

## Temporal trends in inflammatory bowel disease publications over a 19-years period

Yael Weintraub, Francis B Mimouni, Shlomi Cohen

Yael Weintraub, Shlomi Cohen, Pediatric Gastroenterology and Nutrition Unit, "Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Tel Aviv 64239, Israel

Yael Weintraub, Shlomi Cohen, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv 64239, Israel

Francis B Mimouni, Department of Pediatrics, "Dana-Dwek" Children's Hospital, Tel Aviv Medical Center and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv 64239, Israel

Francis B Mimouni, Division of Neonatology, Shaare Zedek Medical Center, Jerusalem 93722, Israel

**Author contributions:** Mimouni FB and Cohen S designed the research; Weintraub Y collected the data; Mimouni FB and Cohen S analyzed the data; and Mimouni FB, Cohen S and Weintraub Y wrote the paper.

**Correspondence to:** Shlomi Cohen, MD, Pediatric Gastroenterology and Nutrition Unit, "Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, 6 Weizman Street, Tel Aviv 64239, Israel. [shlomico@tlvmc.gov.il](mailto:shlomico@tlvmc.gov.il)

Telephone: +972-3-6974519 Fax: +972-3-6974181

Received: April 1, 2014 Revised: April 29, 2014

Accepted: July 24, 2014

Published online: November 28, 2014

### Abstract

**AIM:** To determine whether temporal changes occurred in the pediatric *vs* adult inflammatory bowel disease (IBD), both in terms of number and type of yearly published articles.

**METHODS:** We aimed to evaluate all PubMed-registered articles related to the field of IBD from January 1, 1993 and until December 31, 2011. We searched for articles using the key words "inflammatory bowel disease" or "Crohn's disease" or "ulcerative colitis" or "undetermined colitis", using the age filters of "child" or "adult". We repeated the search according to the total number per year of articles per type of article, for each year of the specified period. We studied randomized controlled trials, clinical trials, case reports, meta-anal-

yses, letters to the editor, reviews, systematic reviews, practice guidelines, and editorials.

**RESULTS:** We identified 44645 articles over the 19 year-period. There were 8687 pediatric-tagged articles *vs* 19750 adult-tagged articles. Thus 16208 articles were unaccounted and not assigned a "pediatric" or "adult" tag by PubMed. There was an approximately 3-fold significant increase in all articles recorded both in pediatric and adult articles. This significant increase was true for nearly every category of article but the number of clinical trials, meta-analysis, and randomized controlled trials increased proportionally more than the number of "lower quality" articles such as editorials or letters to the editor. Very few guidelines were published every year.

**CONCLUSION:** There is a yearly linear increase in publications related to IBD. Relatively, there are more and more clinical trials and higher quality articles.

© 2014 Baishideng Publishing Group Inc. All rights reserved.

**Key words:** Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Randomized clinical trial; Meta-analysis

**Core tip:** Since the first description of inflammatory bowel disease (IBD) in the 1700's, thousand of articles have been published on the topic. This study aimed to determine whether temporal changes occurred in IBD literature. We identified 44645 articles over the 19 year-period starting in 1993. There was an approximately 3-fold increase in all pediatric and adults articles recorded. This significant increase was true for nearly every category of articles but clinical trials, meta-analysis, and randomized controlled trials increased proportionally more than the number of "lower quality" articles such as editorials or letters to the editor. Very few guidelines were published every year.

Weintraub Y, Mimouni FB, Cohen S. Temporal trends in inflammatory bowel disease publications over a 19-years period. *World J Gastroenterol* 2014; 20(44): 16745-16749 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v20/i44/16745.htm> DOI: <http://dx.doi.org/10.3748/wjg.v20.i44.16745>

## INTRODUCTION

In a 2005 article it was noted that a total of 8.1 million journal articles were recorded by MEDLINE between 1978 and 2001<sup>[1]</sup>. During that period, the annual number of MEDLINE articles increased by a factor of 1.46, from an average of 272344 to 442756 per year<sup>[1]</sup>. Such numbers indicate the enormous burden placed upon physicians and scientists in their attempt to stay up to date with their professional literature<sup>[1-3]</sup>. This appears to be a universal phenomenon, already demonstrated in various fields of medicine<sup>[4-9]</sup>.

Inflammatory bowel diseases (IBDs) were described as early as in the 1700's by Giovanni Battista Morgagni<sup>[10]</sup>. They were however recognized as a distinct pathological entity only after the description by Crohn, who reported in 1932 a case series of 14 patients with what he called "terminal ileitis"<sup>[11]</sup>. Since then, thousands of articles have been published on IBD, and the recent development of biological, anti-inflammatory drugs has created a huge field of basic and clinical science trials<sup>[12-21]</sup>.

The aim of the current study was to determine whether temporal changes occurred in pediatric *vs* adult IBD literature, both in terms of number and type of yearly published articles.

## MATERIALS AND METHODS

We used the Internet address: <http://www.ncbi.nlm.nih.gov/entrez> in order to evaluate PubMed articles registered from January 1, 1993 and until December 31, 2012 (a 20 year period). It became obvious at the time of the search on August 13-14, 2013 that not all 2012 articles were recorded in PubMed, thus we elected to remove 2012 and concentrated our search on a 19 years period. We focused upon articles in the field of IBD. In order to do so, we searched for articles using the key words "inflammatory bowel disease" or "Crohn's disease" or "ulcerative colitis" or "undetermined colitis", without species limitations, and using the filters of "ages: child-birth-18 years" (pediatric studies) or "adult: +19 years" (adult studies). We repeated the search year by year according to the total number per year of articles per type of article, for the 19 years of the specified period, analyzed year by year. The type of article was defined according to PubMed own filter. In particular, we studied randomized controlled trials (RCT), clinical trials, case reports, meta-analysis, letters to the editor, reviews, systematic reviews, practice guidelines, and editorials. In order to verify that the categorization and tagging offered automatically by PubMed was accurate, we used a random

sample of 10 studies each year, and in 100% of the cases, PubMed's categorization was found to be accurate.

## Statistical analysis

The Minitab version 16 (Minitab Inc., State College, PA) was used for statistical analyses. We used linear regression to study trends over time. A *P*-value of < 0.05 was considered significant.

## RESULTS

Over the 19 year-period, when we used no age filter, we identified 44645 articles. When we used pediatric *vs* adult filters, we identified 8687 pediatric-tagged articles *vs* 19750 adult-tagged articles. Thus 16208 articles were unaccounted for, and represent articles that were not assigned a "pediatric" or "adult" tag by PubMed. By category studied, when the age filter was used, there were 976 pediatric and 2242 adult clinical trials, 348 pediatrics and 968 adult RCTs, 41 pediatric and 70 adult meta-analysis, 838 pediatric and 1359 adult reviews, 26 pediatric and 32 adult guidelines, 1248 pediatric and 6121 adult case reports, 80 pediatric and 47 adult editorials, and 384 pediatric and 1531 adult Letters. The total number of articles per year as defined exceeds that provided by PubMed, because of overlap among certain categories of articles (for instance all RCTs are recorded also within clinical trials).

When pediatric and adult articles trends over the years were compared by linear regression, there was a significant increase in all articles recorded, from approximately 292 pediatric articles/year in 1993 to 917 in 2011 (*i.e.*, approximately a 3 fold increase,  $r^2 = 0.86$ ,  $P = 0.001$ ), and from 633 adult articles/year in 1993 to 1,939 in 2011 (also approximately a 3 fold increase,  $r^2 = 0.91$ ,  $P = 0.001$ ) (Figure 1A). There was a significant increase in clinical trials recorded, from approximately 16 pediatric articles/year in 1993 to 105 in 2011 (*i.e.*, approximately a 6.5 fold increase,  $r^2 = 0.79$ ,  $P = 0.001$ ), and from 42 adult articles/year in 1993 to 215 in 2011 (approximately a 5 fold increase,  $r^2 = 0.88$ ,  $P = 0.001$ ). There was a significant increase in RCT recorded, from approximately 12 pediatric articles/year in 1993 to 33 in 2011 (*i.e.*, approximately a 3 fold increase,  $r^2 = 0.70$ ,  $P = 0.001$ ), and from 26 adult articles/year in 1993 to 80 in 2011 (approximately a 3 fold increase,  $r^2 = 0.75$ ,  $P = 0.001$ ). There was a significant increase in meta-analysis recorded, from 0 pediatric articles/year in 1993 to 5 in 2011 (*i.e.*,  $r^2 = 0.45$ ,  $P = 0.002$ ), and from 0 adult articles/year in 1993 to 12 in 2011 ( $r^2 = 0.76$ ,  $P = 0.001$ ) (Figure 1B). There was no significant increase in guidelines recorded, from approximately 0 pediatric articles/year in 1993 to 2 in 2011 ( $r^2 = 0.19$ ,  $P = 0.06$ ), while the rise in the number of adult articles (0 in 1993 to 3 in 2011) reached statistical significance ( $r^2 = 0.22$ ,  $P < 0.04$ ). There was a significant increase in reviews recorded, from approximately 34 pediatric articles/year in 1993 to 67 in 2011 (*i.e.*, approximately a 2 fold increase,  $r^2 = 0.69$ ,  $P = 0.001$ ), and from 57 adult articles/year in 1993 to 79 in 2011 (approx-

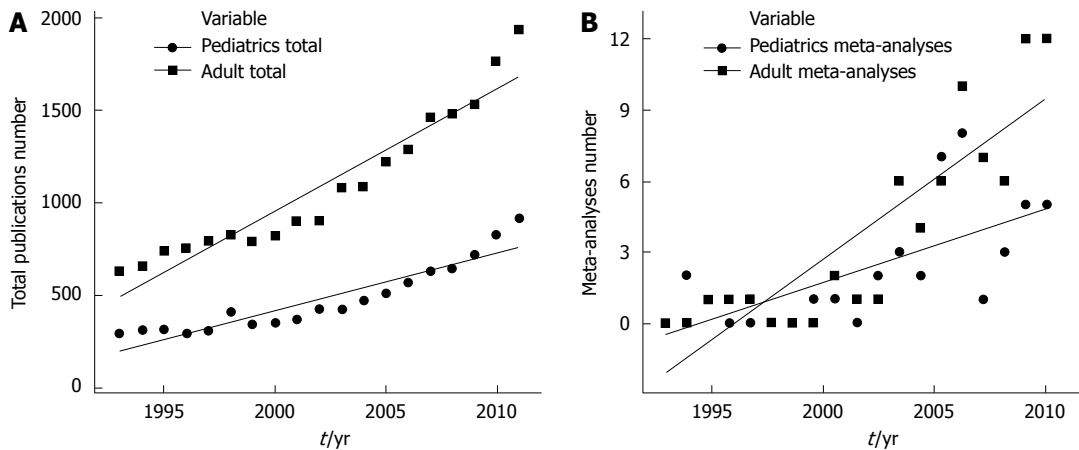


Figure 1 Total number of pediatric and adult articles vs year of publication (A) and number of pediatric and adult meta-analysis vs year of publication (B).

mately a 1.4 fold increase,  $r^2 = 0.42$ ,  $P = 0.003$ ). There was a significant increase in case reports recorded, from approximately 47 pediatric articles/year in 1993 to 95 in 2011 (*i.e.*, approximately a 2 fold increase,  $r^2 = 0.79$ ,  $P = 0.001$ ), and from 205 adult articles/year in 1993 to 448 in 2011 (approximately a 2.2 fold increase,  $r^2 = 0.94$ ,  $P = 0.001$ ). There was a significant increase in RCT recorded, from approximately 12 pediatric articles/year in 1993 to 33 in 2011 (*i.e.*, approximately a 3 fold increase,  $r^2 = 0.70$ ,  $P = 0.001$ ), and from 26 adult articles/year in 1993 to 80 in 2011 (approximately a 3 fold increase,  $r^2 = 0.75$ ,  $P = 0.001$ ). There was a significant increase in letters recorded, from approximately 13 pediatric articles/year in 1993 to 38 in 2011 (*i.e.*, approximately a 3 fold increase,  $r^2 = 0.60$ ,  $P = 0.001$ ), and from 42 adult articles/year in 1993 to 179 in 2011 (approximately a 4.3 fold increase,  $r^2 = 0.82$ ,  $P = 0.001$ ). There was no significant increase in editorials recorded, from approximately 3 pediatric articles/year in 1993 to 7 in 2010 (with a drop to 1 in 2011), and no significant change in adult articles 2/year in 1993 and 1 in 2011.

## DISCUSSION

As hypothesized, we found a significant increase in the IBD-related yearly number of publications. Overall, the yearly number of both pediatric and adult-related articles increased in a similar manner (an approximate 3-fold increase) during this 19 years period, while a little less than a third of the articles were solely related to children. The number of clinical trials increased disproportionately more than other types of articles (a 6.5-fold increase in pediatric literature and a 5-fold increase in adult literature), however the rise in yearly number of RCTs was similar in children and adults, and similar to the overall trend (a 3-fold increase). Since in terms of strength of evidence, RCTs are considered as “stronger” than non-randomized clinical trials<sup>[22-25]</sup>, we speculate that the quality of the articles published in the field of IBD may not have increased more than what was expected from the overall increase. However, due to the large number of articles that

we retrieved, we were not able to determine what kind of papers (*i.e.*, clinical trial for biological therapy, *etc.*) in each category was increased, which is a limitation of this study. Meta-analysis also considered as very high quality in terms of evidence-based-medicine<sup>[22]</sup>, increased apparently dramatically, but this increase is somewhat artificially inflated from the fact that prior to 2000 these articles were practically inexistent, rising from nearly 0 to 5 per year in pediatric literature and 12 per year in the adult literature. Meta-analysis in general cannot be conducted without a sufficient cumulative sample size, often reached only by combining many studies, thus we speculate that in the future, we will see even more of such articles published.

At the other end of the spectrum in terms of strength of evidence, case reports increased by a factor of 2 both in pediatric and adult articles, and editorials did not increase at all. Case reports represent a low level of evidence<sup>[22]</sup> and bring very little academic credit to their authors, which may explain why they did not increase in numbers proportionally to the rest of the IBD literature. This is even truer for Editorials, and we suspect that editors of medical journals are less likely than in the past to seek for the publication such articles, which often represent only the opinion of their author.

In conclusion, there is a linear increase in the number of yearly publications related to the field of IBD. It was not in the scope of this article to compare the rate of increase to that of articles in other fields of gastroenterology, or other fields of medicine. Nevertheless, the increase was significant in terms of the amount of time that a clinician may invest in his/her continuing education through the reading of IBD-specific literature. However, it appears that there are more and more of clinical trials and higher quality articles. We suggest that professional societies related to IBD, such as European Society for Paediatric Gastroenterology Hepatology and Nutrition, European Crohn's and Colitis Organisation, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, Crohn's and Colitis Foundation of America invest more time in such an endeavour, which might require improving their level of organization

and coordination.

## COMMENTS

### Background

An enormous burden is placed upon physicians and scientists in their attempt to stay up to date with their professional literature. Since the initial description of inflammatory bowel diseases (IBD) in the 1700's, thousand of articles have been published on the topic, and the recent development of biological, anti-inflammatory drugs has created a huge field of basic and clinical science trials. Thus, authors aimed to determine whether temporal changes occurred in pediatric and adult IBD literature over the past 2 decades.

### Research frontiers

In this study, they aimed to verify whether the yearly number of high quality articles (such as clinical trials, meta-analysis, and randomized controlled trials) increased relatively more than that of lower quality articles (such as editorials or letters to the editor).

### Innovations and breakthroughs

This article is the first that attempted to critically review trends of the IBD-related medical literature.

### Applications

This article points out to the fact that overall, the quality of IBD-related publications is increasing. However, authors noted that few guidelines are issued every year, which emphasizes the need for more investment in this endeavour by professional societies related to IBD.

### Terminology

The analysis of literature trends is an important tool for the global comprehension of a given medical field in terms of research activity and quality.

### Peer review

Closer collaboration between experts and experts societies is necessary to enable the publication of up-to-date, evidence-based guidelines.

## REFERENCES

- 1 Druss BG, Marcus SC. Growth and decentralization of the medical literature: implications for evidence-based medicine. *J Med Libr Assoc* 2005; **93**: 499-501 [PMID: 16239948]
- 2 Mimouni D, Pavlovsky L, Akerman L, David M, Mimouni FB. Trends in dermatology publications over the past 15 years. *Am J Clin Dermatol* 2010; **11**: 55-58 [PMID: 20000876 DOI: 10.2165/11530190-000000000-00000]
- 3 Tov AB, Lubetzky R, Mimouni FB, Alper A, Mandel D. Trends in neonatology and pediatrics publications over the past 12 years. *Acta Paediatr* 2007; **96**: 1080-1082 [PMID: 17524021]
- 4 Menahem S, Fink D, Mimouni FB. Trends in paediatric, neonatal, and adult cardiology publications over the past 10 years. *Cardiol Young* 2014; **24**: 297-302 [PMID: 23803313 DOI: 10.1017/S1047951113000292]
- 5 Akerman L, Hodak E, Pavlovsky L, Mimouni FB, David M, Mimouni D. Trends in dermatologic surgery research over the past decade. *Eur J Dermatol* 2010; **20**: 196-199 [PMID: 20167567 DOI: 10.1684/ejd.2010.0880]
- 6 Even-Or E, Sichel JY, Perez R, Mimouni FB. Pediatric and adult otorhinolaryngological publications: trends over 15 years (1993-2007). *Int J Pediatr Otorhinolaryngol* 2009; **73**: 1737-1741 [PMID: 19796827 DOI: 10.1016/j.ijporl.2009.09.012]
- 7 Leshem YA, Pavlovsky L, Mimouni FB, David M, Mimouni D. Trends in pemphigus research over 15 years. *J Eur Acad Dermatol Venereol* 2010; **24**: 173-177 [PMID: 19686325 DOI: 10.1111/j.1468-3083.2009.03390]
- 8 Pavlovsky L, Mimouni FB, Hodak E, David M, Mimouni D. From basic research to biological treatments: psoriasis publications over the past 15 years. *Clin Exp Dermatol* 2009; **34**: e91-e93 [PMID: 19438559 DOI: 10.1111/j.1365-2230.2008.03199]
- 9 Marom R, Lubetzky R, Mimouni FB, Ovental A, Mandel D, Cohen S. Secular trends in impact factor of breastfeeding research publications over a 20-year period. *Breastfeed Med* 2014; **9**: 98-100 [PMID: 24283959 DOI: 10.1089/bfm.2013.0090]
- 10 Kirsner JB. Historical aspects of inflammatory bowel disease. *J Clin Gastroenterol* 1988; **10**: 286-297 [PMID: 2980764]
- 11 Crohn BB, Ginzburg L, Oppenheimer GD. Regional ileitis: a pathologic and clinical entity. 1932. *Mt Sinai J Med* 2000; **67**: 263-268 [PMID: 10828911]
- 12 Hlavaty T, Letkovsky J. Biosimilars in the therapy of inflammatory bowel diseases. *Eur J Gastroenterol Hepatol* 2014; **26**: 581-587 [PMID: 24722561]
- 13 D'Haens GR, Sartor RB, Silverberg MS, Petersson J, Rutgeerts P. Future directions in inflammatory bowel disease management. *J Crohns Colitis* 2014; **8**: 726-734 [PMID: 24742736 DOI: 10.1016/j.crohns.2014.02.025]
- 14 Dassopoulos T, Sultan S, Falck-Ytter YT, Inadomi JM, Hanauer SB. American Gastroenterological Association Institute technical review on the use of thiopurines, methotrexate, and anti-TNF- $\alpha$  biologic drugs for the induction and maintenance of remission in inflammatory Crohn's disease. *Gastroenterology* 2013; **145**: 1464-78.e1-5 [PMID: 24267475 DOI: 10.1053/j.gastro.2013.10.046]
- 15 Turner D, Levine A, Escher JC, Griffiths AM, Russell RK, Dignass A, Dias JA, Bronsky J, Braegger CP, Cucchiara S, de Ridder L, Fagerberg UL, Hussey S, Hugot JP, Kolacek S, Kolho KL, Lionetti P, Paerregaard A, Potapov A, Rintala R, Serban DE, Staiano A, Sweeny B, Veerman G, Veres G, Wilson DC, Ruemmele FM. Management of pediatric ulcerative colitis: joint ECCO and ESPGHAN evidence-based consensus guidelines. *J Pediatr Gastroenterol Nutr* 2012; **55**: 340-361 [PMID: 22773060]
- 16 Ruemmele FM, Turner D. Differences in the management of pediatric and adult onset ulcerative colitis--lessons from the joint ECCO and ESPGHAN consensus guidelines for the management of pediatric ulcerative colitis. *J Crohns Colitis* 2014; **8**: 1-4 [PMID: 24230969 DOI: 10.1016/j.crohns.2013.10.006]
- 17 Van Assche G, Dignass A, Bokemeyer B, Danese S, Gionchetti P, Moser G, Beaugerie L, Gomollón F, Häuser W, Herlinger K, Oldenburg B, Panes J, Portela F, Rogler G, Stein J, Tilg H, Travis S, Lindsay JO. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 3: special situations. *J Crohns Colitis* 2013; **7**: 1-33 [PMID: 23040453 DOI: 10.1016/j.crohns.2012.09.005]
- 18 Feagan BG, Rutgeerts P, Sands BE, Hanauer S, Colombel JF, Sandborn WJ, Van Assche G, Axler J, Kim HJ, Danese S, Fox I, Milch C, Sankoh S, Wyant T, Xu J, Parikh A. Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2013; **369**: 699-710 [PMID: 23964932 DOI: 10.1056/NEJMoa1215734]
- 19 Sandborn WJ, Feagan BG, Rutgeerts P, Hanauer S, Colombel JF, Sands BE, Lukas M, Fedorak RN, Lee S, Bressler B, Fox I, Rosario M, Sankoh S, Xu J, Stephens K, Milch C, Parikh A. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med* 2013; **369**: 711-721 [PMID: 23964933 DOI: 10.1056/NEJMoa1215739]
- 20 D'Haens GR, Panaccione R, Higgins PD, Vermeire S, Gasull M, Chowder Y, Hanauer SB, Herfarth H, Hommes DW, Kamm M, Löfberg R, Quary A, Sands B, Sood A, Watermeyer G, Lashner B, Lémann M, Plevy S, Reinisch W, Schreiber S, Siegel C, Targan S, Watanabe M, Feagan B, Sandborn WJ, Colombel JF, Travis S. The London Position Statement of the World Congress of Gastroenterology on Biological Therapy for IBD with the European Crohn's and Colitis Organization: when to start, when to stop, which drug to choose, and how to predict response? *Am J Gastroenterol* 2011; **106**: 199-212; quiz 213 [PMID: 21045814 DOI: 10.1038/ajg.2010.392]
- 21 Hanauer SB, Feagan BG, Lichtenstein GR, Mayer LF, Schreiber S, Colombel JF, Rachmilewitz D, Wolf DC, Olson A, Bao W, Rutgeerts P. Maintenance infliximab for Crohn's



- disease: the ACCENT I randomised trial. *Lancet* 2002; **359**: 1541-1549 [PMID: 12047962]
- 22 **Evidence-based medicine.** (Retrieved on June 1, 2013). Available from: URL: [http://en.wikipedia.org/wiki/Evidence-based\\_medicine](http://en.wikipedia.org/wiki/Evidence-based_medicine)
  - 23 **National Cancer Institute.** Levels of evidence for adult and pediatric cancer treatment studies retrieved on April 28. Available from: URL: <http://www.cancer.gov/cancertopics/pdq/levels-evidence-adult-treatment/HealthProfessional/page2>
  - 24 **Higgins JPT**, Green S. Evaluating the strength of evidence provided by reviews that include non-randomized studies. Cochrane handbook for systematic reviews of interventions. Retrieved on April 28, 2014. Available from: URL: [http://handbook.cochrane.org/chapter\\_13/13\\_7\\_2evaluating\\_the\\_strength\\_of\\_evidence\\_provided\\_by\\_reviews.htm](http://handbook.cochrane.org/chapter_13/13_7_2evaluating_the_strength_of_evidence_provided_by_reviews.htm)
  - 25 **Ho PM**, Peterson PN, Masoudi FA. Evaluating the evidence: is there a rigid hierarchy? *Circulation* 2008; **118**: 1675-1684 [PMID: 18852378 DOI: 10.1161/CIRCULATIONAHA.107.721357]

**P- Reviewer:** Iizuka M, Negreanu L, Stocco G **S- Editor:** Gou SX  
**L- Editor:** A **E- Editor:** Wang CH





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



ISSN 1007-9327

