Globalization of sponsored clinical trials

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We read with interest the recent article in *Nature Reviews Drug Discovery* on trends in the globalization of clinical trials¹, as we have also analysed US clinical trial registry data (ClinicalTrials.gov)² to study the same topic using data downloaded on 4 April 2007.

We identified 188,428 study sites for 8,143 industry-sponsored Phase I–IV trials (recruiting, no longer recruiting/ongoing or completed), compared with 123,713 sites for 6,046 studies identified by Thiers and colleagues¹, and their paper was ultimately based on 74,499 study sites (39.5% of all sites). Among different results obtained in our analysis of our larger data set, the United Kingdom ranked fifth with 4,931 sites, whereas REF. 1 ranked the country eighth with 1,753 sites.

The paper by Thiers *et al.* also ranked countries according to annual growth rate in the number of sites, based on studies registered between 2002 and 2006. However, the US trial register was not utilized on a large scale until the introduction of the International Committee of Medical Journal Editors (ICMJE) publication policy in July 2005 (REF. 3). Before mid-2005, only around 400 new industry-sponsored trials were on average registered annually, compared with 3,400 after mid-2005. Since mid-2005, 24 of the world's top 25 pharmaceutical companies have utilized the register, while several leading companies including Pfizer, AstraZeneca, Boehringer Ingelheim, Wyeth and Takeda rarely registered before this point in time. Furthermore, the majority of sites (67.7%; 40,654/60,037) registered before mid-2005 were US sites, compared with 46.9% (60,270/128,391) from mid-2005 onwards⁴. The number of study sites in the US thus increased by 143%, while all other 49 top-ranked countries showed an increase of at least 200% — with 20 countries showing an increase of more than 400%. Clearly, there was selective registration of trials with ClinicalTrials.gov prior to the implementation of the ICMJE policy in mid-2005.

We also downloaded the US trial register data on 1 November 2007 and kept for analysis industry-sponsored Phase II–IV trials (recruiting, no longer recruiting/ongoing or completed) with at least

Figure 1 | The top 50 countries ranked by the total number of Phase II–IV study sites registered with ClinicalTrials.gov over a 24-month period from October 2005 to September 2007 (rank: number of sites). The annual growth in the number of study sites from the first year to the second year gives a second ranking (rank: growth).

CORRESPONDENCE

Table 1 | Phase II–IV trial protocols and sites registered with ClinicalTrials.gov between Oct 2005–Sept 2006 (Yr 1) and between Oct 2006–Sept 2007 (Yr 2)

Rank	Rank	Rank				Yr 1	Yr 1	Yr 2	Yr 2	Total	Total	Sites per	GROWTH	GROWTH	
Total	Yr 1	Yr 2	Change			Protocols	Sites	Protocols	Sites	Protocols	SITES	Protocol	Protocols	Sites	Rank by Sites
SITES	Sites	Sites	Rank	Region	Country	N	N	N	N	N	N	N	%	%	%
1	1	1	0	North America	United States	1,388	34,131	1,382	24,802	2,770	58,933	21.3	99.6	72.7	34
2	2	2	0	Europe	Germany	547	4,436	491	3,389	1,038	7,825	7.5	89.8	76.4	28
3	3	4	1	Europe	France	406	4,213	303	1,834	709	6,047	8.5	74.6	43.5	48
4	4	3	-1	North America	Canada	440	3,493	325	1,870	765	5,363	7.0	73.9	53.5	44
5	5	6	1	Europe	United Kingdom	378	2,389	307	1,373	685	3,762	5.5	81.2	57.5	41
6	7	5	-2	Europe	Spain	322	1,922	301	1,635	623	3,557	5.7	93.5	85.1	20
7	6	7	1	Europe	Italy	312	1,945	274	1,355	586	3,300	5.6	87.8	69.7	36
8	8	10	2	Asia	Japan	135	1,785	122	922	257	2,707	10.5	90.4	51.7	46
9	9	9	0	E. Europe & Russia	Poland	245	1,235	229	1,093	474	2,328	4.9	93.5	88.5	17
10	11	8	-3	E. Europe & Russia	Russia	181	1,093	178	1,184	359	2,277	6.3	98.3	108.3	6
11	12	11	-1	Oceania	Australia	235	1,082	197	870	432	1,952	4.5	83.8	80.4	25
12	10	12	2	Europe	Belgium	233	1,218	221	683	454	1,901	4.2	94.8	56.1	43
13	13	18	5	Europe	Netherlands	247	1,078	178	574	425	1,652	3.9	72.1	53.2	45
14	14	20	6	Europe	Sweden	184	911	162	529	346	1,440	4.2	88.0	58.1	39
15	18	14	-4	E. Europe & Russia	Hungary	176	706	150	620	326	1,326	4.1	85.2	87.8	18
16	19	15	-4	Latin America	Argentina	146	691	137	620	283	1,311	4.6	93.8	89.7	16
17	15	19	4	E. Europe & Russia	Czech Republic	193	766	145	545	338	1,311	3.9	75.1	71.1	35
18	21	13	-8	Latin America	Brazil	128	627	122	629	250	1,256	5.0	95.3	100.3	8
19	20	16	-4	Asia	India	112	650	115	606	227	1,256	5.5	102.7	93.2	13
20	22	17	-5	Latin America	Mexico	155	601	153	581	308	1,182	3.8	98.7	96.7	10
21	17	28	11	Africa	South Africa	171	709	100	323	271	1,032	3.8	58.5	45.6	47
22	16	29	13	Europe	Denmark	166	725	125	297	291	1,022	3.5	75.3	41.0	50
23	23	23	0	Europe	Austria	156	578	162	428	318	1,006	3.2	103.8	74.0	30
24	28	21	-7	E. Europe & Russia	Ukraine	62	388	72	501	134	889	6.6	116.1	129.1	2
25	29	22	-7	Asia	China	83	377	93	477	176	854	4.9	112.0	126.5	3
26	27	24	-3	Asia	Korea, South	112	439	122	406	234	845	3.6	108.9	92.5	14
27	26	25	-1	Middle East	Israel	117	451	106	390	223	841	3.8	90.6	86.5	19
28	25	30	5	Europe	Finland	139	484	114	277	253	761	3.0	82.0	57.2	42
29	24	35	11	Europe	Norway	105	503	72	207	177	710	4.0	68.6	41.2	49
30	30	26	-4	E. Europe & Russia	Romania	100	349	86	352	186	701	3.8	86.0	100.9	7
31	35	27	-8	Asia	Taiwan	95	284	115	350	210	634	3.0	121.1	123.2	4
32	31	31	0	E. Europe & Russia	Slovakia	81	343	69	253	150	596	4.0	85.2	73.8	32
33	32	32	0	Europe	Switzerland	143	326	117	238	260	564	2.2	81.8	73.0	33
34	34	33	-1	Europe	Greece	86	303	73	224	159	527	3.3	84.9	73.9	31
35	33	36	3	Europe	Portugal	89	315	65	207	154	522	3.4	73.0	65.7	38
36	36	34	-2	E. Europe & Russia	Bulgaria	72	262	52	214	124	476	3.8	72.2	81.7	23
37	38	37	-1	E. Europe & Russia	Turkey	62	153	67	185	129	338	2.6	108.1	120.9	5
38	37	38	1	Asia	Philippines	56	158	46	143	102	301	3.0	82.1	90.5	15
39	39	39	0	Latin America	Chile	71	151	63	142	134	293	2.2	88.7	94.0	12
40	44	41	-3	Asia	Malaysia	47	131	52	126	99	257	2.6	110.6	96.2	11
41	41	42	1	E. Europe & Russia	Lithuania	47	140	50	111	97	251	2.6	106.4	79.3	27
42	42	44	2	Oceania	New Zealand	59	135	47	102	106	237	2.2	79.7	75.6	29
43	45	43	-2	Latin America	Peru	51	129	44	107	95	236	2.5	86.3	82.9	22
44	40	49	9	E. Europe & Russia	Estonia	55	143	39	83	94	226	2.4	70.9	58.0	40
45	43	46	3	Europe	Ireland	60	133	43	91	103	224	2.2	71.7	68.4	37
46	46	47	1	E. Europe & Russia	Latvia	38	114	42	91	80	205	2.6	110.5	79.8	26
47	48	45	-3	Asia	Thailand	55	102	44	102	99	204	2.1	80.0	100.0	9
48	51	40	-11	Latin America	Colombia	30	67	48	134	78	201	2.6	160.0	200.0	1
49	47	48	1	Asia	Hong Kong	65	104	56	87	121	191	1.6	86.2	83.7	21
50	49	51	2	E. Europe & Russia	Croatia	43	94	36	76	79	170	2.2	83.7	80.9	24

*Percentage increase in sites: (number of sites Yr 2) ÷ (number of sites in Yr 1) × 100

one study site address, and first registered after the introduction of the ICMJE policy. Between October 2005 and September 2006, there were 2,597 studies and 74,071 sites registered; between October 2006 and September 2007, there were 2,570 studies and 52,909 sites registered. The explanation for the fewer sites in the second year is that new sites are continuously added for many newly registered trials.

TABLE 1 and FIG. 1 give our ranking of the top 50 countries based on the total number of study sites, as well as ranking based on annual growth, which differ from those presented in REF. 1. Based on our results, Taiwan, Chile, Brazil, Romania, Switzerland and the US had improved rankings of ten positions or more in annual growth of study sites, whereas Estonia,

Portugal, Slovakia, Czech Republic, Lithuania, Peru, Denmark and Japan all slipped down the rankings by 15 positions or more.

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