

THE INGREDIENTS OF A CLINICAL PRACTICE GUIDELINE: A QUALITATIVE ASSESSMENT OF THE RESEARCH USED IN THE DEVELOPMENT OF A PEDIATRIC ASTHMA GUIDELINE

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ABSTRACT

Background: A qualitative assessment of the research used in the development of a widely used Clinical Practice Guideline (CPG) to gain insight into the kinds of evidence that informs the development of CPGs.

Methods: All articles cited within the 2003 Canadian Pediatric Asthma Consensus Guideline (“the Guideline”) were secured, as was the literature cited by these articles. Two independent reviewers coded all 98 articles referenced by the Guideline (“primary citations”), and the 3,167 articles referenced by the primary citations (“secondary citations”), along three schemes: article type, research design and article orientation.

Results: Among the primary and secondary citations Clinical research was the most represented type (53%), followed by Health Services (25%), Population Health (18%), and Biomedical (4%). There was a strong interdependence between Clinical and Health Services Research articles with each type frequently citing the other. Observational study designs were most common (48%), followed by experimental studies (31%) and secondary research (21%).

Discussion: While CPGs rely on significant support from clinical or biomedical randomized controlled trials, the translation of research into practice is non-linear with an important role for Health Services Research and Population Health. This may have implications for funding agencies and other supporters of health research who are working to bridge the gap between research and clinical practice.

Key Words: *Practice Guidelines, Research Funding Policy, Evidence Base*

Abbreviations

CPG – Clinical Practice Guideline

AHRQ – Agency for Healthcare Research and Quality RCT – Randomized Controlled Trials

CIHR – Canadian Institute for Health Research HSR – Health Services Research

NIH – U.S. National Institutes of Health

1. INTRODUCTION

The development and implementation of Clinical Practice Guidelines (CPGs) has been promoted by numerous government organizations (including the Canadian Institutes of Health Research, the U.S. Institute of Medicine, and the U.K.'s National Health Service) as a means to codify best practices, in a readily accessible form, with the goal of addressing patient safety, quality and population health needs [1-3]. CPGs are often used to justify investments in research by funding agencies (e.g., CIHR and NIH) [4-6], with research cited in Guidelines more likely to influence policy and practice [7]. While the diversity of CPGs have resulted in guidelines of varying quality, little assessment has been conducted to explore the variability across the research translational spectrum. As a result, we know more about the rigour and design of CPGs and less about the qualities and approaches of research integrated into recommendations.

With regard to rigour and design, there are now more than 100 rating systems developed and promulgated through medical journals to assess the quality of the evidence base for a recommendation [8], although it has been noted that these rating systems are based on subjective judgments and result in wide variation with respect to quality across guidelines [9-11]. The most prominent rating system for CPGs is the GRADE tool used by Cochrane, the World Health Organization, and the British Medical Journal, among others [12] – which generally point to randomized controlled trials (RCTs) as the “gold standard” for evidence. However, real-world patients and clinical environments are often more complicated than those used in original research [11, 13].

Given the current state of research design and the investments being made toward the establishment of “pragmatic clinical trials” – designed to evaluate the effectiveness of interventions in real-life routine practice conditions – there is a growing focus on the diversity of approaches to research (including observational studies and secondary analyses such as other guidelines, review articles, and qualitative meta-analyses) that inform the evidence base for CPG development. For example, previous research has called into question the fundamental health policy assumption that basic science research feeds into clinical research [14]. A review of cited articles from 15 United Kingdom guidelines found that only 0.2% of articles were from basic science journals [14]. Previous bibliometric analyses of the CPG evidence base has focused on author affiliations, funding acknowledgements, article age, and cited articles' impact scores [5, 14], with few articles including type of article (e.g., basic science versus clinical research) [14].

To address this gap in the literature, this qualitative study examines the kinds of evidence that inform the development of a clinical practice guideline. Taking a widely used CPG for pediatric asthma published by CMAJ as our case study, we performed a content analysis on the scientific literature cited by this guideline. If experimental research is considered the gold standard for CPG development, it is important to determine how observational or review studies add to the evidence. Additionally, if guideline developers often cite health services research and population health studies, this heightens the importance of these types of research within health policy and practice.

2. METHODS

2.1 Classification Schemes

Given the gaps in the literature presented above, three classification schemes were identified to categorize articles: *type*, *design*, and *orientation* (see Table 1 for a list of the categories under each scheme). The first scheme, *article type*, is based on the funding pillars of the Canadian Institute for Health Research (CIHR) [15]. This scheme drives national research funding and clearly identifies the domains of health-focused research, which are:

- *Biomedical Research*: to understand normal and abnormal functioning at the molecular, cellular, organ system and whole body levels. These studies generally do not have a diagnostic or therapeutic orientation.
- *Clinical Research*: focused towards improving the diagnosis and treatment of disease and injury and improving the health and quality of life of individuals.
- *Health Services Research*: to improve the efficiency and effectiveness of health professionals and the health care system through changes to practice and policy.
- *Social, Cultural, Environmental and Population Health*: explores the way in which our social and physical environment impacts our health with the goal of improving population health.

The second scheme classifies articles cited by the CPG according to *research design*. This scheme is used to identify whether a study relied on data gathered by the study authors (primary) or relied on findings gathered by others (secondary). This classification is based on the hierarchy Concato [16] originally explored for rating the purported quality of study design:

- *Experimental (primary)*: research design includes a created control for the purpose of comparison. This excludes natural experiments.
- *Observational (primary)*: design relies solely on observations of the variables of the system under study, rather than manipulation of just one or a few variables as occurs in experimental designs.
- *Secondary*: an approach that looks to the literature to provide synthetic arguments without observation, such as a guideline, meta-analysis or review article.

The third scheme, *orientation*, was developed by Barley, Meyer, and Gash [17] who developed a typology to explore the interface between research and practice, with a particular emphasis on how researchers and practitioners were influencing each other. Orientation refers to whether the article was oriented toward influencing theory, practice or description, as detailed below:

- *Theory*: The article proposes, develops, or expands, a formal conception of the topic it addresses and supports formal propositions with data.
- *Practice*: The article offers methods or advice for addressing pragmatic problems thought to be relevant to managers, consultants, and other individuals who work in or with organizations.
- *Description*: The article aims to inform by reporting facts and opinions about people, events, or issues.

2.2 Choosing a Guideline

Using input from an expert interdisciplinary group, the criteria for the identification of a CPG were established and the Canadian Pediatric Asthma Consensus Guidelines were selected [18].

This CPG represents the current

standard of care for pediatric asthma and reflect the best interpretation of the available evidence published through 2004 for clinical practice, as determined by an expert panel convened by the Canadian Thoracic Society for that express purpose. No updated guidance has been offered in the intervening 10 years.

2.3 Data Collection and Analysis

All references within this article were secured as “primary citations.” Each primary citation was then searched to identify its reference articles that were secured as “secondary citations.” Each cited article was reviewed using the following specific exclusion criteria:

- As the research focus is to explore the nature of the peer-reviewed publication of primary and secondary research, the grey literature was excluded, including National Institutes of Health publications, books, reports, software, dissertations, and article corrections

- Articles written in a language other than English were excluded due to a lack of translation resources.

A checklist was created to categorize each primary and secondary citations according to the three classification schemes. Two different readers evaluated each article’s abstract, and in such cases where the readers disagreed a third reader was used to break the tie.

3. RESULTS

Figure 1 presents a flow diagram of the article extraction process. Of the 98 articles cited by the Canadian Pediatric Asthma Guidelines, four articles were excluded, leaving 94 primary citations. Of the 3,167 secondary citations (bibliography is available upon request), sixty could not be retrieved, 579 were duplicate citations and 138 met other *a priori* exclusion criteria (including 11 non-English articles and 87 books), resulting in 2,390 secondary articles.

Figure 1: Flow Diagram of the article extraction process

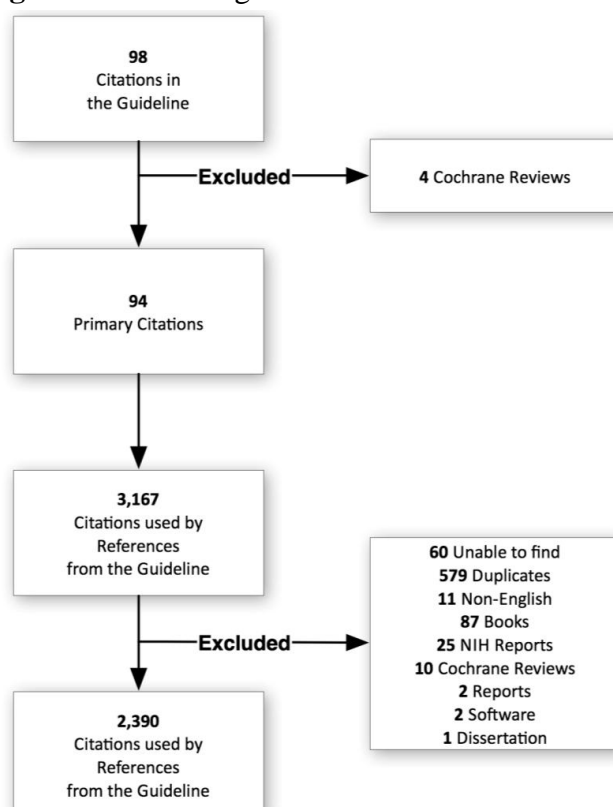


Table 1 presents the classification scheme and outlines the breakdown of the primary and secondary citations along that scheme. Among the primary citations, 4% were coded as Basic Biomedical Research, 61% Clinical, 15% were Health Services Research and 20% were Population Health. The vast majority (84%) of the primary citations were oriented toward practice. Regarding research design, 29% of the citations were experimental designs, half of the articles (49%) were observational, and 22% were secondary analysis (including review articles, guidelines and meta analysis). Also shown in Table 1 is the classification of the referring literature, or secondary citations. The itemization by article type is similar to the primary references with a slightly larger percentage of Health Services Research articles (25% versus 15%) and slightly fewer Clinical articles (53% versus 62%). The research design and orientation categories were also classified similarly to the group of primary citations.

Table 2 presents the primary and secondary references categorized by *research design* within each type and illustrates a diversity of research designs that span not only within the guideline itself but also across the secondary citation frame in each of the four types. For instance, while one might expect experimental designs to dominate basic research, we find that when selecting literature in the development of guidelines, physicians select articles that are diverse in their experimental approach and are predicated on literature that is also similarly diverse in research design. Table 3 further highlights the finding that each type of research cites a diverse array of types of research. Table 4 presents the Barley, Meyer and Gash's typology across the 5 types of research. Analysis finds that in both the primary and secondary research

there is a strong reliance on descriptive research, with practice taking second position in both clinical research (6.4%) and health services research (10.7%).

Table 1. List of categories within the three classification schemes

	Primary Citations (n=94)	Secondary Citations (n=3,167)
Type (CIHR Funding Pillar)		
Biomedical	4	75
Clinical	58	1272
Health Services Research	14	604
Population Health	18	429
Design		
Experimental	27	745
Observational	46	1137
Secondary	0	452
Review Articles	11	0
Guidelines	7	0
Meta Analysis	3	0
Bulletin	0	1
Case Report	0	1
Editorials	0	32
Commentary	0	4
Correspondence	0	4
Position Statements	0	8
Workshop	0	5
Orientation		
Theory	3	85
Practice	79	2132
Description	12	172

Table 2. Classification of secondary citations by type and within type by research design and orientation.

	Number of Articles	% of Articles	Research Design			
			Experimental	Observational	Secondary Analysis	Other
Basic Research	4	4.3%	0	3	1	0
<i>Secondary Citations</i>	272	11.4%	56	162	49	5
Basic Research	20	7.4%	9	8	3	0
Clinical Research	125	46.0%	24	72	26	3
Health Services Research	61	22.4%	3	49	8	1
Population Health Research	66	24.3%	20	33	12	1
Clinical Research	58	61.7%	17	28	13	0
<i>Secondary Citations</i>	1226	51.5%	572	506	128	20
Basic Research	36	2.9%	7	24	5	0
Clinical Research	779	63.5%	395	303	76	5
Health Services Research	347	28.3%	158	140	36	13
Population Health Research	64	5.2%	12	39	11	2
Health Services Research	14	14.9%	6	3	5	0
<i>Secondary Citations</i>	369	15.5%	59	106	182	22
Basic Research	6	1.6%	0	2	4	0
Clinical Research	213	57.7%	23	65	114	11
Health Services Research	120	32.5%	36	33	41	10
Population Health Research	30	8.1%	0	6	23	1
Population Health Research	18	19.1%	4	12	2	0
<i>Secondary Citations</i>	513	21.6%	58	363	83	9
Basic Research	13	2.5%	3	7	3	0
Clinical Research	155	30.2%	19	106	27	3
Health Services Research	76	14.8%	10	45	17	4
Population Health Research	269	52.4%	26	205	36	2
Data on Primary Level Articles	94	100.0%	27	46	21	0

Table 3: Secondary references from the Pediatric Asthma Guideline by type within primary reference type
Secondary Citations by type within each primary citation type

Primary Citations by Type	Basic Research	Clinical Research	Health Services Research	Population Health Research
Basic Research	7.4%	46.0%	22.4%	24.3%
Clinical Research	2.9%	63.5%	28.3%	5.2%
Health Services Research	1.6%	57.7%	32.5%	8.1%
Population Health Research	2.5%	30.2%	14.8%	52.4%

Table 4. Assessment of Primary and Secondary references by type using Barley, Meyer and Gash[22].

	Theory	Practice	Description
Primary	3 (3.1%)	12 (12.7%)	79 (84%)
Basic Research	9 (12%)	6 (8%)	60 (80%)
Clinical Research	34 (2.6%)	82 (6.4%)	1156 (90.8%)
Health Services Research	19 (3.1%)	65 (10.7%)	520 (86%)
Population Health Research	23 (5.3%)	19 (4.4%)	387 (90.2%)

4. DISCUSSION

4.1 *Main Results Summary*

A systematic assessment of the articles cited by a CPG reveals that the developers of this guideline relied on a broad base of evidence, referencing articles across various research types and designs. There is no apparent hierarchy of articles with Basic Biomedical and Clinical RCTs receiving preference. In fact, almost half of cited articles from the guideline studied were in the field of health services research or population health while only 4% were biomedical. Further, there is evidence of an interdependence between Clinical and Health Services Research (HSR), with one-third of Clinical references citing HSR, and half of HSR references citing Clinical articles. Additionally, observational studies and literature-based secondary analyses were prominent study designs, accounting for almost 70% of cited articles.

4.2 *Explanation of findings*

This paper informs knowledge translation efforts by highlighting the need to explore how different types of research, in addition to clinical studies, are integrated and translated into practice. Our study suggests that the translation of research into practice is recursive by nature, rather than a direct flow from basic to clinical to population studies. While Table 2 supports the supposition that Clinical research plays a central role in all aspects of health focused research, Health Services and Population Health account for a significant proportion of the references for both the guideline and the clinical studies that inform them. These intriguing findings require further study in CPGs across disciplines using a similar content analysis method.

Replication of these findings across

a large sample of CPGs could have important implications for health research funding policy because funders of health research consider articles referenced in CPGs as evidence of their funded research's impact on policy and practice [7]. The U.S. National Institutes of Health (NIH) and the Canadian Institute for Health Research, allocate the majority of their research funding based upon silos of disease and research type, respectively.

This focus has resulted in significant resource expenditure toward translational efforts; however, much of this expenditure has been focused on accelerating the basic science-clinical research connection, with significantly less attention on how HSR and population health research feed that process. This has begun to change in the United States with significant resources allocated to patient centered care and comparative effectiveness research through The Patient Centered Outcomes Research Institute (PCORI) and the Agency for Healthcare Research and Quality (AHRQ).

4.3 *Limitations*

It should be noted that our case study approach was very different from a traditional systematic review. There was no environmental scan to clarify either the state of the literature or advances in related science. Additionally, there is no way of judging the relative weight that a cited article might have on the formation of a clinical guideline. For example, one article might be deemed very important while another was evaluated as marginally influential, yet both are weighted equally in our study. Certain types of articles, such as population health, may be used more often in the Introduction. Due to our data collection methods and the arbitrary nature of any weighting system in a case study,

this bias is outside of our ability to comment.

4.4 Strengths

Beyond a specific clinical recommendation, the CPG reviewed here discusses the general management of pediatric asthma, including diagnosis, treatment, prevention, education and follow-up. While the Canadian Pediatric Asthma Consensus Guidelines were selected with expert guidance based on widespread awareness and usage among practitioners, the findings reported here may or may not apply to other CPGs. From a methodological perspective, it would be useful to replicate the systematic evaluation process employed in this paper using a variety of CPGs to further validate this approach. Dissecting the anatomy of a Clinical Practice Guideline, using the approach proffered here, informs our understanding of how research moves to practice. This type of analysis has implications for funding agencies and other supporters of health research who are working to bridge the gap between research and clinical practice.

4.6 Conclusions and implications

Substantiation of our results in a larger sample of CPGs could lead to (1) the need for funding agencies and others to look beyond a linear biomedical to clinical research pathway and consider the range of research that influences clinical practice and (2) to design CPG research quality assessment frameworks to value a diversity of research designs. While basic biomedical research serves to advance the future of medical science by increasing the availability of drugs in the pipeline among other important roles, based on the

references cited in this CPG clinical practitioners demonstrate a clear need for the diverse and outcome oriented research found in health services and population-level research.

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