

Refereed paper

A systematic evaluation of paediatric medicines information content in clinical decision support tools on smartphones and mobile devices

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ABSTRACT

Background Medication information is often poorly delineated for paediatric patients, resulting in high off-label and non-licensed use of drugs in this population. Access to accurate medicines information in this population becomes a necessity in order to avoid medication errors. Clinical decision support tools (CDSTs), which are increasingly available on mobile devices (e.g. smartphones), can provide healthcare providers with convenient access to paediatric medicines information at point of care. However, to date no systematic evaluation of the content in these CDSTs has been conducted.

Objectives To evaluate paediatric medicines information in CDSTs for smartphones and other mobile devices.

Method Evaluation of CDSTs according to scope and completeness was accomplished via weighted categories of 108 questions distributed evenly across three age groups: infants, children and adolescents.

Results Three paediatric-specific databases and six general databases were evaluated. The best performer provided 75.9% of the answers for scope and scored 69.7% for completeness. Databases generally performed less effectively in providing answers sourced from clinical guidelines compared with more conservative sources such as package inserts.

Conclusions Overall, general medicines information CDSTs performed better than paediatric-specific CDSTs in both scope and completeness. Results from this study may help guide CDST selection on mobile devices by healthcare professionals whose patient populations include paediatrics.

Keywords: clinical decision support tools, drug information databases, handheld computers, paediatrics

Introduction

Medication safety and dosing information is often poorly delineated for paediatric patients as 75% of medications demonstrate insufficient labelling for these two purposes.¹ This has resulted in the common practice of off-label or unlicensed use of medications in paediatric patients.^{2,3} Exacerbating matters for paediatric patients is the threat of medication errors. Children are more susceptible than adults to medication errors due to a more narrow therapeutic window, poorly defined medicines information and variability in weight and body surface area, thus complicating pharmacokinetic and pharmacodynamic considerations.⁴ However, a landmark study by Leape *et al* found the most common system failure associated with preventable medical errors was proper dissemination of medicines information.⁵ The use of clinical decision support tools (CDSTs) is one strategy that has demonstrated an ability to help prevent medication errors in paediatrics.⁶

One type of CDST, which is often housed on smartphones (e.g. iPhone, Blackberry) or other mobile devices (e.g. iPad, TabletPC), is the medicines information database. This tool can help to directly address the issue of medicines information dissemination and its value is enhanced by being available at the point of care. A growing number of healthcare professionals (HCPs) have adopted the use of these tools. In particular, paediatricians (80%)⁷ and paediatric residents (89.5%)⁸ report commonly using drug references. However, to date no study has evaluated the ability of CDSTs to provide complete and correct paediatric medicines information. Additionally, no guidance is available to assist HCPs in selecting a particular CDST for paediatric medicines information. The aim of this study was to evaluate paediatric-related medicines information in CDSTs available on smartphones and mobile devices with regard to scope and completeness.

Methods

Question and category development

Seven categories of medicines information questions were developed, including dosing, indications/contraindications, adverse reactions, pharmacokinetics, monitoring, drug interactions and formulations. These categories were selected and weighted based on impact on direct patient care. Category weighting was designed to mirror the distribution of the types of medication use questions encountered in clinical practice. Within

each category, questions were evenly subdivided into three specific age groups: infants, children and adolescents. A total of 108 question and answer pairs were created to populate the categories, with an even distribution of 36 questions across each age group. Answers were generated from conservative, established sources (i.e. package inserts) for 75% of the questions. Owing to the high level of off-label and unlicensed use in paediatric patients, 25% of the answers were derived from paediatric clinical practice guidelines. All aspects of the study methodology (e.g. category and question design, category weighting, question and answer accuracy, relevance to practice) were reviewed by an external panel of paediatricians and pharmacists with expertise in the field of paediatrics. Changes were made based on the recommendations of the panel. A sample of specific medicines information questions is provided in Box 1.

Box 1 Sample of medicines information questions

- Can the sudden appearance of extrapyramidal symptoms in an 11-month-old infant be attributed to administration of metoclopramide by injection?
- What vital signs must be monitored during immune globulin infusion in a 4-year-old with Kawasaki's disease?
- Why should a 17-year-old patient avoid taking drospirenone and ethinyl estradiol and St John's Wort (*hypericum perforatum*) concurrently?
- At what concentration is caffeine citrate for injection available?

Database selection

Both general and paediatric-specific CDSTs were included for evaluation. Inclusion criteria for CDSTs required a satisfactory breadth of information and an electronic downloadable format. 'Satisfactory' was defined as the capacity of a particular database to answer questions in at least five of the seven categories. This criterion insured the medicines information the CDST contained was broad in nature and not too narrow in scope. CDSTs were excluded if they functioned strictly as a specialty database (e.g. a reference comprised exclusively of stability-compatibility data or one limited to identification of drug interactions). Three paediatric-specific and six general medicines information CDSTs satisfied all of the inclusion criteria. Paediatric-specific CDSTs included: British National Formulary for Children (BNFC), Harriet Lane Handbook (HLH) and Paediatric Lexi-Drugs (PLD). General CDSTs included: A to Z Drug Facts (A2Z),

American Hospital Formulary Service Drug Information (AHFS), Clinical Pharmacology OnHand (CP), Epocrates Rx Pro (ERP), Lexi-Drugs (LD) and Thomson Clinical Xpert (TCX). Information on the databases included in the study is shown in Table 1.

Database assessment

Databases were evaluated on two qualities: scope and completeness. Scope was measured by the presence or absence of an answer and was assessed for all 108 questions in all databases. A score of one was assigned if an answer was found and, conversely, a score of zero was assigned if an answer was absent. The scope for each CDST was calculated as a percentage based on the number of answers it yielded. Completeness was a measure of depth defined as a correct, accurate answer. Completeness was assessed on a scale of one to three, with one being the least complete and three being the most complete. If a database scored a zero for scope, then that database also scored a zero for completeness. The completeness scores were calculated and reported as a percentage. Two sets of averages were calculated

for the completeness score, one for questions from conservative, established sources and one from clinical practice guidelines. Each question was assessed independently by two authors and if discrepancies in scoring occurred, discussion ensued until a consensus was reached.

Each discrete CDST was individually evaluated for scope and completeness and the results were also calculated for each question category and age group. Additionally, an overall score combining all results for each category and age group was generated for each CDST.

Statistical analysis

Descriptive statistics were used to summarise the evaluative components. A repeated measures analysis of variance (ANOVA) was used to determine whether significant differences existed for both scope and completeness scores between general and paediatric-specific databases. Statistical analysis of results was conducted using SPSS version 16.0. Significance was set at the 0.05 level.

Table 1 Database information

Databases	Abbreviation	Publisher	Website for additional information
General			
A to Z Drug Facts	A2Z	Wolters Kluwer Health	www.factsandcomparisons.com
American Hospital Formulary Services Drug Information	AHFS	American Society of Health-System Pharmacists	www.ashp.org
CP OnHand	CP	Elsevier, Inc	www.clinicalpharmacology.com
Epocrates RX Pro	ERP	Epocrates	www.epocrates.com
Lexi-Drug	LD	Lexi-Comp, Inc	www.lexi.com
Thomson Clinical Xpert	TCX	Thomson Reuters	www.micromedex.com
Paediatric-specific			
British National Formulary for Children	BNFC	RPS Publishing	www.bnf.org
Harriet Lane Handbook	HLH	Johns Hopkins Hospital	www.skyscape.com
Pediatric Lexi-Drug	PLD	Lexi-Comp, Inc	www.lexi.com

Results

Scope of databases

The top performing database with regard to scope was PLD, with the ability to provide answers to 75.9% of the questions. The lowest scoring database for scope was BNFC (28.7%), which means both the best and worst performing CDSTs were paediatric-specific

databases. Full details of database scope scores for all CDSTs are delineated in Table 2. After all scope scores were calculated, analysis revealed significant differences between CDSTs ($P \leq 0.01$).

Completeness of databases

In terms of completeness of databases, PLD averaged 69.7% completeness and BNFC scored lowest of the

Table 2 Scope of general and paediatric-specific drug information databases

Category	n	General								
		A2Z	AHFS	CP	ERP	LD	TCX	BNFC	HLH	PLD
Dosing	21	14	17	13	15	15	13	2	8	13
Infant	7	5	7	6	7	6	5	1	2	6
Child	7	4	5	2	2	3	2	0	3	3
Adolescent	7	5	5	5	6	6	6	1	3	4
Indications/ contraindications	18	10	11	10	10	10	12	7	8	13
Infant	6	3	3	3	3	2	3	3	3	5
Child	6	5	5	4	5	6	6	2	3	6
Adolescent	6	2	3	3	2	2	3	2	2	2
Adverse reactions	18	14	16	11	16	17	16	9	10	17
Infant	6	4	5	3	6	5	5	3	5	6
Child	6	5	5	4	4	6	5	3	2	6
Adolescent	6	5	6	4	6	6	6	3	3	5
Pharmacokinetics	15	4	5	0	0	4	3	0	0	6
Infant	5	1	3	0	0	2	2	0	0	3
Child	5	2	2	0	0	1	0	0	0	3
Adolescent	5	1	0	0	0	1	1	0	0	0
Monitoring	12	9	7	1	8	5	9	2	2	11
Infant	4	2	0	0	2	2	2	0	1	3
Child	4	3	3	0	3	1	3	0	0	4
Adolescent	4	4	4	1	3	2	4	2	1	4
Drug interactions	12	11	8	12	11	10	8	8	6	10
Infant	4	3	2	4	3	3	2	2	2	4
Child	4	4	3	4	4	4	3	3	2	4
Adolescent	4	4	3	4	4	3	3	3	2	2
Formulations	12	7	8	7	4	10	8	3	4	12
Infant	4	3	3	3	1	3	2	3	2	4
Child	4	1	2	1	1	3	3	0	1	4
Adolescent	4	3	3	3	2	4	3	0	1	4
TOTAL	108	69	72	54	64	71	69	31	38	82
%	100	63.9	66.7	50.0	59.3	65.7	63.9	28.7	35.2	75.9

n=number of questions per category; A2Z=A to Z Drug Facts; AHFS= American Hospital Formulary Service Drug Information; CP=Clinical Pharmacology OnHand; ERP=Epocrates RX Pro; LD=Lexi-Drug; TCX=Thomson Clinical Xpert; BNFC=British National Formulary for Children; HLH=The Harriet Lane Handbook; PLD=Paediatric Lexi-Drug

databases at only 23.4%. Table 3 provides full details of completeness data for each database. Completeness scores were similarly found to be significantly different ($P \leq 0.01$).

Comparison of paediatric-specific and general databases

Performances between paediatric-specific and general databases were not significantly different for either scope or completeness. Although a paediatric-specific CDST performed best in terms of scope, the overall scores for scope in paediatric-specific databases were not significantly better than those of the general databases. The reverse actually held true as general medicines information references scored an average of 61.6% in scope while paediatric-specific databases scored only an average of 46.6%. In terms of completeness, general CDSTs again outperformed paediatric-specific CDSTs with an average score of 53.9% versus 42.0%.

Comparison of package insert and clinical practice guideline-based questions

Most paediatric CDSTs performed better for scope in questions derived from authoritative but conservative sources (e.g. package inserts) versus those answers were sourced from clinical guidelines. For questions from package inserts, BNFC scored the lowest in scope

at 33.0% and AHFS the highest at 71.7%. In the clinical practice guideline-based questions, BNFC scored the lowest in scope at 13.3% and PLD the highest at 63.2%.

In terms of completeness, all CDSTs performed better in questions derived from package inserts, with PLD performing the best and BNFC the worst with 78.3% and 12.3% average completeness respectively. For questions derived from clinical practice guidelines, PLD was the top performer at 59.7% and BNFC the lowest at 12.3% average score for completeness.

Discussion

Principal findings

A misconception may exist that paediatric-specific medicines information databases are better for paediatrics than general medicines information databases. While the best overall performer was paediatric specific, as a group specialty databases performed poorly and typically were only able to answer one-half as many questions as their general counterparts. This is an important distinction as HCPs who generally acknowledge 'gold standard' references such as HLH as their primary medicines information source may be surprised at how ineffective it was in providing basic

Table 3 Completeness (%) of general and paediatric-specific drug information databases

Category	n	General								
		A2Z	AHFS	CP	ERP	LD	TCX	BNFC	HLH	PLD
Dosing	28	60.7	75.0	64.3	60.7	66.7	64.3	7.1	40.5	63.1
Indications/ contraindications	24	43.1	55.6	52.8	47.2	56.9	62.5	34.7	41.7	69.4
Adverse reactions	24	66.7	84.7	51.4	76.4	80.6	66.7	38.9	47.2	86.1
Pharmacokinetics	20	23.3	33.3	0	0	18.3	23.3	0	0	38.3
Monitoring	16	52.1	54.2	6.3	56.3	25.0	60.4	14.6	16.7	77.1
Drug interactions	16	56.3	58.3	87.5	83.3	75.0	52.1	52.1	39.6	68.8
Formulations	16	50.0	56.3	47.9	29.2	77.1	56.3	20.8	35.4	89.6
TOTAL %	100	50.9	61.3	45.6	51.2	58.1	56.0	23.4	32.9	69.7

n=number of questions per category; A2Z=A to Z Drug Facts; AHFS= American Hospital Formulary Service Drug Information; CP=Clinical Pharmacology OnHand; ERP=Epocrates RX Pro; LD=Lexi-Drug; TCX=Thomson Clinical Xpert; BNFC=British National Formulary for Children; HLH=The Harriet Lane Handbook; PLD=Paediatric Lexi-Drug

information about medications (e.g. adverse reactions, drug interactions and dosing).

Implications of the findings

The results from this study can be used to guide HCPs to select the CDST that best suits their individual practice needs. For example, since scope and completeness scores are reported by both category and patient subpopulation, the HCP who is primarily interested in dosing information could choose the database that performed best in that capacity. Similarly, if drug interaction information is the primary concern, the data could be used to eliminate possible CDST choices from contention. Additionally, institutions considering adopting smartphone or mobile device CDSTs to reduce adverse drug events (ADEs) can utilise the results of this study to drive decision making and help provide budgetary justification. The results of our study may be further underscored by the findings of an interventional study in which the mobile device-based use of PLD (the highest overall performer in our study) was implemented and resulted in the significant reduction of 7.1 potential ADEs per 100 orders ($P=0.001$).⁹

One notable categorical performance (irrespective of database) was pharmacokinetic information. Of the full CDSTs that were studied, the average number of questions answered correctly was 1.4 out of 16, with no single database able to provide answers for one-half of the questions. Questions regarding trough and peak concentrations, clearance, volume of distribution and bioavailability went largely unanswered by databases, despite the dire need for information in these areas in paediatrics due to weight and body surface variability. This is an area that practitioners should recognise as a limitation in these CDSTs.

Comparison with the literature

The use of smartphones by physicians has rapidly increased over the past few years, far outstripping the rate of adoption by the general population.¹⁰ Just ten years ago, physician use of mobile phones hovered around 30%, whereas 72% of physicians currently use smartphones and it is believed that number will grow to 81% by 2012.¹⁰ Mobile devices have been used specifically in paediatrics for a variety of applications including depression screening,¹¹ measuring clinical and educational workload¹² and improving resident documentation discrepancies.¹³ However, the most commonly used application is the medicines information database, and studies have demonstrated that CDSTs can help decrease the rate of medication errors in the paediatric population.^{6,9,14} One study specifically

found that the introduction of a mobile device-based medicines information reference significantly reduced potential ADEs in a children's hospital ($P=0.001$).⁹ Databases used as CDSTs on smartphones and mobile devices have previously been assessed for general medicines information,^{15–18} and content from these medicines information databases has also been assessed in order to rate the potential to reduce medication errors.¹⁹ Although there are several studies highlighting the accuracy of general and selected specialty medicines information references, there are no published studies systematically evaluating smartphone databases for paediatric medicines information.

Because of the limited number of medications with approved indications in paediatric patients, the availability of appropriate medicines information to the HCP is vital. Efficacy and safety data from manufacturers is often scarce and provides limited utility for determining the appropriate dosage for paediatric patients. Subsequently, HCPs may rely heavily on CDSTs for guidance. Incomplete or inaccurate information may result in treatment failure or adverse consequences. For example, one question included in the study evaluated the scope and completeness for the dosing of acyclovir for the treatment of herpes simplex virus (HSV) encephalitis. The acyclovir dose for HSV central nervous system infections from birth to three months is listed in the package insert as 10 mg/kg every eight hours for ten days.²⁰ The insert further states that doses of 15–20 mg/kg/dose have also been used, but safety has not been established.²⁰ However, the American Academy of Pediatrics (AAP) Red Book recommends a dosage of 20 mg/kg/day every eight hours for 21 days.²¹ Of the databases reviewed in this study, four of nine (44%) did not meet either scope or completeness for this particular question, including two of the paediatric-specific CDSTs (i.e. HLH and PLD). Subtherapeutic dosing of acyclovir in HSV encephalitis has the potential to result in long-term sequelae, such as brain damage. Another area for potential therapeutic failure is in the treatment of acute otitis media. The most recent AAP clinical guidelines recommend an oral dose of amoxicillin of 80–90 mg/kg/day in two divided doses for ten days.²² In our study, we found that only one of the databases earned full scores in both scope and completeness for this particular question, four years after the release of the guidelines.

Actual adverse events secondary to inaccurate information in CDSTs are unknown. To date, only one paediatric case report has been published regarding errors in CDSTs. In the report, a one-month-old infant presented to the emergency department with symptoms of phenytoin toxicity with a serum phenytoin concentration of 91.8 mcg/mL. Upon investigation, it was realised that the infant had been prescribed phenytoin 2.5 mL of the 30 mg/5 mL suspension based

on the information available in a specific CDST. At the time, the 30 mg/5mL suspension was not available and the pharmacist dispensed an incorrect dose.²³ Inappropriate dosing resulting in ADEs may not be recognised as frequently in the outpatient setting as in the inpatient setting due to fewer monitoring programmes being available in the outpatient setting. One study, however, did find that the potential incidence of outpatient medication dosing errors can be as high as 15%,²⁴ hence the occurrence of similar adverse events in the outpatient environment may not be captured.

Limitations of the method

Not all available CDSTs were evaluated in this study, nor were all possible clinical questions evaluated. HCPs may use different resources for specific types of information than those examined in this study (e.g. using a drug interaction database to identify specific drug interactions). However, the most commonly used comprehensive CDSTs were identified and included in the study. Additionally, while only a subset of all possible evaluation questions was used, the selected categories, age groups and questions were all designed to be a representative sample.

All answers in the evaluation were verified by either the package insert or clinical practice guidelines to minimise differences in opinions based on clinical practice. However, the overall frequency of guideline non-adherence by HCPs is unknown and practice guidelines specific to the USA were primarily used. One study evaluated trends in the management of otitis media since the release of the last AAP guidelines.²⁵ The study showed that of the physicians responding to the survey 57.2% utilised high-dose amoxicillin in patients with non-severe symptoms, but 33.1% continued to prescribe amoxicillin at the traditional, conservative dose. The authors speculated that possible reasons for non-adherence to the guidelines included lack of knowledge about the guidelines, lack of agreement with the guidelines or pharmaceutical industry influence on prescribing. As stated previously, only one of the CDSTs in this evaluation was able to fully answer the otitis media dosing question with regard to scope and completeness, which may provide an additional reason for lack of adherence to the guidelines.

Call for further research

A potential limitation of our study is that only 25% of the questions included were based on clinical practice guidelines. However, because this is the first evaluation of paediatric-specific CDSTs, it was decided to

focus primarily on questions with answers from sources that were not subject to debate. Future evaluations of paediatric medicines information in CDSTs may include a higher percentage of clinical practice guideline questions in order to more closely resemble clinical practice.

Conclusion

No previous systematic and objective evaluations have been conducted to assess the quality of medicines information in CDSTs for paediatrics. Surprisingly, general medicines information CDSTs collectively outperformed paediatric-specific databases in the provision of medicines information. However, PLD was the best overall performer in answering medicines information questions. Overall, general and paediatric-specialty databases have substantial limitations in providing paediatric medicines information. Publishers should re-examine the inclusion of information drawn from clinical guidelines given the frequency of off-label and unlicensed use in the paediatric population. The results from this study may help guide CDST selection by paediatricians and other HCPs whose patient populations include paediatrics.

Box 2 Key findings

- The best and worst performing drug information databases with regard to scope and completeness were both paediatric specific
- Overall, general drug information databases performed better than paediatric-specific databases
- Both general and paediatric-specific databases were unable to answer questions regarding pharmacokinetic parameters in paediatrics

REFERENCES

- 1 Benjamin DK, Smith PB, Murphy MD *et al.* Peer-reviewed publication of clinical trials completed for pediatric exclusivity. *Journal of the American Medical Association* 2006;296:1266–73.
- 2 American Academy of Pediatrics. Committee on Drugs. Uses of drugs not described in the package insert (off-label uses). *Pediatrics* 2002;110:181–3.
- 3 Hawcutt DB and Smyth RL. Drug development for children: how is pharma tackling an unmet need? *IDrugs* 2008;11:502–7.
- 4 Sullivan JE and Buchino JJ. Medication errors in pediatrics: the octopus evading defeat. *Journal of Surgical Oncology* 2004;88:182–8.

- 5 Leape LL, Bates DW, Cullen DJ *et al*. Systems analysis of adverse drug events. ADE Prevention Study Group. *Journal of the American Medical Association* 1995;274:35–43.
- 6 Fortescue EB, Kaushal R, Landrigan CP *et al*. Prioritizing strategies for preventing medication errors and adverse drug events in pediatric inpatients. *Pediatrics* 2003;111:722–9.
- 7 Carroll AE and Christakis DA. Pediatricians' use of and attitudes about personal digital assistants. *Pediatrics* 2004;113:238–42.
- 8 Khan AN, Frank J, Geria R and Davidson S. Utilization of personal digital assistants (PDAs) by pediatric and emergency medicine residents. *Journal of Emergency Medicine* 2007;32:423–8.
- 9 Leonard MS, Cimino M, Shaha S, McDougal S, Pilliod J and Brodsky L. Risk reduction for adverse drug events through sequential implementation of patient safety initiatives in a children's hospital. *Pediatrics* 2006;118:e1124–9.
- 10 Manhattan Research. *Physicians in 2012: the outlook for on demand, mobile, and social digital media*. Taking the Pulse, 2010.
- 11 John R, Buschman P, Chaszar M, Honig J, Mendonca E and Bakken S. Development and evaluation of a PDA-based decision support system for pediatric depression screening. *Studies in Health Technology and Informatics* 2007;129:1382–6.
- 12 MacGregor DL, Tallett S, MacMillan S, Gerber R and O'Brodovich H. Clinical and education workload measurements using personal digital assistant-based software. *Pediatrics* 2006;118:e985–91.
- 13 Carroll AE, Tarczy-Hornoch P, O'Reilly E and Christakis DA. The effect of point-of-care personal digital assistant use on resident documentation discrepancies. *Pediatrics* 2004;113:450–4.
- 14 Stavroudis TA, Miller MR and Lehmann CU. Medication errors in neonates. *Clinics in Perinatology* 2008;35:141–61, ix.
- 15 Enders SJ, Enders JM and Holstad SG. Drug-information software for Palm operating system personal digital assistants: breadth, clinical dependability, and ease of use. *Pharmacotherapy* 2002;22:1036–40.
- 16 Clauson KA, Seamon MJ, Clauson AS and Van TB. Evaluation of drug information databases for personal digital assistants. *American Journal of Health-System Pharmacy* 2004;61:1015–24.
- 17 Knollmann BC, Smyth BJ, Garnett CE *et al*. Personal digital assistant-based drug reference software as tools to improve rational prescribing: benchmark criteria and performance. *Clinical Pharmacology and Therapeutics* 2005;78:7–18.
- 18 Clauson KA, Polen HH and Marsh WA. Clinical decision support tools: performance of personal digital assistant versus online drug information databases. *Pharmacotherapy* 2007;27:1651–8.
- 19 Galt KA, Rule AM, Houghton B, Young DO and Remington G. Personal digital assistant-based drug information sources: potential to improve medication safety. *Journal of the Medical Library Association* 2005;93:229–36.
- 20 Bedford Laboratories. *Acyclovir for Injection Product Information*. Bedford, OH: Bedford Laboratories, 2005.
- 21 American Academy of Pediatrics, Committee on Infectious Diseases. Herpes simplex. In: Pickering LK (ed) *Red Book: 2006 Report of the Committee on Infectious Diseases* (27e). Illinois: American Academy of Pediatrics, 2006, pp. 361–71.
- 22 American Academy of Pediatrics, Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. *Pediatrics* 2004;113:1451–65.
- 23 Lowry JA, Vandover JC, Degreeff J and Scalzo AJ. Unusual presentation of iatrogenic phenytoin toxicity in a newborn. *Journal of Medical Toxicology* 2005;1:26–9.
- 24 McPhillips HA, Stille CJ, Smith D *et al*. Potential medication dosing errors in outpatient pediatrics. *Journal of Pediatrics* 2005;147:761–7.
- 25 Vernacchio L, Vezina RM and Mitchell AA. Management of acute otitis media by primary care physicians: trends since the release of the 2004 American Academy of Pediatrics/American Academy of Family Physicians clinical practice guideline. *Pediatrics* 2007;120:281–7.

CONFLICTS OF INTEREST

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