

# Evaluation of rational prescribing in paediatrics

Imti Choonara 

**To cite:** Choonara I. Evaluation of rational prescribing in paediatrics. *BMJ Paediatrics Open* 2021;**5**:e001045. doi:10.1136/bmjpo-2021-001045

Received 1 February 2021  
Revised 2 March 2021  
Accepted 9 March 2021

Evidence-based medicine is recognised as being important. Clinical trials and subsequent systematic reviews of clinical trials are the key determinants of efficacy of an intervention. Medicines have made a major contribution to the health of children. Antibiotics are essential for the treatment of sepsis and are life-saving medicines. Similarly, antiasthmatic drugs and antiepileptic drugs can be both life-saving and also significantly enhance the quality of life, reducing morbidity from asthma and epilepsy, respectively.

Inappropriate use of medicines, however, may result in problems such as increased resistance to antibiotics or side effects.<sup>1</sup> The rational use of medicines has been recognised as important for the health and well-being of all by the WHO for a long time. Irrational prescribing remains a problem in paediatric patients of all ages. Studies of drug utilisation in neonates have highlighted inappropriate use of new broad spectrum antibiotics and polypharmacy as major problems in neonates.<sup>2,3</sup>

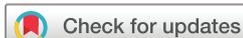
There have been more studies of irrational prescribing in children than in neonates. Overuse of antibiotics in children has been reported in both high-income<sup>4</sup> and low-income countries.<sup>5</sup> Other examples of inappropriate use of medicines are the widespread use of cough medicines in children<sup>6</sup> and polypharmacy.<sup>7</sup> Polypharmacy is associated with an increased risk of drug toxicity. A systematic review of the toxicity of levetiracetam found that polypharmacy was associated with both a greater risk of drug toxicity (64% children compared with 22% children on monotherapy) and discontinuation due to toxicity (4.5% vs 0.9% on monotherapy).<sup>8</sup> There is a risk of toxicity with every medicine and therefore medicines should only be used if they are clinically indicated.<sup>9</sup>

There has been a notable increase in the use of psychotropic medicines in children in many countries. A Norwegian study documented increased use of stimulants and

hypnotic/sedative agents over a decade.<sup>10</sup> The differences in guidelines and licensing for antipsychotics in children and adolescents between different countries demonstrate the lack of a clear evidence base to allow rational prescribing.<sup>11</sup>

In order to facilitate rational prescribing, the WHO has produced numerous guidelines. For example, the WHO guideline on child pneumonia recommends amoxicillin as first-line treatment.<sup>12</sup> Alongside the guidelines, the WHO produced their seventh Essential Medicines for Children list (EMLc) in 2019.<sup>13</sup> The EMLc gives specific guidance re-choice of antibiotic in different clinical situations. The antibiotics included in the EMLc are divided into three groups.<sup>13</sup> The first group (access) have activity against a wide range of commonly encountered pathogens. They also have lower resistance potential than other antibiotics. They are recommended as essential first or second choice empirical antibiotics. The second group (watch) have higher resistance potential and are recommended for a limited number of specific infections. Their use needs to be monitored as key targets of stewardship programmes. The third group (reserve) should be reserved for treatment of confirmed or suspected infections due to multidrug-resistant organisms. Their use needs to be monitored in national and international stewardship programmes. It is to be hoped that this division of the essential antibiotics will minimise irrational use.

Stewardship programmes have been shown to be of benefit in neonates<sup>14</sup> and children.<sup>15</sup> Quality indicators are useful in evaluating antibiotic use and 10 quality indicators have been proposed for use in hospitalised neonates and paediatric patients.<sup>16</sup> Others have proposed 25 quality indicators to evaluate treatment of community acquired pneumonia.<sup>17</sup> Two simple quality indicators have been used for community infections. One is the proportion of children receiving amoxicillin as the first antibiotic (target 50%) and



© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

Child Health, University of Nottingham School of Medicine, Derby, UK

**Correspondence to**  
Emeritus Professor Imti Choonara; Imti.Choonara@nottingham.ac.uk

the other was the proportion of children who received cephalosporins or macrolides (maximum 10%).<sup>18</sup> Both relate to community infections.

It is important to recognise that it is access to health-care and antibiotics rather than choice of antibiotic, that is the main reason for the higher mortality of infections in low-income and middle-income countries. The production of the EMLc enables researchers to study the availability of the essential medicines. Unfortunately, studies usually show limited availability of these essential medicines in many low-income and middle-income countries.<sup>19</sup> Universal access to healthcare and essential medicines are necessary prerequisites for rational prescribing.

Research into the availability of essential medicines in low-income and middle-income countries is to be welcomed and encouraged. There is, however, a need for other types of research in relation to rational prescribing. Tools for the evaluation of rational prescribing have been extensively developed and studied in adults, especially the elderly.<sup>20</sup> A systematic review of rational prescribing tools in 2014 identified 46 tools for adults.<sup>20</sup> In contrast, a systematic review in 2020 of tools for paediatric patients identified only three tools.<sup>21</sup>

The first tool for use in children was developed in France. Pediatrics: Omission of Prescriptions and Inappropriate Prescriptions (POPI) was published in 2014 and contained 105 criteria to evaluate prescriptions.<sup>22</sup> The tool was modified for use in the UK and this tool (POPI-UK) contained 80 criteria.<sup>23</sup> The only other tool was developed for use in primary care by researchers in Ireland and contained 12 criteria, of which six were for the respiratory system.<sup>24</sup> None of these tools are suitable for neonates and the lack of such tools for neonates has been highlighted.<sup>25</sup>

The evidence basis for the rational treatment of children is increasing with recognition that children have the right to receive medicines that are scientifically evaluated for efficacy and safety. Additionally, changes in teaching clinical pharmacology to medical students may promote a greater understanding of the need for rational prescribing.<sup>26</sup> Health professionals need to ensure that the scientific evidence is used appropriately. This can only be ensured by studies evaluating prescribing habits using tools that have been validated. It is encouraging that more tools and indicators are being developed for the paediatric population. Unfortunately, considerably more needs to be done to ensure that every child receives medicines prescribed rationally.

**Contributors** IC is the sole author.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** IC is editor in chief of *BMJ Paediatrics Open*.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not required.

**Provenance and peer review** Commissioned; externally peer reviewed.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

#### ORCID id

Imti Choonara <http://orcid.org/0000-0002-3069-6323>

#### REFERENCES

- 1 WHO global action plan on antimicrobial resistance, 2015. Available: <https://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/> [Accessed 5 Jan 2021].
- 2 Allegaert K. Rational use of medicines in neonates: current observations, areas for research and perspectives. *Health Care* 2018;6:115.
- 3 Al-Turkait A, Szatkowski L, Choonara I, et al. Review of drug utilization studies in neonatal units: a global perspective. *Int J Environ Res Public Health* 2020;17:5669.
- 4 Fleming-Dutra KE, Demirjian A, Bartoces M, et al. Variations in antibiotic and azithromycin prescribing for children by geography and Specialty—United States, 2013. *Pediatr Infect Dis J* 2018;37:52–8.
- 5 Østergaard MS, Kjærgaard J, Kristensen MM, et al. Recurrent lower respiratory illnesses among young children in rural Kyrgyzstan: overuse of antibiotics and possible under-diagnosis of asthma. A qualitative fresh air study. *NPJ Prim Care Respir Med* 2018;28:13.
- 6 Maina M, Akech S, Mwaniki P, et al. Inappropriate prescription of cough remedies among children hospitalised with respiratory illness over the period 2002–2015 in Kenya. *Trop Med Int Health* 2017;22:363–9.
- 7 Bowden N, Thabrew H, Kokaua J, et al. National prescribing rates and polypharmacy for children and young people in New Zealand with and without autism spectrum disorder. *Res Autism Spectr Disord* 2020;78:101642.
- 8 Egunsola O, Choonara I, Sammons HM. Safety of levetiracetam in paediatrics: a systematic review. *PLoS One* 2016;11:e0149686.
- 9 Allegaert K, Choonara I. All medicines have side effects. *Arch Dis Child* 2016;101:951–2.
- 10 Hartz I, Skurtveit S, Steffanak AKM, et al. Psychotropic drug use among 0–17 year olds during 2004–2014: a nationwide prescription database study. *BMC Psychiatry* 2016;16:12.
- 11 Putignano D, Clavenna A, Reale L, et al. The evidence-based choice for antipsychotics in children and adolescents should be guaranteed. *Eur J Clin Pharmacol* 2019;75:769–76.
- 12 WHO. Pneumonia. Available: [https://www.who.int/health-topics/pneumonia#tab=tab\\_1](https://www.who.int/health-topics/pneumonia#tab=tab_1) [Accessed 28 Feb 2021].
- 13 World Health Organization. *World Health organization model list of essential medicines for children*. 7th edn. Geneva: World Health Organization, 2019.
- 14 Gustavsson L, Lindquist S, Elfvin A, et al. Reduced antibiotic use in extremely preterm infants with an antimicrobial stewardship intervention. *BMJ Paediatrics Open* 2020;4:e000872.
- 15 Donà D, Barbieri E, Daverio M, et al. Implementation and impact of pediatric antimicrobial stewardship programs: a systematic scoping review. *Antimicrob Resist Infect Control* 2020;9:3.
- 16 Versporten A, Bielicki J, Drapier N, et al. The worldwide antibiotic resistance and prescribing in European children (ARPEC) point prevalence survey: developing hospital-quality indicators of antibiotic prescribing for children. *J Antimicrob Chemother* 2016;71:1106–17.
- 17 Li W, Zeng L, Li J, et al. Development of indicators for assessing rational drug use to treat community-acquired pneumonia in children in hospitals and clinics. *Medicine* 2017;96:e9308.
- 18 Piovani D, Clavenna A, Cartabia M, et al. Assessing the quality of paediatric antibiotic prescribing by community paediatricians: a database analysis of prescribing in Lombardy. *BMJ Paediatrics Open* 2017;1:e000169.
- 19 Droti B, O'Neill KP, Mathai M, et al. Poor availability of essential medicines for women and children threatens progress towards sustainable development goal 3 in Africa. *BMJ Global Health* 2019;4:e001306.
- 20 Kaufmann CP, Tremp R, Hersberger KE, et al. Inappropriate prescribing: a systematic overview of published assessment tools. *Eur J Clin Pharmacol* 2014;70:1–11.
- 21 Corrick F, Conroy S, Sammons H, et al. Paediatric rational prescribing: a systematic review of assessment tools. *Int J Environ Res Public Health* 2020;17:1473.

- 22 Prot-Labarthe S, Weil T, Angoulvant F, *et al.* POPI (pediatrics: omission of prescriptions and inappropriate prescriptions): development of a tool to identify inappropriate prescribing. *PLoS One* 2014;9:e101171.
- 23 Corrick F, Choonara I, Conroy S, *et al.* Modifying a paediatric rational prescribing tool (POPI) for use in the UK. *Health Care* 2019;7:33.
- 24 Barry E, O'Brien K, Moriarty F, *et al.* PIPc study: development of indicators of potentially inappropriate prescribing in children (PIPc) in primary care using a modified Delphi technique. *BMJ Open* 2016;6:e012079.
- 25 van den Anker J, Allegaert K. Rational use of antibiotics in neonates: still in search of tailored tools. *Health Care* 2019;7:28.
- 26 Brinkman DJ, Monteiro T, Monteiro EC, *et al.* Switching from a traditional undergraduate programme in (clinical) pharmacology and therapeutics to a problem-based learning programme. *Eur J Clin Pharmacol* 2021;77:421–9.