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Transparency in Clinical Research and Status in Turkey & Middle East

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Abstract: Though there have been on-going discussions about transparency in clinical research for the last three decades, the first piece of regulation toward this end only came into being in 2005. Today many regulations and registry systems are in use globally and in Middle East countries naturally. Attempts to attain transparency in clinical research are currently paving the way for universal disclosure of all clinical trials.

Keywords: Clinical, disclosure, registry, research, transparency, trial.

HISTORY OF TRANSPARENCY IN CLINICAL RESEARCH

In 1986 the first paper was published by John Simes [1] about the need for transparency in clinical research to inhibit publication bias. In the early part of the twenty first century, initiatives for achieving clinical research transparency were in their infancy providing for opportunities to violate known protocols for reporting adverse events. Not surprisingly several scandals involving violation of reporting of adverse events by well known pharmaceutical companies broke out during this period. Following the scandals, marketing authorizations of some drugs were withdrawn. However during the process of withdrawal decision, the reluctance of the pharmaceutical sector and some physicians to share clinical research data has put the sectors' and academics' reliability in question [2, 3]. The pressure was not only towards the sector and the academia but also towards the regulators who were forced to put into effect the transparency policies with sanctions.

There had been some attempts to ensure clinical trial transparency before www.clinicaltrials.gov web site of NIH had come into effect in 2000. But it was the year 2004, when the International Committee of Medical Journal Editors [4] declared that they would not publish the medical articles unless the related clinical trial was registered on a publicly accessible web site. This was a breaking point and the pharmaceutical industry declared its support for transparency initiatives through its associations [5]. In 2005 the pharmaceutical companies prepared and published their policies on transparency in clinical research and the first regulation on disclosure of clinical trials came into force in USA. Following these events, the registration of clinical trials increased remarkably [6, 7]. However, disclosure of results of most of the clinical trials is improving but not complete 100%.

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REGISTRIES WORLDWIDE AND IN THE MIDDLE EAST

Clinicaltrials.gov, first of the publicly accessible registry database, is taken as the reference database generally. It currently contains registration information for more than 195,000 clinical trials and summary results for more than 18,000 [9]. However WHO's portal "International Clinical Trial Registry Platform" is the hub that pulls together all the registries that are in compliance with WHO criteria worldwide. This is the most comprehensive media on clinical research transparency since 2006.

A decade ago the investigation on clinical research was performed on clinicaltrials.gov [10, 11] website in order to analyze the trials running worldwide. Analysis based on the number of registered trials in the clinicaltrials.gov may suffer from several issues of internal validity and reliability. For example; Iran has 8557 clinical trials registered in its local database (Iranian Registry of Clinical Trials-IRCT) but 711 registered in clinicaltrials.gov. Because all clinical trials in Iran should have registration with IRCT, the IRCT database may be far more reliable with exhaustive coverage of trials in Iran than the clinicaltrials.gov [12]. In Turkey the situation is vice versa. Turkey has announced its official clinical trial registry website (kap.titck.gov.tr) in November 2014 and the number of registered trials is 318 whereas it is 1940 in clinicaltrials.gov since Turkey started to register to its local database very recently [13].

Iran, Israel, Turkey and Saudi Arabia stands out in the Middle East region in terms of transparency initiatives in clinical trials by having local databases and/or local regulations [14, 15].

Nevertheless Iran is one step ahead among all with its local registry (IRCT) that is compliant with WHO criteria and official data provider to WHO International Clinical Trials Registry Platform (ICTRP).

It is of utmost importance for Middle East countries to have registry databases or regulations to ensure disclosure. This will not only complete the mission for patients but also

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Table 1. Major events in the history of transparency initiatives in clinical research.

Date	Event
1997	FDA-*Food and Drug Administration* mandated the disclosure of clinical trials with serious and life-threating conditions
2000	*ClinicalTrials.gov* (1st version) was published
September 2004	ICJME- *The International Committee of Medical Journal Editors* declared the requirement of the clinical trial to be registered in a publicly accessible registry, as a condition of consideration for publication
January 2005	IFPMA-*International Federation of Pharmaceutical Manufacturers & Associations* declared its support to disclose late stage clinical trials in a publicly accessible database
October 2005	The first law on registering clinical trials *"An Act Regarding Advertising by Drug Manufacturers and Disclosure of Clinical Trials"* came into force in Maine, USA
May 2006	WHO formed a portal "International Clinical Trial Registry Platform" to access all registered clinical trials from a single hub
October 2008	Items 35 & 36 were added with the title of "Research Registration and Publication and Dissemination of Results" which require the disclosure of clinical trials to the latest version of Helsinki Declaration [8]
January 2015	Under the new EMA- *European Medicines Agency* policy on publication of clinical data, the Agency proactively publishes the clinical reports submitted as part of marketing-authorization applications for human medicines after January 1st, 2015

Table 2. Number of registered studies from middle east region in clinicaltrials.gov.

Region Name	Number of Studies
World	195,996
Middle East	8,167
Cyprus	47
Iran, Islamic Republic of	711
Iraq	18
Israel	5,304
Jordan	99
Kuwait	49
Lebanon	258
Oman	20
Katar	66
Saudi Arabia	357
Syrian Arap Republic	32
Turkey	1,940

will pave the way for investigators to collaborate on research and inhibit unintentional multiplications in clinical trials. Additionally it will considerably improve the quality of clinical trials in the Middle –East. In Turkey specifically, the desired target should be primarily to have the local database in English and secondarily to improve the local database to be fully compliant with the WHO portal on clinical research and become a data provider registry.

FUTURE OF TRANSPARENCY IN CLINICAL RESEARCH

The conversation about transparency in clinical research has shifted from whether you share what you do to what types of data do you share, when do you share, and where do you share it. Regulators can access the results of every trial but this is not sufficient for public opinion any more. Regulators have the responsibility to be transparent in their decision making processes as EMA established recently [17-19] with the policy on publication of clinical data for medicinal products for human use.

Table 3. Data providers to WHO international clinical trials registry platform (ICTRP) [16].

Data Providers to WHO ICTRP	Every week	Every 4 weeks
	Australian New Zealand Clinical Trials Registry	Brazilian Clinical Trials Registry (ReBec)
	Chinese Clinical Trials Registry	Clinical Trials Registry, India
	ClinicalTrials.gov	Clinical Research Information Service, Republic of Korea
	EU Clinical Trials Register (EU-CTR)	Cuban Public Registry of Clinical Trials
	ISRCTN	German Clinical Trials Register
	The Netherlands National Trial Register	Iranian Registry of Clinical Trials
		Japan Primary Registries Network
		Pan African Clinical Trial Registry
		Sri Lanka Clinical Trials Registry
		Thai Clinical Trials Register

It is inevitable that transparency initiatives in clinical data sharing will evolve more worldwide [20]. Alltrials.net is a relatively new initiative that intends "all trials past and present to be registered and the full methods and results reported" [21]. Very recently the investors declared their support on disclosure of more clinical data because 30% of a pharmaceutical company's valuation is based on results from its Phase III trials [22]. Alltrials.net initiative will conduct audits on pharmaceutical companies' for investors and publish their scores on transparency. These developments will contribute to full transparency in clinical trials.

CONFLICT OF INTEREST

The author confirms that this article content has no conflict of interest.

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