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A historical review of classic Helicobacter pylori publications in science citation index expanded

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Yuh-Shan Ho

Which Helicobacter pylori publications in the Web of Science are classic? This study identified classic papers by referring to the Science Citation Index Expanded, which covers 59,904 documents related Helicobacter pylori publications in the Web of Science from 1900 to 2016. The present paper lists classic Helicobacter pylori papers published between 1991 and 2007. Classic documents that have been cited at least 1,000 times from the Web of Science Core Collection were assessed regarding language of publication, document type publication outputs, distribution of outputs in journals and Web of Science categories, publications of authors, institutions, countries as well as citation life cycles of classic documents. An article published by Parsonnet et al. in 1991 obtained the highest number of citations from the Web of Science Core Collection during the period from its initial publication to the end of 2016. The most impactful article in 2016 was published by Uemura et al. in 2001 with 163 citations in 2016. In addition, results showed that three main research focuses in H. pylori study were gastric cancer, low-grade gastric lymphoma, and the CagA gene.

Keywords: Bibliometric, Citation, Classic article

1. Introduction

An early, highly cited Helicobacter pylori (H. pylori)-related article entitled “Prospective double-blind trial of duodenal-ulcer relapse after eradication of campylobacter pylori” [1] was published by Marshall et al. from Royal Perth Hospital and Curtin University in Australia. It was the first report regarding patients with both duodenal ulcer
and *Campylobacter pylori* infection. In 2005, Marshall and Warren won the Nobel Prize in physiology or medicine for their discovery of the bacterium *H. pylori* and its role in gastritis and peptic ulcer disease.

Scholars have studied classic papers [2] on various medical topics, for example liver transplantation [3], Guillain-Barré syndrome [4], lumbar spine surgery [5], melanoma [6], digestive disease [7], Tourette syndrome [8], Parkinson’s disease [9], orthopedic surgery [10], critical care medicine [11]. Classic papers have been used to teach organometallic chemistry [12], physiology [13], capillary filtration, and presentation skill development [14]. In recent years, the Web of Science Core Collection has presented classic publications with at least 1,000 total citations from publication to the latest recent year; presentations have been made for articles [15], single-author articles [16], and reviews [17] in the Science Citation Index Expanded. Classic articles in surgery [18] and psychology [19] have also been studied.

In this study, we analyzed classic *H. pylori*-related publications with at least 1,000 total citations from publication to the end of 2016 in the Web of Science Core Collection for citation histories, recent impact, journals, Web of Science categories, and publication performance of countries, institutions, and authors.

### 2. Methodology

The methodology used in this study was based on the Science Citation Index (SCI-EXPANDED) database, which indexed the Web of Science from Clarivate Analytics (updated on 10 August 2017). To identify *H. pylori* research, documents with Helicobacter pylori, *H. pylori*, campylobacter pylori, and *C. pylori* keywords [20] in the title, abstract, author keywords, or KeyWords Plus were downloaded. Selecting publications between 1900 and 2016, we found 59,904 *H. pylori*-related documents in SCI-EXPANDED. KeyWords Plus supplies additional search terms extracted from the titles of articles cited by authors in their bibliographies and footnotes in the ISI (now Clarivate Analytics) database, and substantially augments title-word and author-keyword indexing [21]. The documents that can only be found by KeyWords Plus are less likely to be related to *H. pylori*. In recent years, Ho’s group proposed that a “front page” filter [22,23,24] — which searches only documents with specified keywords on the front page, including only the title, abstract, and author keywords — might avoid introducing unrelated publications for analysis [22]. To determine which of these publications might be called classic publications, we used three indicators:

\[
C_{\text{year}} : \text{the number of citations in the Web of Science Core Collection in a particular year. } C_{2016} \text{ means the number of citations in 2016 only [25].}
\]

\[
TC_{\text{year}} : \text{the total number citations from publication to the end of the latest recent year [26,27]. It is 2016 (} TC_{2016} \text{) in this study.}
\]

\[
CPP_{\text{year}} : \text{citations per publication (} CPP_{2016} = TC_{2016}/TP \text{) [25].}
\]
To provide another filter, we defined classic \( H. \) pylori publications as those with \( TC_{2016} \geq 1,000 \) \[18,28\]. Finally, we found 22 publications (0.037% of the 59,897 total publications) to be classic publications in \( H. \) pylori-related research. Hard copies of these 22 publications were analyzed; these records were downloaded into spreadsheet software, and additional coding was manually performed using Microsoft Excel 2013 for analysis \[29\]. In subsequent analysis, publications originating from England, Scotland, Northern Ireland, and Wales were classified as being from the United Kingdom \[30\]. The impact factor (\( IF_{2016} \)) as reported in Journal Citation Reports 2016 was then determined for each journal that published classic publications.

3. Results and Discussion

The “front page” filter \[22\] was used to improve bias from KeyWords Plus in the Web of Science. It was pointed that highly cited articles unrelated to a relevant study topic can be analyzed if the analyst uses KeyWords Plus \[31\]. Another possible bias is that a search may include \( H. \) pylori publications that do not include keywords such as Helicobacter pylori, \( H. \) pylori, campylobacter pylori, and \( C. \) pylori on the front page. Some papers that are related to \( H. \) pylori may not have the expected keywords on their front pages. All of 22 classic \( H. \) pylori publications (\( TC_{2016} \geq 1,000 \)) were checked by a senior gastroenterologist to avoid detectable bias. One example was an article entitled “Inference of population structure using multilocus genotype data: linked loci and correlated allele frequencies” \[32\] that had a \( TC_{2016} \) of 3,992. In the most highly cited article, authors described extensions to the method of Pritchard et al., and \( H. \) pylori was an example, but this article was not focused on \( H. \) pylori research. In the article “C-reactive protein in wealthy subjects: Associations with obesity, insulin resistance, and endothelial dysfunction — A potential role for cytokines originating from adipose tissue?” \[33\], cytokines constituted the main research topic, but \( H. \) pylori was mentioned in passing. Similarly, in the article “The genome sequence of the food-borne pathogen Campylobacter jejuni reveals hypervariable sequences” \[34\], Campylobacter pylori was mentioned, but Campylobacter jejuni was the focus of the research. Associations between baseline values of four different circulating markers of inflammation, future risk of coronary heart disease, potential triggers of systemic inflammation, and other markers of inflammation were presented in “Low-grade inflammation and coronary heart disease: Prospective study and updated meta-analyses” \[35\]. We concluded that no strong associations of these factors with Helicobacter pylori were observed. In total, 18 classic \( H. \) pylori publications, including 15 articles, two reviews, one note, and one proceedings paper were further studied.

3.1 Language of Publication and Document Type

We found that 18 classic \( H. \) pylori publications (\( TC_{2016} \geq 1,000 \)) were published in SCI-EXPANDED between 1991 and 2007. All classic publications were published in English. The average value of \( TC_{2016} \) was 1,543 and the maximal value \( TC_{2016} \) was 2,964. The 18
classic publications were found within four Web of Science document types. Table 1 lists characteristics of document types. Most documents (83% of the 18 classic publications) were articles. The average number of authors per publication (APP) was 12; the average number of citations per publication (CPP\textsubscript{2016}) was 1,558. Since the discovery of \textit{H. pylori} in the human stomach, infection by these bacteria has been shown to be strongly associated with gastric lesions, including chronic atrophic gastritis [36,37], intestinal metaplasia [38,39], and gastric cancer [39]. Epidemiological studies, in combination with results from animal models, confirm that eradication of \textit{H. pylori} effectively prevents gastric carcinogenesis [40,41], and mild gastritis without severe atrophy or intestinal metaplasia [41]. The classic proceedings paper entitled “\textit{Helicobacter pylori} infection and the development of gastric cancer” [39] in \textit{New England Journal of Medicine} by Uemura and other eight co-authors from Kure Kyosai Hospital and Fukuoka University in Japan had the highest CPP\textsubscript{2016}. In this proceedings paper, the authors concluded “Gastric cancer develops in persons infected with \textit{H. pylori} but not in uninfected persons.” But the CPP\textsubscript{2016} values of the reviews were found to be lower than those of any other document type. The APP values of the reviews were also much lower than those of other documents.

3.2 Publication Outputs

Starting in 2014, Ho’s group proposed a relationship between the annual number of highly cited articles and their citations per publication (CPP\textsubscript{year} = TC\textsubscript{year}/TP) by decades [42,43] and years [44]. Figure 1 depicts the aforementioned relationship, which indicates that four classic \textit{H. pylori} publications were found in 1991 whereas no classic publications were found in 1998, 2003, 2004, and 2005. The highest CPP\textsubscript{2016} for the publications occurred in 1997. This was attributed to the publication entitled “The complete genome sequence of the gastric pathogen \textit{Helicobacter pylori}” [45] with a TC\textsubscript{2016} of 2,606. This paper published the first complete genome of \textit{H. pylori}, which had been cultured from a gastritis patient in the United Kingdom. It general, time is typically required to accumulate citations for highly cited articles [24,46]. However time was not related to the accumulation of citations for classic \textit{H. pylori} publications. The striking and creative ideas of a classic publication might cause it to have a high TC\textsubscript{2016}.

3.3 Journal and Web of Science Category

Table 2 characterizes 18 classic \textit{H. pylori} papers in 10 journals in five Web of Science categories in SCI-EXPANDED, including general and internal medicine (9 papers; 50% of 18 publications), multidisciplinary sciences (4; 22%), oncology (3; 17%), one in biochemistry and molecular biology, and one in gastroenterology and hepatology. The \textit{New England Journal of Medicine} published the highest number of classic \textit{Helicobacter pylori} papers, namely five papers (28% of the 18 publications), including four articles, one proceedings
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paper, and one review. The New England Journal of Medicine also had the highest CPP\textsubscript{2016}, namely 1881, and an IF\textsubscript{2016} of 72.406. As expected, the classic publications were published in journals with high impact factors [47]. The Journal of Biological Chemistry had the lowest impact factor (IF\textsubscript{2016} = 4.125).

3.4 Collaborations

Among the classic Helicobacter pylori publications, seven publications (39\% of 18 publications) were international collaborations by 13 countries and 11 (61\%) were not international. Papers that were not international were published by researchers in advanced countries (the USA, the UK, Japan, and Italy). The average citations per publication (CPP\textsubscript{2016} = 1,550) for the seven international publications was slightly higher than that for the 11 noninternational publications (CPP\textsubscript{2016} = 1,539). The average number of authors for the international publications (16 authors) was greater than that for the noninternational publications (8.1 authors). Ho reported that a high percentage of the classic articles in SCI-EXPANDED had been published by single authors [15]. Similarly, few classic reviews in SCI-EXPANDED had multiple authors [17]. The USA had the highest rank in all six of these indicators, namely total publications (11 publications), country-independent publications (6), international publications (5), first-author publications (10), corresponding-author publications (10), and single-author publications (1). The UK ranked second in five indicators.

In total, 14 publications (78\% of 18 publications) were interinstitutional collaborations by 56 institutions and four (22\%) were institutionally independent publications by four institutions, namely Louisiana State University in the USA, Chiron Vaccines in Italy, University College and Middlesex School of Medicine in the UK, and University of Oxford in the UK. Vanderbilt University in USA published the most classic H. pylori publications (with four articles) and also ranked top in interinstitutional collaborations (4 articles) and first-author papers (3 articles). Only four institutions (including Vanderbilt University and Stanford University in the USA) published two corresponding-author papers.

3.5 Authors of the 18 Classic Helicobacter pylori Publications

In total, 18 classic H. pylori publications were authored by 164 authors from 60 institutions in 14 countries, including 16 first authors from 8 institutions in the USA, four in the UK, two in Germany, and one in each of Japan and Italy, respectively as well as 16 corresponding authors from eight institutions in the USA, four in the UK, and one in each of Germany, Italy, Japan, and Switzerland. Blaser from Vanderbilt University in the USA was the only classic author who published three classic H. pylori articles, including one first-author article and one corresponding-author article. Only two classic H. pylori papers were published by single authors, namely the article entitled “Human gastric carcinogenesis: A
multistep and multifactorial process — First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention” [48] in Cancer Research by Correa of Louisiana State University in the USA, and the review entitled “The global health burden of infection-associated cancers in the year 2002” [49] in International Journal of Cancer by Parkin of the University of Oxford in the UK. Table 3 shows that Vanderbilt University in the USA had four classic authors (first authors or corresponding authors): Blaser and Nomura each had one first-author classic article and one corresponding-author classic article; Cover had one corresponding-author classic article; and Atherton had one first-author classic article. Chiron Vaccines in Italy and University College London in the UK had two classic authors. Parsonnet from Stanford University in the USA was the only classic author who published two first-author and corresponding-author classic articles. Both Wotherspoon and Isaacson from University College London in the UK published one classic article and one classic note as first author and corresponding author.

3.6 The Lifespan of the 18 Classic Helicobacter pylori Publications

Table 4 lists 18 classic H. pylori publications (15 articles, 2 reviews, 1 proceedings paper, and 1 note). H. pylori infection is the paramount risk factor for the development of gastric cancer [39]. Seven of classic H. pylori publications study the relation between H. pylori and gastric cancer. In addition, H. pylori colonization is strongly associated with mucosa-associated lymphoid tumors [50,51], and eradication of H. pylori often leads to improvement in tumor histology [52]. Three classic H. pylori publications explore the relation between H. pylori infection and low-grade gastric lymphoma [50,51,53].

Three classic publications report the role of cytotoxin-associated antigen A (CagA) in the pathogenesis of H. pylori [54,55,56]. Infection with strains of H. pylori that carrying the CagA gene is associated with gastric carcinoma [57]. Many of the alterations in gastric epithelial cells caused by H. pylori are attributable to CagA, which is secreted and translocated into cells through a type IV secretion system [58].

Figure 2 lists the histories of citations of the top ten high-impact classic H. pylori publications in SCI-EXPANDED in 2016 (C_{2016} ≥ 36). Only four of the 18 classic H. pylori publications, namely Uemura et al., [39] with a C_{2016} of 163, Parkin [49] with a C_{2016} of 130, Correa [48] with a C_{2016} of 105, and Suerbaum and Michetti [59] with a C_{2016} of 101 had high impact values in the most recent year. All these studies discussed chronic infection with H. pylori as a cause of gastric cancer. The discovery of H. pylori in 1983 [60,61] and subsequent demonstration that it was the main cause of gastritis culminated the long search for the cause of gastritis, which had long been known to be closely associated with gastric atrophy and with gastric cancer [39]. H. pylori was the first bacterium linked to human cancer [62] and was classified as a group 1 carcinogen by the International Agency for Research on Cancer in 1994 (IARC Helicobacter pylori Working Group, 2014) [63].
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Figure 3 shows the top ten highly cited H. pylori classic publications in SCI-EXPANDED, with $TC_{2016} > 1,360$. Since the classic article entitled “The complete genome sequence of the gastric pathogen Helicobacter pylori” [45] was published in 1997, the number of citations of this article have increased rapidly; the rate of new citations reached a peak in 1998. The publication of the genome sequences of H. pylori opened new avenues for research in the molecular biology of this gastric pathogen, and much attention has been paid to topics related to genomic and postgenomic analysis, which has contributed enormously to our understanding of the pathogenesis of H. pylori infection [64].

Classic articles entitled “Helicobacter pylori infection and the development of gastric cancer” [39], “Human gastric carcinogenesis: A multistep and multifactorial process — First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention” [48], and “Helicobacter pylori infection and the risk of gastric carcinoma” [37] were ranked in the top five for both $TC_{2016}$ and $C_{2016}$. These articles had high impact values in 2016 and were highly cited classic articles. The study topic of gastric cancer increased gradually and did not fluctuate notably in the study periods, which implies that the development of H. pylori research in gastric cancer was basically steady and concentrated over the past 16 years.

4. Conclusion

In total, 18 classic H. pylori publications were reviewed in this study. They were mainly published in the New England Journal of Medicine; for most of them, the Web of Science category was “general,” and the research area was “internal medicine.” English was the only language used in these publications. The USA published the most classic publications, followed by the UK. Vanderbilt University in the USA held the highest rank. Blaser from Vanderbilt University was the only classic author who published three classic papers. The most three common research fields of class H. pylori publications were gastric cancer, low-grade gastric lymphoma, and the CagA gene. It can be concluded that research on these topics will remain a crucial direction of H. pylori research in the future.

Table 1

Characteristics of document type

<table>
<thead>
<tr>
<th>Document type</th>
<th>$TP$</th>
<th>%</th>
<th>$AU$</th>
<th>$APP$</th>
<th>$TC_{2016}$</th>
<th>$CPP_{2016}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Article</td>
<td>15</td>
<td>83</td>
<td>173</td>
<td>12</td>
<td>23,824</td>
<td>1,588</td>
</tr>
<tr>
<td>Review</td>
<td>2</td>
<td>11</td>
<td>3</td>
<td>1.5</td>
<td>2,603</td>
<td>1,302</td>
</tr>
<tr>
<td>Note</td>
<td>1</td>
<td>5.6</td>
<td>4</td>
<td>4.0</td>
<td>1,350</td>
<td>1,350</td>
</tr>
<tr>
<td>Proceedings paper</td>
<td>1</td>
<td>5.6</td>
<td>9</td>
<td>9.0</td>
<td>2,182</td>
<td>2,182</td>
</tr>
</tbody>
</table>

$TP$: number of publications; $AU$: number of authors; $APP$: number of authors per publication; $TC_{2016}$: the total number of citations from Web of Science Core Collection since publication to the end of 2016; $CPP_{2016}$: number of citations ($TC_{2016}$) per publication ($TP$).
Table 2
Characteristics of 10 journals.

<table>
<thead>
<tr>
<th>Journal</th>
<th>TP (%)</th>
<th>TC&lt;sub&gt;2016&lt;/sub&gt;</th>
<th>CPP&lt;sub&gt;2016&lt;/sub&gt;</th>
<th>IF&lt;sub&gt;2016&lt;/sub&gt;</th>
<th>Web of Science category</th>
<th>Research area</th>
</tr>
</thead>
<tbody>
<tr>
<td>New England Journal of Medicine</td>
<td>5 (28)</td>
<td>9405</td>
<td>1881</td>
<td>72.406</td>
<td>general and internal medicine</td>
<td>general and internal medicine</td>
</tr>
<tr>
<td>Nature</td>
<td>3 (17)</td>
<td>5412</td>
<td>1804</td>
<td>40.137</td>
<td>multidisciplinary sciences</td>
<td>science and technology - other topics</td>
</tr>
<tr>
<td>Cancer Research</td>
<td>2 (11)</td>
<td>2906</td>
<td>1453</td>
<td>9.122</td>
<td>Oncology</td>
<td>oncology</td>
</tr>
<tr>
<td>Lancet</td>
<td>2 (11)</td>
<td>2924</td>
<td>1462</td>
<td>47.831</td>
<td>general and internal medicine</td>
<td>general and internal medicine</td>
</tr>
<tr>
<td>British Medical Journal</td>
<td>1 (5.6)</td>
<td>1091</td>
<td>1091</td>
<td>20.785</td>
<td>general and internal medicine</td>
<td>general and internal medicine</td>
</tr>
<tr>
<td>Gut</td>
<td>1 (5.6)</td>
<td>1110</td>
<td>1110</td>
<td>16.658</td>
<td>gastroenterology and hepatology</td>
<td>gastroenterology and hepatology</td>
</tr>
<tr>
<td>International Journal of Cancer</td>
<td>1 (5.6)</td>
<td>1238</td>
<td>1238</td>
<td>6.513</td>
<td>Oncology</td>
<td>oncology</td>
</tr>
<tr>
<td>JAMA-Journal of the American Medical Association</td>
<td>1 (5.6)</td>
<td>1264</td>
<td>1264</td>
<td>44.405</td>
<td>general and internal medicine</td>
<td>general and internal medicine</td>
</tr>
<tr>
<td>Journal of Biological Chemistry</td>
<td>1 (5.6)</td>
<td>1066</td>
<td>1066</td>
<td>4.125</td>
<td>biochemistry and molecular biology</td>
<td>biochemistry and molecular biology</td>
</tr>
<tr>
<td>Proceedings of the National Academy of Sciences of the United States of America</td>
<td>1 (5.6)</td>
<td>1361</td>
<td>1361</td>
<td>9.661</td>
<td>multidisciplinary sciences</td>
<td>science and technology - other topics</td>
</tr>
</tbody>
</table>

TP: total number of classic papers; TC<sub>2016</sub>: the total number of citations from Web of Science Core Collection since publication to the end of 2016; CPP<sub>2016</sub>: number of citations (TC<sub>2016</sub>) per publication (TP); IF<sub>2016</sub>: impact factor in 2016.
### Table 3
First authors and corresponding authors of the 18 classic *Helicobacter pylori* publications.

<table>
<thead>
<tr>
<th>Authors</th>
<th>TP</th>
<th>FP</th>
<th>RP</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.J. Blaser</td>
<td>3</td>
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<td>Vanderbilt University, USA</td>
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<tr>
<td>T.L. Cover</td>
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<td>P.G. Isaacson</td>
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<td>0</td>
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<td>University College London, UK</td>
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<td>A. Nomura</td>
<td>2</td>
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<td>1</td>
<td>Vanderbilt University, USA</td>
</tr>
<tr>
<td>J. Parsonnet</td>
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<td>2</td>
<td>2</td>
<td>Stanford University, USA</td>
</tr>
<tr>
<td>A.C. Wotherspoon</td>
<td>2</td>
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<td>0</td>
<td>University College London, UK</td>
</tr>
<tr>
<td>R.A. Alm</td>
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<td>1</td>
<td>1</td>
<td>Astra Research Center Boston, USA</td>
</tr>
<tr>
<td>J.C. Atherton</td>
<td>1</td>
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<td>0</td>
<td>Vanderbilt University, USA</td>
</tr>
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<td>S. Censini</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>Chiron Vaccines, Italy</td>
</tr>
<tr>
<td>P. Correa</td>
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<td>University of Michigan, USA</td>
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</tbody>
</table>

*TP*: total number of classic publications; *FP*: number of first-author classic publications; *RP*: number of corresponding-author classic publications.
### Table 4
The 18 classic *Helicobacter pylori* publications in Science Citation Index Expanded

<table>
<thead>
<tr>
<th>Rank <em>(TC\textsubscript{2016})</em></th>
<th>Rank <em>(C\textsubscript{2016})</em></th>
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<th>Publication information</th>
</tr>
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<table>
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<th>Page</th>
<th>No.</th>
<th>Type</th>
<th>Article Title</th>
<th>Authors</th>
<th>Journal Name / Volume</th>
</tr>
</thead>
</table>


TC_{2016}: the total number of citations from Web of Science Core Collection since its date of publication to the end of 2016; C_{2016}: the total number of citations in 2016 only.

**Figure 1**

Distribution of number of classic publications and their citations per publication by year.
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Figure 2
The top ten high impact *Helicobacter pylori* classic publications in SCI-EXPANDED in 2016

Figure 3
The top ten highly cited *Helicobacter pylori* classic publications in SCI-EXPANDED with $TC_{2016} > 1,360$
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