



## Therapeutic risk score for pharmaceutical follow-up prioritization

Ketlin Leite dos Santos<sup>1</sup>, Débora Driemeyer Wilbert<sup>1</sup>, Marcus Vinícius Terashima de Pinho<sup>2</sup>

<sup>1</sup>Faculdade de Medicina da Universidade Santo Amaro, UNISA, São Paulo/SP, Brasil.

<sup>2</sup>Faculdade de Medicina da Universidade de São Paulo/USP, São Paulo/SP, Brasil.

### ABSTRACT

#### OBJECTIVE

To develop an instrument for assessing pharmacotherapeutic risk factors (score) to prioritize patients in pharmacotherapeutic monitoring.

#### METHODS

An analysis of the Martinbiancho methodology was carried out, considered as a model study focusing on the need for parameter modifications according to the profile of pediatric patients treated in a public hospital in the south of São Paulo. Associated with data from the methodology used as a model, a literature review was carried out regarding risk factors for the pediatric population in relation to the use of medications, pharmacokinetics, pharmacodynamics, polypharmacy, risk of adverse reactions to medications, and clinical pharmacy. The following factors were found: age, polypharmacy, use of high-alert medications, use of intravenous medications, route of feeding (tubes and parenteral nutrition), liver and kidney failure, heart and lung problems. It was decided to add the use of screening medications, use of antibiotics, use of sedoanalgesic and/or vasoactive medications and non-standardized medications in the institution. In total, 11 important parameters in pediatrics were selected.

#### RESULTS

After choosing the relevant criteria, a form was developed to apply the score.

#### CONCLUSION

The developed score is expected to be an efficient instrument for detecting and prioritizing patients at greater risk of developing drug-related problems (DRPs), enabling a greater contribution to care in relation to therapeutics for the pediatric population.

#### DESCRIPTORS

Pharmacotherapeutic monitoring, Pediatrics, Clinical pharmacy, Therapeutic risk score.

#### Corresponding author:

Débora Driemeyer Wilbert.

Programa de Residência Multidisciplinar da Universidade Santo Amaro - UNISA. R. Prof. Enéas de Siqueira Neto, 340 - Jardim das Imbuías, São Paulo - SP, Brasil. São Paulo/SP, Brasil.

E-mail: [dwilbert@prof.unisa.br](mailto:dwilbert@prof.unisa.br)

ORCID ID: <https://orcid.org/0000-0003-1485-8473>.

**Copyright:** This is an open-access article distributed under the terms of the Creative Commons

Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided that the original author and source are credited.

#### DOI:

**INTRODUCTION**

The clinical pharmacist is the professional able to promote the rational use of medicines through the review of pharmacotherapy, treatment monitoring and health education, as described in Resolution No. 585/2013 of the Federal Pharmacy Council (CFF)<sup>2</sup>. One of the clinical services provided by the pharmacist is pharmacotherapeutic monitoring, where problems related to medications and negative results of pharmacotherapy are identified, analyzing their causes and making documented interventions, aiming to resolve or prevent them<sup>3</sup>.

Pharmacotherapeutic monitoring aimed at pediatric patients constitutes an important challenge for the pharmaceutical area, especially clinical pharmacy, since this population presents peculiar characteristics related to physiological maturity, which alter their capacity to absorb, metabolize and excrete medications and constitute important information not only always considered in clinical decisions related to the selection and use of drugs<sup>4</sup>. Evidence of more significant changes is observed in relation to pharmacokinetics because important stages such as drug absorption and metabolism can be influenced by variations in pH, gastric emptying time, gastrointestinal motility, enzyme deficiency and liver immaturity.

Approximately 75% of medications available on the market have not been adequately studied in the pediatric population. Therefore, drug therapy in children may result in an increased risk of adverse drug events<sup>5</sup>.

The development and validation of tools that prioritize patients is important to guide the work of clinical pharmacists, as the number of these professionals is often insufficient to meet all hospital needs<sup>6</sup>. Creating a therapeutic risk stratification score targeted to the needs of pediatric patients is an excellent way to improve pharmacist performance and patient therapy. The score can be used to characterize risk groups, enabling time optimization, without compromising the routine functioning of the clinical pharmacist in other services, in addition to enabling pharmaceutical assistance to patients whose underlying disease or therapy risk factors require greater care<sup>7</sup>.

In this scenario, the objective of the present study was to develop an instrument for evaluating pharmacotherapeutic risk factors (score) according to the profile of patients hospitalized in the pediatric sectors of a public hospital in the south of São Paulo, for prioritization in pharmaceutical monitoring.

**METHODS**

This is a cross-sectional study that proposes an adaptation of the Therapeutic Risk Score designed by a group of pharmacists from another institution with the addition and/or modification of criteria, based on the specificities of the pediatric population served. Therefore, this instrument will be developed according to aspects of therapy and standardized clinical protocols in the pediatric sectors of a public hospital in the south of São Paulo.

Martinbiancho<sup>1</sup> methodology assesses the risk of complications associated with the use of medications in hospitalized patients. Eight indicators are defined with scores ranging from zero to four points, and the sum is categorized as: (AR) - High-risk prescription ( $\geq 9$  points); (RM) - Moderate risk prescription (5 - 8 points); and (RB) - low risk prescription ( $\leq 4$  points).

Associated with data from the methodology used as a model, a literature review was carried out regarding risk factors for the pediatric population in relation to the use of medications, pharmacokinetics, pharmacodynamics, polypharmacy, risk of adverse reactions to medications and regarding clinical pharmacy and pharmaceutical care at Scielo, LILACS, Medline and Pubmed databases, using the following descriptors: pharmacotherapy follow up combined with pediatrics, clinical pharmacy and therapeutic risk score. This review aimed to support the modifications and additions of some criteria to the developed therapeutic risk score.

Based on these data, a scale consisting of 11 items/criteria

was formulated and a therapeutic risk score model was proposed. To apply the score, the following factors were considered relevant, making it necessary to collect these data from medical prescriptions and patients' records: age, polypharmacy, use of intravenous medications, use of high-alert medications, use of antibiotics, use of vasoactive and/or sedoanalgesics, use of tube medications and parenteral nutrition, liver and kidney failure, heart and/or lung problems, medications not standardized in the institution and tracer medications.

After choosing the criteria considered relevant, a form was developed to apply the score.

**RESULTS**

Based on the objective of the study, guidance for filling out the proposed form is found on table 1.

Table 1 - Guidance for filling out the proposed form

Risk classification criteria for defining monitoring from patients in pediatric inpatient departments	
Patient age	Need to identify age range in patient records.
Kidney and/or liver problems	Kidney and/or liver failure. Checked against medical records.
Heart and/or lung problems	COPD, mechanical ventilation (MV), heart failure, cardiogenic, septic, hypovolemic shock. Checked against medical records.
Nutritional Support	NGT (nasogastric tube), SNE ( nasoenteral tube ), GTT (gastrostomy), JT (jejunostomy) and NP (parenteral nutrition). Verified in the patient's electronic medical record.
Number of medicines	Calculate the number of oral and intravenous medications. Consider all items except those prescribed, if necessary (Y/N), items at medical discretion (ACM), creams and ointments. Verified in the patient's medical prescription.
Intravenous medications	Calculate the number of intravenous items prescribed, including nutrition items, excluding those prescribed if necessary (Y/N) and items at medical discretion (ACM). Verified in the patient's medical prescription.
High alert medications	List of standardized medications at the institution: sodium bicarbonate 8.4% 10 mL and 250 mL, potassium chloride 19.1%, sodium chloride 20%, potassium phosphate, calcium gluconate 10%, glucose 25% and 50%, magnesium sulfate 10% and 50% and Regular and NPH insulin. Verified in the patient's medical prescription.
Sedoanalgesic and/or Vasoactive Medications	Most medications used in the institution's pediatric sectors: midazolam, diazepam, lorazepam, propofol, ketamine, dexmedetomidine, and fentanyl. Verified in the patient's medical prescription.
Antimicrobial Medications	List of restricted-use medications provided by the institution's SCIH: cefepime, ceftriaxone, meropenem, piperacillin + tazobactam, polymyxin B, teicoplanin and vancomycin. Verified in the patient's medical prescription.
Non-standard medicines	Consider items for continuous use brought by the patient and items purchased via the hospital's purchase request process. Verified in the patient's medical prescription.
Tracker medications	Main triggers in pediatrics according to the profile of adverse reactions in the institution's pediatric sectors: diphenhydramin, flumazenil, protamine, desloratadine, vitamin K, naloxone, promethazine dexchlorferinamine oral solution, hydroxyzine oral solution, polyethylene glycol sachet and 20% mannitol sulfate.

Source: Prepared by the authors based on the Martinbiancho methodology<sup>1</sup>

The criteria were scored and grouped as shown in table 2.

Table 2 - Form for application and interpretation of adapted risk scores

Patient-related	Punctuation
0 – 12 months	two

13 – 24 months	1
>24 months	0
<b>Risk factors and comorbidities</b>	
Liver and/or kidney problems	1
Heart and/or lung problems	1
<b>Nutritional support</b>	
Does not use a probe	0
In use of SNE, SNG, VJ, VG	1
Using parenteral nutrition	two
<b>Related to pharmacotherapy</b>	
1 – 3 medications	0
4 – 10 medications	1
11 – 15 medications	two
>15 medications	3
<b>Intravenous medications</b>	
None	0
1 – 3 medications	1
4 – 6 medications	two
>6 medications	3
<b>High vigilance</b>	
None	0
1 – 5 medications	1
6-10 medications	two
>10 medications	3
<b>Vasoactive and/or sedative</b>	
None	0
1-2 medicines	1
3-4 medications	two
>medicines	3
<b>Antimicrobials</b>	
None	0
1-2 medicines	1
3-4 medications	two
>medicines	3
<b>Non-standard medicines</b>	
No	0
Yes	1
<b>Tracker medications</b>	
No	0
Yes	1
<b>Sum of criteria</b>	

Source: Prepared by the authors based on the Martinbiancho methodology<sup>1</sup>

The risk classification of patients for pharmaceutical monitoring adopted in this study is shown in table 3.

Table 3 - Risk classification for pharmaceutical monitoring

Score	Risk rating	Description
≥ 12 points	High Risk	Patients with a high-risk factor for medication-related problems. They need priority in pharmacotherapeutic monitoring. Daily monitoring of medical prescriptions, analysis of drug interactions, incompatibilities and active search for adverse drug reactions every 2 days.
7 – 11 points	Moderate Risk	They need monitoring, but not urgently. Daily monitoring of medical prescriptions, analysis of drug interactions and incompatibilities, active search for adverse drug reactions every 3 days.
≤ 6 points	Low Risk	Patients who should only be observed and monitored. Daily monitoring of medical prescriptions.

Source: Prepared by the authors based on the Martinbiancho methodology<sup>1</sup>

**DISCUSSION**

In addition to the criteria used in the Martinbiancho metho-

dology<sup>1</sup>, 4 criteria considered relevant in pediatrics and in pharmacotherapeutic monitoring carried out by clinical pharmacists at the institution where the study was developed were added to the score, namely: use of antibiotics, use of vasoactive and/or sedoanalgesic drugs, use of tracer medications and use of non-standardized medications in the institution.

To compose the list of antimicrobials, it was necessary to contact the institution's hospital infection control service, where they were informed which drugs were restricted for use. In a study evaluating the profile of antibiotic use in a pediatric intensive care unit, it was measured that 47.71% of errors in prescriptions were for restricted-use antibiotics, the most prescribed, respectively, were: vancomycin, cefepime, meropenem, piperacillin+tazobactam and polymyxin B<sup>8</sup>. In 50% of cases the prescription may be inappropriate, in addition to being the therapeutic class responsible for the majority of adverse events<sup>9</sup>.

Sedoanalgesic medications were included in the score, the main representatives of this class and most used are: midazolam, diazepam, lorazepam, propofol, ketamine, dexmedetomidine and fentanyl. Excessive and incorrect use of sedoanalgesia can have negative repercussions, leading to a prolongation of the need for ventilatory support, length of hospital stays and increased risk of infection. This occurs because the body begins to develop mechanisms that lead to physical dependence, determining the need to receive the drug in increasingly higher doses to maintain the clinical effect<sup>10</sup>.

Vasoactive drugs are potent and can produce harmful effects on the patient's life, which is why they should only be used under strict monitoring and in specific units<sup>11</sup>. Among the most used medications are: dobutamine, dopamine, epinephrine, milrinone and norepinephrine.

The non-standardized medications included in the present study can be brought from home by the patient if they use them continuously, or they can be purchased through a doctor's request and go through the hospital's purchasing process. This topic was added to the score because the pharmacist must monitor the process of prescription, acquisition, duration of treatment, dispensing and administration of such medications, to ensure that the treatment is carried out appropriately and has the expected therapeutic effect.

The use of trackers is an alternative method to reviewing medical records and an active form of pharmacovigilance. With the help of adverse event trackers, it is possible to locate the classes or medications that have a greater tendency to cause harm. For this score criterion, a selection of the main trackers in pediatrics was made<sup>12</sup>.

The immunosuppression criterion used in the Martinbiancho methodology<sup>1</sup> was removed from the present study because it is a general hospital in which, normally, immunocompromised pediatric patients treated are referred to specialized reference centers.

In a study, Falconer et al. (2014)<sup>13</sup> talk about the creation of an electronic tool for prioritizing patients, considering factors such as age, polypharmacy and comorbidities, high-risk medications (hyperglycemic agents, anticoagulants, antimicrobials, cardiovascular agents) and other factors that were included in the tool. In total, the online tool consisted of 38 risk flags, which were divided into five groups. These flags received scores, at the end of the summation they were classified as high, medium or low risk. In eight months of use, 765 patients were prioritized by pharmaceutical services, 526 errors involving medications were prevented, 174 of these were classified as moderate to serious. Carlson and Phelps (2015)<sup>14</sup> developed an electronic tool that aims to carry out interventions, medication reconciliations, monitoring of some medications and laboratory tests (work similar to that of Falconer et al. (2014))<sup>13</sup>, with this tool the improvement in the role of clinical pharmacy and it was possible to generate medication history of patients admitted by emergency. In these works similar to the score developed, it was observed that the points of relevance are very similar (presence of polypharmacy, comorbidities, use of antibiotics etc.) and follow a pattern when it comes to prioritization, having their particularities according to the group that belongs to needs to be prioritized.

The article by Pernassi and collaborators (2017)<sup>4</sup> evaluated the general scoreable risk in the pediatric intensive care sector at the Hospital das Clínicas in Ribeirão Preto, and the risk factors were: renal failure, potentially dangerous medications and liver failure, thus demonstrating a profile of patients and diverse results. Also using the risk outcome for the development of adverse reactions, through a bibliographic review via PubMed, Science Direct, CINAHL and MEDLINE, Zhou and Rupa (2018)<sup>15</sup> found that polypharmacy received the highest reporting rate, an important finding, given that the risk score proposal classified medication addition in an increasing manner. Thus, several data demonstrate common risk factors for the develo-

ment of drug-related problems (DRPs).

Thinking about applying the score in other institutions, it was observed that the use of 11 criteria could be too expensive to carry out manually. Its application would be faster if carried out automatically by a computerized system. If the use of the computerized system is not possible, we could eliminate some less important criteria by making the appropriate adjustment to the sum of points for applying the score.

Among the criteria presented in this study, we could suggest the removal of 4 criteria depending on the maturity of the service where it would be applied: The first would be the criterion related to the patient's age, which does not necessarily reflect the severity of the patient. The second criterion would be the use of high alert medications. This criterion can be critical when we think about the severity of the error associated with this type of medication, but a well-trained nursing team can mitigate most of these errors. The third and fourth criteria would be the use of non-standardized medications and tracer medications, both of which depend on how the institution handles these demands. In the context in which we have the suppression of the four suggested criteria, the scores for high, moderate and low risk could be reduced to greater than or equal to 10, between 5 and 8 and less than 5, respectively.

Finally, the overall score could also be adapted to the reality of the application site, by eliminating a smaller number of criteria or even other criteria not mentioned.

We must remember that this study did not extend to the validation phase of the proposed score, being only a pilot for prioritization in the hospital in question. Therefore, careful validation must be carried out regarding the time used to apply the score against the time that would be used to evaluate patients. Another point to evaluate is the team's experience in evaluating prescriptions. An experienced team takes less time to evaluate more complex patients compared to a team with little experience.

Therefore, the strategy of developing a risk score targeted to the needs of a sector acts to improve the quality and functionality of care, which are often limited by the low number of professionals. In this way, high-risk patients can receive more intensive interventions with the aim of reducing negative outcomes, increasing safety and improving the cost-effectiveness of therapy.

## CONCLUSION

It is expected that the score developed will be an efficient instrument for detecting and prioritizing patients at greater risk of developing drug-related problems (DRPs), enabling a greater contribution to care in relation to the therapy of the pediatric population treated in a public hospital in the area, South of São Paulo. However, it is necessary to carry out another study to apply and evaluate the effectiveness of the proposed score.

## REFERENCES

1. Martinbiancho JK, Zuckermann J, Mahmud SDP, *et al.* Development of risk score to hospitalized patients for clinical pharmacy rationalization in a high complexity hospital. *Latin American Journal of Pharmacy.* 2011;30: 1342-47.
2. Brasil. Resolução nº 585, de 29 de agosto de 2013. Regulamenta as atribuições clínicas do farmacêutico e dá outras providências. *Diário Oficial da União, Brasília, DF, n.186, p. 186- 188, 25 set. 2013, Seção 1.*
3. Conselho federal de farmácia (CFF). Serviços farmacêuticos diretamente destinados ao paciente, à família e à comunidade: contextualização e arcabouço conceitual: Acompanhamento farmacoterapêutico; p.87 [Internet]. 2017 [Citado 04 jan 2024]. Disponível em: [https://www.cff.org.br/userfiles/Profar\\_Arcabouco\\_TELA\\_FINAL.pdf](https://www.cff.org.br/userfiles/Profar_Arcabouco_TELA_FINAL.pdf).
4. Pernassi MGS. Desenvolvimento e validação de escore (BRAPP) para priorização de pacientes no acompanhamento farmacoterapêutico do medicamento clínico em CTI pediátrico [Internet]. Ribeirão Preto; 2017 [citado 20 dez 2023]. Disponível em: <https://pesquisa.bvsalud.org/portal/resource/pt/ses-35135>.
5. Santos L, Torriani MS, Barros E. Medicamentos na Prática da Farmácia Clínica. 1. ed. Porto Alegre: Editora Artmed;2013. Capítulo 7, Farmácia Clínica; p. 83-85.
6. Audurier Y, Roubille C, Manna F, Zerkowski L, Faucanie M, Macioce V, Castet-Nicolas A, Jalabert A, Villiet M, Fesler P, Lohan-Descamps L, Breuker C. Development and validation of a score to assess risk of medication errors detected during medication reconciliation process at admission in internal medicine unit: SCOREM study. *The international journal of clinical practice [Internet].* 2021 [citado 28 dez 2023];75(2):e13663: DOI 10.1111/ijcp.13663. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/32770845/>.
7. Alshakrah MA, Steinke DT, Lewis PJ. Patient prioritization for pharmaceutical care in hospital: A systematic review of assessment tools. *Res Social Adm Pharm.* 2019 Jun;15(6):767-779. doi: 10.1016/j.sapharm.2018.09.009. Epub 2018 Sep 20. Erratum in: *Res Social Adm Pharm.* 2020 Jul;16(7):993. PMID: 30268841.
8. Xavier MM. Perfil de segurança das prescrições de antibióticos de uso restrito numa Unidade de Terapia Intensiva Pediátrica [Internet]. Bahia: Faculdade de Farmácia da Universidade de Coimbra; 2015 [citado 28 dez 2023]. 124 p. Disponível em: [https://estudogeral.uc.pt/bitstream/10316/30999/1/Milena\\_MFA.pdf](https://estudogeral.uc.pt/bitstream/10316/30999/1/Milena_MFA.pdf).
9. Magalhães TC, Ferrari CKB, David FL. Aspectos críticos da prescrição de medicamentos em pediatria. *ev. [Internet].* 21º de junho de 2013 [citado 05 jan 2024];13(1):5-18. Disponível em: <https://periodicos.unoesc.edu.br/evidencia/article/view/2755>.
10. Araújo MM, Gomes JL, Rodrigues RNV, Cruz LKLP. Perfil do uso de sedoanalgesia em crianças sob ventilação mecânica em unidade de terapia intensiva. *Resid Pediatr.* 2019;9(3):246-251 DOI: 10.25060/residpediatr-2019.v9n3-09.
11. Garcia PCR, Tonial CT, Piva JP. Septic shock in pediatrics: the state-of-the-art. *J Pediatr (Rio J) [Internet].* 2020Mar; 96:87-98. Disponível em: <https://doi.org/10.1016/j.jped.2019.10.007>.
12. Silva LT, Loze PM, Modesto ACF, Lopes FM. Avaliação de eventos adversos a medicamentos em pacientes pediátricos hospitalizados. *Rev. Eletr. Farm. [Internet].* 18º de setembro de 2017 [citado 10 jan 2024];14(2). Disponível em: <https://revistas.ufg.br/REF/article/view/45912>.
13. Falconer N, Nand S, Liow D, Jackson A, Seddon M. Development of an electronic patient prioritization tool for clinical pharmacist interventions. *Am J Health Syst Pharm.* 2014 Feb 15;71(4):311-20. doi: 10.2146/ajhp130247. PMID: 24481156.
14. Carlson MK, Phelps PK. Use of an electronic clinical scoring system to prioritize patients' medication-monitoring needs. *Am J Health Syst Pharm.* 2015 Dec 1;72(23):2032, 2034, 2038. doi: 10.2146/ajhp140827. PMID: 26581928.
15. Zhou L, Rupa AP. Categorization and association analysis of risk factors for adverse drug events. *Eur J Clin Pharmacol.* 2018 Apr;74(4):389-404. doi: 10.1007/s00228-017-2373-5. Epub 2017 Dec 8. PMID: 29222712.