



Interrater reliability of a tool to assess omission of prescription and inappropriate prescriptions in paediatrics

Aurore Berthe-Aucejo^{1,2} · N. P. K. Khan Nguyen¹ · François Angoulvant^{2,3} · Rym Boulkedid^{2,4} · Xavier Bellettre⁵ · Thomas Weil¹ · Corinne Alberti^{2,4} · Olivier Bourdon^{1,6,7,8} · Sonia Prot-Labarthé^{1,2,6}

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Abstract

Background Potentially inappropriate medication (PIM) and potential prescription omission (PPO) are common issues in pharmacotherapy in vulnerable populations. A first tool to assess PIM's and PPO's targeting pediatric populations: POPI «Pediatrics Omission of Prescriptions and Inappropriate Prescriptions» was created in 2014. **Objective** This study aimed to evaluate inter-rater reliability between healthcare professionals who apply POPI. Setting: Mother and child emergency ward of a university hospital. **Method** Twenty cases with or without PIM or PPO were identified in a previous retrospective PIM-PPO prevalence study on 15,973 patients. One doctor and one pharmacist, who participated in the creation of POPI tool, identified PIM and PPO (“gold standard response”). These cases were reviewed independently by eleven clinicians (generalists, pediatricians, pharmacists, residents), with no previous experience of this tool. Interrater agreement was calculated by using the Kappa agreement test. Main outcome measure: Inter-clinician agreement. **Results** A high level of agreement of PIM and PPO detection was recorded (PIM: median = 0.80; PPO: median = 0.71). **Conclusion** POPI demonstrated a good interrater reliability. This validation by many clinicians proves that POPI is a reliable tool. Other multicenter and prospective studies should be conducted to evaluate economical and clinical impacts of POPI.

Keywords France · Inappropriate prescription · Inter-rater reliability · Pharmacist · Physician

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✉ Aurore Berthe-Aucejo
aurore.berthe84@gmail.com

- ¹ Department of Pharmacy, Robert-Debré Hospital AP-HP, Paris, France
- ² U1123, INSERM ECEVE, Paris, France
- ³ Department of Pediatric Emergency, Necker-Enfants Malades Hospital AP-HP, Paris Descartes University, Paris, France
- ⁴ Clinical Epidemiology Unit, Robert-Debré Hospital AP-HP, Paris, France
- ⁵ Emergency Unit, Robert-Debré Hospital AP-HP, Paris, France
- ⁶ Groupe Pédiatrie de la Société Française de Pharmacie Clinique, Paris, France
- ⁷ Clinical Pharmacy, Paris Descartes University, Sorbonne Paris Cité, Paris, France
- ⁸ Laboratoire Educations et Pratiques de Santé, Paris XIII University, Bobigny, France

Impacts on practice

- The scoring of potentially inappropriate medications and prescribing omissions with the POPI tool shows a high level of agreement.
- The usefulness for measuring impact on outcomes of the POPI-tool needs to be further evaluated.

Introduction

Children are vulnerable population concerning medication errors [1]. Safety data on children are very limited, as most drug studies are performed on adults [2]. The risk of adverse events is more significant in children due to the lack of information on prescription drug labelling [3]. Studies showed that adverse drug events are not only related to medication errors, such as inappropriate prescribing [4]. The term “inappropriate prescribing” (IP), first coined by Dr. Mark Beer in 1991, is nowadays well known [5]. It encompasses

both (potentially) inappropriate medication (PIM) as well as (potential) prescription omissions (PPO) [6]. PIM is defined as a prescription which has clinical indication, with the possibility of adverse drug events or treatment risks potentially outweighing benefits. PPO, or the under-use of appropriate medication, is the absence or insufficient prescription of a drug that is beneficial to the patient [7]. Inappropriate prescribing is a significant challenge to clinicians because of its link to adverse events [8]. As reported by World Health Organisation (WHO) already in 2009, 50% of medicines are inappropriately prescribed [9]. Many studies reported high rates of off-label (9–78.7%) and unlicensed (0.3–35%) drug use in different pediatric patient settings [10]. According to our studies, of which the preliminary results are now available, the PIM rate and PPO rate in pediatrics (0–18 years) are respectively 3.3% and 2.6% at the emergency ward and 26.4% and 13.2% at the community pharmacy.

Various tools have been created to detect PIM and PPO in geriatric populations such as: Beers' criteria, MAI (Medication Appropriate Index), STOPP/START (Screening Tool of Older Person's Prescriptions/Screening Tool to Alert doctor to Right Treatment) [5, 11, 12]. STOPP/START is the newest tool and it has had a broad impact. Its performance in the prevention of adverse drug events has been demonstrated. It prevented 35% of adverse effects resulting from prescribed medications [13]. Furthermore, these criteria are logically constructed and have demonstrated to have ease and speed of use [14].

The first pediatric tool, POPI: «Pediatrics: Omission of Prescriptions and Inappropriate Prescriptions» was developed to improve drug use and decrease adverse events in a pediatric population. Diseases of interest difference between paediatric and geriatric populations. For example, respiratory and digestive diseases are typical in paediatric and cardiovascular and nervous central diseases are more common in geriatric population [15, 16]. The POPI tool allows the detection of inappropriate prescriptions and omissions of prescription for some of the most frequent pediatric diseases [17, 18]. It has 101 criteria (76 PIMs, 25 PPOs). A literature review was done to obtain criteria. Criteria were categorized according to the main physiological systems (gastroenterology, respiratory infections, pain, neurology, dermatology and miscellaneous) and validated by 2-round-Delphi consensus technique. For example, use of domperidone in case of vomiting is a PIM; omission of oral rehydration solution in diarrhoea is a PPO. POPI is designed as a tool for healthcare practitioners (physicians, pharmacists) in their daily practice.

Because the tool can be used in a hospital or ambulatory setting, it is necessary to have a substantial rate of agreement amongst the scores of different healthcare professionals [19]. In geriatrics, STOPP/START's tool received an excellent

rate of agreement amongst six European centers [19] and a similar rate of agreement is also found amongst hospital pharmacists and community pharmacists [20].

Aim of the study

Our main objective was to evaluate inter-rater reliability of POPI criteria between different healthcare professionals (physicians and pharmacists).

Ethics approval

This project was approved by the Robert-Debré research ethics committee (no. 2015/218) which approved a waiver of the need for consent for raters. Informed consent was obtained from all individual raters included in the study.

Methods

Study procedure

Twenty clinical cases were selected from patient's cases. Datasets were drawn from a cohort of 15,973 patients aged < 18 years old who consulted the emergency ward (article in submission). The choice of cases was determined by the prevalence of children's diseases and corresponded to physiological systems of POPI. Each file presented patient data (age, sex, weight), and drugs prescribed (International Non-proprietary Names (INN), posology, frequency and duration of treatment). Current and past diagnoses and clinical exams were taken into account.

From the 20 cases presented, 58 prescriptions lines had to be rated.

Thirteen raters participated in the study and two groups were formed. The first group, named "Rater A", was composed of a pharmacist and a pediatrician who participated in POPI's development. Their analysis and discussion of these cases created the "gold standard response". These results were compared to the ratings of each professionals, referred to as the second group (raters 1–11). This group was composed of French professionals with no prior experience of POPI. Professionals were selected according to the following criteria: experience/seniority, speciality, exercise environment (hospital, community). Selected raters were pediatricians (3 in hospital and 2 in community settings), two general practitioners, one medical resident and three pharmacists (1 in hospital setting, 1 in community setting, 1 residency). Their role in the study and the study's evaluation procedure were explained to them by telephone. Description of cases (characteristic's patient, prescription

...), instructions to complete the survey (SurveyMonkey®), the POPI tool and the hyperlink were submitted to the raters by email [21].

For each case, raters had to select POPI criteria detected (PIM and/or PPO). A case could present none, one or more PIM/PPO. A screen copy is presented in Fig. 1.

Raters could write comments for each prescription. Raters noted the time needed to analyze the 20 prescriptions.

Outcome measures

The main outcome measure was inter-clinician agreement in the use of the POPI tool, and the second outcome measure was the median time needed for the use of the tool.

Statistical analysis

Data analyses was performed using SAS Version 9.3 (SAS Institute, Cary, NC, USA software). Data are presented as median and interquartile range (25th–75th percentiles) for continuous variables and numbers (percentages) for categorical variables.

Kappa statistics were used to evaluate the level of agreement between raters (inter-rater reliability, Rater A vs. 2nd

Group). Degree of reliability was determined as poor if $\kappa \leq 0.2$; as fair if $0.21 \leq \kappa \leq 0.4$; as moderate if $0.41 \leq \kappa \leq 0.6$; as substantial if $0.61 \leq \kappa \leq 0.8$ and as good if $\kappa \geq 0.81$ [22].

Results

Characteristics of cases

Among the 58 prescriptions assessed, 19 were rated as PIM by rater A with POPI and concerned 15 cases out of 20. Among the 20 cases assessed, only 10 were rated as having PPO by rater A and this concerned 9 cases (2 PPO were detected in a single case).

Characteristics of the patients and their diseases were presented in Table 1. Medications with PIMs and PPOs more frequently affected were amoxicillin, salbutamol and oxomemazine.

Characteristics of raters

The characteristics of the raters are described on Table 2. Median age was 39 years (first quartile-third quartile: 32.0–48.5). Women represented 46% of professionals.

Survey d'utilisation de l'outil POPI (Pédiatrique: Omissions & Prescriptions Inappropriées)

Critères détectés par POPI

1/3 33%

Ce questionnaire vous permet de renseigner le(s) prescription(s) inappropriée(s) ou omission(s) que vous avez détectée(s) grâce à l'outil POPI.
Chaque ordonnance peut contenir un critère, deux critères, plusieurs critères ou aucun...
Attention, la première ligne doit obligatoirement être remplie avant de passer au cas suivant.
Vous avez également la possibilité de laisser un commentaire pour chaque cas (facultatif).

A vous de jouer !

* 1. Cas 1 - Anne

Problème détecté	Inappropriée	Omission
Problème détecté n°1		
Problème détecté n°2	AI-1. Prescription en 1e intention de deux antipyrétiques...	
Problème détecté n°3	AI-2. Prescription en 1e intention d'un médicament autre... AI-3. Paracétamol par voie rectale en 1e intention. AI-4. Association de deux AINS. AI-5. Ibuprofène en solution buvable en plus de 3 prises...	
Commentaire	AI-6. Opiacés dans le traitement de la crise migraineuse BI-1. Nitrofurantoïne en prophylaxie BI-2. Nitrofurantoïne en curatif avant 6 ans ou si autre... BI-3. Antibio prophylaxie après un premier épisode... BI-4. Antibio prophylaxie en cas de bactériurie... CI-1. Apport de fluor avant 6 mois. DI-1. Répulsifs cutanés avant 6 mois... DI-2. Essence de citronnelle (huile essentielle)... DI-3. Les bracelets anti-insectes pour se protéger... DI-4. Les appareils sonores à ultrasons... EI-1. Métoclopramide. EI-2. Dompéridone. EI-3. Antisécrétoire gastrique pour un reflux simple...	

* 1. Cas 1

Problème détecté	Inappropriée	Omission
Problème détecté	EI-2. Dompéridone.	Aucun
Problème détecté		
Problème détecté		

Commentaire (pas obligatoire)

Fig. 1 Screen copy of survey completed by raters 1–11

Table 1 Characteristics of cases (A raters reference)

Characteristics	N=20
Age (years) [Median (min; max)]	4 (1.6–8.0)
Sex [% female]	35%
Number of prescribed drugs [Median (q1; q3)]	3 (2; 3)
Total number of lines of prescriptions	58
Number of prescription per case [Median (min; max)]	3 (2; 6)
Total number of lines of inappropriate prescriptions detected by Raters A per total number of lines of prescription	19/58
Total number of omission of prescriptions detected by Raters A per total number of omission detection opportunities	10/21*
Diseases requiring emergency treatment	
Respiratory disorders	65% (N=13)
Neuropsychiatric disorders	10% (N=2)
Dermatological disorders	10% (N=2)
Digestive disorders	10% (N=2)
Others (migraine)	5% (N=1)
Proportion of chronic diseases among cases presented	25% (N=5)

*For 8 cases, 1 PPO was detected per case, and for 1 case 2 PPOs were detected. Therefore, there was a total number of 21 omission detection opportunities

Median numbers of years of general experience and in pediatric respectively were 16.0 (6–22.5) and 9.0 (3–22.5) in pediatrics. All of them gave their written consent to participate.

Interrater reliability

Statuses of agreement are indicated in Tables 3 and 4. The practitioner within greatest agreement concerning POPI concerning PPO and PIM is a community pediatrician

with 16 years of experience of which 15 are in pediatrics ($\kappa = 0.96$ for PIM, $\kappa = 1$ for PPO). The pharmacist resident obtained the lowest agreement concerning PIM ($\kappa = 0.61$). The least agreement rate for PPO is observed in a general practitioner with 25 years of experience in pediatrics and in a hospital pharmacist with 20 years of experience, one of which was in pediatrics.

Items concerning tixocortol pivalate and H1-antihistamine were less commonly detected by raters. Issues concerning antihistaminic antitussives or metoclopramide were detected by all raters. “Doses in mg for drinkable (solutions of) amoxicillin or josamycin” is the most frequent of PPO not detected by medical raters.

With POPI, other potential omissions of prescription are also detected by 10/11 of the raters (for example: prescription of vitamin D, the offer of a pertussis booster or an inhalation chamber adapted to the age). A third of the raters considered the prescription of tixocortol pivalate to be inappropriate but they did not find corresponding items in the POPI tool. Some criteria were expressed only with pharmacology class and not with INN; for example: “corticosteroid therapy in case of nasopharyngitis” (Item II5-Annexe 1) or “H1-antihistaminine in case the asthma” (Item JI1-Annexe 1). Other criteria which specified the trade name or INN such as oxomemazine, ethanolamine tenoate, metoclopramide etc. received 100% rate of agreement amongst raters.

Duration of analysis

Median length of time for analyzing each case was 2 min 45 s (q1; q3: 2 min 25 s – 3 min 25 s). Total median time of analysis was 55 min for raters and 40 min for rater A familiar with POPI.

Table 2 Characteristics of raters

Medical profession	Number of rater	State	Situation	Total experience (years)	Experience in pediatrics (years)
Pediatrician	1	Seine et Marne (77)	Community	26	25
Pediatrician	2	Yvelines (78)	Hospital	20	20
Pediatrician	3	Paris (75)	Community	16	15
Pediatrician	4	Paris (75)	Hospital	7	5
Pediatrician	5	Paris (75)	Hospital	5	5
General physician	6	Val-d'Oise (95)	Community	31	31
General physician	7	Hauts de Seine (92)	Community	25	25
Medicine resident	8	Paris (75)	Hospital	1	1
Pharmacist	9	Paris (75)	Community	9	9
Pharmacist	10	Loire-Atlantique (44)	Hospital	20	1
Pharmacy resident	11	Paris (75)	Hospital	2	1

Table 3 Interrater reliability of POPI criteria between rater A and rater 1–11: PIM

Rater combination	Ppos % (n/N)	Pneg % (n/N)	Kappa [95% CI]
<i>Physicians</i>			
Rater A* Rater 3	98.3 (57/58)	1.7 (1/58)	0.96 [0.88–1]
Rater A* Rater 2	94.8(55/58)	5.2(3/58)	0.88 [0.74–1]
Rater A* Rater 8	94.8 (55/58)	5.2 (3/58)	0.88 [0.74–1]
Rater A* Rater 4	94.8 (55/58)	5.2 (3/58)	0.88 [0.74–1]
Rater A* Rater 5	93.1 (54/58)	6.9 (4/58)	0.83 [0.68–0.99]
Rater A* Rater 1	91.4 (53/58)	8.6 (5/58)	0.80 [0.63–0.97]
Rater A* Rater 6	91.4 (53/58)	8.6 (5/58)	0.79 [0.62–0.96]
Rater A* Rater 7	89.7 (52/58)	10.3 (6/58)	0.75 [0.57–0.94]
Median (interquartile ranks)	94.0	6.0	0.86 (0.79–0.88)
<i>Pharmacists</i>			
Rater A * Rater 10	91.4 (53/58)	8.6 (5/58)	0.79 [0.62–0.96]
Rater A * Rater 9	86.2 (50/58)	13.8 (8/58)	0.65 [0.44–0.86]
Rater A * Rater 11	84.5 (49/58)	15.5 (9/58)	0.61 [0.39–0.83]
Median (interquartile ranks)	86.2	13.8	0.66 (0.63–0.72)
Total median (interquartile ranks)	91.4	8.6	0.80 (0.77–0.88)

Rater A: Standard defined by physician and pharmacist who participated in POPI's tool development

Ppos proportion of positive agreement, *Pneg* proportion of negative agreement, *n* number of positive (or negative) agreement, *N* total number of prescription or total opportunities for omissions, *CI* confidence interval

Table 4 Interrater reliability of POPI criteria between rater A and rater 1–11: PPO

Rater combination	Ppos % (n/N)	Pneg % (n/N)	Kappa [95% CI]
<i>Physicians</i>			
Rater A* Rater 3	100 (21/21)	0	1 [0.42–1]
Rater A* Rater 4	95.2 (20/21)	4.8 (1/21)	0.90 [0.72–1]
Rater A* Rater 5	90.5 (19/21)	9.5 (2/21)	0.81 [0.56–1]
Rater A* Rater 6	85.7 (18/21)	14.3 (3/21)	0.71 [0.42–1]
Rater A* Rater 8	81.0 (17/21)	19.0 (4/21)	0.61 [0.3–0.93]
Rater A* Rater 2	76.2 (16/21)	23.8 (5/21)	0.51 [0.19–0.84]
Rater A* Rater 1	76.2 (16/21)	23.8 (5/21)	0.51 [0.19–0.84]
Rater A* Rater 7	71.4 (15/21)	28.6 (6/21)	0.41 [0.09–0.73]
Median (interquartile ranks)	83.4	16.6	0.66 (0.51–0.86)
<i>Pharmacists</i>			
Rater A* Rater 9	90.5 (19/21)	9.5 (2/21)	1 [1]
Rater A* Rater 11	71.4 (15/21)	28.6 (6/21)	0.81 [0.56–1]
Rater A* Rater 10	90.5 (19/21)	9.5 (2/21)	0.41 [0.09–0.73]
Median (interquartile ranks)	90.5	9.5	0.81 (0.61–0.91)
Total median (interquartile ranks)	85.7	14.3	0.71 (0.51–0.90)

Rater A: Standard defined by physician and pharmacist who participated in POPI's tool development

Ppos proportion of positive agreement, *Pneg* proportion of negative agreement, *n* number of positive (or negative) agreement, *N* total number of prescription or total opportunities for omissions, *CI* confidence interval

Discussion

This study is the first to estimate the interrater reliability of the POPI tool. The raters are healthcare professionals

who will be future users of POPI. A good inter-rater rate of agreement was observed amongst the professionals $\kappa = 0.80$ (0.77–0.88). Our results are similar to tools of detection for geriatrics [12, 19]. There is a higher risk at an old age of being given an inappropriate prescription or

an omission of prescription [23, 24]. Our results are similar to those observed in geriatrics where the concordance of detection of one PIM was higher than the detection of the omissions [14, 19]. As with STOPP/START, the number of PIM criteria is higher than those of omission. The inappropriate prescriptions are “present”, thus more easily detected than the omissions. Furthermore, only three pharmacists participated in our study, but their small number was compensated by their varied professional experiences (hospital/community, resident, pharmacist, physician).

POPI obtained an excellent rate of agreement between the doctors, and its result was also good amongst pharmacists for inappropriate prescription (κ median of 0.86 and 0.66, respectively). In the future, we want to link the POPI tool with prescription management systems which would permit an alert in case of PIM whether the drug is prescribed with the INN or the trade name.

The detection of the omission of prescription obtained a good agreement between the professionals [$\kappa = 0.71$ (0.51–0.90)]. The disagreements concerned the criterion “Doses in mg for drinkable (solutions of) amoxicillin or josamycin”. This item concerned 33% of the PPOs detected in the prescriptions by the second group. The highest level of detection of this item was amongst the pharmacists. Due to the misuse of the spoon measurement to administer oral suspension, pharmacists have the important task of detecting omissions of prescriptions in order to intervene if necessary [25]. Other PPOs are also noted by raters concerning long-term medication as vitamins, vaccinations. Indeed, these treatments are not prescribed in the emergency ward but by community practitioners. The use of the POPI tool could raise awareness among practitioner to this issue.

In geriatrics, concordance between professionals using the STOPP tool was excellent κ : 0.75–0.95 [12, 14, 19]. However, the number of the participants on the inter-judge rate of agreement could have an impact. The first STOPP/START inter-rater study was performed by two geriatricians ($k = 0.75$) [12]. The second multicentric study obtained an excellent rate of agreement ($k = 0.93$) amongst 9 hospital geriatricians [19]. Thirteen healthcare professionals belonging to different professions participated in our study. In the geriatric study, only specialists in geriatrics were questioned and the study showed excellent agreement rates, contrary to our study in which agreement rates were good. However, a good concordance for our tool between professionals remains acceptable. The user panel (work environment, years of practice etc.) strengthens the reliability of the POPI tool.

Less than a third are not fully satisfied by the time of analysis of 20 datasets. This can be explained by the successive analyses of the patient cases. Lap time includes reading the clinical case, followed by the analysis and the evaluation of prescribed medicine. The time per case is

here over-estimated compared to POPI used for one’s own patients. Becoming accustomed to using the tool will also decrease time spent detecting IP and use will become more automatic. The use of a paper version of the tool can be a delaying factor in the detection by users. A software or phone application version could increase the ease of use. Professionals could use the tool anywhere. Some study have shown global satisfaction about use of medical phone application [26, 27]. Phone application could permit to have directly accessed PPO or PIM according to diseases or medical diagnosis and could promote the speed of detection.

Our study has some limitations. All diseases of POPI could not be analyzed. It was not possible to represent the diversity of items presented in POPI in twenty files. The retrospective evaluation of the clinical cases is a bias in this analysis. POPI must be used in real practice condition i.e. in front of patients. However, it is the only way to use same patients’ cases to evaluate reliability amongst physicians and pharmacists. The detection of IP could be favored by a prospective use of POPI. In some hospitals, analysis of prescriptions is absent or partial. In these cases, the tool is a real advantage for doctors, and also for pharmacists, allowing them to target certain points of their analysis.

Conclusion

Our study showed a good rate of agreement for the detection of PIM and PPO amongst various healthcare professionals with the POPI tool. These results confirmed that POPI can be used more widely, and a prospective, multicenter study can be initiated to evaluate the impact of this tool for the detection of PIM and PPO in pediatrics.

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