CMAJ OPEN
MEDICAL RESEARCH FOR ALL

Development of a provisional essential medicines list for children in Canada

Journal:	*CMAJ Open*
Manuscript ID	CMAJOpen-2017-0129
Manuscript Type:	Descriptive
Date Submitted by the Author:	05-Oct-2017
Complete List of Authors:	Persaud, Navindra; St Michael's Hospital, Family Medicine Woods, Hannah ; St. Michael's Hospital, Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute Oronsaye, Efosa; St. Michael's Hospital, Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute Bali, Anjli; St. Michael's Hospital, Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute Rajakulasingam, Yathavan; St. Michael's Hospital, Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute Lee, Taehoon; Li Ka Shing Knowledge Institute, St. Michael's Hospital Umali, Norman; St. Michael's Hospital, Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute Cohen, Eyal Finkelstein, Yaron Offringa, Martin; The Hospital for Sick Children, Child Health Evaluative Sciences
Keywords:	Family medicine, general practice, primary care, Pediatrics, Pharmacoepidemiology
More Detailed Keywords:	
Abstract:	Background: Worldwide, many countries have developed a list of essential medicines for children to improve prescribing. We aimed to create an essential medicines list for children in Canada. Methods: We adapted the previously created list of essential medicines for adults in Canada and the WHO Model List of Essential Medicines for Children to create a provisional list of essential medicines for children in Canada. Canadian clinicians made suggestions for changes. Literature relevant to each suggestion was presented to clinician-scientists who used a modified nominal group technique to make recommendations on the

	suggestions. The Ontario Public Drug Programs prescription data was reviewed to identify commonly prescribed medications missing from the list. Literature relevant to these medications was shared with a clinician-scientist review panel to determine which should be added, and a revised list was developed. Results: 76 removals from the list of essential medicines for adults in Canada were made because they were not indicated for use in children; 7 medications were added to the child list based on Ontario Public Drugs Programs prescribing data and clinician-scientist review. Suggestions to add, remove, or substitute medications were made by peer-reviewers and resulted in one medication removal and one medication replacement. The process produced a provisional list of 64 medications for children. Interpretation: A provisional list of 64 essential medicines for children was developed. The list should be further developed based on wider input and continuously revised based on emerging evidence of safety and effectiveness of these medicines in all pediatric age groups

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **N/A**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Page 2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **Page 3**
Objectives	3	State specific objectives, including any prespecified hypotheses **Page 4**
Methods		
Study design	4	Present key elements of study design early in the paper **Pages 4-9**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Pages 4-9 (some of the above is not applicable)**
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants **N/A**
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case **N/A**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **N/A**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **N/A**
Bias	9	Describe any efforts to address potential sources of bias **N/A**
Study size	10	Explain how the study size was arrived at **N/A**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why

		N/A
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions **N/A**
		(*c*) Explain how missing data were addressed **N/A**
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy **N/A**
		(*e*) Describe any sensitivity analyses **N/A**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **N/A**
		(b) Give reasons for non-participation at each stage **N/A**
		(c) Consider use of a flow diagram **N/A**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **N/A**
		(b) Indicate number of participants with missing data for each variable of interest **N/A**
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) **N/A**
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time **N/A**
		Case-control study—Report numbers in each exposure category, or summary measures of exposure **N/A**
		Cross-sectional study—Report numbers of outcome events or summary measures **N/A**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **N/A**
		(*b*) Report category boundaries when continuous variables were categorized **N/A**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **N/A**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity

		analyses **N/A**
Discussion		
Key results	18	Summarise key results with reference to study objectives **Pages 9-12**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Page 14-15**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Pages 12-14**
Generalisability	21	Discuss the generalisability (external validity) of the study results **N/A**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **N/A**

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Hannah Woods, BHSc, MSc, Efosa Oronsaye, MBBS, MPH, Anjli Bali, MD, Yathavan Rajakulasingam, MD, Taehoon Lee, MD, MPH, Norman Umali, RPh, Eyal Cohen, MD, MSc, Yaron Finkelstein, BMedSc, MD, Martin Offringa, MD, PhD, Nav Persaud, BA, BSc, MD, MSc

Affiliations: Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, St Michael's Hospital (Woods, Oronsaye, Bali, Rajakulasingam, Lee, Umali, Persaud); St. Michael's Hospital; Department of Family and Community Medicine (Persaud); The Hospital for Sick Children (Cohen, Finkelstein, Offringa); University of Toronto (Persaud, Cohen, Finkelstein, Offringa); Institute of Health Policy, Management and Evaluation (Cohen).

Corresponding Author: Dr. Nav Persaud. 30 Bond Street, Toronto, Ontario, Canada, M5B 1W8. nav.persaud@utoronto.ca, Phone: 416-360-4000 Ext. 77578

Keywords: family medicine, general practice, pediatrics, pharmacoepidemiology, primary care

Word count: 2669

Competing Interests: *The authors have no competing interests*. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Funding Statement: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Contributions: NP conceived of the study; NP, HW, EO, AB, YR, TL, EC, YF and MO conducted the study; NP, HW, EO, AB, YR, TL, EC, YF, and MO interpreted the findings. HW and NP wrote the first manuscript draft; NP, HW, EO, AB, YR, TL, EC, YF, and MO were involved in revising it critically for important intellectual content and all approved of the final version. All authors will be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgement: The authors thank Lee Dupuis for helpful comments on the article.

Development of a provisional essential medicines list for children in Canada

ABSTRACT

Background: Worldwide, many countries have developed a list of essential medicines for children to improve prescribing. We aimed to create an essential medicines list for children in Canada.

Methods: We adapted the previously created list of essential medicines for adults in Canada and the WHO Model List of Essential Medicines for Children to create a provisional list of essential medicines for children in Canada. Canadian clinicians made suggestions for changes. Literature relevant to each suggestion was presented to clinician-scientists who used a modified nominal group technique to make recommendations on the suggestions. The Ontario Public Drug Programs prescription data was reviewed to identify commonly prescribed medications missing from the list. Literature relevant to these medications was shared with a clinician-scientist review panel to determine which should be added, and a revised list was developed.

Results: 76 removals from the list of essential medicines for adults in Canada were made because they were not indicated for use in children; 7 medications were added to the child list based on Ontario Public Drugs Programs prescribing data and clinician-scientist review. Suggestions to add, remove, or substitute medications were made by peer-reviewers and resulted in one medication removal and one medication replacement. The process produced a provisional list of 64 medications for children.

Interpretation: A provisional list of 64 essential medicines for children was developed. The list should be further developed based on wider input and continuously revised based on emerging evidence of safety and effectiveness of these medicines in all pediatric age groups.

INTRODUCTION

In 1977, the World Health Organization (WHO) created a model list of essential medicines that is updated every 2 years based on up-to-date evidence for efficacy, safety and tolerability. (1-2) The WHO recommends that each country evaluate and adapt the list in order to create a list of essential medicines that is appropriate for its own environment. Previously, we adapted the WHO model list of essential medicines to create a list of essential medicines for adults in Canada. (3) This list may contribute to improved quality of care where a short list of essential medications may make it easier for clinicians to prescribe the most effective, safe and appropriate medication (4-6) and more appropriate use of drugs. (7-8)

The WHO developed its first model list of essential medicines for children in 2007 in an effort to make safe and effective medicines as available for children as for adults. (9-10) The current 5th edition lists medications deemed to be the most efficacious, safe and cost-effective for priority conditions and diseases. The WHO recommends that the list of essential medicines for children be adapted by countries according to local context and policy.

In Canada, there is no list or central source of information related to safety, efficacy, and tolerability of medication forms and formulations for children. This, in combination with the large number of medications available for children with unknown safety and efficacy profiles in Canada (11-13) poses a challenge for clinicians treating children. An essential medicines list for children in Canada may contribute to improvements in quality of care while also generating cost savings. (7, 8, 12, 14, 15)

Our aim was to develop a list of essential medicines for children in Canada based on the WHO model list of essential medicines for children and on the adult essential medicines list we previously created. (3, 16) The provisional child list was created through a peer-reviewed, multi-step process based on current clinical evidence, Canadian clinical practice guidelines and historic prescribing data and is publicly posted at http://cleanmeds.ca/.

METHODS

Adaptation of WHO essential medicines list

As previously described, (3) we adapted the 2013 WHO Essential Medicines list (16) to create a preliminary essential medicines list for adults in Canada. The purpose of this process was to identify the medicines on the WHO list that are applicable to Canada. Removals from the WHO list were made for 1 of 5 reasons: items were not medications, other medications on the list had better tolerated routes of administration (e.g., oral medication available instead of intravenous), the medications had the same indication as other listed medications, the medications were used for conditions that are uncommon in Canada, or the medications were not medications prescribed by primary care providers. Any disagreements were resolved through discussion and consensus. (3)

After reviewing the WHO list, we considered adding medications applicable to Canada that were not on the WHO list. We reviewed the following resources to determine if there were medications applicable to Canada that were not on the WHO list: Canadian clinical practice guidelines, systematic reviews, health technology assessment reports and child formularies in other countries. This part of the process generated a draft of the list for wider feedback.

Development of the provisional list of essential medicines for children in Canada

We started with medications that were on both the Canadian adult list (3), and the WHO Model List of Essential Medicines for Children 5th edition (9). All medications on our adult essential medicines list that also appeared on the WHO model list for children were added to our draft essential medicines list for children. Medications that were on the WHO model list for children but not on our provisional list were identified for potential inclusion. For each of these medications research team members determined if there was an equivalent medication on the Canadian child list or if the indication for which the medication was prescribed using RxTx (formerly eCPS) or if the medicine was not used in Canada (e.g. treatment for tropical disease). If there was an equivalent, or if the medication was not relevant in the Canadian healthcare context, the medication was not added to our provisional list of essential medicines for children in Canada..

Peer review feedback

Peer reviewers included pediatricians, primary care physicians, nurse practitioners, pharmacists and consultants or specialists practicing in Canada. The initial child list of essential medicines was made publicly-available via a website (www.cleanmeds.ca) and feedback on suggested changes to medications on the list was collected through the website. Each proposed change was classified as a replacement, an addition to or removal from the list, and could be justified by at least one of the following: evidence of efficacy, evidence of safety, route of administration and tolerability, dosing schedule, usefulness for other medical conditions, and interactions with other medications. Respondents were allowed to make suggestions for any reason.

The website has been active since January 2017 and changes can be suggested at any time.

Peer reviewers were carefully selected based on expertise, publications and academic involvement. We searched Canadian clinical practice guidelines using the repository maintained by the Canadian Medical Association and publications in the *Canadian Medical Association Journal, Canadian Family Physician and Paediatrics and Child Health* in the last two years for authors of papers in different pediatric therapeutic areas. Thirteen peer reviewers were contacted through mail, fax or email with a description of the project and the website (www.cleanmeds.ca) where they could submit their proposed list changes. Four peer reviewers suggested changes to the list; the response rate was 31%.

Based on the suggested additions, subtractions or substitutions to the adapted list made by the peer reviewers, we developed questions focused on efficacy and safety with support from an information scientist and performed a literature search for each question. Five literature searches were performed (one for each suggestion that was made). No searches were run for medicines that remained from the WHO list. Duplicate or similar suggestions were grouped together in one question. Evidence was gathered from systematic reviews, meta-analyses, randomized control trials, the Compendium of Pharmaceuticals and Specialties, clinical practice guidelines and health technology assessment reports. Members of the research team (AB, EO, HW, YR and NP) reviewed the results of the literature searches and compiled the information into an evidence report document. Literature search questions and search strategies were included in the evidence report and are publicly posted online (at cleanmeds.ca/list/suggest-changes/).

Five clinician-scientists who were all involved in the treatment of children and active researchers were invited to join a panel to discuss the suggestions made by the peer reviewers. They were asked to participate based on their familiarity with clinical issues relevant to the medications on the list, their experience critically appraising clinical evidence (i.e., research training, experience), and a lack of relevant conflicts of interest (including those with pharmaceutical industry). The response rate was 100%; all five clinician-scientists agreed and participated. A meeting was held on 30 March 2017 to discuss changes that were suggested by peer reviewers via the website. Three voting members (clinician-scientists) and NP were present at the meeting. Each participating clinician-scientist was given the evidence report document to review 2 weeks prior to the meeting. Clinician scientists used the information in the documents to form an evidence-based recommendation on addition, removal, or replacement for each suggested medication change. Comments on each suggestion were submitted to the research team by clinician-scientists prior to the meeting. The comments were compiled by research assistants (AB, TL, EO, YR and HW) and presented to all clinician-scientists during the meeting to facilitate discussion among the clinician- scientists. Each voting member discussed their opinion without interruption, followed by open discussion. After each group discussion, the participating clinician-scientists voted by independently recommending whether or not the suggested change should be made based on the evidence gathered and from their own clinical expertise. The meeting employed a modified nominal group technique, involving independent consideration prior to the meeting, group discussion and voting on recommended changes to the adapted list. (3, 17)

The strength of each recommendation (strong or weak) was determined by the 3 participating clinician-scientists. The final recommendations were deemed strong if all clinician-scientists were in agreement for or against the recommendation and at least 2 had made strong recommendations. If this criterion was not met, the recommendation was deemed weak in the direction of the majority of clinician-scientist votes. The strength of evidence supporting each recommendation was determined by vote, using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. (3, 18) The strength of the recommendation reflects the importance of the decision, while the strength of the evidence reflects how unlikely it is that new evidence would change the recommendation.

Identification and addition of commonly prescribed medications

To identify commonly prescribed medications missing from the list, the Ontario Public Drug Programs prescription data was reviewed. For each medication, if there was an equivalent on the draft child essential medicines list according to the Canadian RxTx, the medication was not selected for further review. Medications were considered equivalent if they treated the same condition and/or were from the same class of medications. The medications that were not already on the provisional essential medicines list for children and for which there were no equivalents were selected for further review. Evidence reports presenting current information about the effectiveness and safety of these medications were created and disseminated to clinician-scientists for review. A clinician-scientist meeting was held on 23 March 2017 where clinician-scientists deliberated and voted for or against addition of each medication to the child essential medicines list. Three voting members (clinician- scientists) and NP were

present at the meeting. Where there was consensus, the medication was added or not added to the list accordingly and the website was updated. If consensus was not reached, the decision whether to add the medication was deferred until more evidence could be provided.

Patient and Community Involvement

The process for developing and revising the list was co-developed with a panel of 11 community members who owere recruited from the area surrounding St Michael's Hospital, Toronto by canvassing, random digit dialing and through existing community groups. The community guidance panel met every one to two months during the development of the list and provided input on issues including the criteria used to select medications, how to maintain the list and the knowledge translation strategy. The community guidance panel members did not suggest particular changes to the medications on the list.

Ethics approval

The study was approved by the Research Ethics Board of St Michael's Hospital, Toronto.

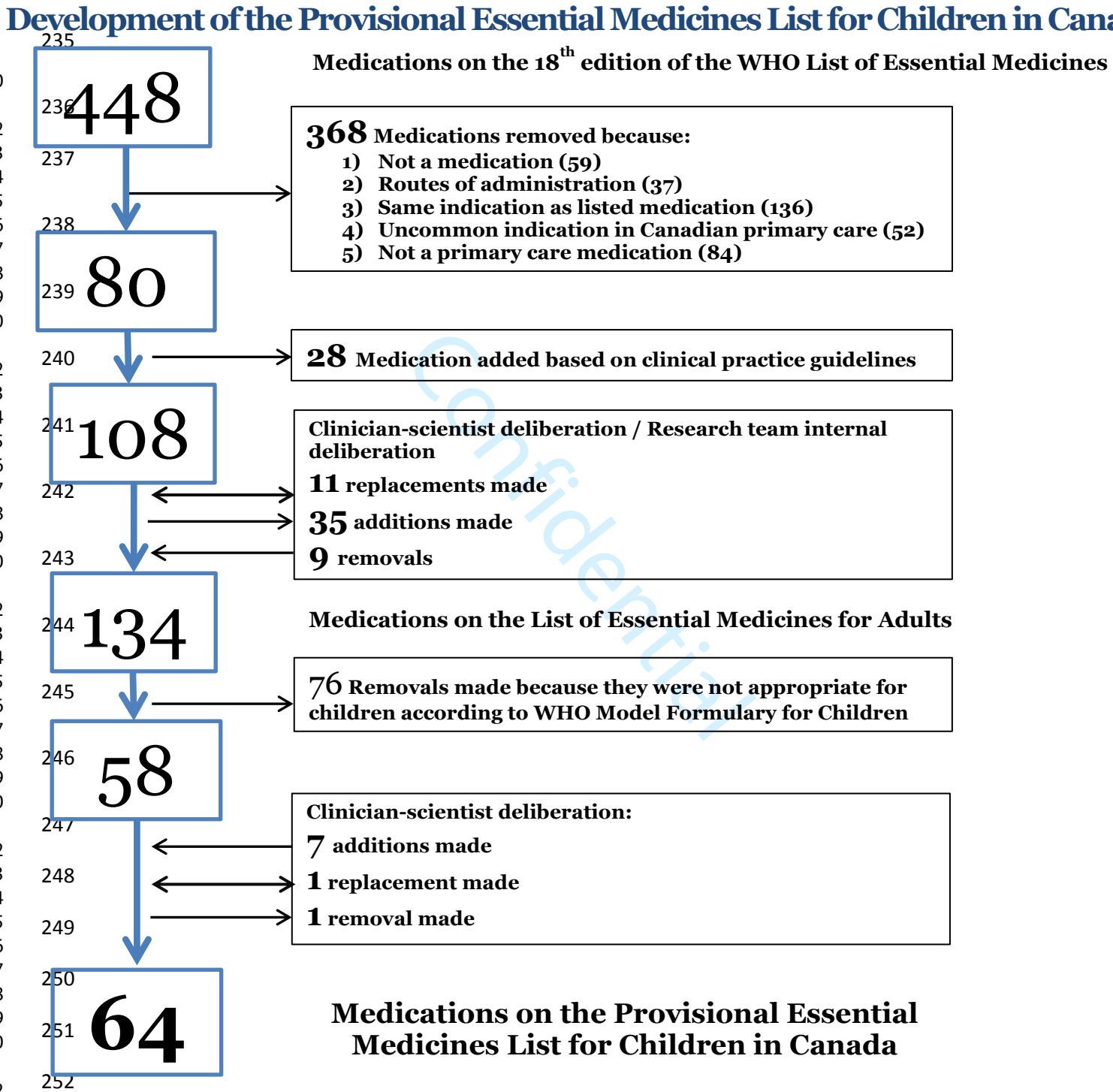
RESULTS

Adaptation of the Essential Medicines List for Adults

As previously reported, the provisional Essential Medicines List for Adults contained 134 items. (3) In creation of our provisional list for children, 76 removals from the adult list were made because they were not indicated for use in children in the WHO Model Formulary for Children. This resulted in a provisional child list of 58

essential medicines. Figure 1 illustrates the development process for the child list of essential medicines. The list can be found at cleanmeds.ca.

Figure 1. Flow diagram summarizing the development of the provisional essential medicines list for children in Canada



Clinician-scientist review

Evidence reports for the potential additions to the list based on Ontario Public Drug Program prescribing data were presented to clinician-scientists for review and a clinician-scientist meeting was held where deliberation took place. As a result of this process, 7 medications were added to the essential medicines list for children in Canada.

Peer-review suggestions

Suggestions to add, remove, or substitute medications on the list were made by peer-reviewers. An evidence report for each suggestion was created based on up-to-date scientific evidence and provided to clinician-scientists for further review. Deliberations that took place at clinician-scientist meetings lead to one medication removal and one medication replacement for a total of 64 medications on the initial list for children.

INTERPRETATION

We adapted the Essential Medicines List for Adults development scheme, using a 4-step process involving a small group of Canadian clinicians and clinician-scientists. The provisional child essential medicines list for Canada contains 64 medications. This is a work-in-progress, and the list will likely be revised and grow as further input is gathered. The current short list may allow clinicians to learn more about fewer drugs and could improve appropriateness of clinician prescribing. (3, 19)

Child essential medicine lists differ from country to country in the way they are developed and presented; some countries include details of the list development process and guidelines for preparation, prescribing, and how to use the document. Some lists are standalone documents specific to children while others are a pediatric section within a larger list or formulary. The number of medications included in child essential

medicine lists or formularies ranges from 4 (Egypt) to over 1000 (United Kingdom). (20-21) List information by country is presented in Table 1.

Details on the development process for pediatric lists and formularies are not readily available for all countries; however, some countries make this information publicly available. The British National Formulary for Children and the Kinderformularium (The Dutch Paediatric Formulary) present information on the development of their child formularies including the contributing bodies, the sources of information and how the information has been validated. (21-22) While these are not essential medicines lists, their purpose is similar to that of our child essential medicines list- to aid decisions on prescribing, dispensing and administration of medicines. (21-22) The process for developing the British National Formulary for Children and the Dutch Paediatric Formulary is aligned with the process for developing our child essential medicines list: collaboration; consulting expert clinical advisors, literature, systematic reviews, consensus guidelines, reference sources, comments from readers; and continuous revision are important components. The British National Formulary for Children also includes information on how to use the formulary, selecting suitable preparations, dose selection, writing prescriptions, and so on. (21) Likewise, South Africa includes these details around the development process for their Standard Treatment Guidelines and Essential Medicines List for hospital level paediatrics as does India for their Essential Medicines List for Children. (24-25) The processes and methods used in other jurisdictions will continue to be consulted while further developing and maintaining the provisional essential medicines list for children in Canada.

The provisional list of essential medicines for children we have created lists medications in alphabetical order or therapeutic area and includes contraindications, drug interactions or cautions, adverse effects, dosing information, monitoring, and the source of the suggestion. Further details and the presentation of our child list are to be decided through additional input and collaboration.

Table 1. Child essential medicines lists and child formularies in several countries

	Essential Medicines List or formulary	# of medicines	Development process described
Canada	Essential Medicines List	64	No
Democratic Republic of Congo (26)	Essential Medicines List	48	No
Egypt (20)	Formulary	4	No
India (25)	Essential Medicines List	134	Yes
Kiribati (27)	Formulary	21	No
Netherlands (28)	Formulary	726	Yes
New Zealand (29)	Formulary	Not available	Not available
South Africa (24)	Essential Medicines List	249	Yes
Togo (30)	Essential Medicines List	219	No
United Kingdom (21)	Formulary	over 1000	Yes

Limitations

The process was dependent on evidence for the individual medicines and high quality evidence in children was often lacking. It is unclear if it would be better to consider lower quality studies. More quality evidence would facilitate the child essential

medicines list development. In many cases, there is not a clear basis for prescribing advice in children.

The list was peer reviewed by a small number of individuals. Other medications, including those usually prescribed by sub-specialists (e.g. seizure disorder medications), may have been suggested if there were more peer reviewers. The small number of clinician-scientists making the final decisions meant that the final composition of the list could have been dependent on the judgments of just a few individuals.

Using commonly prescribed medications as one of the starting points for list development could reinforce inappropriate prescribing practices, however, evidence reports regarding the safety and efficacy for each medication were created and disseminated to clinician-scientists prior to final recommendations on whether to add these medications.

We did not consider local availability of medications in creating the provisional essential medicines list for children in Canada; the current availability of medicines as products that can be ordered through Canadian pharmacy wholesalers was not within the scope of this research.

CONCLUSION

We have developed a provisional short list of essential medications for children that can be refined in the future based on wider input. The list should be continuously revised based on new evidence. Future work should determine the applicability of the list across Canada, the impact of list adoption on actual prescribing, and the effects of list-driven prescribing on patients.

REFERENCES

1. WHO. Essential medicines selection - National Medicines List/Formulary/Standard Treatment Guidelines; 2014. Available from: http://www.who.int/selection_medicines/country_lists/en/

2. WHO. The selection of essential drugs: report of the WHO Expert Committee; 1977;(615):1-36.

3. Taglione MS, Ahmad H, Slater M, Aliarzadeh B, Glazier RH, Laupacis A, Persaud N. Development of a preliminary essential medicines list for Canada. CMAJ open. 2017 Jan;5(1):E137.

4. Yakabowich MR, Keeley G, Montgomery PR. Impact of a formulary on personal care homes in Manitoba. CMAJ: Canadian Medical Association Journal. 1994 May 15;150(10):1601.

5. Feely J, Chan R, Cocoman L, Mulpeter K, O'Connor P. Hospital formularies: need for continuous intervention. BMJ. 1990 Jan 6;300(6716):28-30.

6. King MA, Roberts MS. The influence of the Pharmaceutical Benefits Scheme (PBS) on inappropriate prescribing in Australian nursing homes. Pharmacy world & science. 2007 Feb 1;29(1):39-42.

7. Eom G, Grootendorst P, Duffin J. The case for an essential medicines list for Canada. Canadian Medical Association Journal. 2016 Jun 13:cmaj-160134.

8. Sketris IS, Lummis H, Langille E. Optimal prescribing and medication use in Canada: challenges and opportunities. In: Canada HCo, editor.: Citeseer; 2007.

9. WHO. Model list of essential medicines for children. 5th list; 2015. Available from: http://www.who.int/medicines/publications/essentialmedicines/en/index.html

10. World Health Organization. World Health Assembly: Resolution WHA60.20 better medicines for children; 2007. Available from: http://www.who.int/entity/childmedicines/publications/WHA6020.pdf

11. Ontario Public Drug Programs - Formulary - Drugs Funded by Ontario Drug Benefit (ODB) Program; 2014 [cited 2017 June]. Available from: http://www.health.gov.on.ca/en/pro/programs/drugs/odbf_mn.aspx

12. Alberta Health - Alberta Drug Benefit List (ABDL); 2015 [cited 2017 June]. Available from: http://www.health.alberta.ca/services/drug-benefit-list.html

13. Prescription drug insurance - Prescription drugs covered - Prescription drugs covered by the Public Prescription Drug Insurance Plan; 2015 [cited 2017 June]. Available from: http://www.ramq.gouv.qc.ca/en/citizens/prescription-drug-insurance/pages/prescription-drugs-covered.aspx

14. Quittner AL, Modi AC, Lemanek KL, Ievers-Landis CE, Rapoff MA. Evidence-based assessment of adherence to medical treatments in pediatric psychology. Journal of pediatric psychology. 2008 Oct 1;33(9):916-36.

15. Council of Canadian Academics. Improving medicines for children in Canada. The expert panel on therapeutic products for infants, children, and youth; 2014. Available from: http://www.scienceadvice.ca/uploads/eng/assessments%20and%20publications%20and%20news%20releases/therapeutics/therapeutics_fullreporten.pdf

16. WHO. Model List of Essential Medicines; 2013. Available from: http://www.who.int/medicines/publications/essentialmedicines/18th_EML_Final_web_8Jul13.pdf

17. Nair R, Aggarwal R, Khanna D. Methods of formal consensus in classification/diagnostic criteria and guideline development. Seminars in arthritis and rheumatism. 2011;41(2):95-105.

18. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ (Clinical research ed.). 2008 Apr 26.

19. Avery AJ, Walker B, Heron T, Teasdale SJ. Do prescribing formularies help GPs prescribe from a narrower range of drugs? A controlled trial of the introduction of prescribing formularies for NSAIDs. British Journal of General Practice. 1997;47(425):810-4.

20. Ministry of Health and Population Central Administration of Pharmaceutical Affairs. Egyptian national formulary; 2007. Available from: http://apps.who.int/medicinedocs/documents/s17411e/s17411e.pdf

21. Paediatric Formulary Committee. British National Formulary for Children (2015). London: BMJ Group. 2015.

22. van der Zanden TM, de Wildt SN, Liem Y, Offringa M, de Hoog M. Developing a paediatric drug formulary for the Netherlands. Archives of disease in childhood. 2016 Oct 31:archdischild-2016.

23. Kelly LE, Ito S, Woods D, Nunn AJ, Taketomo C, de Hoog M, Offringa M. A Comprehensive List of Items to be Included on a Pediatric Drug Monograph. The Journal of Pediatric Pharmacology and Therapeutics. 2017 Jan;22(1):48-59.

24. The National Department of Health. Standard treatment guidelines and essential medicines list for South Africa. 2013 edition; 2013. Available from: http://www.kznhealth.gov.za/pharmacy/PaedsSTG2013LR.pdf

25. Indian Academy of Pediatrics. List of essential medicines for children of India. First list-2011. Available from: http://apps.who.int/medicinedocs/documents/s19040en/s19040en.pdf

26. Ministere de la Sante des Affaires Sociales et de la Famille. Republique du Congo strategies plaintes -traitements enfants; 2006. Available from

http://www.who.int/selection_medicines/country_lists/Congo_STGChildren_2006.pdf?ua=1

27. Kiribati Ministry of Health. Obstetrics, gynaecology, paediatrics and dental drug guidelines December 2007. Available from: http://www.who.int/selection_medicines/country_lists/kir_book4.pdf?ua=1

28. Foundation Dutch Knowledge Centre for Pharmacotherapy in children (NKFK). Kinderformularium. Available from: https://www.kinderformularium.nl

29. New Zealand Formulary for Children (NZFC). NZFC;2013. Available from: www.nzfchildren.org.nz

30. Defence for Children International. Liste nationale des medicament essentiels sous dci pour les enfants (<14 ans); 2012. Available from: http://www.who.int/selection_medicines/country_lists/Togo_LNME_Enfant_2012.pdf?ua=1