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## A Bibliometric Analysis of Clinical and Translational Research in Pediatric Gastroenterology from 1970 to 2017

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## Abstract

**Objectives**—Pediatric gastroenterology is a clinical and research discipline principally developed over the past 50 years. Bibliometric methods provide quantitative analysis and identify research trends. Study aims were to characterize the growth and trends in pediatric gastroenterology clinical and translational research using citation analysis.

**Methods**—Using citations analysis software, a search strategy specific for pediatric gastroenterology was implemented for the years 1970–2017. The 50 most-cited research articles per decade were identified. These 250 articles were coded for topic and study attribute. Analysis included authors, affiliations, journals, countries, and funding sources.

**Results**—Overall average annual growth rate for pediatric gastroenterology publications was significantly higher than for general pediatrics (51.7% vs 6.2%; p < 0.05). Among the top 250 cited articles, the distribution of study focus was epidemiology (43%), pathophysiology (18%), treatment (16%), diagnosis (8%), prevention (8%), and comorbidities of gastrointestinal diseases (7%). There were 38 different topics represented and there was a notable shift in topic focus over time. Cholestasis, biliary atresia, and total parenteral nutrition were common topics from 1970–1989 and obesity, nonalcoholic fatty liver disease, and eosinophilic esophagitis were common topics after 1990. Notably, 2.3% of the authors accounted for 30% of the top 250 articles.

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Conflicts of Interest: none

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Kimberly P. Newton MD: analysis and interpretation of data, revision of the manuscript for important intellectual content Jeffrey B. Schwimmer MD: study concept and design, analysis and interpretation of data, critical revision of the manuscript for important intellectual content; study supervision

**Conclusion**—Pediatric gastroenterology research has undergone rapid growth yielding advancements in the management of gastrointestinal conditions in children. The emergence of new diseases in need of better diagnostics and therapeutics led to a temporal shift in research focus. Further advancements will require multidisciplinary collaborations and continued funding for pediatric gastroenterology research.

#### Keywords

citation analysis; hepatology; nutrition; obesity

## INTRODUCTION

The field of pediatric gastroenterology has rapidly evolved over the past fifty years. In the 1950's and 1960's there were medical advances in diagnosis and treatment that led to an increased survival of children with complex gastrointestinal conditions and thus a need for pediatric physicians with gastrointestinal expertise (1–2). The beginning of pediatric gastroenterology was marked by the development of dedicated research societies, established in Europe in 1968 and North America in 1973, and the publication of specialty textbooks, such as <u>Pediatric Clinical Gastroenterology</u> authored by Silverman, Roy, and Cozzetto in 1971 (3). Many hospitals were designated as centers of excellence for the treatment of gastrointestinal diseases, and over time developed formal gastroenterology fellowship programs. Training guidelines were created in the 1980s and subspecialty board examinations were established in 1990. In 1982, the North American Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) published the first journal dedicated to pediatric gastroenterology, hepatology, and nutrition, cementing the field as a discrete subspecialty of pediatrics (2).

In recent years, the field of pediatric gastroenterology has seen substantial increases in research and literature production. As a field grows, bibliometric methods can identify historical advances in knowledge. Additionally, they provide quantitative analysis of research within a field, identifying trends in research within a given body of literature and papers most likely to have long-term impact. While there have been citation analyses of disease-specific research, a bibliometric analysis of pediatric gastroenterology as a field has not been performed; such an analysis may delineate the impact of specific research and how it shapes the current field (5–8). Therefore, the aims of this study were to characterize the growth and trends in pediatric gastroenterology clinical and translational research from 1970–2017.

### METHODS

#### **Growth Rate**

To determine the growth rate of publications, the total numbers of publications per year during the targeted time period (1970–2017) were extracted from Medline using the search term "pediatric gastroenterology" in February 2018. For comparative purposes, Medline search term "pediatrics" over the same time period was also performed.

#### **Bibliometric Analysis**

Bibliometric analysis was performed examining research output in Web of Science (Clarivate Analytics, Philadelphia, PA) from 1970–2017. Web of Science was selected because it has the most complete coverage for the complete study period. The search strategy and keywords were developed to identify articles from overlapping areas of "pediatrics" and "gastroenterology" in consultation with a health science librarian. The search terms for pediatrics included: "pediatric", "pediatrics", "youth", "baby", "infant", "newborn", "toddler", or "adolescent". The search terms for gastroenterology are shown in supplemental Appendix 1 and included 135 terms representing disorders and disease processes relevant to pediatric gastroenterology derived from a standard reference textbook (1). Because the study focus was clinical and translational research, we included studies that met criteria for patient-oriented research, epidemiologic and behavioral studies, and/or outcomes research and health services research. Additional inclusion criteria were, peerreviewed, original research studies, primarily focused on pediatric gastroenterology, and abstracts in English. Preclinical and animal studies were excluded.

The search was performed in February 2018 and was applied separately for five decades (1970–1979, 1980–1989, 1990–1999, 2000–2009, and 2010–2017). The 50 most cited articles were identified from each decade, totaling 250 articles over the full research period. The resulting output was manually verified by three independent pediatric gastroenterologists to ensure that articles met inclusion criteria. Target information was then abstracted from each article, and included citation score, coding by topic (e.g. disease or process), study attributes (epidemiology, pathophysiology, diagnosis, treatment, outcomes, comorbidities, and prevention), area of interest (gastroenterology, hepatology, or nutrition), author(s), institutional and departmental affiliation, country of research production, journal of publication, and reported funding organizations.

#### Data Analysis

Data were reported as number, frequency, or percentage. The annual growth rate of publications was calculated as [(Current Year Total–Previous Year Total)/Previous Year Total] for the studied time period. Differences in growth rates were determined using repeated measures ANOVA. Chi- square was used to determine differences between categorical variables. Significance was defined *a priori* at a value of 0.05. Analyses were performed using IBM SPSS Statistics for Windows, Version 24.0 (Armonk, NY: IBM Corp).

## RESULTS

Searches of Medline for the terms "pediatric gastroenterology" and "pediatrics" yielded 15,409 and 828,470 and publications respectively over the search period. The annual trend of publications is shown in Figure 1. From 1970–2017, the average annual growth rate for pediatric gastroenterology publications was 52.0%, whereas the average annual growth rate for pediatric publications was 6.3% (p = 0.035). When the analysis was constricted to a more recent timeframe, 1990–2017, the average annual growth rate of pediatric gastroenterology research remained significantly higher than the annual growth rate for pediatrics overall (13.1% versus 5.6%, p = 0.032). The top 50 research articles by citation

score for each of the 5 decades were retrieved from Web of Science and are listed in Supplemental Table 1a–1e. Among these 250 papers, gastroenterology was the most common discipline (62%), followed by hepatology (21%) and nutrition (17%). In addition, the most common type of study was epidemiology (43%), followed by pathophysiology (18%), treatment (16%), diagnosis (8%), prevention (8%), and comorbidities of gastrointestinal diseases (7%). Full reference details for each of the 250 publications are provided in Supplemental Appendix 2.

Notably, there were 38 different topics represented; the most common of these are listed in Table 1. Obesity was the most common topic and was the primary focus of 19% of the most cited articles. Some topics commonly represented in the 1970's and 1980s, including cholestasis, cystic fibrosis, jaundice, biliary atresia, and total parenteral nutrition (TPN), were not common subject matters among articles with the highest citation score in subsequent decades. Other topics such as nonalcoholic fatty liver disease (NAFLD) and eosinophilic esophagitis (EoE) had no representation among top cited articles in the 1970s and 1980s, but became of increasing interest in later decades. In contrast many disease processes, including diarrhea, necrotizing enterocolitis, and celiac disease, were consistently represented in the top 50 articles across all decades studied.

Temporal changes were also noted for disease etiologies and the age groups experiencing the reported conditions. For example, infectious gastrointestinal conditions accounted for 32% of the most commonly cited papers from 1970–1989; whereas, this category accounted for only 11% of these papers after 1990. In contrast, diseases of immune dysregulation such as EoE, celiac disease, food allergy, and inflammatory bowel disease (IBD) were discussed in only 4% of the most highly cited articles from 1970–1989, yet this category accounted for 32% of these articles after 1990. Also, there was a significant difference in age groups represented in earlier versus later publications (p<0.001). Highly cited research in earlier decades focused primarily on diseases of infancy; this population was the focus of 67% of articles in the 1970s and 1980s. In comparison, 78% of the most highly cited research after 1990 focused on diseases of school aged children and/or adolescents.

The 250 highly-cited articles were published in 61 different journals. The ten journals accounting for 62% of these articles are shown in Table 2. The focus of these journals included general medicine (4), general pediatrics (2), gastroenterology (2), allergy (1), and nutrition (1) (Table 2). Over 400 institutions contributed to these 250 articles. Ten institutions accounted for 46% of the publications (Table 3). The U.S. Centers for Disease Control and Prevention published the most articles (19), followed by the University of London (15), UC San Diego (12), and Harvard University (12).

Research articles with the highest citation score originated from 40 different countries and 6 different continents. A majority of the most-cited research publications came from the United States, with an increase in cited research over time, from 48% of the highest cited articles between 1970 and 1979 to 72% after 2000. Overall, England produced 10% of publications, Canada produced 6%, Germany produced 4%, and Italy, Australia, and Japan each produced 3% of the most cited research publications. Supplemental Table 2 details the

18 countries contributing three or more of the highly cited articles in pediatric gastroenterology.

There were 1,421 authors that contributed to the identified 250 articles, and 33 authors that had three or more publications within this group. Combined, these 33 authors published 30% of the most highly cited articles identified in this study. Primary topics of interest amongst these authors were obesity (10), eosinophilic esophagitis (7), infant nutrition (4), nonalcoholic fatty liver disease (4), viral hepatitis (3), inflammatory bowel disease (2), food allergy (2), and microbiome (1). A list of the 33 authors who had three or more publications among the most highly cited articles is available in Supplemental Table 3.

The majority of research funding was provided by governmental agencies from the United States of America, the United Kingdom, and Australia. Individual institutes of the National Institutes of Health (NIH) including National Institute of Diabetes, Digestive, and Kidney Diseases, National Institute of Child Health and Human Development, National Heart, Blood, and Lung Institute, National Institute of Allergy and Infectious Diseases, and National Center for Research Resources funded 27% of the identified research articles. A list of the ten most common funding organizations noted in research articles identified by this study is available **in** Supplemental Table 4. Other common funding organizations identified were a non-profit medical charity (Wellcome Trust) and a pharmaceutical company (AstraZeneca).

## DISCUSSION

We performed a bibliometric analysis of clinical and translational research in the field of pediatric gastroenterology, evaluating research citations from 1970 to 2017. Notably, the volume of pediatric gastroenterology research increased rapidly across this time period. Over time there was a shift in the specific diseases represented in the most highly cited research. In addition, we observed that approximately one percent of author accounted for nearly one-third of the most highly cited research. Similar trends were noted for institutions and journals (4). Finally, pediatric gastroenterology research was generated by many investigators across a wide range of scientific disciplines.

In accordance with observed growth in research across most medical disciplines, our findings demonstrated a vast increase in literature production in pediatric gastroenterology since 1970. An analysis of Medline publication data over time indicates an average annual growth rate of pediatric gastroenterology citations of 52.0% since 1970, compared with an average growth rate of 6.3% for general pediatric citations. This overall increase is likely multifactorial due in part to digital technologies, which increased the efficiency of information retrieval and transmission and created a new space for online academic publication (5). However, there was a significantly faster rate of growth in pediatric gastroenterology compared to the field of pediatrics in general; the reasons of this accelerated growth are not clear. We hypothesize that contributing factors could be the emergence of novel therapeutics specific to gastrointestinal diseases, the growth in absolute number of trained pediatric gastroenterologists over time, which has more than doubled in the past 15 years, and the increasing prevalence of emerging diseases within the field such as

obesity, nonalcoholic fatty liver disease, food allergy, and diseases of immune dysregulation (9–16).

Diseases most referenced during a particular time period seemed to parallel both the emergence of novel treatments and an increasing prevalence of specific clinical conditions. For example, with the advent of TPN in the late 1960s, nearly 14% of the most cited articles in the 1970's were about TPN or TPN-related complications such as cholestasis (17). Similarly, after successful immunosuppression with the introduction of cyclosporine in the 1980s, pediatric liver transplant centers rapidly developed across the country. Nearly 10% of the most cited articles from the 1980s and 1990s addressed issues associated with liver transplantation (18). Mirroring the increasing prevalence rates of obesity in the United States, an increasing number of top cited articles focused on obesity in the 1990s, a focus that persisted over subsequent decades (19). This focus was followed by highly-cited publications demonstrating the increasing recognition of obesity related co-morbidities, in particular related to liver morbidity of nonalcoholic fatty liver disease (NAFLD), now the most common chronic liver disease in children (10).

Of note, this bibliometric analysis highlighted the multidisciplinary nature of pediatric gastroenterology research. Among the most highly cited authors, many were researchers principally based in disciplines other than gastroenterology, such as epidemiology, endocrinology, or allergy and immunology. This may be in part due to differences in citation practices among subspecialty disciplines, but may also be a reflection of the innate complexity of gastrointestinal pathophysiology (5). The gastrointestinal tract is central in both delivery of nutrients and immunological responses to environmental triggers, acting simultaneously as a doorway and a barrier to the outside world. Additionally, the field of gastroenterology encompasses not only the gastrointestinal tract and its associated role in immunology and nutrition, but also includes complex metabolic processes of the liver and exocrine functions of the pancreas. As a result, problems arising in the gastrointestinal tract often present with multisystem manifestations, leading to the involvement of multiple subspecialties in their evaluation. Moreover, specific gastrointestinal disease processes with increasing prevalence such as EoE, NAFLD, pediatric obesity, and food allergies are conditions where management and comorbidities cross disciplinary boundaries. These emerging gastrointestinal conditions constituted nearly two-thirds of the most cited publications after 1990. Thus, further progress in pediatric gastroenterology is likely to depend upon broad collaborative efforts across multiple disciplines.

Governmental agencies, especially individual institutes of the National Institutes of Health, funded the majority of pediatric gastroenterology clinical and translational research, and play a critical role in the advancement of child health outcomes. Given that the prevalence of pediatric gastrointestinal diseases such as NAFLD, inflammatory bowel disease, eosinophilic esophagitis, and celiac disease is increasing, continued research efforts are needed (9,10,12,13). Moreover, multiple studies measuring the financial impact of disease have demonstrated a significant economic burden secondary to both acute and chronic pediatric gastrointestinal disease. In the United States for the year 2007, there were 4.2 billion dollars of emergency department charges due to pediatric gastrointestinal diseases alone (20). The financial impacts of chronic gastrointestinal disease in children such as IBD

and EoE are also substantial with annual costs of \$663 million and \$472 million respectively (21–24). Largest of all is the increasing prevalence and consequence of childhood obesity, with annual direct costs exceeding \$14.3 billion (25). Moreover, the complexity of chronic diseases in children is further demonstrated by data that consistently show that the cost of treatment for an individual child exceeds the cost of treatment for an individual adult (21, 23). Finally, many gastrointestinal disorders in adults have their origins in childhood via factors including epigenetics, nutrition, and adverse childhood experiences. Thus pediatric gastroenterology research has the potential for impact in both children and adults.

Allocating resources to ensure sustainable funding from governmental institutes is crucial to the continued advancement of care in pediatric gastroenterology. Yet in recent decades, there has been a decline in the availability of research dollars. Between 2003 and 2015, there was a 22% decrease in National Institute of Health research funding secondary to sequestration, decreasing research budgets, and inflationary losses (26). Moreover, NIH R01 equivalent annual funding limits for researchers have not increased in constant dollars since 1998 (27). The impact of these policies is particularly difficult for interdisciplinary fields, where the need for expertise in multiple subspecialties increases a project's research personnel costs. Within this financial climate, it is likely that funding from foundations and industry will play a larger role. The overall implication of shifting funding practices on both research questions and output is unknown.

The current bibliometric analysis of pediatric gastroenterology had notable strengths and limitations. The Web of Science database encompasses a broad geographical publication range and detailed citation metrics, and thus is among the most frequently used database in bibliometric studies (5, 29). Furthermore, the created list of search parameters was developed specifically for this study using the standard pediatric gastroenterology textbook (1). Limitations of the analysis are similar to those of other bibliometric studies and include inconsistency or inaccuracy of citation data, biased citation practices such as language and geographic biases inherent in databases used, and variation in citation practices between subspecialties (5, 30). As our study was limited to clinical and translational research, we did not address contributions to the field of pediatric gastroenterology from basic biomedical research. To do so would require a unique search strategy to capture the breadth of basic research studies that are applicable to pediatric gastroenterology with an appreciation that many of these are done by research scientists who are in other fields of study. It is also important to note that citation analysis is not necessarily a metric of study quality and is not the only methodology to assess research impact. (30) Furthermore, despite the comprehensive and thorough methodology utilized in this analysis, there may be a study that despite being highly cited was not identified. We encourage future studies to consider focusing on additional aspects of pediatric gastroenterology and/or the use of additional databases.

Pediatric gastroenterology research has undergone rapid growth over the past fifty years yielding numerous advancements in the management of gastrointestinal conditions in children. The temporal shift in disease focus and research populations evidenced in this study may reflect advances in diagnostics and treatment of established diseases and the emergence of novel disease processes. It may also be an indication that management of

emerging gastrointestinal diseases crosses disciplinary boundaries, broadening the appeal of gastrointestinal scholarship to a wider audience. The economic impact of childhood gastrointestinal conditions is significant, and further advancements will require continued research support for pediatric gastroenterology research, whether from traditional or nontraditional funding sources. An understanding of the historical trends of research and an awareness of its complexities and challenges may lay the groundwork future scholarship in pediatric gastroenterology.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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#### What Is Known

- Quantitative bibliometric evaluation of citation data is a research tool to identify research trends and scholarship with lasting impact.
- There has not been a bibliometric analysis of clinical and translational research in the field of pediatric gastroenterology.

#### What Is New

- Average annual growth rate for pediatric gastroenterology publications was 51.7%.
- In highest cited articles, age composition of study populations and diseases of interest have changed over time.
- Fewer than **5%** of authors and institutions accounted for one-third to one-half of top cited research articles.

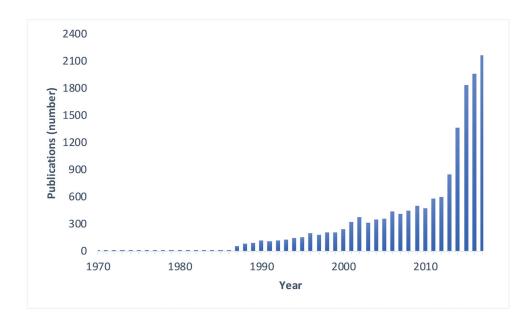




Table 1

Common Subjects of Pediatric Gastroenterology Research with the Highest Citation Index.

Subject		Ye	Year of Publication	on		Number of Research Articles
	1970–1979	1980-1989	6661-0661	2000-2009	2010-2017	
Obesity	4	3	8	26	6	47
Diarrhea	5	7	4	0	4	20
IBD	0	2	9	5	5	18
Food Allergy	0	0	5	5	L	17
Eosinophilic Esophagitis	0	0	2	4	8	14
Microbiome	4	0	0	5	9	15
Necrotizing Enterocolitis	4	4	1	2	2	13
Viral Hepatitis	2	6	4	0	0	12
Cystic Fibrosis	6	4	0	0	0	10
Liver Transplant	0	4	5	0	1	10
TPN	3	6	0	0	0	6
Cholestasis	8	0	0	0	0	8
NAFLD	0	0	2	2	4	8
Celiac Disease	1	1	1	0	3	7
Functional Abdominal Pain	0	2	3	0	1	6
Biliary Atresia	3	1	0	0	0	4
Jaundice	3	0	0	0	0	3

### Table 2

Top Ten Journals Containing the Most Highly Cited Articles in Pediatric Gastroenterology from 1970–2017.

Journal	Number of Articles	Citations
Journal of Pediatrics	31	4,522
Pediatrics	27	8,093
New England Journal of Medicine	18	13,385
Journal of Allergy and Clinical Immunology	16	5,987
Gastroenterology	16	4,897
JAMA-Journal of The American Medical Association	14	16,181
Lancet	12	4,761
American Journal of Clinical Nutrition	9	3,499
British Medical Journal	7	10,231
Journal of Pediatric Gastroenterology and Nutrition	6	1,952

#### Table 3

Institutions of Most Highly Cited Research Publications in Pediatric Gastroenterology from 1970–2017.

Institution	Location	Articles	Citations
Centers for Disease Control Prevention	Atlanta, Georgia	19	26,770
University of London	London, England	15	13,038
University of California, San Diego	La Jolla, California	12	4,120
Harvard University	Boston, Massachusetts	12	3,627
Baylor College of Medicine	Houston, Texas	11	3,472
Children's Hospital of Philadelphia	Philadelphia, Pennsylvania	11	3,317
Cincinnati Children's Hospital Medical Center	Cincinnati, Ohio	10	6,141
Hospital for Sick Children	Toronto, Ontario	9	2,428
Johns Hopkins University	Baltimore, Maryland	9	4,510
Pennsylvania State University	Centre County, Pennsylvania	8	1,527