Growing Trend of China’s Contribution to Global Diabetes Research

A Systematic Literature Review

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Abstract: China, as a rapidly developing country with the largest population in the world, is playing an increasingly important role in diabetes research. There are >10,000 diabetes doctors who care for a large population of diabetic patients. The quantity and quality of research on diabetes from 3 major regions of China, including Mainland China (ML), Taiwan (TW), and Hong Kong (HK), is unknown. We aimed to analyze the contributions of each of these 3 regions to diabetes research.

Articles on diabetes originating from ML, TW, and HK that were published from 2005 to 2014 were retrieved from the Web of Science. The quantity of articles, citations, article types, and articles published in high-impact journals were analyzed.

A total of 9302 articles were retrieved from the 3 regions of China. There were 6775 from ML, 1993 from TW, and 534 from HK, with an increasing trend in publications from 2005 to 2014. After 2006, the number of publications from ML exceeded TW and HK. The largest total number of citations (48,296) was from ML. The highest mean citations, however, were from HK (15.90). PLoS One was the most popular journal in all 3 regions. The greatest number of RCTs, clinical trials, meta-analyses, and articles published in high-impact journals were from ML.

There has been a significant increase in the number of articles published on diabetes research from China during the past 10 years. Most of the articles were published by authors in ML, and an increasing trend began in 2006. HK had the highest quality research output in terms of mean citations per article.

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METHODS

Search Strategy

The Research Ethics Committee of Guang’anmen Hospital approved this study. Our study was based on previous publications.14–27 We used the Web of Science database to carry out a computerized search for publications. The search was performed on April 12, 2015. We chose Web of Science because it is the world’s leading database for citation information and other academic impact information. Also, it has been widely used in studies that are similar to ours. The search terms...
“diabetes” or “diabetic” were used as the topic of the search and the publication years were limited to 2005 to 2014. The criteria for inclusion were as follows: the papers were original articles and reviews; the study was related to diabetes and its comorbidities; the authors were from Mainland China, Taiwan, or Hong Kong; the year of publication was during 2005 and 2014. The criteria for exclusion were publications of letters, editorials, and corrections. The source region was based on the “Reprint Address” for each article. Articles from the 3 regions of China were selected and recorded. Refining conditions were address = (Taiwan); address = (Hong Kong); and address = (China NOT Hong Kong NOT Taiwan). In addition, according to the latest update of Essential Science Indicators, the top 5 countries listed by articles (i.e., United States, China, Germany, Japan, and the United Kingdom) were also searched for comparisons.

Data Extraction
To maintain the focus on diabetes research, article selection and data extraction were performed by 2 independent reviewers. Discussion was used to resolve disagreements. A third reviewer was consulted if a consensus was not met between the 2 initial reviewers. The quantity of research output was the number of publications found in the 10-year period. The citation reports of articles were used as an assessment of the quality of the research. The total number of articles, total number of citations, and mean number of citations for each article were recorded for ML, TW, and HK. The journals that were used most often for publication were determined for each region, and the quantity of articles published in high-impact journals in the 3 regions was also analyzed. We determined the impact factor (IF) ≥ 6 as high-impact journals, according to Journal Citation Reports in 2013 established by the Institute for Scientific Information. Also, the impact factor for publications in the subject categories of “endocrinology and metabolism” and the 4 most important general medicine journals including The New England Journal of Medicine, Lancet, JAMA (Journal of the American Medical Association), and BMJ (British Medical Journal) were also analyzed. Based on the previous study, the research type was divided into basic research, clinical study, review, and meta-analysis. The clinical studies included randomized controlled trial (RCT), nonrandomized controlled trial (non-RCT), cross-sectional study, cohort study, case-control study, case series, and case report.

Statistical Analysis
Descriptive statistics (e.g., mean and total) were used for analysis in this study. Significant changes in trends between 2005 and 2014 were assessed by regression analysis. SPSS version 19.0 (SPSS, Inc., Chicago, IL) was used for data analysis and \( P < 0.05 \) was considered as statistically significant.

RESULTS

Total Number of Articles
Figure 1 shows that in the past 10 years, the United States was the most productive (34,332), followed by China (9302), United Kingdom (9114), Japan (7046), and Germany (6224). The total number of articles from China exceeded Germany and Japan since 2009, and the United Kingdom since 2011. The total number of articles published on diabetes research in all 3 regions of China between 2005 and 2014 was 9302. Figure 2 shows the selection process. The total number of articles that were published annually increased significantly from 2005 to 2014 (205–2026; \( P = 0.000 \)), which was a 9.88-fold increase. ML published the most articles (6775/9302, 72.83%), with Taiwan following at 1993/9302 (21.43%) and with Hong Kong publishing the least number of articles (534/9302, 5.74%). The results for the total number of articles published are shown in Figure 3. The number of articles
published annually in ML significantly increased (from 79 to 1645; \( P = 0.000 \)), which was a 20.82-fold increase. TW showed an increase from 96 to 310 (\( P = 0.000 \)), which was 3.23-fold, and Hong Kong had an increase in the number of published articles from 30 to 71 (\( P = 0.001 \)), which was a 2.37-fold increase. As of 2006, the number of articles originating from ML exceeded the numbers from TW and HK (Table 1).

**Article Type**

Between 2005 and 2014, 4997 basic science articles, 3364 clinical studies, 457 reviews, and 484 meta-analyses originated from the 3 regions of China. ML published 4007 basic science articles, 1978 clinical studies, 322 reviews, and 468 meta-analyses. TW published 786 basic science articles, 1128 clinical studies, 70 reviews, and 9 meta-analyses. HK published 204 basic science articles, 258 clinical studies, 65 reviews, and 7 meta-analyses (Figure 4). The subtype of the clinical study included 379 RCTs, 700 non-RCTs, 671 cross-sectional studies, 789 cohort studies, 290 case-control studies, 392 case series studies, and 143 case reports originated from the 3 regions of China. ML published the most non-RCTs, whereas TW and HK published the most cohort studies, compared with other subtypes (Table 2).

**Citations**

Citations of articles published between 2005 and 2014 in ML (48,296) were the highest in number compared to TW (19,265) and HK (8492; Table 1). HK, however, had the highest mean for citations per article (15.90), which was followed by TW (9.67) and then ML (7.13; Table 1).

Considering the subtypes of clinical studies, ML had 2335 citations of RCTs, 3431 citations of non-RCTs, 3479 citations of cross-sectional studies, 1476 citations of cohort studies, 1356 citations of case-control studies, 815 citations of case series, and 123 citations of case reports. TW had 1123 citations of RCTs, 1233 citations of non-RCTs, 1376 citations of cross-sectional studies, 3721 citations of cohort studies, 583 citations of case-control studies, 972 citations of case series, and 235 citations of case reports. HK had 572 citations of RCTs, 105 citations of non-RCTs, 261 citations of cross-sectional studies, 1881 citations of cohort studies, 182 citations of case-control studies, 257 citations of case series, and 3 citations of case reports. HK had the highest mean citations of RCTs, non-RCTs, cohort studies, case-control studies, and case series, whereas ML had the highest mean citations of cross-sectional studies and TW had the highest mean citations of case reports (Table 2).

We also analyzed the top 10 cited articles on diabetes by authors from the 3 regions of China (Table 3). The citations ranged from 155 to 843. Six of the top 10 cited articles were from ML, whereas 2 were from TW, and 2 were from HK. The research type of the top 10 cited articles included 7 basic science articles, 1 review, 1 cross-sectional study, and 1 RCT. The top cited article was a cross-sectional study on the prevalence of diabetes among men and women in China, which was published...
in *The New England Journal of Medicine* by Yang WY\(^34\) from ML. The second most cited article was a review on diabetes entitled “Asia: epidemiology, risk factors, and pathophysiology,” which was published in *JAMA*, by Chan JCN\(^35\) from HK. The third most cited article was a basic research study on elevated plasma level of visfatin/pre-B cell colony-enhancing factor in patients with type 2 diabetes mellitus, which was published in *The Journal of Clinical Endocrinology & Metabolism* by Chen MP\(^36\) from TW.

**Journal Analysis**

All of the diabetes publications originating in the 3 regions of China 2005 to 2014 were published in a total of 1498 journals. The journals *PLoS One* and *Diabetes Research and Clinical Practice* were the top 2 most popular journals in the 3 regions of China, whereas *Chinese Medical Journal* ranked as number 2 of the top 3 most popular journals in ML. *Diabetes Care* ranked number 3 of the top 3 most popular journals in TW, and *Diabetes Care* ranked number 1 with *PLoS One* in the top 3 most popular journals in HK (Table 4). According to the 2013 Journal Citation Report, high-impact journals were designated by impact factors ≥ 6. The number of articles published in high-impact journals by authors in ML was 322 (322/6775, 4.75%) and the number of high-impact journals included was 63. TW published papers in 40 high-impact journals and the number of papers was 164 (164/1993, 8.22%). For HK, 101 articles (101/534, 18.91%) were published in 28 high-impact journals. Considering the 4 most important general medicine journals, that is, *The New England Journal of Medicine*, *Lancet*, *JAMA*, and *BMJ*, ML published 1 article in each of the 4 journals, TW published 1 article in *BMJ*, and HK published 2 articles on *JAMA*. As for specialized journals, authors from ML published 46 and 57 articles in *Diabetes Care* and *Diabetes*, respectively, whereas TW published 42 and 14 articles in *Diabetes Care* and *Diabetes*, respectively, and HK published 25 and 17 articles on *Diabetes Care* and *Diabetes*, respectively (Table 5).

**Diabetes, its Complications, and Comorbidities**

For clinical studies, most of the articles focused on type 2 diabetes (1155), whereas 148 articles focused on pre-diabetes, 103 articles focused on type 1 diabetes, and 84 articles focused on gestational diabetes. As for complications, the top 3 most common topics were diabetic nephropathy, diabetic retinopathy, and diabetic foot disease. Cardiovascular disease, cancer, and cerebrovascular disease were the top 3 most common topics on comorbidities (Figure 5). Traditional Chinese medicine (TCM) was analyzed in 156 articles, including 49 basic research studies, 97 clinical studies, 9 reviews, and 1 meta-analysis.

**DISCUSSION**

There has been significant progress and development in science and medicine in China as a result of the tremendous socioeconomic changes that have occurred in China.\(^3\,^5\,^12\) Research on diabetes has also dramatically evolved in China over the past decades.\(^6\,^37\) The contribution of China’s researchers in many biomedical fields has been reported in recent years.\(^14\,^27\) Reports on the status of research by Chinese scientists on diabetes, however, have not been published. Our study is the first to analyze the quality and quantity of publications on diabetes by researchers in China.

In this study, some of the most exciting evidence for change was the total number of articles published from China

| Year | Total Citations | HK | TW | ML |
|------|-----------------|----|----|----|
| 2005 | 1355            | 761| 1823| 25.37 |
| 2006 | 2676            | 1242| 2604| 28.23 |
| 2007 | 4769            | 1303| 2313| 30.30 |
| 2008 | 5721            | 1326| 1947| 25.50 |
| 2009 | 6794            | 1259| 2599| 26.23 |
| 2010 | 7314            | 939 | 2211| 14.45 |
| 2011 | 6693            | 763 | 2396| 12.11 |
| 2012 | 6937            | 449 | 2163| 8.98 |
| 2013 | 4843            | 355 | 986 | 5.22 |
| 2014 | 1194            | 95  | 223 | 1.34 |
| Total| 48296           | 8492| 19265| 15.90 |
in diabetes research, which has increased significantly during the past 10 years and exceeded Japan, Germany, from 2009, and the United Kingdom from 2011. However, compared with the United States, the number of articles from China is still less. Furthermore, our results provide an overview of research output on diabetes in China over a 10-year period. China was increasingly productive in diabetes research from 2005 to 2014, and ML was the most productive relative to TW and HK since 2006. HK, however, produced the highest quality research according to the mean citation rate per publication.

China has become increasingly productive in scientific research in many biomedical fields, and this includes research on diabetes, according to our study. The year 2006 was shown to be the time when the ML publication rate on diabetes research exceeded the biomedical research production rates for TW and HK, which previously lagged behind TW and HK. The trend after 2006 was also identified for other medical fields.

Several reasons have been suggested for the increase in China’s contribution to research on diabetes. First, the economy

| Rank | Article | Citations | Region |
|------|---------|-----------|--------|
| 1    | Yang W, Lu J, Weng J et al. Prevalence of diabetes among men and women in China. *N Engl J Med*. 2010; 362:1090–101. | 843 | ML |
| 2    | Chan JC, Malik V, Jia W et al. Diabetes in Asia: epidemiology, risk factors, and pathophysiology. *JAMA*. 2009; 301:2129–40. | 513 | HK |
| 3    | Chen MP, Chung FM, Chang DM et al. Elevated plasma level of visfatin/pre-B cell colony-enhancing factor in patients with type 2 diabetes mellitus. *J Clin Endocrinol Metab*. 2006; 91:295–9. | 356 | TW |
| 4    | Qin J, Li Y, Cai Z et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. *Nature*. 2012; 490:55–60. | 313 | ML |
| 5    | Sun C, Zhang F, Ge X et al. SIRT1 improves insulin sensitivity under insulin-resistant conditions by repressing PTP1B. *Cell Metab*. 2007; 6:307–19. | 288 | ML |
| 6    | Weng J, Li Y, Xu W et al. Effect of intensive insulin therapy on beta-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial. *Lancet*. 2008; 371:1753–60. | 224 | ML |
| 7    | Zhang D, Jiang W, Liu M et al. Highly efficient differentiation of human ES cells and iPSCs into mature pancreatic insulin-producing cells. *Cell Res*. 2009; 19:429–38. | 199 | ML |
| 8    | Ng MC, Park KS, Oh B et al. Implication of genetic variants near TCF7L2, SLC30A8, HHEX, CDKAL1, CDKN2A/B, IGF2BP2, and FTO in type 2 diabetes and obesity in 6,719 Asians. *Diabetes*. 2008; 57:2226–33. | 194 | HK |
| 9    | Jiang W, Shi Y, Zhao D et al. In vitro derivation of functional insulin-producing cells from human embryonic stem cells. *Cell Res*. 2007; 17:333–44. | 168 | ML |
| 10   | Chen YH, Lin SJ, Lin FY et al. High glucose impairs early and late endothelial progenitor cells by modifying nitric oxide-related but not oxidative stress-mediated mechanisms. *Diabetes*. 2007; 56:1559–68. | 155 | TW |

HK = Hong Kong, ML = Mainland China, TW = Taiwan.
in China has grown rapidly, which has allowed increasing funds to be spent on medical research. Second, ML has been able to recruit more participants because of its very large population as well as the higher prevalence of diabetes. These 2 factors may also explain the increase in the number of clinical studies. In our study, we showed that research on diabetes has thrived in ML because there were many more basic research studies, clinical studies, reviews, and meta-analyses published in ML than in TW and HK. Third, ML has the largest number of physicians specializing in diabetes, and research ability in terms of conducting studies and writing manuscripts has improved in ML. For these reasons, ML will likely continue to increase the rate of publications on diabetes in the future.

ML published more basic science articles compared to clinical studies, reviews, and meta-analyses, according to our study. The reason may be related to the National Natural Science Foundation of China, the largest funding source for biomedical research in China, which prefers to support basic sciences compared to clinical studies. This result is similar with previous publications. There may be several reasons for the research status in ML. ML has an advantage in population for previous publications. There may be several reasons for the research status in ML. ML has an advantage in population for

### TABLE 5. Articles Published in New England Journal of Medicine, Lancet, JAMA, BMJ, and the High-Impact Endocrinology and Metabolism Journals from Mainland China, Taiwan, and Hong Kong. (IF ≥ 6)

| Journal | 2013 IF | ML | TW | HK |
|---------|---------|----|----|----|
| New England Journal of Medicine | 54.42 | 1 | 0 | 0 |
| Lancet | 39.207 | 1 | 0 | 0 |
| JAMA—Journal of the American Medical Association | 30.387 | 1 | 0 | 2 |
| BMJ—British Medical Journal | 16.378 | 1 | 1 | 0 |
| Endocrine Reviews | 19.358 | 0 | 0 | 0 |
| Cell Metabolism | 16.747 | 1 | 0 | 1 |
| Nature Reviews Endocrinology | 12.958 | 0 | 0 | 1 |
| Trends in Endocrinology and Metabolism | 8.868 | 0 | 0 | 0 |
| Diabetes Care | 8.570 | 46 | 42 | 25 |
| Diabetes | 8.474 | 57 | 14 | 17 |
| Obesity Reviews | 7.859 | 4 | 0 | 0 |
| Journal of Pineal Research | 7.812 | 0 | 2 | 0 |
| Antioxidants and Redox Signaling | 7.667 | 3 | 0 | 2 |
| Frontiers in Neuroendocrinology | 7.581 | 0 | 0 | 0 |
| Diabetologia | 6.880 | 46 | 17 | 13 |
| Journal of Bone and Mineral Research | 6.580 | 1 | 0 | 0 |
| Journal of Clinical Endocrinology & Metabolism | 6.310 | 24 | 10 | 7 |

BMJ = British Medical Journal, HK = Hong Kong, JAMA = Journal of the American Medical Association, ML = Mainland China, TW = Taiwan.
participant recruitment, but most people do not have high-quality healthcare,\(^45\) which helps them join clinical trials. Insufficient funding, lack of available time, an unsupportive research environment, and a deficient clinical research teaching program may have contributed to fewer clinical studies from ML\(^4,46\).

There are controversies about the best way to assess the quality of research articles.\(^15,16\) However, the number of citations is a commonly used tool.\(^14–27\) The region of China that had the most citations, indicating it had the most overall influence, was ML. ML may have the most citations because they have the most publications; however, HK had the greatest mean number of citations per publication. This may suggest that HK produced publications that were of higher quality than ML or TW. Also, HK had the highest mean number of citations of cross-sectional studies and TW had the highest mean number of citations of case reports. This may indicate that the quality and evidence level of clinical studies in HK was higher than ML and TW.

The topics of the 7 basic science articles in the top 10 most cited articles were related to visfatin/pre-B cell colony-enhancing factor,\(^36\) gut microbiota\(^47\) in type 2 diabetes, SIRT1 (silent mating-type information regulator 2 homolog 1) improving insulin sensitivity,\(^48\) human embryonic stem differentiation into mature pancreatic insulin-producing cells,\(^49,50\) genetic variants in type 2 diabetes,\(^51\) and mechanisms of high glucose impairing endothelial progenitor cells.\(^52\) These topics are areas of focus in diabetes research and provide the foundation for further investigations.

ML published the most articles in high-impact journals both in the most important general medical journals and in specialized journals. However, when considering the proportion of publications in high-impact journals relative to the total number of publications, HK was ranked first, followed by TW and then ML. This suggested that the quality of research in HK may be superior, which may be due to HK having an advantage because of a longer and more solid foundation in research experience, including articles written in English.\(^41\)

For clinical studies, type 2 diabetes was the most popular, followed by cardiovascular disease and diabetic nephropathy. This indicated that studies on diabetic complications received increasing attention. TCM originated in China, including Chinese herbal medicine, acupuncture, Qigong, and Tai Chi. There were only 1.7% of the articles in the study of TCM, and most of them were from ML. This may be related to many excellent articles being published in Chinese journals. To spread TCM throughout the world, there should be more attempts in the future to publish more articles on TCM in English.

Our study had some limitations. First, data from Macau, which is another region of China, were collected but not used; the number of articles published by authors from Macau was too few. It would have been better to have been able to include all regions of China and not just the major 3 regions. Second, articles that were published in non-Web of Science journals were not included in the search. These articles, however, may have contributed to research production in the 3 regions of China. Third, this study evaluated the research contributions of ML, TW, and HK according to the number of publications and citations, which was not a perfect assessment. However, the quality and quantity of articles in a region are often used to evaluate national research productivity and these assessments have been used in many other medical fields.

**CONCLUSIONS**

Our study was the first to assess the quantity and quality of research publications on diabetes in the 3 major regions of China. Our results provide an overview of diabetes research in China and suggest possible reasons for the emerging increasing trend. There was a significant increase in the number of articles.
published by Chinese authors from 2005 to 2014. Most of the articles were published by authors in ML and the increasing trend began in 2006. The region that produced the highest quality research as measured by the mean number of citations per article was HK. However, compared with the United States, there is still much room for Chinese authors to expand diabetes research in the future.

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