J Exp Clin Med 2014;6(4):111–117

Contents lists available at ScienceDirect

Journal of Experimental and Clinical Medicine

journal homepage: http://www.jecm-online.com

REVIEW ARTICLE

A Bibliometric Study on Second-generation Antipsychotic Drugs in the Asia–Pacific Region

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ARTICLE INFO

Article history:
Received: May 7, 2014
Revised: May 19, 2014
Accepted: May 29, 2014

KEY WORDS:
atypical antipsychotic drug;
bipolar disorder;
risperidone;
schizophrenia

In this review, we analyzed the status and changes in the research on second-generation (atypical) antipsychotic drugs in the Asia–Pacific region (i.e., Japan, South Korea, Taiwan, Hong Kong, Singapore, and Australia). We also performed a bibliometric study of the literature in this region on atypical antipsychotic drugs (e.g., clozapine, risperidone, olanzapine, ziprasidone, quetiapine, sertindole, aripiprazole, paliperidone, amisulpride, zotepine, asenapine, iloperidone, lurasidone, perospirone, and blonanserin). We applied bibliometric indicators of production and dispersion (i.e., Price's law on the increase of scientific literature and Bradford's law, respectively). We also calculated the participation index of different countries. The data were also correlated with relevant social and health data from the Asia–Pacific region (e.g., the per capita gross domestic product and total per capita expenditure on health and gross domestic expenditure on research and development). All data are discussed together. We also analyzed the different aspects among the six countries in the region.

1. Introduction

The advances in antipsychotic drugs in the past 20 years are important because of the clinical introduction of many second-generation (atypical) antipsychotic drugs (SGAs) such as risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole. These agents have improved the quality of life of psychotic patients and have contributed to weakening the stigmatization of psychiatric diseases. The acceptance of SGAs has resulted from their improved therapeutic efficacy and patients' adherence to therapy, which reduces relapses.[1] Since 2003, the approved indication of SGAs for the treatment of bipolar disorder (BD) has considerably advanced the research related to these drugs. Research in the countries of the Asia–Pacific region—some consolidated countries (e.g., Japan and Australia) and others emerging countries (e.g., South Korea, Taiwan, Hong Kong, and Singapore)—is not an exception at this point because they have powerful economies. The four countries, South Korea, Taiwan, Hong Kong, and Singapore, called "the Asian Tigers" or "Asian Dragons", have exceptionally high growth rates (>7% per year). South Korea is one of the great 20–50 class economic powers of East Asia, and is the most industrialized member country of the Organization for Economic and Co-operative Development (OECD). Hong Kong is a special administrative region of China and, as one of the world's leading international financial centers, has a reputable capitalist economy. However, Singapore is an emergent country with a highly developed market-based economy, but it has a short psychiatric history. Taiwan adds a consolidated psychiatric tradition to its strong economic growth. In Japan, political, social, and

Conflicts of interest: The authors declare no potential conflicts of interest, including financial support, for the current study.

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http://dx.doi.org/10.1016/j.jecm.2014.06.001

economic conditions have greatly influenced the development of psychiatry during the past 3 decades. In Australia, mental health reforms have been occurring in parallel with similar developments in other Western nations. In this review, we analyze jointly and comparatively the published results of the bibliometric studies in Japan,[2] South Korea,[3] Taiwan,[4] Hong Kong,[5] Singapore,[6] and Australia.[7]

2. A brief description of methods in the bibliometric SGA studies in the Asia–Pacific region

We used EMBASE Biomedical Answer web (Elsevier B.V., Amsterdam, The Netherlands), which consists of MEDLINE (*Index Medicus*, United States National Library of Medicine, Bethesda, MD, USA), and *Excerpta Medica* (Elsevier Science Publishers, Amsterdam, The Netherlands). The bibliometric method used in the previously listed article has been described elsewhere.[2,3,4,5,6,7] In brief, we included documents that contained in the author address section the descriptors "Japan", "South Korea", "Taiwan", "Hong Kong", "Singapore", or "Australia"; and in the title section, the descriptors "atypic* (atypical*)", "antipsychotic*", "second-generation antipsychotic*", "clozapine", "risperidone", "olanzapine", "ziprasidone", "quetiapine", "sertindole", "aripiprazole", "paliperidone", "amisulpride", "zotepine", "asenapine", "iloperidone", "lurasidone", "perospirone", and "blonanserin". We confined the year of publication until 2011. We considered all original articles, reviews, editorials, and letters to the editor. Duplicated documents were deleted.

2.1. Bibliometric indicators

Price's law was used to analyze productivity by fitting exponential growth models.[8] To assess the dispersion of scientific information, we applied Bradford's law. Bradford proposed a model of concentric zones of productivity with decreasing density of information.[9] This model permits the identification of the journals most widely used or with the greatest weight in a given field of scientific production. We also used the impact factor (IF) for 2011. Another indicator included in these analyses is the national participation index (PI) of different countries for overall scientific production (i.e., the ratio of the number of documents generated by a specific country and the total number of documents on this topic). The PI has also been compared to the global PI in the biomedical and health sciences (and in particular in the psychiatry and neurology field). The PI has likewise been correlated with some health data such as the per capita gross domestic product, total per capita expenditure on health, and gross domestic expenditure on research and development (R&D). The health data were obtained from the 2011 OECD Health Division and 2011 World Health Organization Department of Health Statistics and Informatics. Other data were obtained from different sources such as the Statistics Office of Department of Health of Taiwan (2009) Taipei, Taiwan or the Census and Statistical Department and Department of Health of Hong Kong (Hong Kong, 2011).

3. Important findings of bibliometric studies on SGAs in the Asia–Pacific region

3.1. Growth of scientific literature on SGA drugs

After studying the analyzed database, we obtained 669 original documents that dealt with different aspects of SGAs in Japan during the period 1982–2011.[2] For the period 1993–2011, we obtained 438 original papers from Australia,[7] 359 papers from Taiwan,[4] 326 papers from South Korea,[3] 51 papers from Singapore,[6] and 44 papers from Hong Kong.[5] On performing a joint analysis of the evolution of scientific production on SGAs in the period 1993–2011 ($n = 1857$), we found a markedly increased number of documents generated over the past 20 years, without evidence (until the end of the period studied), of the process of saturation postulated by Price[8] in his theory of expansion of scientific literature. To assess whether the growth of scientific production in SGAs follows Price's law, we made a linear adjustment of the data, based on the equation $y = 13.43x - 39.351$; and we made another adjustment to the exponential curve, based on the equation $y = 10.729e^{0.763x}$. As Figure 1 shows, the mathematical adjustment to the exponential curve permitted us to obtain a correlation coefficient of $r = 0.8978$, which indicates that 4.91% of variance is unexplained by this fitting. By contrast, the linear adjustment of the measured values provides a correlation coefficient of $r = 0.8149$, and therefore 18.17% of unexplained variance. With these data, we can conclude that the analyzed database was more in keeping with an exponential fitting than a linear fitting and that the postulates of Price's law were fulfilled.

This phenomenon is extensive to the individual analysis of Japan,[2] South Korea,[3] and Taiwan.[4] However, the repertoire of Australia,[7] Hong Kong,[5] and Singapore[6] did not meet the postulates of Price's law; in the latter two countries, this may be because of the small sample of publications. In Hong Kong, we speculated that, although 15 SGAs were included in the current literature search, only nine SGAs—amisulpride, aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, risperidone, sertindole, and ziprasidone—had been licensed and were available in Hong Kong during the study period. In the Australian case, this discrepant finding may be because this country has more of an interest in doing post-marketing studies because regulatory clinical trials tend be performed in European-based or United States-based countries. Regulatory agencies in Taiwan, South Korea, and Japan all demand that the data demonstrate the same efficacy for their citizens that is as good as the efficacy demonstrated in the original Caucasian population in the United States of America and the United Kingdom. This may be the reason psychiatrists in Taiwan[4] and South Korea[3] have more of an interest in doing efficacy-related studies, compared to psychiatrists in Australia[7]; however, all three countries do not have any pharmaceutical drug companies on their soil.

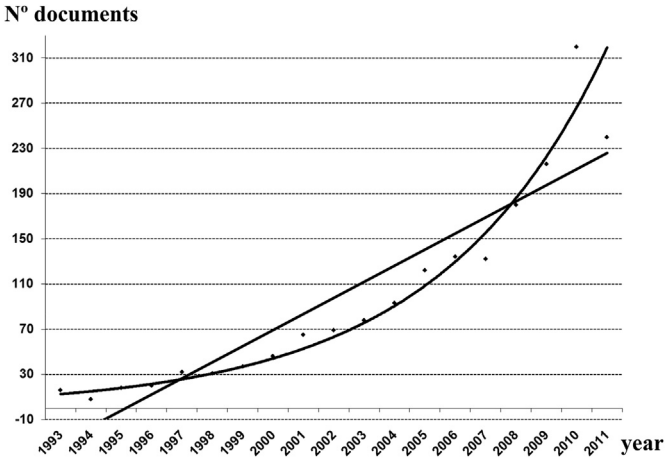

Figure 1 Growth of scientific production on SGAs in the Asia–Pacific region. A linear adjustment of the data and a fitting to an exponential curve were performed to check whether production follows Price's law of exponential growth. Linear adjustment: $y = 13.43x - 39.351$ ($r^2 = 0.8183$). Exponential adjustment: $y = 10.729e^{0.176x}$ ($r^2 = 0.9509$). SGAs = second-generation antipsychotics.

The introduction of SGAs to the market in different countries and their approved indications for treating bipolar disorder (BP) have contributed substantially to the increase in scientific production in the Asia–Pacific region. This date precisely coincides with the authorization by the United States Food and Drug Administration (US FDA; Silver Spring, Maryland, USA) and other international regulatory agencies to use risperidone, aripiprazole, quetiapine, and ziprasidone for the treatment of manic episodes in BD. Furthermore, olanzapine and aripiprazole have been authorized to prevent relapses in patients with BD whose manic episodes previously responded to treatment with these antipsychotics.[10] Quetiapine is indicated as a monotherapy for the acute treatment of depressive episodes associated with BD, and olanzapine (in combination with the antidepressant fluoxetine) is indicated for the treatment of treatment-resistant depression. In 2007, aripiprazole was approved by the US FDA for the treatment of major depression when used adjunctively with an antidepressant medication.[10] Risperidone and aripiprazole were approved to treat irritability in people with autism. However, SGAs are also commonly used (and studied) for numerous off-label indications.[11,12] In this sense, there has been an important upsurge in the most recent 5-year period (2007–2011). This upsurge coincides with the period of clinical development immediately prior to the official approval of the new antipsychotics and approval of new indications for SGAs.

Figure 2 illustrates the cumulative growth (by 5-year periods) of scientific papers in the six countries. The country with the highest cumulative growth figures is South Korea, followed by Taiwan; Japan is the country with the lowest cumulative growth. Australia has experienced notable significant growth in the past quinquennium (335.71%), primarily because of publications on clozapine and olanzapine. This growth was always higher (in the 3 consecutive 5-year periods), compared to the global growth of science in biomedicine and health, and to the specific field of psychiatry and neurology in all countries analyzed, except Hong Kong and Singapore.

The great growth in the scientific literature in this area leads us to conclude that the field of SGAs is in the prime of its development from a clinical perspective and basic research perspective within the field of psychiatry. There are no specific data on SGAs published in this field, although some authors (who also applied bibliometric tools) have reported that the research activity in the field of schizophrenia is superior to that in other fields of psychiatry.[13]

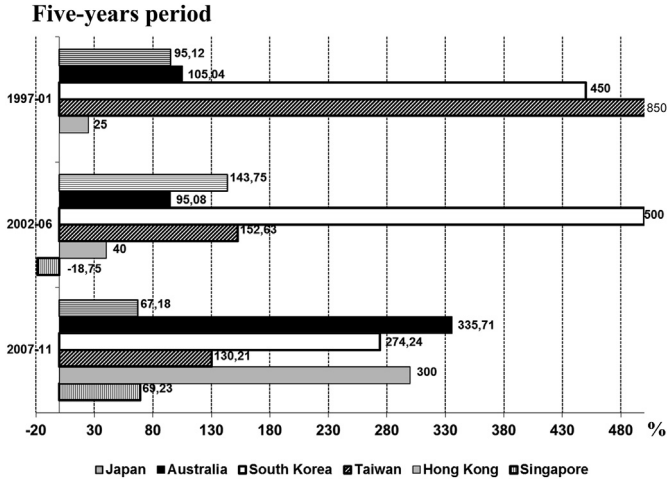

Figure 2 Cumulative growth by 5-year periods of scientific production on SGAs in six countries of the Asia–Pacific region. Data from each 5-year period refer to evolution over the previous period. The period of reference is 1992–1996. The data are expressed in percentages. SGAs = second-generation antipsychotics.

Without using bibliometric tools, Bai[14] has recently confirmed a great investigative interest in pharmacotherapy for schizophrenia in Taiwan.

Another interesting aspect is the close correlation between these bibliometric data and the prescription data in this region, as revealed in the pharmacoepidemiological study of the Research on Asian Psychotropic Prescription (REAP) Project.[15] The prescribing patterns in 2001, 2004, and 2008 showed a significant increase of SGA use at 45.5%, 64.7%, and 76.6%, respectively.[16,17] A similar result occurred in Australia. Between July 1995 and December 2001, the SGA use increased in Australia from an estimated 0.27 to 3.83 defined daily doses (DDD) per 1000 population per day.[18] Stephenson et al[19] more recently reported a 217.7% increase in the dispensing of SGAs in DDD per 1000 population per day from 2000 to 2011.

3.2. Research topics and antipsychotic drugs: differences between countries

After a study of the analyzed database, risperidone emerged as the agent most widely studied (with 467 documents) from clinical and safety points of view, followed in decreasing order by clozapine (391 documents), olanzapine (336 documents), aripiprazole (275 documents), quetiapine (136 documents), perospirone (60 documents), zotepine (58 documents), amisulpride (49 documents), paliperidone (48 documents), ziprasidone (40 documents), blonanserin (29 documents), lurasidone (19 documents), sertindole (11 documents), and asenapine (4 documents). No document was devoted to iloperidone. Perospirone is only available in Japan, blonanserin is available in Japan and South Korea, amisulpride is not available in Japan, and iloperidone and lurasidone are not available in Australia.

In the analysis of individual SGAs, clozapine is the agent most widely studied in Hong Kong, Singapore, Taiwan, and especially in Australia (which has 36.98% of the country's production and 41.43% of all articles for clozapine). In Australia, the increased number of publications on clozapine since 2005 was strikingly correlated with the increase in the clinical use of this antipsychotic; this coincided with the release of the Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines.[20] According to these guidelines, clozapine should be used early in the treatment course—as soon as treatment resistance to at least two antipsychotic drugs has been demonstrated. The daily dosage of clozapine use in Australia has increased nearly 80% during the past 10 years, and 19% of schizophrenia patients in Australia are currently on clozapine therapy.[21,22] Data on clozapine use in Singapore have similarly shown some increase in prescriptions; this contributed to the analyses within the REAP study, which is associated with more severe illness (e.g., more frequent admissions, greater severity of delusions, disorganization, negative symptoms), but associated with fewer extrapyramidal symptoms.[23] The REAP project also detected a clear relationship between the increase in publications on clozapine since 2007 and the increase in the clinical use of this antipsychotic in Korea.[23]

Using manual coding after studying the title and/or abstracts of the articles, we divided the papers into four groups: "experimental pharmacology," "clinical efficacy," "tolerance and/or safety," and "not specified group" (consisting of primarily reviews, pharmacoeconomic analysis, and articles of prescribing patterns and quality of life). Figure 3 shows the results that we obtained. Japan has more research on SGAs for "experimental pharmacology" (40.06%) and Korea, for clinical trials (54.61%). By contrast, Taiwan and Australia dominate papers on aspects related to tolerance (40.11%) and safety (39.27%). Clinical studies are primarily devoted to schizophrenia and BD, and to a lesser extent to other disorders

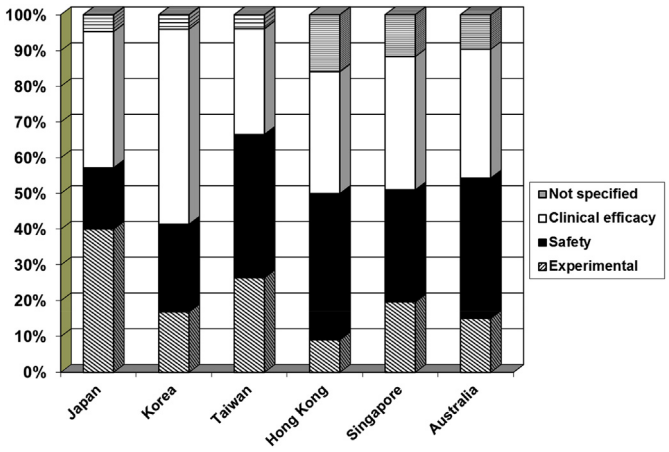

Figure 3 Thematic distribution of the analyzed database in the six countries of the Asia–Pacific region.

(e.g., Parkinson's disease, post-stroke psychosis, depressive disorders, panic disorder, dementia, ADHD).

3.3. Dispersion of scientific literature on SGA drugs

Applying Bradford's model showed that the mean number of articles was 232.12 articles per Bradford zone (even if we discarded the last zone, the accuracy of which was also obviously lower because the mean would be 254.57 articles). Table 1 shows the division of Bradford's areas of the material under study. The nucleus or first zone consisted of the *Progress in Neuro-Psychopharmacology and Biological Psychiatry* and the *Journal of Clinical Psychopharmacology* (with 149 articles and 101 articles, respectively). The second zone included three journals: *Australian and New Zealand Journal of Psychiatry*, *European Neuropsychopharmacology*, and the *International Journal of Neuropsychopharmacology* (with 95 documents, 86 documents, and 76 documents, respectively). The remaining journals analyzed were included in zones 3–8. A total of 352 different journals published material pertinent to this topic, but it was notable that the 10 most used journals accounted for 41.62% of all their publications.

The extensive use of domestic journals by Australian researchers is also notable. In fact, the *Australian and New Zealand Journal of Psychiatry* accounted for 19.18% of total production and with *Australasian Psychiatry* and the *Medical Journal of Australia* reached 25.8% of publications on SGAs in Australia. This is less striking in some other countries such as South Korea where the local journal *Psychiatry Investigation* ranks eighth (for local ranking).

3.4. Quality of publications on SGA drugs

Another aspect of interest in relation to scientific production that we have analyzed is quality. The 10 journals most extensively used for the diffusion of works on SGAs in the Asia–Pacific region have high IFs (all journals have an IF > 2; 6 journals have an IF > 4). The fact that prestigious journals such as the *Journal of Clinical Psychiatry* (IF = 5.799), *Journal of Clinical Psychopharmacology* (IF = 4.857), *Schizophrenia Research* (IF = 4.748), *International Journal of Neuropsychopharmacology* (IF is 4.578), or the *Journal of Clinical Psychopharmacology* (IF = 4.098) publish articles on SGAs from countries in the Asia–Pacific region is an important factor in this regard. This indicates the clinical and social relevance that these countries have acquired in recent years.

The use of the Science Citation Index (SCI) impact factor to determine the merit or quality of scientific contributions is debatable. The citation count applied in calculating the impact factor may not directly reflect the importance or quality of one study; on the contrary, it may only represent the topic of a given study as "more fashionable," or even "not yet mature" and/or "in need of more studies."

3.5. Differences between countries in the research activity on SGA drugs

The general scientific contribution of the six countries of the Asia–Pacific region within this thematic area represents a global PI of 9.58 with respect to world production in period analyzed (i.e., 1993–2011). Among the countries generating research on SGAs, the most significant, as Table 2 shows, is the United States whose PI is 29.11; this is followed in decreasing order by the United Kingdom (PI = 6.27), Germany (PI = 5.72), Canada (PI = 4.58), and Italy (PI = 4.29). Japan ranks sixth (PI = 3.37) and Australia ranks ninth (PI = 2.26). However, on considering the paper productivity of these countries in the field of psychiatry and neurology, only Spain from among the 10 largest producers in biomedicine and health sciences devoted a higher percentage of attention to the SGA. This reflects this country's special interest in SGA research. Within the Asia–Pacific region, Taiwan and South Korea also show a similar special interest in SGA research. Similar to Japan, Hong Kong—another well-developed capitalist economy in the Asia–Pacific region—appeared only at the bottom rank with respect to SGA publications. (This indicates the lower relative interest in these drugs within the context of their general production in psychiatry.) What is surprising is that from 1993 to 2011 Taiwan,

Table 1 Distribution of the journals in Bradford's zones.*

Zones	No. of journals	No. of articles	Bradford's constants
1	2	250	
2	3	257	1.5
3	5	266	1.66
4	12	257	2.4
5	24	252	2
6	57	250	2.37
7	174	250	3.05
8	75	75	—

* Total number of articles is 1857 articles. The total number of journals is 352 journals. The average number of articles is 232.12 articles. The average number of articles, excluding the last Bradford zone, is 254.57 articles.

Table 2 Distribution of papers on atypical antipsychotic drugs in the world's 10 most productive countries in biomedicine and health sciences and in the countries of the Asia–Pacific region for the period 1993–2011.*

	Country	%	Psychiatry–Neurology† (%)	SGAs (%)	SGAs/Psychiatry-Neurology
1	USA‡	25.84§	35.58	29.11	0.99
2	UK‡	7.35§	9.90	6.27	0.77
3	Japan‡	6.59§	6.81	3.37	0.70
4	Germany‡	6.29§	7.91	5.72	0.88
5	France‡	4.53§	4.93	3.02	0.75
6	China‡	4.00§	2.94	1.93	0.80
7	Italy‡	3.87§	4.76	4.29	1.09
8	Canada‡	3.69§	5.03	4.58	1.11
9	Spain‡	2.69§	2.90	3.36	1.41
10	Australia‡	2.47§	3.07	2.26	0.89
	South Korea	1.31	1.17	1.61	1.90
	Taiwan	0.99	0.94	1.79	2.43
	Hong Kong	0.47	0.46	0.23	0.65
	Singapore	0.37	0.33	0.32	1.23

* The total documents for 1993–2011 was 13,778,264 articles. The total documents in the neurology and psychiatry area for 1993–2011 was 1,590,693 articles

† Psychiatry–Neurology = the area of focus is neurology and psychiatry; SGAs = second-generation antipsychotics

‡ Indicates this country is within the world's 10 most productive countries in biomedicine and health sciences for the period 1993–2011

§ Indicates the countries' productivity (in percent) in the discipline of psychiatry and neurology.

which has only approximately one-fifth the population (23 million people) of the Japanese population, had produced more than one-half of the papers produced by Japan and had published them in comparably prestigious journals.[2,4] Figure 4 illustrates this aspect.

The two major English-speaking countries, the United States of America (USA) and the United Kingdom (UK), head the ranking of SGA-producing countries. Between them, they generate more than one-third (35.38%) of the total scientific production in this field. These two countries are home to the pharmaceutical companies responsible for the development of SGAs: olanzapine by Eli Lilly (USA); risperidone and paliperidone by Janssen Pharmaceutica (USA); quetiapine by AstraZeneca (UK); ziprasidone by Pfizer (USA); and aripiprazole by Bristol–Myers Squibb/Otsuka Pharmaceutical Co. (USA/Japan). This fact may explain this high PI.

Japanese pharmaceutical companies such as Dainippon Sumitomo Pharma, Otsuka Pharmaceutical, and Fujisawa Pharmaceutical also have relevant roles. Japan is responsible for the development of five SGAs: zotepine, perospirone, aripiprazole, blonanserin, and lurasidone. These SGAs have notably improved the quality of life of psychotic patients and have contributed to weakening stigmatization. Mental health in Japan is greatly important, particularly in the area of schizophrenia. In 2002, this country was the first Asian country to rename schizophrenia "togo-shicchou-sho" in an attempt to destigmatize people with this disorder.[24] However, the lower relative weight of Japan in SGA research regarding psychiatric research in general may have several explanations. One reason could have been the delay in Japan of licensing new drugs or approving new indications for a drug, especially for neurological[25] and psychiatric[26] medications. The Japanese regulatory process has been notoriously slow; the median review time (from approval application to final approval) was 23 months for 13 psychiatric drugs introduced in Japan between September 2000 and July 2011. This review time was considerably longer than the review times in the European Medicines Agency and the US FDA (13.5 months and 10.0 months, respectively).[26] The patients in South Korea and Taiwan can usually obtain the needed SGAs for their patients in 2–3 years, after approval by the US FDA.

A second reason could be that Japan had produced a higher percentage of basic research papers on SGAs (40.06%) than clinical papers (38.30%), compared to other countries in the Asia–Pacific area such as Taiwan (29.53% for basic research papers and 40.11% for clinical papers).[4] The productivity of basic research by Japanese psychiatrists has always been admired by their counterparts in other Asian countries. However, executing clinical drug trials and implementing institutional review board for protecting human research participants in Japan have recently become popular. These phenomena indicate that remarkable improvement in the productivity of clinical research papers in Japan would be expected in the near future.

A similar situation can be found in Hong Kong. It would be interesting to explore the reason for Hong Kong's bottom-ranking on the PI despite her excellent research on early psychosis.[27] Scientific SGA production in Singapore, although small, is important in the context of its psychiatric production. As noted by Chong,[28] the impact of mental health research activity on Singapore is not evident. Some studies in the mid-2000s suggested that only 1% of all scientific publications in Korea were focused on mental health;[29] however our results confirm that during the period 1993–2011, the percentage of papers in the area of psychiatry and neurology accounted for 9.55% of the total scientific production in Korea. Scientific SGA research, especially in the field of clinical research, is a fast growing field within the field of psychiatry.

The most productive institutions in the Asia–Pacific region with regard to the material under study are the Seoul National University Bundang Hospital, Chongrogu (Seoul, Korea; $n = 45$), the Department of Psychiatry of the Taipei Veterans General Hospital (Taipei, Taiwan; $n = 42$), and the Department of Neuropsychiatry in the Graduate School of Medicine at Hirosaki Graduate University (Hirosaki, Japan; $n = 39$).

3.6. Socioeconomic correlations

With regard to social-health parameters, on correlating the scientific documents contributed by the principal producers of SGA literature (and the six countries of the Asia–Pacific region) with the per capita gross domestic product, we observed a homogeneous distribution for a large group of countries: Hong Kong, France, Japan, Spain, Italy, Germany, United Kingdom, and Canada. However, there is less interest in this topic in relation to their economic potential in countries such as Singapore and Australia (Figure 5).

Figure 6 shows the correlation of scientific production in SGAs with the per capita health expenditure and the gross domestic expenditure on R&D of each country. This offers a parallel view of

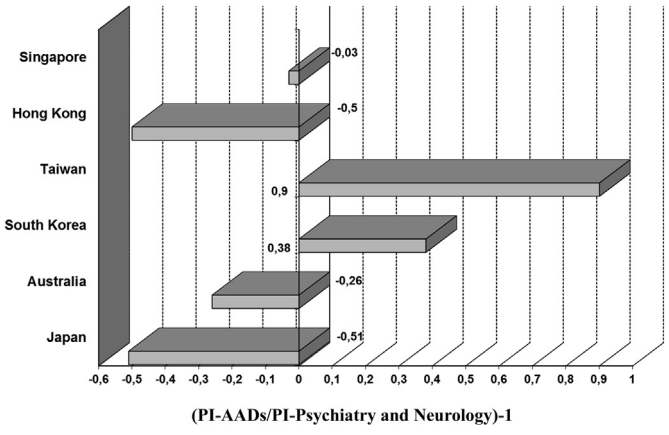

Figure 4 The relationship between the production of scientific literature on SGAs and the total production in the field of psychiatry and neurology in the six countries of the Asia–Pacific region. PI = participation index; SGAs = second-generation antipsychotics.

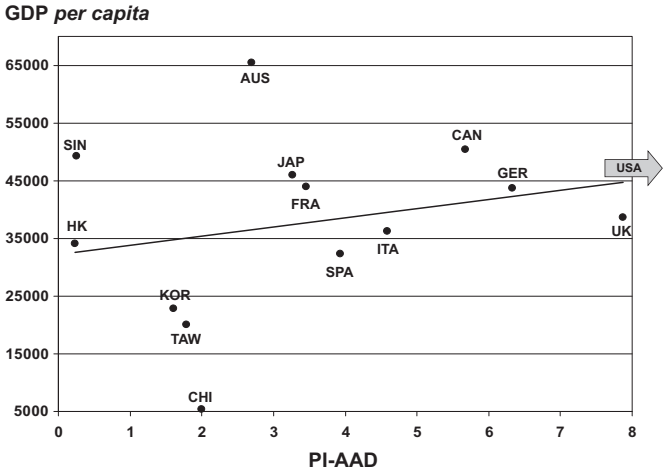

Figure 5 The relationship between the production of scientific literature on SGAs and the per capita gross domestic product in the world's 10 most productive countries in biomedicine and health sciences and countries of the Asia–Pacific region. We excluded the United States from the graph to give a clearer reflection of the rest of the countries. The economic data were obtained from the website of the World Health Organization (http://www.who.int/country/es/). The economic data are expressed in international dollars. GDP = gross domestic product; PI = participation index; SGAs = second-generation antipsychotics.

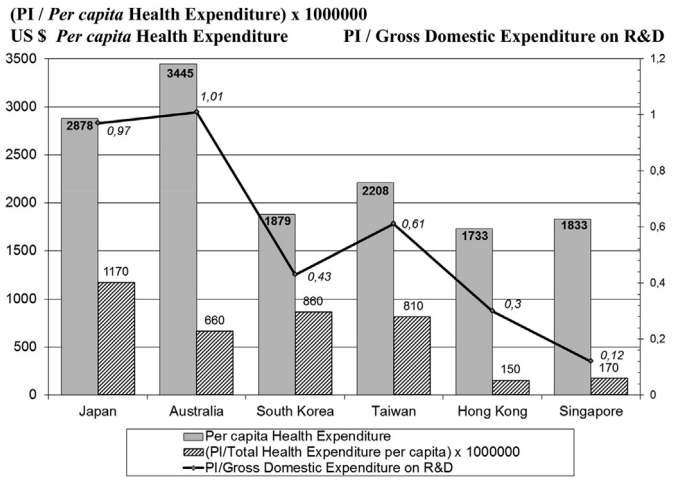

Figure 6 The relationship between the production of scientific literature on SGAs and the per capita health expenditure and gross domestic expenditure on research and development (R&D) in the six countries of the Asia–Pacific region. The total health expenditure per capita purchasing power parity (PPP) in US$ [data from the Organization for Economic and Co-operative Development (OECD) 2009]. Japan and Australia (data 2008). Gross domestic expenditure (%) on R&D. The data is from the OECD 2010, except for Taiwan and Japan (for which the data is from OECD 2009). PI = participation index.

this phenomenon. In general, this confirms the finding that the higher the spending on health and R&D, the greater the research production. It is striking however to observe the low ratios of both city-states. In the rest of the Asia–Pacific region the distribution is similar, although the ratios are much lower than the ratios for 10–15 countries of the most productive countries in biomedicine and health sciences, which we have found in previous studies.[2,3,4,5,6,7]

Despite recently being the world's first seven countries to meet the gross domestic product (GDP) per capita [purchasing power parity (PPP), US $29,997.00], South Korea has a health expenditure that is relatively low for a developed country (it ranks 28th with 6.9% of the GDP). In addition, only 6% of health care expenditures by the government health department are devoted to mental health.[30]

A similar finding exists with the two city-states. Hong Kong, as one of the world's countries with the highest GDP per capita city (PPP, US $49,137.00), reportedly spends 5.5% of her GDP on health care, out of which only approximately 0.24% is distributed to mental health.[27] Singapore, which has the world's third highest GDP per capita (PPP, US $59,936.00), similarly has a relatively "prudent" health expenditure for a developed country.

In addition, there is another problem contributing to these low ratios: a short psychiatric history in countries such as Singapore, Hong Kong, and Taiwan, and a deficiency in the development of policies on mental health where a substantial proportion of people rely on a mixture of Western medicines and traditional medicines.[28] Advances in South Korea have been much greater. However, it is problematic that patients with schizophrenia are predominantly treated by hospitalization in Korea, and a patient's mean length of stay is greater than in other countries. The infrastructure to support the implementation of the mental health policy has yet to be strengthened.[30] Japan and Australia are among the 10 most productive countries in biomedicine and health sciences, and they have a great tradition in the care of patients with schizophrenia. Japan has the biggest number of psychiatric beds in the world (with 1600 psychiatric hospitals).[24] During the 15-year period between 1992 and 2008, national spending on mental health in Australia increased from $132 per head of population to $251. Furthermore, in recent years, mental health has been a central focus of Australian government activity, which was marked by the Mental Health Reform in 2011.

4. Conclusion

Despite the limitations that are characteristic of bibliometric studies, we have been able to offer a picture of the representativeness and evolution of international research on SGAs in the Asia–Pacific region. We have observed a significant growth in the scientific literature on SGAs in this region, and we found that the research paper productivity on SGAs was different between the analyzed countries, which can be related to the differences described by other authors in antipsychotic prescribing patterns between Japan and other countries.[15,31]

In 2008 in the USA, the SGAs as a group of pharmaceutical class became number 1 in market sales (US $14.6 billion per year).[10] We trust that research in this field will continue to grow in the coming years in the countries of the Asia–Pacific region while bearing in mind (1) that the ideal antipsychotic drug has not yet been found,[1] the etiopathogeny of schizophrenia is still mostly unknown, and the clinical indications of these drugs is ever-expanding; and (2) the high economic growth of these countries, their short psychiatric development, and the reforms that are being implemented in mental health.

Acknowledgment

This study was supported by a grant (UCJC 2012-01) from Camilo José Cela University (I Convocatoria de Ayudas a la Investigación Competitiva; Madrid, Spain).

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