

Original research

Prescribing, dispensing and administration indicators to describe rational use of oral dosage forms of medicines given to children

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Abstract

Background Owing to lack of indicators, researchers are compelled to use non-specific indicators to assess rational use of medicines in children. Thus, paediatric-specific issues are poorly described. This study aims to develop a set of indicators to describe rational use of oral dosage forms of medicines given to children.

Methods A modified RAND/UCLA Appropriateness Method was used. A comprehensive draft list of 40 indicators was compiled, based on the results of a literature review. Twelve experts rated these indicators in two rounds, using a nine-point Likert scale, first in an online survey, for clarity, necessity and scientific merit, and secondly in a face-to-face meeting, for necessity, feasibility and predictive value. An overall panel median score of ≥ 7 and agreement within the experts were used in indicators. The indicators were ranked independently by the research team and a final list of indicators was prepared. These indicators were pilot-tested for acceptability and interrater reliability.

Results Nine prescribing indicators, such as weight, appropriate dose and age-appropriate dosage form; five dispensing indicators, such as adequacy of labelling and inappropriate manipulation by pharmacists; and five administration indicators, such as inappropriate manipulation by parents and full completion of dose, were finalized in the second round.

Conclusion This novel approach has provided a set of indicators to describe the use of oral dosage forms of medicines given to children, which can be used by researchers as a supplement to the World Health Organization's drug use indicators when investigating rational use of medicines in children.

Keywords: children, indicators, medicines, oral dosage forms, rational use

Background

The World Health Organization (WHO) defines rational use of medicine (RUM) as patients receiving "medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community".¹ RUM reduces risks, improve benefits, saves money, prevents wastage of resources and helps equity.² It is not limited to selecting the right medicine, but it also involves selecting the right dose, dosage form, route of administration, dosing interval and duration of treatment.³ Appropriate prescribing, dispensing and administration practices are core components in ensuring RUM.⁴ WHO encourages its Member States to establish programmes to promote RUM.⁵

The first step in promoting any strategy is to assess the current situation. Difficulties in measuring RUM quantitatively

prompted WHO to develop core and complementary drug use indicators to measure use of medicines.⁶ Many researchers worldwide have used the WHO drug use indicators to describe RUM.⁷ These drug use indicators are "time-tested" over three decades and have been found by researchers to be useful, user-friendly, reproducible, valid, reliable and applicable to multiple settings, and can be used with limited data and by individuals who are not specifically trained.⁸ One drawback of the WHO drug use indicators is that their generic nature means they were designed neither to measure RUM in a particular age group or special population, nor to describe the potential challenges for RUM in those groups. This is a major limitation in employing the WHO drug use indicators alone to measure RUM in a paediatric age group. RUM in children has many distinctive challenges, not least because children are not just small adults.⁹ It is not limited to selecting the suitable medicine

for the child but also extends to selecting the appropriate dose and suitable dosage form. In addition, administering medicines to children poses special challenges. The generic WHO drug use indicators cannot identify the unique challenges in paediatric pharmacotherapy, as they lack the ability to assess the issues related to dose, dosage form, administration, palatability and acceptability: all of these are key obstacles for RUM in children. While paediatric studies using the WHO indicators have described generic issues related to medicine use in children, they have failed to identify the specific challenges for RUM in this population.¹⁰ These challenges are most notable for oral dosage forms of medicines, owing to the overall lack of “child size” medicines and suitable paediatric dosage forms.¹¹

Medicine use is rational (appropriate, proper, correct) when patients receive the appropriate medicines, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost both to them and to the community. Irrational (inappropriate, improper, incorrect) use of medicines is when one or more of these conditions is not met. To be effective in children, medicines must be available in formulations that allow doses to be easily adjusted to reflect a child’s size, stage of development and condition. The lack of availability of medicines that fit these criteria for children is a major reason for irrational practices. Examples include splitting tablets or opening capsules and estimating the dose to be administered.

To the best of the authors’ knowledge, there are no indicators for RUM in children in the world literature. Hence, the objective of this study was to develop a set of indicators to measure RUM of oral dosage forms of medicines given to children.

Methods

The RAND/UCLA Appropriateness Method¹² was employed to develop the indicators. This method depends on finding the most appropriate indicators for conditions that cannot be measured by numerical scale. Unlike the Delphi method, which involves multiple questionnaire-driven rounds to obtain the opinion, the RAND/UCLA Appropriateness Method involves a round of individual rating, followed by a round of face-to-face discussion with experts. It is the only systematic method of combining expert opinion and evidence,¹³ as well as having inter-panellist discussion. A literature review is done and sent to the panellists so they can base their opinion on scientific evidence.¹⁴ This method has also been shown to have predictive, face and content validities, and a high level of reproducibility.¹⁵ It also includes a rating of the feasibility of collecting data, a key requirement in the application of indicators. The design comprises two key components: (i) identification of indicators; and (ii) a two-round consensus process.

Identification of indicators: literature review

As described in best practice documents for the RAND/UCLA Appropriateness Method,¹² a literature review was conducted to locate articles on use of oral dosage forms of medicines in children. The key research questions used as the basis for developing the search strategy for the literature review were: (i) what are the irrational ways of prescribing, dispensing and administering oral dosage forms of medicines to children?;

(ii) what is the level, nature and quality of the research evidence for drug manipulations at the point of prescribing, dispensing and administration of oral dosage forms?; (iii) what are the effects of prescribing adult oral dosage forms to children?; and (iv) what are the effects of manipulating oral dosage forms, using methods employed at the point of drug dispensing and administration, on dose accuracy, palatability, bioavailability and stability? In the context of this project, “irrational” practices were defined as manipulation of oral dosage forms of medicines for children, such that they are inappropriately, improperly or incorrectly prescribed, dispensed or administered. The word “irrational” therefore does not reflect on an individual’s action but is used as a general term to contrast with “rational” use of medicines.

All type of articles published in English between January 1985 and January 2016 on children aged ≤ 12 years were eligible. Based on the research questions, the search terms, including their synonyms and spelling variants, were: “child”, “infant”, “paediatrics”, “paediatric”, “baby”, “pharmacist”, “nurse”, “doctor”, “health-care professional”, “parent”, “guardian”, “drug formulation”, “drug manipulation”, “splitting”, “opening”, “dosage form”, “crushing and dispersing oral solid dosage forms”, “oral drug”, “tablet”, “capsule”, “syrup”, “solution”, “suspension”, “dispensing”, “prescribing”, “administration”, “organoleptic properties”, “swallowing”, “refuse acceptability”, “taste”, “palatability”, “flavour”; “administration devices”, “droppers”, “oral/enteral syringes”, “measuring cups”, “measuring spoons”, “household spoons”, “irrational use”, “patient compliance”, “treatment refusal”, “stability”, “rational use”, “quality”, “bioavailability”, “safety”, “indicators” and “side-effect”. Multiple alternative search terms joined by the Boolean operators “OR” and “AND” were built up to search for articles in PubMed and Scopus. “OR” exploded the search and marked it highly sensitive. Using “AND” at the end of the process narrowed the search.

Titles and abstracts were screened initially to identify all English-language guidelines, reports and articles on oral dosage forms of any drug in children. Duplicate studies were identified and deleted. When studies met the inclusion criteria or when a decision to include a study could not be made based solely on review of the title or abstract, full-text copies were obtained. Selected full-text articles were carefully reviewed to identify the articles that were aimed at answering the key questions. As per the RAND/UCLA-recommended good practices,¹² the first author extracted all relevant information from the articles and summarized the literature search with links to full articles (or the print version of full articles) for the expert panel.

From these data, the first draft of indicators to measure rational use of oral dosage forms of medicines in children was developed by the authors, after several rounds of discussion. The indicators were grouped into three categories, namely prescribing, dispensing and administration.

Two-round consensus process

A multidisciplinary panel of 12 experts, in the fields of clinical pharmacology, pharmacology, paediatrics, pharmacy, nursing and community medicine were selected. The local experts ($n = 10$) were nominated by relevant postgraduate institutes and societies; the international experts ($n = 2$) were selected by writing to experts in the field.

Round one: online survey

Rating forms using a nine-point Likert scale were prepared to assess the clarity, necessity and scientific merit (see Table 1) of each indicator in the first draft. These were converted to an online form using Survey Monkey.¹⁶ The following were sent to the panellists: (i) a rating form for the list of indicators; (ii) instructions for rating; (iii) a summary of the literature review; (iv) a detailed summary of articles with citations; and (v) a covering letter that explained the purpose, process and outcomes of the study.

Round two: face-to-face meeting

Before the meeting, panellists were given a personalized form giving the panellist's own rating and the rating by the panel as a group. During the meeting, panellists discussed each indicator in terms of given criteria. After the discussion, panellists independently rated feasibility and predictive value and re-rated necessity on a nine-point Likert scale (see Table 1).

Analysis of criteria

Rates given by the panellists for the five criteria, namely clarity, necessity, scientific merit, predictive value and feasibility, were computed and the median score for each criterion was calculated. When the overall panel median score was ≥ 7 for all criteria, with agreement within the panellists, and when no more than two panel members rated the statement outside a three-point distribution around the median for any of the criteria, the indicators were considered as appropriate. These selected indicators were subjected to further scrutiny by the authors.

Final list of indicators

Similar to the WHO drug use indicators, the authors decided to limit the indicators of each category to fewer than 10. The research team ranked the important indicators independently and the final list of indicators was prepared. Open comments made by the experts were also taken into consideration when the final list was prepared. As per the method adopted, this list of indicators satisfies content validity, predictive value, reproducibility, feasibility, necessity and clarity.

Pretesting of the indicators**Acceptability to users**

To refine the finalized list further, the indicators were also tested for acceptability, defined as whether "the indicator is acceptable to both those being assessed and those undertaking the assessment".¹⁷ Since these indicators will be administered by researchers, prescribers, pharmacists and parents, eight participants were selected from each category.

For the professionals, selection was via nominations from the postgraduate institute/society. The parents were selected with the help of the in-charge medical officer of a child welfare clinic. Participants were given rating forms with the Likert scale of 1–9 and were requested to rate relevant indicators for acceptability (score of 1–3 not accepted; 4–6 uncertain acceptability; and 7–9 acceptable). When participants' scores were analysed, indicators with a median score of less than 7 and indicators with non-agreement (2 members marking 3 points away from the median) were either removed or amended.

Use in health-care settings

In order to apply in health-care settings, the indicators were converted to user-friendly interviewer-administered data-collection instruments, mainly in the form of checklists and data-collection sheets. The data-collection instruments and the measurement of indicators were pretested in a paediatric ward, clinic and outpatient department of a teaching hospital, to determine whether they allow calculation of all the indicators and user-friendliness. Information for prescribing and dispensing indicators were collected from patients' records; for administration, indicators were collected via interviews with parents.

Interrater reliability

Interrater reliability was also assessed during this pilot study. Interrater reliability was defined as the relative consistency of the judgements that are made of the same stimulus by two or more raters.¹⁸ In order to determine interrater reliability, two raters independently reviewed each indicator in the records of children who were given oral dosage forms of medicines in the study setting during the pilot study. Cohen's kappa was calculated to determine the interrater reliability. A kappa value above 0.7 was considered as good agreement.¹⁹

Minor amendments were made to the data-collection instruments and indicators. Since the set of indicators will be unique in identifying different issues in paediatric prescribing, dispensing and administration practice, it was decided to leave them as stand-alone indicators similar to WHO drug use indicators, rather than scoring each indicator and determining a cut-off value.

This concluded assessment of the validity of indicators.

Ethical considerations

Ethical approval was obtained from the Ethics Review Committee, Faculty of Medicine, University of Colombo, Sri Lanka. Parental informed consent and assent from children were obtained.

Table 1. Criteria assessed in rounds 1 and 2 by the expert panel

Criterion	Description	Round
Clarity	This indicator is clear to the reader in the context of the content and language	1. Online survey
Necessity	This indicator will drive the rational use of oral paediatric dosage forms of medicines in children This indicator can detect the current gaps in rational use of oral paediatric dosage forms of medicines in children	1. Online survey and 2. face-to-face meeting
Scientific merit	The evidence supports the indicator This indicator represents the concept being assessed	1. Online survey
Feasibility	Valid, reliable and consistent data are available and collectable for this indicator	2. Face-to-face meeting
Predictive value	Use of this indicator has the capacity for predicting outcomes for rational use of medicine	2. Face-to-face meeting

Results

Identification of indicators: literature review

Literature review

Paediatric clinical pharmacology is a relatively new discipline, and thus there were relatively few reports of problems of oral dosage forms in children. There were no existing indicators in the literature for measurement of RUM in children. There were 1229 publications on the theme of challenges faced by children in RUM, mostly around issues of prescribing, dispensing and administration.

Of the 80 records identified as being relevant to answering the key questions, 66 were journal articles and 14 were guidelines/reports. The full details of the results of the literature

review, as presented to the expert panel, are available on request from the corresponding author. The results, which were grouped into 12 topics, are summarized in Box 1.

Since no existing indicators that could be used as a template were found, the authors developed 14 prescribing, 11 dispensing and 15 administration indicators, based on the results of the literature review. The 40 draft indicators appear in Box 2.

Two-round consensus process

All 12 experts participated in the first-round online survey. Seven of the 12 panellists attended the second-round face-to-face meeting. Of the five panellists who could not attend the face-to-face meeting, two international experts contributed to

Box 1. Summary of results of literature review for developing indicators

1. The need for a prescribing dose that is adequate for the age and weight

Children respond to medicines differently. Pharmacodynamic differences could affect the action and toxicity of medicines, as in warfarin and ciclosporin. Pharmacokinetics influence the efficacy, toxicity and dosing regimens of medicines. Some adverse effects occur only in children and not in adults. Medicines should be tailored to children's age, body weight and physiological conditions.

2. Manipulation of solid oral dosage forms

Owing to non-availability of suitable paediatric dosage forms, and inability to swallow certain dosage forms, health-care providers and parents tend to give the medicine by various methods, such as crushing the tablets, dissolving the tablet in solvents or giving the powder contained inside a capsule.

3. Clinical and pharmacokinetic outcome of manipulation of oral dosage form

Manipulation of oral dosage forms affects the dissolution rate and thereby changes the bioavailability of manipulated dosage forms from the intact dosage form for some drugs. Health-care professionals should be aware of the consequences of manipulating oral dosage forms, especially with drugs that have a narrow therapeutic range.

4. Quality of manipulated dosage forms

Manipulation leads to inaccurate dosing and uneven distribution of drug and excipient in the manipulated segments. There are also quality issues for the stability of the manipulated dosage forms. Sex, age, education and prior experience in tablet splitting do not have a predictive effect on the manipulation.

5. Effect of use of a splitting device

Different devices split tablets in different proportions. The quality of the split tablet varies with the device used.

6. Co-administration with food/drink

The drug is mixed with food or drink to improve adherence to the therapy, but interaction of food or drink with drugs can alter the effect of the drug.

7. Palatability of drugs

The palatability of a drug plays an important role in paediatric oral dosage form. Preference of taste varies with age, sex and disease type.

8. Liquid volumes and dosing devices

The volume of the liquid used must be acceptable to the child, and the dosing device should be able to measure the volume accurately. Dose amounts vary with different devices. Dosing errors are also associated with the type of device used. Inaccurate dosing can result in a potentially serious risk to the health of children.

9. Formulation preferences and issues

Children prefer different types of dosage forms. Uncoated mini-tablets seem to be a very promising alternative to liquid dosage forms and could be used in paediatric drug therapy at an earlier age than previously anticipated.

10. Health-care professionals' knowledge of rational use of oral dosage forms in children

Health-care professionals from different disciplines displayed a variety of perspectives on manipulation and of knowledge about the consequences of medication manipulation.

11. Problems faced by nurses/caregivers when administering oral dosage forms of medicines

Rejection of drugs due to bad taste, size and shape were some of the problems experienced during administration. Lack of appropriate equipment for administering the drugs also caused difficulty during administration.

12. Cost of manipulated dosage forms

Tablet splitting is used as a method of reducing the cost of prescription drugs. Splitting of tablets has usefulness as a cost-reduction strategy, but there are hidden costs arising due to splitting, such as wastage of drug during splitting.

Box 2. Draft set of 40 indicators shared with the expert panel

A. Prescribing indicators

1. % of oral dosage forms (ODFs) of medicines prescribed in a dose that is adequate for the weight of the child
2. % of ODFs of medicines prescribed in a dose that is adequate for the age of the child
3. % fixed solid ODFs of medicines prescribed for children aged 5 years or under
4. % of tablets prescribed for children aged ≤ 5 years
5. % of capsules prescribed for children aged ≤ 5 years
6. % of flexible ODFs (e.g. dispersible tablets) of medicines prescribed for children aged ≤ 5 years
7. % of ODFs prescribed with a written direction of use
8. % of age-appropriate ODFs prescribed for children
9. % of occurrences where the prescribed liquid oral dose volume is not in a multiple strength of 5 mL
10. % of liquid ODFs prescribed as drops
11. % of occurrences where the prescribed liquid oral dose needs an oral syringe to measure the volume
12. % of occurrences where the number of solid ODFs to be taken is five or more at a time for a child aged 12 years or under
13. % of occurrences where the volume of liquid dosage forms to be taken is 10 mL or more at a time for a child aged 12 years or under
14. % of prescribed oral paediatric dosage forms of medicines registered under the national drug regulatory authority

B. Dispensing indicators

1. % of correct doses dispensed as per prescription
2. % of correct dosage forms dispensed as per prescription
3. % of tablets split and dispensed
4. % of tablets/capsules manipulated and powder dispensed as sachet
5. % of liquid ODFs reconstituted as liquid by the pharmacist before dispensing
6. % of ODFs dispensed with correct reconstitution advice by the pharmacist
7. % of ODFs dispensed with manipulation by the pharmacist
8. % of ODFs for which the pharmacist instructed the parent/guardian to manipulate
9. % of ODFs dispensed with written directions/labelling for use
10. % of occurrences where the pharmacist advised the parent/guardian to use an administration device
11. % of occurrences where the pharmacist advised the parent/guardian about the storage conditions

C. Administration indicators

1. % of tablets split and administered
2. % of capsules opened and content administered
3. % of ODFs mixed in water and administered
4. % of ODFs mixed in other liquids (fruit juices/milk, etc.)/vehicles and administered
5. % of ODFs mixed with other medicines and administered
6. % of ODFs mixed with food and administered
7. % of ODFs that were difficult for the child to swallow during administration
8. % of ODFs where the child vomited soon after administration
9. % of ODFs the child refused to take
10. % of liquid ODFs administered with an appropriate measuring device
11. % of solid ODFs swallowed using boiled cooled water
12. % of occurrences where there was a need to repeat the dose
13. % of occurrences where accurate dosing was administered
14. % of occurrences where the frequency and duration of dosing interval were maintained
15. % of occurrences where the ODF was hygienically administered

the process electronically and rated the indicators through an online survey and another two were met on a different day by the research team; one panellist did not participate in round two.

Analysis of criteria

In round one, the 40 draft indicators were graded by the expert panel in terms of clarity, necessity and scientific merit. The expert

panel considered all of them appropriate to assess rational use of oral dosage forms of medicines in children (overall panel median rating of 7–9 with agreement). In the second-round, face-to-face meeting, the 40 indicators were graded by the expert panel in terms of feasibility and predictive value, and regraded in terms of necessity. Again, the panel rated all indicators as appropriate (median score ≥ 7 with none marked 3 points away from the median), but it noted several instances where several

indicators on the same theme could be consolidated into a single overarching indicator. The panel also recommended the way in which indicators could be rephrased.

Final list of indicators

After consolidating groups of indicators on the same themes and incorporating the suggested rephrasing, 19 indicators were finalized. The logistics of applying the indicators in health-care facilities were also taken into consideration when compiling the final list of nine prescribing, five dispensing and five administration indicators to measure rational use of oral dosage forms of medicines for children (see Table 2).

Pretesting of the indicators

Acceptability to users

Each of the 19 indicators in the finalized list was scored as acceptable (median ≥ 7) in each group of participants: researchers, prescribers, pharmacists and parents.

Use in health-care settings

The data-collection instruments were used by the first author to collect data on 30 instances of prescribing, dispensing and administration of oral dosage forms of medicines in 20 children in a paediatric ward, clinic or outpatient department of a teaching hospital. It was found that numerators and denominators could be readily obtained, allowing efficient calculation of all indicators.

Interrater reliability

The records of the 20 children who were given 30 oral dosage forms of medicines from the pretesting were reviewed independently by the first author and an independent rater. The kappa value was above 0.7, indicating high agreement between the two raters.

Finalized list of indicators

The finalized list of the indicators, their purpose and the numerator and denominator for the calculation of each are given in Table 2.

Discussion

This study followed an extensive well-tested process to develop indicators to describe the use of oral dosage forms of medicines given to children. To the best of the authors' knowledge, this is the first time that a set of evidence-based indicators has been developed to measure rational use of oral dosage forms of medicines in children.

Since the WHO core drug use indicators are generic, their use will detect broad issues of RUM in children that are common to RUM in adults. We therefore suggest that the indicators from this study can serve as supplementary indicators to the WHO core indicators. Researchers interested in rational use of oral dosage forms of medicines in children should also consider using these supplementary indicators. These indicators will be useful for researchers, paediatricians, clinical pharmacologists, clinical pharmacists, medical administrators and policy-makers. They can be used at a national, regional, hospital or even ward level, to understand the issues in rational use of oral dosage forms of medicines in children. The indicators will allow quantification

of the issue, as well as determining the type of irrational use, finding out the reasons and explaining the contributing factors. This will facilitate implementation of interventions to improve the existing practice, if it is deficient, and reassessment after some time to measure the outcome of implementation. The indicators cover the entire cycle of medicine issues in children, namely prescribing, dispensing and administration. Since they are stand-alone indicators, researchers can use a particular group of indicators that are relevant to them; for example, the chief pharmacist of a hospital can use dispensing indicators to investigate issues related to dispensing practices.

It is interesting to note that almost all the prescribing indicators are related to dosing of medicines in children. In addition, the majority of articles identified during the literature review related to prescribing and dosing accuracy in children. It is the authors' perception that awareness of the need "to scale the dose to function and not to size" and that "one size does not fit all" is quite high in Sri Lanka, and this may also be true of other resource-limited settings. This may be the result of initiatives such as the WHO campaign "Make medicines child size", which was launched in 2007 to raise awareness of and accelerate action to meet the need for improved availability and access to child-specific medicines.²⁰ Given the expertise and up-to-date knowledge of the expert panel, it is unsurprising that this issue was strongly represented.

The majority of dispensing indicators were focused on quantifying the problem of non-availability of paediatric strengths and dosage forms. Studies have reported that lack of paediatric strength and dosage forms is a major problem in resource-limited settings.²¹ The indicators from the present study can be used to quantify and describe the different type of issues related to this problem in dispensing oral dosage forms of medicines to children. This can be done at national level, as a survey when a representative sample is studied, or even as a hospital-level audit. Results will not only quantify the issues but also describe different types of issues related to rational dispensing practice of oral dosage forms of medicines in children. The indicators can also be used to compare the problem in different settings (for example, different levels of hospitals in the public sector, provincial differences, public versus private sector and even intercountry)

The need to ensure appropriate administration of medicines to children has become more represented in the published literature in recent years. Most of the publications are from resource-rich countries,²² with few from resource-limited countries.²³ It is a relatively new topic for many resource-limited countries, which are struggling to improve the availability and affordability of medicines for children. However, the acceptability of medicines is also a component in access to medicines.²⁴ Even if affordable medicines are made available, the objective of treatment can be met only if the medicines are given to children properly. Hence, the set of administration indicators will be a useful tool to assess this neglected area of rational use of oral dosage forms of medicines in children in resource-limited countries. The indicators mainly focus on issues in administration, which may lead to dosing errors. Since antibacterial agents are the commonly prescribed medicines in children,²⁵ dosing errors have many implications, including emergence and spread of antibiotic resistance.²⁶

Interestingly, all 40 indicators developed by the authors were found to be appropriate in terms of feasibility, necessity and

Table 2. Finalized indicators and their purpose and calculation method

Indicator	Purpose	Indicator measurement	
		Numerator	Denominator
Prescribing indicators			
1. Mean number of ODFs of medicines per child	To measure the degree of medicines burden in children	Total number of ODFs prescribed to children	Total number of children to whom ODFs were prescribed
2. % of ODFs of medicines prescribed in a dose that is appropriate for the weight of the child	To measure the tendency for prescribing to be based on the weight of the child	Number of ODFs of medicines prescribed in a dose appropriate for the weight of the child	Total number of ODFs prescribed
3. % of solid ODFs of medicines prescribed	To measure the tendency to prescribe a solid ODF to a child	Number of solid ODFs of medicines prescribed	Total number of ODFs prescribed
4. % of ODFs of medicines prescribed as tablets	To measure the tendency to prescribe tablets to a child	Number of ODFs of medicines prescribed as tablets	Total number of ODFs prescribed
5. % of ODFs of medicines prescribed as capsules	To measure the tendency to prescribe capsules to a child	Number of ODFs of medicines prescribed as capsules	Total number of ODFs prescribed
6. % of ODFs of medicines prescribed as a dosage form that is suitable for the child's age	To measure the tendency to prescribe a dosage form based on the age of the child	Number of ODFs of medicines prescribed that were suitable for age	Total number of ODFs prescribed
7. Mean number of tablets prescribed per child	To measure the degree of tablet burden	Total number of tablets prescribed	Total number of children to whom ODFs were prescribed
8. Mean number of capsules prescribed per child	To measure the degree of capsule burden	Total number of capsules prescribed	Total number of children to whom ODFs were prescribed
9. Mean volume of liquids prescribed per child	To measure the degree of liquid medicine burden	Total volume of liquids prescribed	Total number of children to whom ODFs were prescribed
Dispensing indicators			
1. % of instances where alternative ODFs (to what was prescribed) were dispensed	To measure the degree to which health-care facilities are able to provide the dosage forms that were prescribed	Number of instances where alternative ODFs (to what was prescribed) were dispensed	Total number of ODFs dispensed
2. % of ODFs adequately labelled	To measure the degree to which pharmacists document essential information on the medicine packages they dispense	Number of ODFs that were adequately labelled	Total number of ODFs dispensed
3. % of solid ODFs irrationally manipulated by the pharmacist before dispensing	To measure the irrational ^a dispensing of medicines	Number of solid ODFs irrationally manipulated by the pharmacist before dispensing	Total number of solid ODFs dispensed
4. % of solid ODFs that need manipulation before administering a single unit	To measure the degree to which health-care facilities are able to provide the required prescribed dose with manipulation	Number of solid ODFs that need manipulation before administering a single unit	Total number of solid ODFs dispensed
5. % of instances where ODFs were dispensed with correct advice on storage	To measure the degree to which pharmacists correctly advise on storage	Number of instances where ODFs were dispensed with correct advice on storage	Total number of children to whom ODFs were dispensed
Administration indicators			
1. % of instances where the child swallowed the intact tablet/capsule	To measure the degree to which a child can swallow the intact tablet/capsule	Number of instances where the child swallowed the intact tablet/capsule	Total number of solid ODFs administered
2. % of instances where crushed tablet was dissolved and administered	To measure the irrational administration of ODF	Number of instances where crushed tablet was dissolved and administered	Total number of solid ODFs administered
3. % of liquid ODFs administered using an oral syringe	To measure the degree to which the correct dose amount is administered	Number of liquid ODFs administered using an oral syringe	Total number of liquid ODFs administered
4. % of instances where safe water ^b was used in preparing the medicine	To measure the availability of safe water for preparing the medicine	Number of instances where safe water was required to prepare the medicine for the child	Number of instances where water was required to prepare the medicine for the child
5. % of instances where the prescribed dose is correctly completed	To measure the degree of dose completion	Number of instances where the prescribed dose is correctly completed	Total number of ODFs prescribed

ODF: oral dosage form.

^a In the context of this project, "irrational" practices were defined as manipulation of ODFs of medicines for children, such that they are inappropriately, improperly or incorrectly prescribed, dispensed or administered. The word "irrational" in this context does not reflect on an individual's action but is used as a general term to contrast with "rational" use of medicines.

^b Safe water: water that does not cause any significant risk to health after consumption, e.g. boiled water, bottled water.

predictive value. The number of indicators remained the same even after two rounds of expert review. This could be due to the extensive search done by the authors before developing the initial set of indicators and shortlisting to 40 indicators from a longer list. Since the authors also represent the same expertise as the panel members, it is perhaps unsurprising that the panellists found all 40 shortlisted indicators appropriate. The authors nevertheless reduced the number of indicators to 19, considering the time required to complete the data-collection form; this was aided by open comments given by the panellists and consolidating indicators, which were variations of the same theme. Finally, these indicators are not meant to measure the appropriateness of prescribed medicines for children. They were developed for health-care settings; further validation is needed if they are to be used in the community setting.

Conclusion

This study developed a set of indicators to measure rational use of oral dosage forms of medicines in children, using a standard method. The indicators satisfied the criteria for appropriateness. They can be used together with the WHO drug use indicators to identify issues in rational use of oral dosage forms of medicine in children.

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