines for children, and further strengthen the supervision of medicines procurement for children. Moreover, since the ‘National Essential Medicines List (2012 Edition)’, China has made efforts to expand the coverage of medicines for children and increase the proportion of medicines whose medicine package inserts only included indications and usage for children on the ‘National Essential Medicines List’.<sup>27</sup> There were nearly 200 medicines that could be used in children on the ‘National Essential Medicines List (2012 Edition)’,<sup>28</sup> including more than 70 whose medicine package inserts only included indications and usage for children and covering granules, oral solutions, suspensions, dry suspensions agent, etc. Based on children’s medication needs, the ‘National Essential Medicines List (2018 Edition)’,<sup>29</sup> added 22 new medicines for children. The medicines were all urgently needed in clinical practice (eg, caffeine citrate injection essential for primary apnea in preterm neonates, bovine pulmonary surfactant for injection essential for neonatal respiratory distress syndrome, pegaspargase injection essential for childhood acute lymphoblastic leukaemia) and some child-friendly dosage formulations of the original medicines (a low-dose Clindamycin dispersible tablet (0.075 g) was added.<sup>30</sup> In 2021, the ‘Administrative Measures for the National Essential Medicine List (NEML) (Draft)’ proposed that the new NEML would list essential medicines for children separately, which reflected the government’s continuous attention of medicines for children.<sup>31</sup> Moreover, to further improve the availability of essential medicines, the State Council proposed to ‘promote the priority procurement and use of essential medicines, increase the proportion of essential medicines used, timely adjust the ‘National Essential Medicines List’ and gradually realise that the proportions of essential medicines in primary medical institutions, secondary public hospitals and tertiary public hospitals are more than 90%, 80% and 60%, respectively’ in 2019.<sup>32</sup>



### Improve the affordability of medicines for children, including some anticancer and rare disease medicines

To reduce the price of medicines and improve the affordability of medicines for children, the National Healthcare Security Administration and the Ministry of Human Resources and Social Security of the People's Republic of China proposed that 'Priority would be given to medicines for children' in the 'National Reimbursement Drug List (NRDL) Adjustment Work Plan'.<sup>33</sup> Thirty-eight medicines for children were added to the NRDL in 2019.<sup>34</sup> In the latest NRDL (2021 edition),<sup>35</sup> there were 109 medicines for children (medicine package inserts only included indications and usage for children). Meanwhile, for diseases, such as haematological diseases and malignant tumours for children, the 'Announcement on Medical Treatment and Security Management in Children with Haematological Diseases and Malignant Tumours' was issued in 2019,<sup>36</sup> which stated that 'Gradually include more eligible medicines for haematological diseases, malignant tumours and other major or catastrophic diseases for children into the NRDL'. In 2021, the National Healthcare Security Administration and the National Health Commission proposed a 'dual-channel' mechanism for negotiating drugs in the NRDL. Reimbursement is available for purchases at designated medical institutions and designated retail pharmacies. The proposal was made to solve the problem that some high cost drugs in the NRDL are not always available in hospitals (not purchased or in short supply). Purchases from private pharmacies cannot be reimbursed by medical insurance.<sup>37</sup> At present, 19 provinces have published a 'dual-channel' drug list (the number of drugs ranges from 23 to 291) in China. For example, in Sichuan Province of China, Pegaspargase (acute lymphoblastic leukaemia) and Nusinersen (spinal muscular atrophy) were included in the 'dual-channel' drug list. From 1 January 2022, the high cost drug Nusinersen (original price of ¥700 000) was included in the NRDL and the price has dropped to ¥33 180. After being reimbursed by medical insurance, patients only need to pay about ¥9000 (€1321) out of pocket.<sup>38</sup>

In recent years, China has paid more attention to the affordability of medicines for children and prioritised including medicines for children on the NRDL. However, the medicines for children on the NRDL were limited. The proportion of medicines for children on the latest NRDL was less than 6%. Most of them were mainly antibiotics, antitussives, decongestants, antihistamines and antipyretics.<sup>39</sup>

### EXPECTATIONS FOR THE FUTURE

With the full implementation of the 'three-child policy' in China<sup>40</sup> (a series of policies and supporting measures for encouraging a couple to have three children to cope with the ageing of the population and improve population structure), it is foreseeable that the number of children will continue to increase and the market demand

for medicines for children will also increase.<sup>41</sup> Compared with WHO Model Lists of Essential Medicines for Children (EMLc), China's NEML has fewer child-friendly dosage formulations (eg, oral solution). Many medicines included in EMLc are not available in China, such as acyclovir oral solution, oseltamivir oral solution, phenobarbital oral solution, ciprofloxacin oral solution, linezolid oral solution, etc.<sup>42</sup> Improving the accessibility of medicines for children in appropriate dosage formulations and strength is still the long-term national goal and mission.

With the support of relevant policies, pharmaceutical companies should focus on the technical barriers to the development and production of medicines for children. Children of different ages have different needs for drug strength and dosage formulations. The European Medicines Agency divided children's growth period into five stages, and recommended different drug dosage formulations according to the physiological and psychological development characteristics of children at different stages to improve children's medication compliance, which comprehensively and accurately provided direction for the development and production of children's medicines.<sup>43</sup> There are few studies on the demand of drug dosage formulations or strength for children at different ages in China. Therefore, it is suggested to carry out relevant studies to provide scientific and reasonable guidance for helping pharmaceutical companies to fill the gaps in the children's medicine market and improve the accessibility of children's medicines.

For improving the affordability of medicines for children, relevant government departments also need to revise and improve relevant medical insurance policies and control medicine prices (especially for oral solutions, oral suspensions, dispersible tablets and scored tablets which have higher costs but are more suitable for children). Moreover, comprehensively considering the burden of disease for children in China, economic level, marketed drug dosage forms and so on, the government could learn experience from the WHO, South Africa and other established children's essential medicine list organisations or countries, and cooperate with experts from universities or research institutions to rationally select essential medicines for children to form the 'National Essential Medicines List for Children'. As a priority list of medicines for procurement and use in medical institutions, it will contribute to improving the accessibility of essential medicines and ensure the needs for essential medicines for children.

### CONCLUSION

Since August 2011, China has successively issued a number of policies to ensure the accessibility of medicines for children, covering research and development, production, supply, procurement and prices of medicines. The accessibility of medicines for children has been partially improved, but still needs continuous improvement.

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