

Report

Iranian Registry of Clinical Trials: A Four-year Steady Progress

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Abstract

Background: Iranian Registry of Clinical Trials (IRCT) commenced its activities as a member of WHO registry network on fourth of December 2008. We explored the progress it has made within its first four years both in terms of quantity of registrations as well as its timeliness.

Materials and Methods: We downloaded all the approved trial records until 22nd of September 2012 from the registry website. The number of registrations per calendar year was calculated and plotted over time. We assessed the timing of the registrations by categorizing them according to the date of registration in relation to the start date of recruitment into prospective, borderline prospective, borderline retrospective, and retrospective. We looked at the trends of timeliness of the registrations over time both according to registration year and the year that the recruitment had started.

Results: There were 3145 valid registrations in IRCT until 22nd of September 2012. The number of trials increased steadily over the years from 26 in the last three months of 2008 and 182 in 2009 to 771 and 1138 in 2010 and 2011 respectively and is expected to reach 1310 in 2012. Among the 182 registrations that took place in 2009, only 16 % were prospective or borderline prospective while this figure was doubled in 2012. When we categorized registrations according to the year of recruitment, the increasing trend was more marked from 5 % and 15 % in 2009 and 2010 to 27 % and 62 % in 2011 and 2012.

Conclusion: IRCT has made an outstanding progress within four years from its establishment both in terms of quantity and timeliness. Registration movement has succeeded in getting the message across to the research community and clinical trial registration has now become an integral part of research sphere in Iran.

Keywords: Clinical trials, Iran, registry

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Introduction

Iranian Registry of Clinical Trials (IRCT) was established in 2008 and acquired its World Health Organization (WHO) primary registry status^{1,2} on fourth of December 2008. Its development was a complementary step in a set of events that started in 1985 when medical education was integrated into the Iranian national health system.³ The 1985 reform caused a major boost in problem oriented medical research and created a need for a tighter regulation of its conduct. In 1997 a group of leading researchers sponsored by the Ministry of Health and Medical Education (MOHME) set up the 26-item national ethical guideline to safeguard human participants in experimental research.⁴ This was in continuation of Helsinki declaration and to make the ethical principles more relevant to the local religious, cultural, and judiciary norms. Parallel to the events happening nationally, a global movement for greater transparency in interventional medical research

was on the making.

The international movement was led by International Committee of Medical Journal Editors (ICMJE). ICMJE came to the conclusion that the current state of affairs between pharmaceuticals that sponsor and fund medical research on new drugs and medical journals that disseminate the findings coming out of this research does not fully serve the rights of patients who are participating in clinical trials with mainly altruistic intentions. Findings perceived to be a threat to the financial interests of the sponsors are likely not to find their way into medical literature. This also includes negative findings. Therefore, greater transparency and timely public disclosure of all protocol information was at the heart of their 2004 and 2005 editorials^{5,6} simultaneously published in all member journals. The editorial called for the registration of key protocol information in a database that is in public domain before the recruitment of the first patient. Soon after, WHO gave its backing to the movement⁷ by establishing International Clinical Trial Registry Platform (ICTRP) and giving it the task of creating a network of registries that are abide by minimum standards set by WHO and a portal that keeps all the registered trials in one place and facilitates retrieval of protocol information for those who need them. In line with global endorsement of the movement, World Medical Association in its 59th annual assembly in 2008 added a clause to Helsinki declaration making registration of clinical trials before the recruitment of their first patient an ethical necessity.⁸

Given the abovementioned national and international context, Iranian Registry of Clinical Trials started its activities with the goal of upholding ethical principles and promoting culture of

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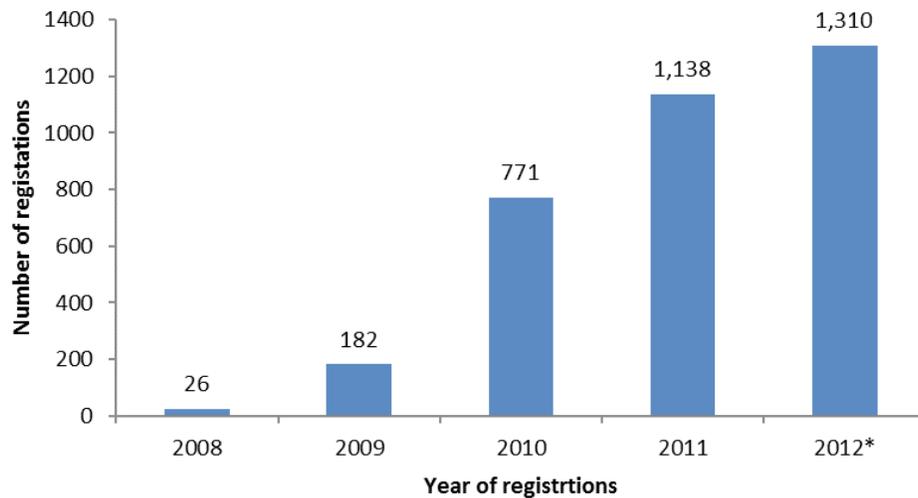


Figure 1. The number of registrations of clinical trials in IRCT according to the year of registration; *Number estimated based on 1028 registrations until 22nd of September 2012.

transparency in medical research. It had also the additional advantage of making research conducted by Iranian researchers more internationally visible. Now four years on, we are examining the progress it has made so far both in terms of quantity of registrations as well as its timeliness. We are using the latter as an indicator of the degree that the registration movement has succeeded to establish itself among members of the research community in the Islamic Republic of Iran.

Materials and Methods

We downloaded all the approved trial records until 22nd of September 2012 from the registry website. The number of registrations per calendar year was calculated and plotted over time. We assessed the timing of the registrations by categorizing them according to the date of registration in relation to the date of recruitment. Those registered before the start of recruitment were called prospective registrations in contrast to retrospective ones which were those trials registered after the date that recruitment ended. For those in between of the start and end dates of recruitment, we regarded them as borderline prospective if they had completed the registration within 30 days of the start of recruitment, otherwise they were regarded borderline retrospective. We looked at the trends of timeliness of the registrations over time both according to the registration year and the year that the recruitment had started. Stata 11 statistical software was used for the analysis.

Results

There were 3145 valid registrations in IRCT until 22nd of September 2012. The number of trials increased steadily over the years from 26 in the last three months of 2008 and 182 in 2009 to 771 and 1138 in 2010 and 2011 respectively (Figure 1). Based on 1028 trials registered until the date of data extraction for the current study and assuming a constant rate the number of trials registered for 2012 is expected to be about 1310. The annual increase in the number of registrations went up from 75 % in 2010 to 3.2 times in 2011 compared to their previous year while gradu-

ally coming down to 48 % in 2011 and is expected to be around 15 % in 2012.

Among the 182 registrations that took place in 2009, only 16 % were either prospective or borderline prospective while this figure was doubled in 2012 (Figure 2). When registrations were categorized according to the year of recruitment, the increasing trend was more marked from 5 % and 15 % in 2009 and 2010 to 27 % and 62 % in 2011 and 2012, respectively (Figure 3).

Discussion

We found that the number of registrations in IRCT has gone up steadily from 182 in 2009 to 1138 in 2011 and is expected to reach 1310 in 2012. The annual increase in the number of registrations on the other hand has slowed down and is expected to be only 15 % in 2012 compared to its previous year. The proportion of prospectively registered trials has increased in a sign of more timely registrations suggesting that the registration process has become an integral part of conduct of a clinical trial among Iranian researchers.

The steady increase in the number of registered clinical trials in IRCT during the first four years since its conception is an indication of outstanding progress. It happened in the context of a rapid rise in the research output and overall scientific ranking of Islamic Republic of Iran.⁹⁻¹² Many factors may have contributed to this increase, among them were the support that IRCT received from the authorities at the MOHME and the Iranian Society of Medical Journal Editors (ISMJE) both in terms of funding (from MOHME) and enforcing new regulations making registration mandatory for publication of clinical trial results in Iranian Journals. It was expected that the number of registrations should go up before it reaches a plateau and the slowdown in the rate of increase to 15 % in 2012 is a sign of this adaptation. This is the result of a balance between number of trials conducted and the proportion that is being registered.

We found that the proportion of trials that are being retrospectively registered is decreasing and the number of prospectively registered trials is increasing. This is reassuring as this is the first

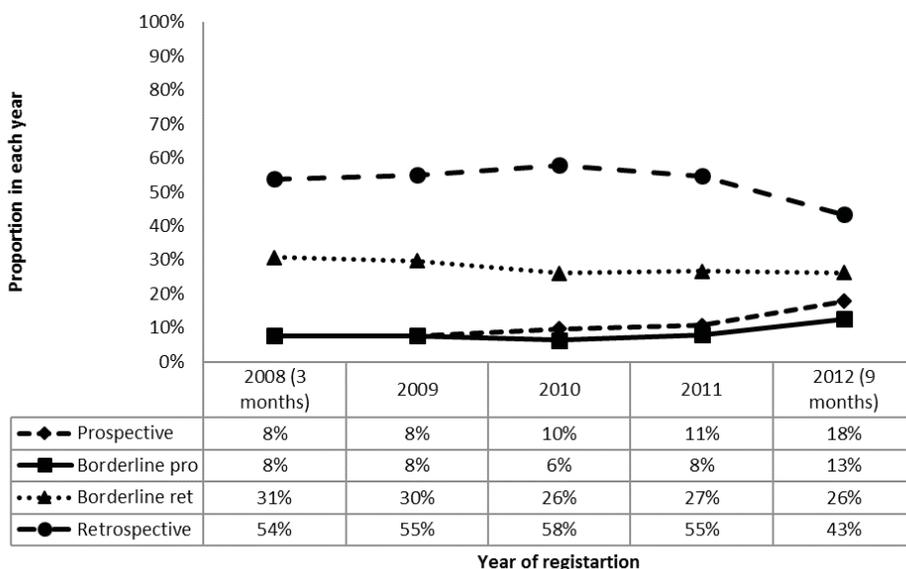


Figure 2. Timeliness of registration according to the year of registration in clinical trials registered in IRCT.

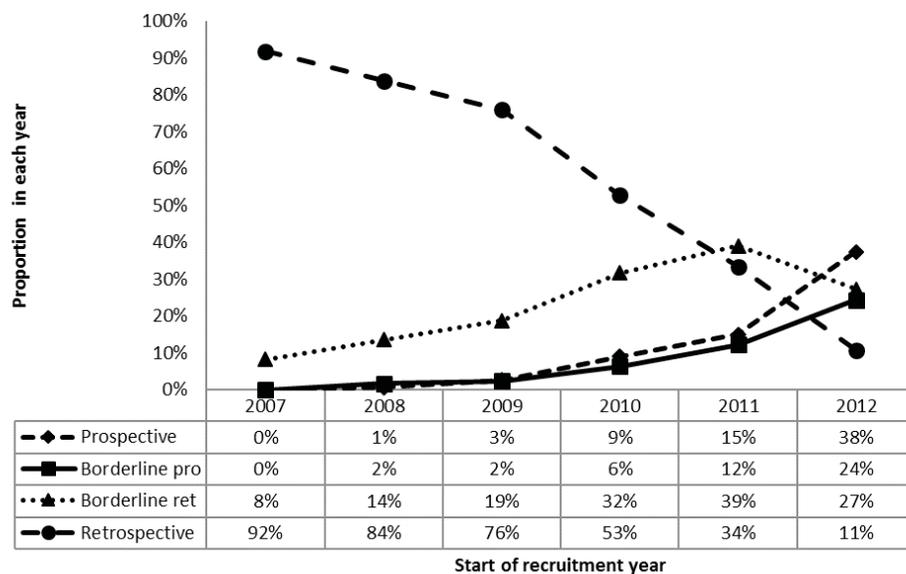


Figure 3. Timeliness of registrations according to the start of the recruitment year in clinical trials registered in IRCT.

time we are witnessing signs of improvement in this index. Retrospectively registered trials are a potential problem in all registries and it has been reported that about 40 % of trials registered in ICTRP are either retrospective or borderline retrospective by our current study's definition. Their presence could be the result of ignorance in part of sponsor or the investigator if the study is investigator initiated to the existing ethical guidelines governing medical research. This, however, is not very likely particularly when it comes to major pharmaceutical companies but still might be relevant to small scale investigator initiated trials. It was potentially worrying when we first found a high proportion of trials that were retrospective or borderline retrospective in our previous study.¹³ We speculated that this could be partly due to lack of awareness by investigators and partly due to forceful implementation of measures to expand the coverage of registrations to all eli-

gible trials conducted in Iran. Although we couldn't provide any evidence to back our claim at the time, the emerging trend suggests that as IRCT enters into its establishment phase the impact of old trials that are being referred for retrospective registration as they want to publish their results is decreasing. A further evidence of this phenomenon emerged when we categorized registered trials based on their year of start of recruitment (Figure 3). Although the figures for 2012 might not be reliable because not enough time has passed to provide a chance for retrospective registrations, but a clear trend towards an increase in proportion of prospective registrations over time are supportive of our claim. It also shows that the message of global registration movement has reached the research community in Iran and has started to make its impact on the way clinical trial research is being conducted in Iran.

A national clinical trial registry could not fully succeed without

strong support by policy makers. The first attempt to set up a registry of clinical trials compliant with WHO standards was in 2007 by Tehran University of Medical Sciences (TUMS)¹⁴ which had limited success. Building on the experiences of TUMS registry, work on a Clinical Trial Registry with national remits sponsored by MOHME started a year later and IRCT was founded. However, this was only the beginning. Some critical changes in the regulations were also needed besides the database that holds the protocol information and the interface that is used to communicate and interact with users. This was the key to make sure that the registry will survive and flourish. The strong political support that IRCT enjoyed enabled it to bring about the necessary regulatory changes. The first key change was to make registration of clinical trials a mandatory condition for publication in any Iranian Medical Journal. This was enforced by a great deal of support from individual editors and ISMJ. The second was to ask medical universities to release the funds for clinical trials only after they complete the registration process. The latter that was more recent contributed greatly to the timely registration of trials.

IRCT has made an outstanding progress within four years from its establishment both in terms of quantity and timeliness. Registration movement has succeeded in getting the message across to the research community and clinical trial registration has now become an integral part of research sphere in Iran.

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