Int J Clin Exp Med 2016;9(6):10684-10694
www.ijcem.com /ISSN:1940-5901/IJCEM0020678

Original Article

A cross-sectional analysis of China-sponsored clinical trials registered with ClinicalTrials.gov

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Received November 27, 2015; Accepted February 14, 2016; Epub June 15, 2016; Published June 30, 2016

Abstract: To evaluate the quality of the information that is available for clinical trials that are sponsored by institutes in China, Hong Kong, and Taiwan and are registered with the ClinicalTrials.gov database. A search of ClinicalTrials.gov was performed on March 31, 2014 to identify trials that were sponsored by institutes located in mainland China, Hong Kong, and Taiwan. The details of these trials were examined and compared using statistical analysis. Among the included trials (N=5820), 72.5% were interventional studies, 26.3% were observational studies, 1.1% were patient registries, and 0.1% were expanded access situations. Moreover, 53.2%, 10.0%, and 36.8% of the trials were sponsored by mainland China, Hong Kong, and Taiwan, respectively. Thirty-three percent of the studies were registered before the trial had been started, while 65.0% were registered after the start or upon completion of the trial. Only 20.7% of all of the studies examined provided links to published results, and the trials based in mainland China were significantly more likely to be published than those based in Hong Kong or Taiwan ($P<0.05$). The total number of registered trials increased over the time period examined, and they predominately encompassed small- and medium-sized interventional studies. Randomized controlled trials (RCTs) only represented approximately one-fourth of the registered trials. Since October 2007, the number of clinical trials sponsored by China has increased significantly, and the publication of study results has also gradually increased. The current transparency of the registry information associated with clinical trials based in China, Hong Kong, and Taiwan is imperfect, and the publication record falls short of expectations. Thus, the capacity and input of clinical research should be enhanced, and the quality and quantity of registered trials needs to be improved.

Keywords: Clinical trials, China, clinical trial registration

Introduction

Clinical trials have important significance for the prevention, diagnosis, and treatment of disease states [1]. Moreover, the registration of clinical trials provides a means for the public to access information regarding study design and to track research progress prior to official implementation of a trial [2]. Trial registration is also necessary to ensure the transparency of information and to improve the quality of clinical trials [3, 4]. In February 2000, clinical trial registration became more readily accessible following the establishment of the website, ClinicalTrials.gov, by funding provided by the U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the National Library of Medicine [5]. In September 2004, the International Committee of Medical Journal Editors (ICMJE) proposed a policy that the registration of clinical trials should be a precondition for publication, and this policy became effective in 2005 [6]. These guidelines are particularly relevant for researchers who intend to publish their results in international journals. In 2004, the ICMJE also announced that clinical trials would need to meet twenty key minimum requirements in order to be accepted into the registry [7]. Similarly, in October 2005, the Chinese Clinical Trial Register (ChiCTR) was established by The Chinese Cochrane Center [8], and in Aug 2005, the World Health Organization International Clinical Trial Registration Platform (WHO ICTRP) was established [9]. The initiative of the latter was to develop a just and equitable clinical trial registration process and to increase transparency on a global scale [10]. Previous research

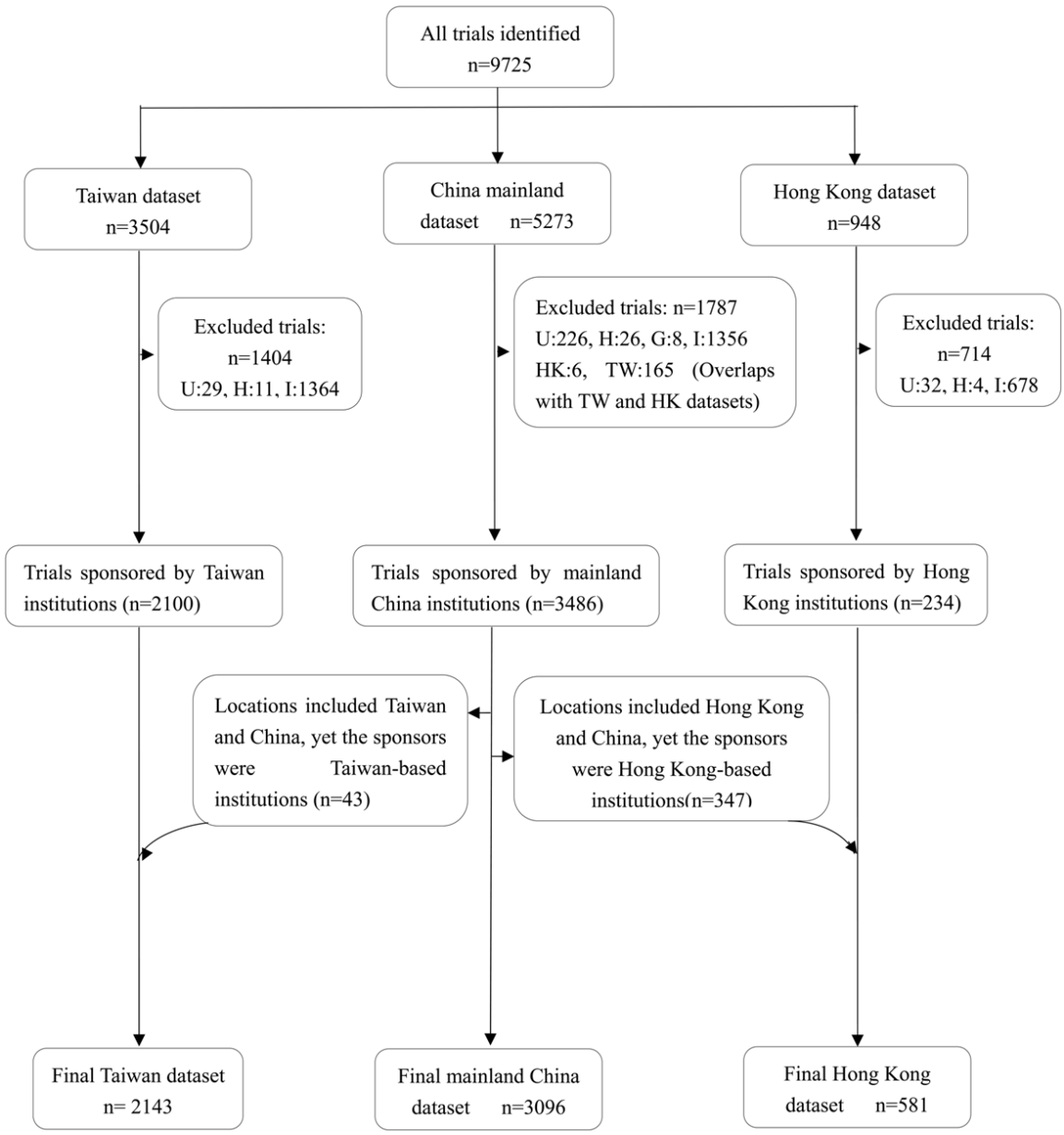

Figure 1. Selection of the trials registered with ClinicalTrials.gov for this study. Trials that were excluded from the analysis were those sponsored by an institution that was not based or affiliated with China. U: university; G: government; H: hospital; I: industry.

showed that registered information pertaining to Chinese clinical trials was incomplete, and the number of Chinese trials was small [11, 12]. Thus, to promote an environment that would foster clinical research in China, the government supplemented clinical trial funding, systematically trained clinicians, and created an integrated platform for the analysis of results.

Currently, ClinicalTrials.gov is the most advanced and informative registry platform available. Previously, the registered information available in ClinicalTrials.gov has been assessed in regards to the minimum required data set [11, 12], yet no published reports to date have conducted a complete investigation of the information available for the Chinese clinical trials that are registered with ClinicalTrials.gov. Therefore, the objective of the present study was to provide a comprehensive statistical analysis of the status of the clinical trials registered by research groups in China, as well as by research groups in Hong Kong and Taiwan, in

Table 1. Characteristics of the interventional trials that have been sponsored by mainland China, Taiwan, and Hong Kong and have been registered with ClinicalTrials.gov

Characteristics examined	Mainland (N=2522)		Taiwan (N=1202)		Hong Kong (N=498)	
	n	%	n	%	n	%
Study Design						
Randomized	1803	71.49%	817	67.97%	411	82.53%
Non-randomized	263	10.43%	202	16.81%	35	7.03%
Missing	453	17.96%	183	15.22%	52	10.44%
Classification						
Safety	85	3.37%	54	4.49%	16	3.21%
Safety/efficacy	1651	65.46%	501	41.68%	186	37.35%
Efficacy	586	23.24%	428	35.61%	224	44.98%
Bio-equivalence	11	0.44%	4	0.33%	2	0.40%
Bio-availability	8	0.32%	2	0.17%	0	0
Pharmacokinetics	11	0.44%	16	1.33%	0	0
Pharmacokinetic/dynamics	23	0.91%	7	0.58%	3	0.60%
Pharmacodynamics	8	0.32%	2	0.17%	1	0.20%
Missing	139	5.51%	188	15.64%	66	13.25%
Intervention Model						
Parallel	1797	71.25%	770	64.06%	373	74.90%
Single group	625	24.78%	320	26.62%	89	17.87%
Factorial	49	1.94%	40	3.33%	8	1.61%
Cross-over	45	1.78%	66	5.49%	25	5.02%
Missing	6	0.24%	6	0.50%	3	0.60%
Masking						
Open	1522	60.35%	599	49.83%	222	44.58%
Single	349	13.84%	266	22.13%	103	20.68%
Double	645	25.57%	333	27.70%	170	34.14%
Missing	6	0.24%	4	0.33%	3	0.60%
Primary purpose						
Treatment	2017	79.98%	831	69.13%	389	78.11%
Prevention	298	11.82%	119	9.90%	39	7.83%
Diagnostic	54	2.14%	75	6.24%	17	3.41%
Screening	16	0.63%	9	0.75%	0	0
Supportive	51	2.02%	44	3.66%	21	4.22%
Health service research	22	0.87%	39	3.24%	15	3.01%
Basic science	22	0.87%	32	2.66%	2	0.40%
Other	0	0	7	0.58%	0	0
Missing	42	1.67%	46	3.83%	15	3.01%
Study phase						
0	22	0.87%	11	0.92%	0	0
I	136	5.39%	56	4.66%	17	3.41%
I/II	134	5.31%	36	3.00%	15	3.01%
II	562	22.28%	187	15.56%	57	11.45%
II/III	127	5.04%	35	2.91%	16	3.21%
III	320	12.69%	114	9.48%	74	14.86%
IV	497	19.71%	252	20.97%	84	16.87%
Missing	724	28.71%	511	42.51%	235	47.19%

the ClinicalTrials.Gov database.

Material and methods

Clinical trial criteria

There were more than 140,000 studies registered with ClinicalTrials.gov as of March 31, 2014 [13]. Therefore, we limited our study sample to "China sponsored" trials which were defined as "studies led by Chinese (including Hong Kong and Taiwan) organizations and conduct the experiments or provide subsidized technology". Trials that were excluded from the analysis were those that included Chinese participants yet were sponsored by an institution that was not based or affiliated with China.

The terms, "China", "Hong Kong", and "Taiwan", were used for the database search. Three XML data sets were subsequently downloaded and these comprised 9725 clinical investigations that had been registered with ClinicalTrials.gov as of March 31, 2014.

Questionnaire design

Based on the features of the "Tabular view" of the ClinicalTrials.gov website, we designed a questionnaire to obtain detailed information about each trial. In addition, reason for exclusion, agency class, registration before/after enrollment of first participant, and study location were recorded. Each trial was classified

Table 2. Characteristics of the observational studies that have been sponsored by mainland China, Taiwan, and Hong Kong and have been registered with ClinicalTrials.gov

	Mainland (n=508)		Taiwan (n=940)		HongKong (n=83)	
	n	%	n	%	n	%
Observational Model						
Cohort	193	37.99%	234	24.89%	32	38.55%
Case-control	168	33.07%	231	24.57%	20	24.10%
Case-only	70	13.78%	178	18.94%	20	24.10%
Case-crossover	5	0.98%	12	1.28%	0	0
Family-based	3	0.59%	17	1.81%	0	0
Ecologic or community	9	1.77%	6	0.64%	2	2.41%
Other	4	0.79%	145	15.43%	1	1.20%
Missing	56	11.02%	117	12.45%	8	9.64%
Time perspective						
Cross-sectional	54	10.63%	233	24.79%	17	20.48%
Prospective	355	69.88%	389	41.38%	57	68.67%
Retrospective	74	14.57%	155	16.49%	5	6.02%
Other	5	0.98%	80	8.51%	1	1.20%
Missing	20	3.94%	83	8.83%	3	3.61%
Duration						
N	507	99.80%	921	97.98%	83	100%
Y	1	0.20%	19	2.02%	0	0
Biospecimen						
With DNA	113	22.24%	118	12.55%	15	18.07%
Without DNA	65	12.80%	69	7.34%	5	6.02%
Non-retained	9	1.77%	12	1.28%	1	1.20%
Missing	321	63.19%	741	78.83%	62	74.70%
Sampling Method						
Probability Sample	260	51.18%	256	27.23%	19	22.89%
Non-probability	239	47.05%	457	48.62%	59	71.08%
Missing	9	1.77%	227	24.15%	5	6.02%

as: interventional, observational, observational [patient registry], or expanded access.

Common baseline features included: primary/study completion date type, first received date, start date, primary completion date, study result, gender, enrollment of healthy volunteers, study location, has DMCs (Data Monitoring Committees), number of collaborators (1, 2, 3, 4, ≥5, missing), number of outcome measures (1, 2, 3, 4, ≥5, missing), number of study arms (1, 2, 3, 4, ≥5, missing), and number of publications (1, 2, 3, 4, ≥5, missing).

Sponsor institutions were classified as university, hospital, research institute/organization, government, industry, and other. Individual sponsors were classified based on their affiliation to a unit or organization. Trials were also categorized based on therapeutic area: neurological, stroke, cardiovascular, respiratory, infectious, diabetes, tumor, and other. Age of the participants was classified as: ≥18 years, <18 years, or missing. More than one classification for age was chosen if the participants included children and adults. Trial enrollment was based on the total number of participants and was divided into five levels: 0-100, 101-500, 501-1000, >1000, and missing.

Additional details that were recorded regarding the interventional studies were: study design (randomized, non-randomized, missing), endpoint classification (safety, safety/efficacy, efficacy, bioequivalence, bioavailability, pharmacokinetics, pharmacokinetics/dynamics, pharmacodynamics, missing), interventional model (parallel, single group, factorial, cross-over, missing), masking (open, single-blind, double-blind, missing), primary purpose (treatment, prevention, diagnostic, screening, supportive care, health services research, basic science, others, missing), and phase (0, I, I/II, II, II/III, IV, missing).

Observational/observational [patient registry] features that were recorded included: model (cohort, case-control, case only, case-crossover, family-based, ecologic or community, others, missing), time perspective (cross-sectional, prospective, retrospective, other, missing), target follow-up duration, biospecimen (samples with/without DNA, non-retained, missing), biospecimen (blood, DNA, tissue, urine, feces, others, missing), and sampling method (probability, non-probability, missing).

The expanded access recruitment studies were classified as: available, no longer available,

Table 3. Multiple choice items for the interventional and observational studies that have been sponsored by mainland China, Taiwan, and Hong Kong and have been registered with ClinicalTrials.gov

	Mainland		Taiwan		Hong Kong	
	n/N	%	n/N	%	n/N	%
Condition						
Neurological	151/3072	4.92%	202/2164	9.33%	65/586	11.09%
Stroke	65/3072	2.12%	71/2164	3.28%	16/586	2.73%
Cardiovascular	322/3072	10.48%	122/2164	5.64%	26/586	4.44%
Respiratory	130/3072	4.23%	125/2164	5.78%	32/586	5.46%
Infectious	201/3072	6.54%	113/2164	5.22%	21/586	3.58%
Diabetes	133/3072	4.33%	106/2164	4.90%	21/586	3.58%
Tumor	1029/3072	33.50%	407/2164	18.81%	90/586	15.36%
Other	1041/3072	33.89%	1018/2164	47.04%	315/586	53.75%
Intervention						
Drug	1637/3389	48.30%	615/2223	27.67%	223/616	36.20%
Procedure	457/3389	13.48%	202/2223	9.09%	101/616	16.40%
Biological	206/3389	6.08%	32/2223	1.44%	13/616	2.11%
Behavioral	57/3389	1.68%	130/2223	5.85%	57/616	9.25%
Device	219/3389	6.46%	153/2223	6.88%	79/616	12.82%
Radiation	98/3389	2.89%	17/2223	0.76%	3/616	0.49%
Dietary Supplement	50/3389	1.48%	49/2223	2.20%	9/616	1.46%
Genetic	14/3389	0.41%	17/2223	0.76%	0	0
Other	261/3389	7.70%	215/2223	9.67%	68/616	11.04%
Missing	390/3389	13.00%	793/2223	35.67%	63/616	10.23%
Age						
N	97/3071	3.16%	225/2297	9.80%	32/592	5.41%
<18	358/3071	11.66%	267/2297	11.62%	41/592	6.93%
≥18	2787/3071	90.75%	1805/2297	78.58%	519/592	87.67%
Description						
Blood	137/543	25.23%	134/970	13.81%	16/83	19.28%
DNA	9/543	1.66%	23/970	2.37%	2/83	2.41%
Tissue	48/543	27.26%	36/970	3.71%	1/83	1.20%
Urine	10/543	1.84%	10/970	1.03%	0	0
Feces	0	0	0	0	0	0
Other	19/543	3.50%	25/970	2.58%	3/83	3.61%
Missing	320/543	58.93%	742/970	76.49%	61/83	73.49%

temporarily unavailable, and approved for marketing.

Statistical analysis

All of the above items were listed on separate lines. The following items are multiple choices: ages, description, condition, intervention. For the trials that were excluded, only the NCT number, sponsor, and reason for exclusion were recorded.

These questionnaires were converted into an electronic form and SPSS 18.0 was used to perform statistical analyses. Chisquare (χ^2) tests were used to examine associations between study characteristics and regions. The statistical tests were two-tailed with a type I error of 0.05.

Results

A search of the ClinicalTrials.gov database identified 9725 studies (**Figure 1**). Among the listed trials, 5273 were sponsored by mainland China, 948 were sponsored by Hong Kong, and 3504 were sponsored by Taiwan. In the data set for mainland China ("China" is included in

Table 4. Common characteristics of the interventional and observational studies that have been sponsored by mainland China, Taiwan, and Hong Kong and have been registered with ClinicalTrials.gov

	Mainland n=3030		Taiwan n=2142		Hong Kong n=581	
	n	%	n	%	n	%
Recruitment status						
Unknown	606	20.00%	829	38.70%	117	20.14%
Recruiting	1636	53.99%	1115	52.05%	194	33.39%
Completed	747	24.65%	691	32.26%	277	47.68%
Not yet Recruiting	262	8.65%	108	5.04%	35	7.28%
Active, not recruiting	251	8.28%	123	5.74%	46	7.92%
Rolling invitation	82	2.71%	43	2.01%	4	0.69%
Terminated	26	0.86%	40	1.87%	19	3.27%
Suspended	14	0.46%	5	0.23%	4	0.69%
Withdrawn	12	0.40%	17	0.79%	2	0.34%
Primary completion date type						
Actual	807	26.63%	636	29.69%	234	40.28%
Anticipated	2112	69.70%	902	42.11%	248	42.69%
Missing	111	3.66%	604	28.20%	99	17.04%
Study completion date type						
Actual	721	23.80%	630	29.41%	251	43.20%
Anticipated	2020	66.67%	958	44.72%	255	43.89%
Missing	289	9.54%	554	25.86%	75	12.91%
Registration is:						
Before[a]	1245	41.09%	593	27.68%	183	31.50%
After	1773	58.51%	1518	70.87%	386	66.44%
Undetermined	12	0.40%	31	1.45%	12	2.07%
Agency class						
Industry	330	10.89%	119	5.56%	20	3.44%
University	1340	44.22%	46	2.15%	444	76.42%
Hospital	1230	40.59%	1909	89.12%	51	8.78%
Government	69	2.28%	60	2.80%	58	9.98%
Organization	38	1.25%	3	0.14%	8	1.38%
Other	17	0.56%	5	0.23%	0	0
Collaborator						
1	494	16.30%	401	18.72%	120	20.65%
2	136	4.49%	59	2.75%	35	6.02%
3	55	1.82%	13	0.61%	9	1.55%
4	43	1.42%	8	0.37%	3	0.52%
≥5	136	4.49%	44	2.05%	6	1.03%
Missing	2166	71.49%	1617	75.49%	408	70.22%
Study arm						
1	705	23.27%	498	23.25%	87	14.97%
2	1548	51.09%	672	31.37%	304	52.32%
3	302	9.97%	169	7.89%	50	8.61%
4	140	4.62%	49	2.89%	14	2.41%
≥5	75	2.48%	31	1.45%	3	0.52%
Missing	260	8.58%	723	33.75%	123	21.17%
Publication						
1	301	9.93%	186	8.68%	65	11.19%

2	102	3.37%	59	2.75%	19	3.27%
3	54	1.78%	29	1.35%	8	1.38%
4	48	1.58%	19	0.89%	7	1.20%
≥5	161	5.31%	104	4.86%	52	8.95%
Missing	2364	78.02%	1745	81.47%	430	74.01%
Study result						
Y	45	1.49%	43	2.01%	8	1.38%
N	2985	98.51%	2099	97.99%	573	98.62%
Enrollment						
0-100	1367	45.12%	1224	57.14%	301	51.81%
101-500	1177	38.84%	698	32.59%	204	35.11%
501-1000	211	6.96%	91	4.25%	32	5.51%
>1000	243	8.02%	83	3.87%	35	6.02%
Missing	32	1.06%	46	2.15%	9	1.55%
Gender						
Both	2674	88.25%	1878	87.68%	517	88.98%
Male	56	1.85%	55	2.57%	15	2.58%
Female	300	9.90%	205	9.57%	49	8.43%
Missing	0	0	4	0.19%	0	0
Accepting healthy volunteers						
Y	419	13.83%	581	27.12%	103	17.73%
N	2606	86.01%	1544	72.08%	425	73.15%
Missing	5	0.17%	17	0.79%	53	9.12%
DMC						
Y	2144	70.76%	849	39.64%	198	34.08%
N	683	22.54%	784	36.60%	248	42.69%
Missing	203	6.70%	509	23.76%	135	23.24%

Abbreviations: DMC, data monitoring committee; Y, yes; N, no. [a]Before: when a study was conducted after the trial registration. After: when a study was conducted before registered.

the location), there were 43 trials sponsored by Taiwan institutions and 347 trials sponsored by Hong Kong institutions. Based on the inclusion and exclusion criteria for the current study, only 5820 trials were eligible, including 3096 that were sponsored by mainland China, 581 that were sponsored by Hong Kong, and 2143 that were sponsored by Taiwan. Among the 3905 excluded trials, 1787, 1404, and 714 trials were sponsored by mainland China, Taiwan, and Hong Kong, respectively.

Interventional trials accounted for more than 50% of the total trials registered (mainland China: 81%, Taiwan: 56%, Hong Kong: 86%), while observational studies comprised the second most frequent study type (mainland China: 16%, Taiwan: 44%, Hong Kong: 14%). In addition, there were 61 observational [patient registry] studies, five expanded access studies from mainland China, and one expanded access study from Taiwan.

Table 1 lists selected characteristics of all the interventional trials that were examined, as well as the comparisons that were made between the data for each of the three regions. The frequency of the randomized trials that were based in mainland China, Taiwan, and Hong Kong were 71.49% (n=1803), 67.97% (n=817), and 82.53% (n=411), respectively. Safety/efficacy and efficacy trials accounted for most of the trials that were examined (China: 88.7%, n=2237; Taiwan: 77.29%, n=929; Hong Kong: 82.33%, n=410). In addition, parallel and open-label interventional models constituted a large proportion of the trials (China: 71.25% and 60.35%, Taiwan: 64.06% and 49.83%, Hong Kong: 74.9% and 44.58%, respectively in each case). Approximately 25-34% of the trials had a double-blind design, while intent-to-treat analyses comprised 80% of the trials based in China, 69.13% of the trials based in Taiwan, and 78.11% of the trials based in Hong Kong. Furthermore, phase II and phase IV studies

Table 5. The number of publications associated with the trials sponsored by mainland China, Taiwan, and Hong Kong and have been registered with ClinicalTrials. gov[a]

Trial sponsors	Numbers of publications								
	<5	5-9	10-19	20-29	30-39	40-49	≥50	Total	%
Mainland China	505	103	44	9	4	-	1	666/3096	21.50%
Taiwan	286	55	31	11	3	1	2	389/2143	18.15%
Hong Kong	99	28	19	4	1	-	-	151/581	25.99%
Total	890	186	94	24	8	1	3	1206/5820	20.72%

[a]Comparison of these three regions was performed by using a Chi-square test (x^2=12.723, P<0.05).

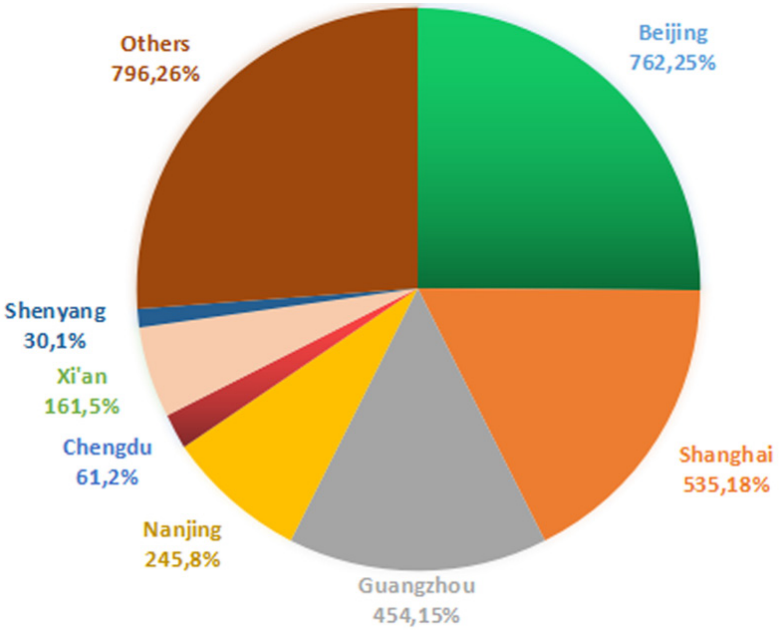

Figure 2. Regional distribution of the trials sponsored by institutions in mainland China.

comprised the first and second largest proportion of interventional trials, while nearly one-third to one-half of the studies examined did not indicate the study phase.

Table 2 lists selected characteristics of all the observational studies that were examined. Cohort studies represented the largest proportion (China: 37.99%, Taiwan: 24.89%, Hong Kong: 38.55%), followed by case-control and case-only studies. In addition, there were a large number of prospective studies (China: 69.88%, Taiwan: 41.38%, Hong Kong: 68.67%), followed by cross-sectional and retrospective studies.

Additional multiple choice items that were included in the questionnaire used to examine the eligible trials addressed: therapeutic area, intervention type, patient age, and biospecimen availability (**Table 3**). Tumor trials comprised the largest group among all of the therapeutic areas (China: 33.5%, Taiwan: 18.81%, Hong Kong: 15.36%), and the top two types of intervention studies involved drugs and procedures. An "unknown" status was applied by the registry to trials that had not been updated in the last three months. **Table 4** demonstrates that the highest proportion of "unknown"-labeled trials were from Taiwan (38.70%, n=829), while approximately 20% were from China or Hong Kong. The vast majorities of all of the trials were still actively recruiting participants or were completed (80%). When the start and registry dates of the trials were compared, only about one-third of the trials were found to be registered before the official start of the studies.

Overall, 20.72% of published trials could be found in peer-reviewed biomedical journals indexed by Medline, and for only 5.6% of all of the completed trials, the results were published within 15 ± 14.4 months of trial completion (**Table 5**). Furthermore of the published trials, approximately 26% were funded primarily by Hong Kong-associated institutes, followed by institutes in mainland China (21.5%) and Taiwan (18.15%, P<0.05 for Hong Kong vs. mainland China). It was also observed that 25% of the trials from mainland China were sponsored by Beijing-based institutions compared

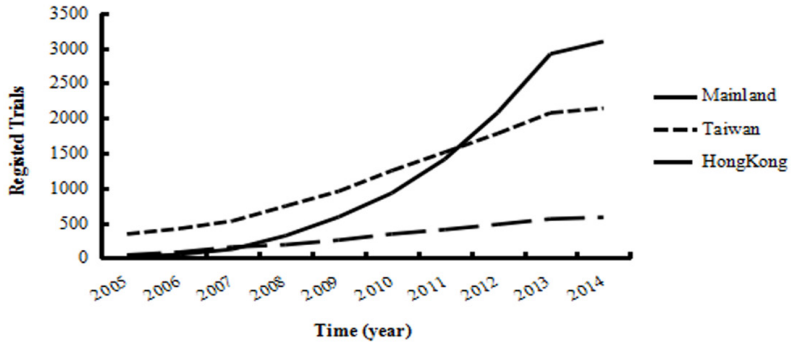

Figure 3. Cumulative number of trials registered with ClinicalTrials.gov between 2005 and 2014.

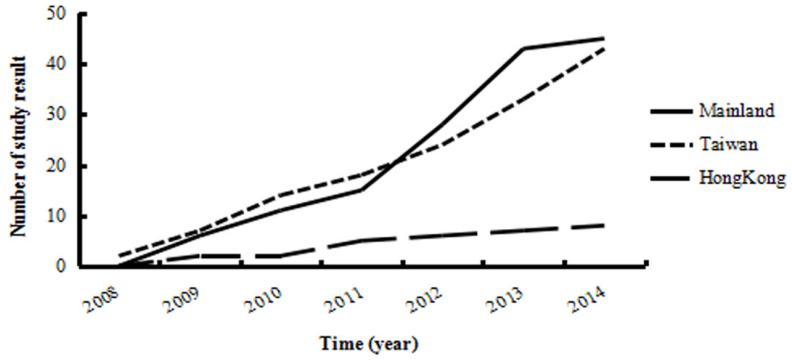

Figure 4. Cumulative number of published studies. The Chi-square test was used to compare the data for the three regions (x^2=4.214, P>0.05).

to 18% and 15% of the trials that were sponsored by institutes based in Shanghai and Guangzhou, respectively (**Figure 2**). Since the establishment of the ChiCTR, the number of clinical trials based in mainland China has increased significantly, and was found to be much greater than the numbers for the other two regions after 2012 (**Figures 3** and **4**). Mainland also gradually began to publish study result and published the biggest number of papers in the three regions after 2011 (**Figure 4**).

Discussion

When we examined the clinical trials that have been sponsored by institutes in China and registered with ClinicalTrials.gov, we determined that the number of registered trials had increased with each year, particularly after the establishment of the ChiCTR in 2007. There was also a gradual increase in the number of published findings. The types of trials that were predominantly registered included small and medium-sized interventional, single-center studies, while 80% of the trials represented randomized, open-label trials. In contrast, randomized controlled trials only comprised about one-fourth of all the China-sponsored studies that were examined.

The present study demonstrates that China-sponsored clinical trials were primarily funded through local universities and industries, while the proportion of studies that were funded by Chinese industries was very low (3.44-10.89%). Furthermore, of the clinical trials that did not satisfy the inclusion criteria for the present study, most of these were sponsored by fully reinforced international enterprises. In contrast, the clinical research industries in Europe and America are the leading sponsor (~36%) of interventional trials, and these trails accounted for 59% of all of the clinical trials registered between 2007 and 2010 [14]. Company was also the primary source of funding for 85% of the randomized controlled drug trials that were published up until March 27, 2012 [15], as well as for 96 registered trials (73%) that were published in 19 high-impact journals [16]. These differences potentially reflect a weakness of Chinese companies, and in particular, a weakness of the clinical trial registration process.

Regarding the predominant therapeutic areas of the clinical trials examined, tumor trials accounted for the highest proportion of studies that were based in mainland China, Taiwan, and Hong Kong, and are similarly represented by other domestic and foreign institutions [16-18]. This indicates that China, as well as other nations, have a common interest in the treatment of tumors and other chronic diseases.

A relatively high percentage of missing entries were found, and some of the missing items tended to be associated with important trial design details. These findings indicate that

Chinese researchers who are responsible for registering clinical trials do not always have sufficient information to provide a complete registration, and this highlights the need for a more professional and serious attitude towards completing each registration entry [19]. Accordingly, research groups in China have prioritized specialized training for the registration of clinical trials due to the majority of registered trials with incomplete entries.

Before April 30, 2008, only 11% of the completed trials that were examined were published. In comparison, publications of European and American clinical trials have spanned several years, while China has only recently begun publishing trial results. Moreover, the accuracy and integrity of the latter have been recognized as needing improvement [20-22]. Forty-six percent of the trials funded by the NIH are published in peer-reviewed biomedical journals indexed by Medline within 30 months of a trial's completion, with only about one-third of trials remaining unpublished after 51 months [22]. However, the publication of all China-sponsored studies (including Hong Kong and Taiwan) were only about 20.7% and the reported study result were 5.6%. The results of the present analysis also indicate that a significant proportion of the registered trials that were examined were not published following completion of the trials.

Research has shown that industry-funded trials are more likely to exhibit greater publication bias than those funded by academic institutions [29]. However, in the present study, registered trials funded by non-profit organizations were published more frequently than those funded by commercial organizations. Therefore, integrating the information from this comprehensive collection of clinical trials may facilitate the presentation of both negative and positive data and prevent publication bias.

An important finding was that approximately 50% of the interventional and observational studies that were examined included fewer than 100 participants. Small trials can be useful in early-phase drug evaluations or biological investigations [23, 24]. However, there are risks associated with reliably establishing the efficacy of treatments that exert modest effects in a small trial, particularly when clinical practice guidelines are developed based on the results obtained from a small, and potentially unrepresentative, sample population [25-28]. Therefore, the utility of small trials should be addressed cautiously. Additional limitations to consider are that the data available on ClinicalTrials.gov are recorded by trial sponsors or principal investigators, and therefore may include recording errors. Furthermore, some records may have been modified, such as the recruitment status, during the study period.

Conclusions and perspectives

This study revealed the status of China-sponsored clinical trials registered with ClinicalTrials.gov to date. Due to the consistent efforts of Chinese researchers, clinical trial registration has been widely recognized and implemented in recent years; however, the quality and quantity of clinical investigations are still affected by country/regional laws, regulations, economic conditions, research and technology, as well as other factors. In 2013, the Chinese government officially launched 13 national clinical research centers in order to strengthen the country's research capacity and experience, and this was an important step in building China's clinical research unit towards becoming a global leading force [30].

Disclosure of conflict of interest

None.

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