Study Designs Used by Japanese Clinical Researchers: A quantitative estimate of randomized controlled trials, cohort studies, case-control studies and meta-analysis

Mahbubur Rahman,*1 Mayuko Saito,*2 Tsuguya Fukui*2

Abstract
Background Japanese biomedical researchers are said to have been using less sophisticated study designs in terms of clinical research, and studies on quantitative estimates based on randomized controlled trials (RCT), cohort studies (CS), case-control studies (CCS) and meta-analyses (MA) are not available in this regard to date.

Methods We searched PubMed database to estimate the number of RCT, CS, CCS and MA published by Japanese researchers during the period 1994–2003, and compared it with that of rest of the countries as a whole. The search criteria we employed included publication year (1994–2003), language (English), tag (human), publication type (MA, RCT), and medical subjects headings (cohort studies, case-control studies, odds ratio). Nonparametric tests for trends were performed to determine any significant changes in the number and proportion of publication types over the period in question.

Results During the period 1994–2003, 98,774 RCT, 174,898 CS, 5,489 CCS, and 6,993 MA were published as a whole while Japanese researchers contributed 3,148 (3.19%), 8,985 (5.36%), 268 (4.03%), and 62 (0.89%) papers respectively. For the year 1994, the respective percentages were 2.58%, 4.02%, 2.25%, and 0%, and for the year 2003 they were 3.39%, 5.36%, 5.49%, and 1.15%. Japan’s contribution has increased significantly over the period of time, in all categories in absolute terms, but not always in proportion to the total number of articles in respective categories.

Conclusions Although the number of publications has increased over time, the Japanese share of published studies in RCT, CS, CCS and MA categories were lower compared with the average figures for the rest of the world.

Key words Randomized controlled trials, Meta-analysis, Cohort studies, Case-control studies, Japan, Research productivity, Biomedical publication, Research design

Introduction
Randomized controlled trials (RCT), cohort studies (CS), case-control studies (CCS) and meta-analysis (MA) are considered to be very important study designs in terms of generating evidence for clinical practice.1 However, it has been reported that Japanese clinical researchers have not been using the more sophisticated study designs to help accumulate clinical evidence.2 Different studies have shown that Japan contributed 8.8% of the total journal articles indexed in PubMed,3 1.1% of epidemiology
articles, 0.6–11.4% of clinical science articles and 3.8–11.9% of articles in basic science categories. However, no estimate is available for the Japanese contribution to the range of different study design categories, although one study has reported on RCT based on 1995–1999 data. The objective of the present investigation was to quantify RCT, CS, CCS and MA that originated from Japan and to compare this with that of other countries as a whole.

**Methods**

We searched PubMed in February 2005 to obtain the total number of RCT, CS, CCS and MA indexed in this database and published during the period 1994–2003. Subsequently, a similar search was performed to generate the number of publications by authors affiliated to Japanese institutions. To identify the percentage of the Japanese contribution to a particular study design category, we used the number of articles with the study design affiliated to Japanese institutions as numerator, while the total number of articles with similar design originated from all over the world was used as denominator. In addition, we conducted a search on the total number of journal articles (excluding published letters) that originated from Japan and the rest of the world together to elicit the proportion of a particular study design article relative to the total number of articles.

We used another indicator based on the total number of a particular study design affiliated to Japanese institutions as numerator and total articles from Japan in all categories as denominator. The search strategies and criteria used to find the relevant information are listed in Table 1. We used ‘publication type’ option for RCT and MA, and Medical Subject Headings (MeSH) words for CS (“cohort studies”) and CCS (“case-control studies” and “odds ratio”) as other options were not available to identify the numbers in the latter two categories. Separate estimates for each year (from 1994 to 2003) were generated with a view to examining the trend over the whole period of time.

**Statistical Analysis**

Trends for the total number and proportion of articles with different study design that originated from Japan and the rest of the world were examined using non-parametric tests for trends.
Fig. 1 Number of articles in the Pubmed database during 1994–2003 based on different study designs in logarithm scale: (a) from Japan and (b) from the rest of the world

Y-axis indicates the number of publications in logarithm scale. The numbers have increased significantly over the period of time in all categories as P values were always less than .05 for each of the categories both for articles from Japan and the rest of the world in logarithm and normal scale.

Fig. 2 Comparison of Japanese contribution in each of the research study design categories with that of the rest of the world

X-axis indicates year of publication while y-axis indicates percentage of total articles in respective categories. In CS, CCS and MA categories, Japan and the rest of the world’s contribution as a proportion of the total articles were found to have increased significantly. In RCT however, the contributions remained unchanged.
results

Overall numbers
From 1994 up to December 2003, 98,774 RCT, 174,898 CS, 5,489 CCS, and 6,993 MA were published as a whole while Japanese researchers contributed 3,148 (3.19%), 8,985 (5.36%), 268 (4.03%), and 62 (0.89%) articles, respectively. The respective figures were 2.58%, 4.02%, 2.26%, and 0% during 1994, and 3.39%, 5.36%, 5.49%, and 1.15% during 2003. In terms of number, both Japanese and the rest of the world's contributions have increased significantly over time in each of the categories. Figure 1 shows contribution trends from Japan and the rest of the world in logarithm scale.

Contribution as a share of total articles indexed in pubmed
Figure 2 presents articles from Japan and the rest of the world in each of the RCT, CS, CCS, and MA categories as a proportion of total articles from the respective category as indexed in the Pubmed database. Both Japanese and the rest of the world's share of published articles have increased significantly in CS (P = .05 vs .04), CCS (P = .01 vs .01), and MA (P = .01 vs .01) categories over time and remained unchanged in RCT category (P = .16 vs .13).

Japanese situation as a proportion of total articles in a particular study design
Figure 3 shows the Japanese position in terms of proportion of total articles in a particular study design category. Japan's share as a proportion of total articles has increased in RCT (P = .02), CCS (P = .01) and MA (P = .01) categories significantly and marginally in CS (P = .08) categories. On the other hand, the Japanese overall share of articles has remained unchanged during this period (P = .12).

Discussion
This study presents information on Japan's contribution to each of the categories of study design, which helps generate evidence for clinical practice. In terms of number, Japan's contribution has increased over the period in question, but not always proportionally. Japan's contribution to different categories of study design articles are comparable to that of high impact factor journals in different subject areas. Its share of RCT was a little lower if we compare it to that reported for the publication period 1995–1999 (5% of total). This could be due to the fact that more stringent inclusion criteria were set up in this study (reviews, letters, practice guidelines and editorials were all excluded). Japan's contribution to MA design was generally lower, but comparable in the case of highly reputable general medicine (0.7% of the total) and epidemiology journals (1.1% of total). Journals in the general medicine and epidemiology categories use epidemiological study designs which are not wide-spread among clinicians and researchers in Japan. MA is one of the latest epidemiological study designs, which summarizes a group of studies/trials to provide pooled evidence. Thus it is not surprising that Japanese contribution to MAs articles (0.89%) was far lower than its overall contribution to biomedical articles (8.8%).

There are limitations to this study. Since there are no options available in Pubmed database to quantify the number of case-control and cohort studies, we estimated the numbers based on MeSH words which might not represent the
actual number in this regard. Again, we included articles indexed in PubMed database only, while there could be additional articles in other databases, and some articles from Japan and other countries could remain unpublished or simply as reports. In this case, our estimates could differ somewhat if the proportions from Japan and other countries were different in this regard.

Although the average Japanese contribution (as a proportion of total articles originated from Japan) to a particular study design was lower compared to that of the rest of the world (as a proportion of total articles from the rest of the world), the situation has improved significantly over the last 10 years. Policy makers and clinical researchers need to work together to improve this situation further. The language barrier, funding shortages for clinical research and the lack of appropriate infrastructure are the main areas that require initial attention. A few other steps are also necessary for a visible improvement to be achieved in the near future. First, in order to improve the situation, it is crucial that the undergraduate and graduate students currently enrolled in clinical and public health departments be made aware of methodologies related to RCT, CS, CCS and MA. Second, to facilitate clinical research with sophisticated study designs, faculty experienced in clinical/epidemiological research should be recruited. Third, there should be training programs on how to write scientific articles in English for the clinical researchers in Japan. These programs should be conducted by noted scholars from the English speaking countries.

In conclusion, the number of articles with sophisticated study designs that originated from Japan is not up to the mark if we compare it with the average from the rest of the world, although it has increased over the period of time analyzed. Appropriate interventions are a prerequisite to improving the situation.

References
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