Discussion

OPTIMAL eCRF DESIGN, USER FRIENDLY INTERFACE AND PROPER TRAINING: QUINTESSENTIAL FOR HIGH QUALITY DATA IN REAL WORLD EVIDENCE (RWE) STUDIES

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ABSTRACT

Background: The success of a Real World Evidence (RWE) study lies in collecting and processing high quality data. Data in RWE study can be collected in a paper format as in a Case Report Form (CRF) or electronically in the format of electronic Case Report Form (eCRF). For a multi-country/multi-centric study, eCRF can offer advantages over the conventional paper CRF for collection of data. An approach which is a combination of optimal eCRF design, user friendly interface and proper training can facilitate in collection of high quality data. **Aim**: The aim of this article is to highlight the significance of optimal eCRF design, user friendly interface and proper training in RWE studies. **Conclusion**: Implementation of EDC system with eCRF can be advantageous for a multi-country/multi-centric RWE studies, as it facilities real time monitoring, which can yield adequate data of high quality. Implementation of eCRF can be cost and time effective.

Keywords: Electronic Case Report Form (eCRF), Electronic Data Capture (EDC), Patient Registry, Real World Evidence (RWE), Stakeholders

INTRODUCTION

A patient registry (an example of RWE study) is an organized system that uses observational study methods to collect uniform data to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes. If designed and conducted properly it can provide useful data on the real-world view of clinical practice, patient outcomes, safety and comparative effectiveness [1]. Apart from the study protocol the most important element of a RWE study is the tool designed and used to collect data. CRFs and questionnaires have been traditionally used for collecting data in clinical studies. Data collection in CRF though simple is time-consuming, tedious and error prone [2]. Moreover in cases where the study is spread over a larger geographical area, the logistics associated with paper based CRF is substantial and cumbersome. An Electronic Data Capture (EDC) system is a computerized system designed for the collection of clinical data in electronic format.

EDC system typically has eCRF, which is basically the CRF in electronic format into which data is populated directly with the help of an appropriate browser. The convenience of eCRF from data collection point of view is that the data can be monitored and evaluated in real time. The system allows the study monitor to access anonymous data from centers throughout the study duration and check them on a real time basis. A well designed eCRF also has numerous edit checks within itself, thereby

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prompting the investigator/end user if the data entered is incorrect or illogical.

Some of the core features of the EDC system are ideally characterized by:

1. Different levels of user access so that data can be monitored at multiple levels
2. Secured platform with password protection and validated by electronic signatures
3. Facilitates remote data capture and real time monitoring
4. Reduced data redundancy as data captured once is populated in relevant fields
5. Facilitates real time query management thus reducing total turnout time
6. Generation of reports which has data on recruitment and other parameters
7. Central storage of anonymous data with back up
8. Automation leading to faster study start up and closure
9. Early database lock leading to timely study completion [3]
10. Cost effective as compared to paper based CRF in certain scenarios [4]

eCRF Design; Designing the eCRF is a critical step in conduct of a RWE study. Contrary to randomized clinical trials, generally, in RWE studies or patient registries, the protocol does not mandate the investigator for any intervention. The investigator collects and populates patient data as per the standard clinical practice and local guidelines/regulations. A particular RWE study conducted on a multi-country, multi-centric platform involving data collection from different geographical regions typically follows a trend specific to local practices and requirements of that particular region. Keeping the above in view, optimal eCRF design becomes quintessential if the right amount and right quality of data have to be collected to yield meaningful analysis and results.

The fundamental basis of eCRF design is that it should ideally be FDA 21 CFR Part 11 compliant [5,6].It should also have appropriate internal and external security safeguards [7].The operations team ideally plays a crucial role in the design and validation of the eCRF. The team responsible for designing the database and eCRF should receive the study protocol as soon as possible and the initiation of eCRF design need not wait for the protocol to be finalized, but can start in parallel to the review and finalization of the protocol. The data parameters derived ideally from the protocol are listed down,

logically segregated into sections/visits and transcribed into paper CRF. The CRF should undergo thorough review by clinical/scientific experts to make sure that all the data parameters necessary to satisfy the data requirements of the primary and secondary objectives/outcomes of the protocol are considered and included. An easy to use eCRF, both from an investigator and a data analyst perspective is one that has maximal drop down menus and radio buttons/check boxes for collection of data and minimal free text entry. End-to-end testing of the eCRF portal is critical. The eCRF should be rigorously tested by populating dummy data and all types of user scenarios to ensure that all real life events are considered and replicated without any errors. The training eCRF portal should be fully tested, validated and approved before release. Training needs to be delivered to individual investigators and all other end users identified at that stage of the study. Indicative approach to eCRF designing is outlined in Figure 1. To maintain the sanctity of data and restrict the access to various types of functionality on the eCRF portal, relevant user specific access rights should be generated and provided as agreed and approved between the sponsor and other stakeholders. Despite best trainings, a user guide should be made available to the respective sites and other stakeholders.

User Interface: No matter how technically correct the eCRF portal might be, it fails to serve its purpose if the investigators/end users find it difficult to use. The interface needs to have the following basic components which would make it widely acceptable in studies which are conducted across the world within multi-cultural setups:

1. Compatibility with different browsers
2. Minimal hardware requirements
3. Minimal internet bandwidth requirement
4. Simple log in and log out procedures
5. Dedicated drop down menus or icons for different functionalities
6. Ease of toggling from page to page
7. Secure and easily retrievable password protection
8. Help option next to login screen listing frequently encountered eCRF issues with possible resolutions
9. Clear and simple user guide with local language support
10. 24 hour helpdesk to solve any technical queries

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Acceptability of the eCRF portal is enhanced if the investigators/end users find it simple and uncluttered. One of the important aspects of the interface is that it should have provision for remote access by the technical team in case the investigator/end user encounters difficulties in populating data or using any of the functionalities.
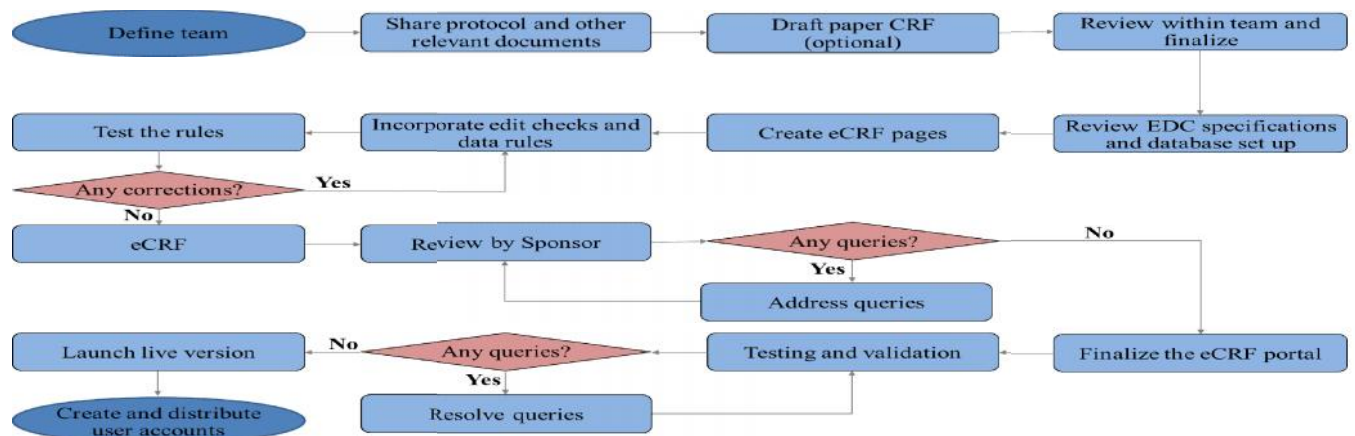

Fig 1: Schematic approach to eCRF design and validation (indicative only)

Training: A very important aspect of the entire activity is ensuring that the investigators/end users are properly trained and understand how to use the eCRF portal.

It is quite common to encounter some level of resistance and hesitancy from a handful of investigators towards the eCRF approach of data collection. It is always better to identify such investigators prior to their enrolment on the study. Some investigators express their resistance towards eCRF once the study has been initiated and patient enrolments are on-going. Hence, the eCRF training sessions should also encompass a module which clearly enumerates the reasons why this study is on eCRF and the benefits it provides to all in terms of time, efforts, money and the ease of conducting studies. Wherever required and applicable, a case study objectively portraying these variables in tangible terms and/or numeric values should always be targeted. Such portrayal has a tendency to simplify the explanations and hence can have a higher probability of connecting with the intended audience who are mostly physicians.

Trainings, however good should never be a standalone activity. Trainings for a longer duration study or for those studies where numerous changes are consistently incorporated in the protocol/eCRF needs to be repetitive in nature. Such repeat sessions may not necessarily be face to face but can be web based interactive sessions with voice support and live video transmission wherever applicable/possible. Repeat training for minor updates in protocol affecting the eCRF data collections can also be scheduled using the simple teleconference mode.

The trainer needs to be well prepared and equipped with all the support documents and tools necessary to impart such training sessions effectively. The list of frequently asked questions (FAQs) should always be shared well in advance with the sites/ investigators/end users along with the technical requirements documents. The trainer should always know the targeted audience's linguistic and cultural gaps. Based on this assessment if the services of interpreters are necessary then they should be appointed for the training sessions and the relevant audience informed of the same well before the start of the session.

The training session needs to have inbuilt checks and balances to periodically assess whether the training serves its intended purpose and the audience is able to well comprehend the contents. This can be done through frequent questions on whatever has been discussed till that point and getting an online/telephonic feedback based responses. Based on the responses gathered, the trainer should always assess any gaps in the understanding of the audience and modulate his/her further sessions/slides accordingly. During remote trainings it is always sought that the training platform's login credentials have been first shared with all. It should be ensured

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that all have successfully logged into it and proceed on that platform with the new dummy data entries as per the training document pre-shared with them. The trainer should always ensure that the pace maintained for the trainings never exceed beyond a point even if audience seems very receptive. Neither should it be too slow to keep pace with slow learners as this can trigger negative interests among the bulk of those who have been receptive and in sync with the trainer. If required, the trainer can conduct an additional session with the slow learners on need basis. The option of submitting questions should always be incorporated. All the questions collated by the end of the session should be answered. If the time doesn't permit to discuss all the questions, then the trainer should request them to submit their remaining questions and assure them of a time bound email based response. The trainer should maintain a question and answer log of that session and share it within a specified time period post training with all the audience via email. The trainer should also share his/her contact details with them for any future correspondence or queries related to the training imparted and must ensure that prompt responses are provided to all correspondences.

DISCUSSION

With ever increasing need of more data and better data by pharmaceutical companies and other stakeholders involved, the future of EDC system seems promising. Technology has bridged the gap between different stakeholders promoting their active participation in any particular study. Newer devices and interfaces are being developed at a rapid rate and the EDC system will have to keep pace with them in order to be compatible. As the acceptability of technology increases, EDC systems will have to be made device and platform agnostic. The EDC system will need to evolve to provide interoperability between differential clinical and e-health systems among several standard consortiums [8,9]. In this modern age of automation, large scale integration of processes on a real time basis is desirable to obtain credible results within justified and acceptable timelines. Paper based CRF have been used extensively in the past but as studies get expansive and diversified, integration of EDC system for data collection will be critical for study success. A study evaluating EDC in developing country has

demonstrated that if EDC system is well designed and introduced with care, and work processes are adjusted to EDC, it will become a more time effective, potentially more accurate and therefore cost effective method than the standard paper-based data collection method [10].

CONCLUSION

In multi-country/multi-centric RWE studies, implementation of EDC system with eCRF can be advantageous as it facilities real time monitoring, which can yield adequate data of high quality. Collection of data in eCRF can be cost and time effective. In order to encourage acceptance of investigators/end users to EDC system, implementation of an approach which combines optimal eCRF design, user friendly interface and proper training could be critical for success.

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