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Review Article

CLINICAL DATA MANAGEMENT SYSTEMS, SOFTWARE USE, ARTIFICIAL INTELLIGENCE(AI) AND RECENT UPDATES

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ABSTRACT

Clinical data management system is extensively used to manage the data that's collected during the clinical trials. This system offers chromatic comfortable techniques via which the data can be collected, managed and stored fluently for additional use. The points regarding the clinical data management that are covered in this review paper are the introductory establishment covering the general aspects of the clinical data management system and chromatic clinical data management softwares plus the use and the significance of case report forms in CDM and the data management procedures that are being followed up for the proper direction of the data so that it's fluently accessible by the staff. Also, the use of chromatic softwares in the clinical data management process has been talked over depicting how the softwares perform chromatic functions to keep the data in a managed, secured and an accessible form. As an end point, chromatic coming challenges and options are considered which give a detailed idea about the growth of clinical data management in the Pharmaceutical Industry.

The effective use of data- catch tools may guarantee that high- quality data are available for early review and fast decision- making. A well- designed, Protocols- driven, regularized, position workflow- acquainted and validated database, peopled via effective data feed mechanisms, will insure nonsupervisory and marketable questions admit rapid-fire responses. When information from a guarantor's clinical database or data storehouse develops into commercial knowledge, the value of the drug can be realized. Also, regulators, payer groups, cases, activist groups, patient advocacy groups, and employers are growing more educated consumers of drug, requiring financial value and quality, and seeking out up-to date medical information supplied by biopharmaceutical companies.

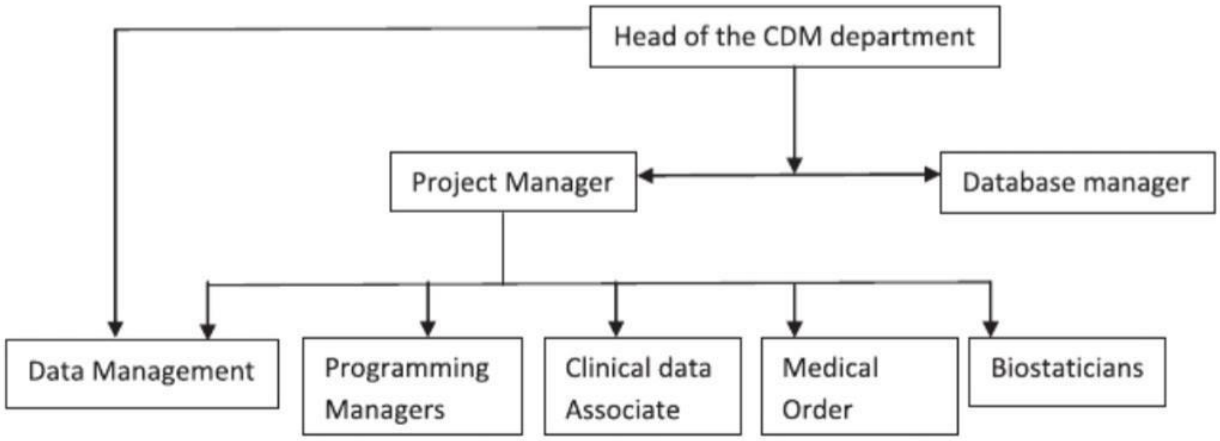
KEYWORDS: Clinical data management (CDM), Case report forms (CRF) , Data management Clinical data management softwares, Electeronic data-capturing, Clinical systems

INTRODUCTION:

Clinical Data Management is involved in all aspects of processing the clinical data, working with a range of computer applications, database systems to support collection, cleaning and management of subject or trial data.[5]

When the clinical trials are performed, the high duty of the investigators is tocollect the data of the case's good after a specific interval oftime.Further, this data is given to the trial guarantor who quantifies and qualifiesthe given data by statistical means. When the blessing of new medicines is to be made by the nonsupervisory agencies it's reliant upon the clinical trial data presented. The trust on the clinical data is generally stuck to the quality practices and norms of the clinical trials performed [1,2]. Thus, the associations assure that the clinical trials performed and the dataobtained are in the hands of well qualified and trained staff and a inflow flowchart representing the staff that's involved in the clinical data manage-ment system is represented. Therefore, the crucial ideal of CDM is to offer high quality data by observing the crimes and missing data andkeeping it as low as possible to congregate maximum data foranalysis.Various practices have been developed to insure that the data attained iscomplete, reused rightly and dependable. This has been fluently achievedby the use of operations of the software that presents royal detec-tion and stir of data disagreement and is used to maintain inspectiontrials.In clinical data operation, softwares are generally needed to addressthe electronic data prisoner, medication of the electronic FDA submission, acceleration of the clinical trial operation processes. A tabularform representing the use of software systems in colorful managementstages of the clinical data has been depicted [2,3]. These sophisticated inventions have helped in maintaining data quality incomplex trials and handle large trials. One more question that now arises is " what is a high quality data?" A high quality data is defined as the datawhich is suitable and accurate for statistical quantification. The datashould satisfy the protocol specific parameters should be compliable withthe protocol musts. This tells us that when the data isn't compliablewith the protocol specifications we can count the tolerant from theultimate database. It should be conceded that in some cases regu-latory agencies can be occupied in viewing similar data. Probing further,

generally lost data is also a matter of apprehension for the scientists, talking about high quality variation in the data that would not impact the result of the study inthe future. The data should convene with the nonsupervisory musts thatare handed for high quality of the data.[2,4]



Manpower involved in clinical data management.

During the clinical trial, the investigators collect data on the patients' health for a defined time period. This data is sent to the trial sponsor, who then analyzes the pooled data using statistical analysis.

Responsibilities of CDM [5]

Study Setup

• CRF design and development (paper/e-CRF)

• Database build and testing

• Edit Checks preparation and testing

Study Conduct

• Data Entry

• Discrepancy Management

• Data Coding (using MedDRA and WHODDE dictionaries)

• Data review (Ongoing QC)

• SAE Reconciliation

• Data Transfer

Study Closeout

• SAE Reconciliation

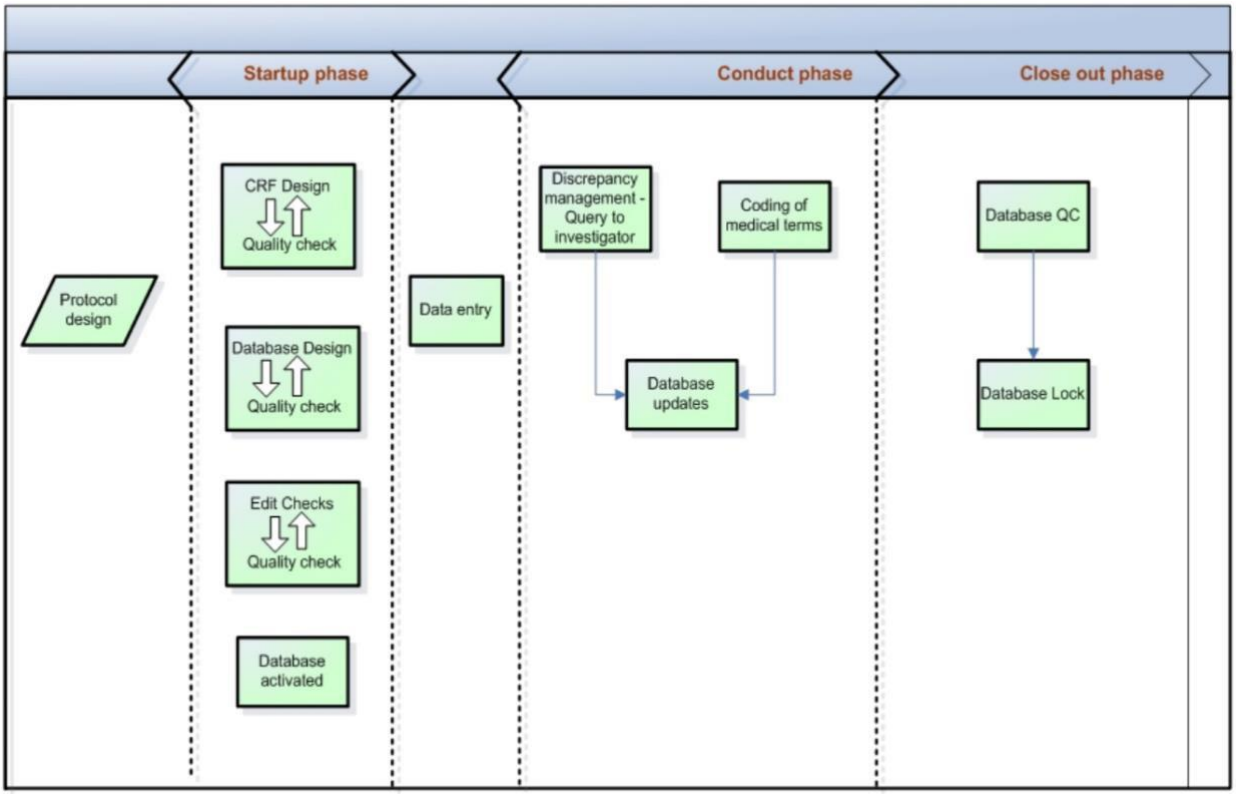
• Quality Control

• Database Lock

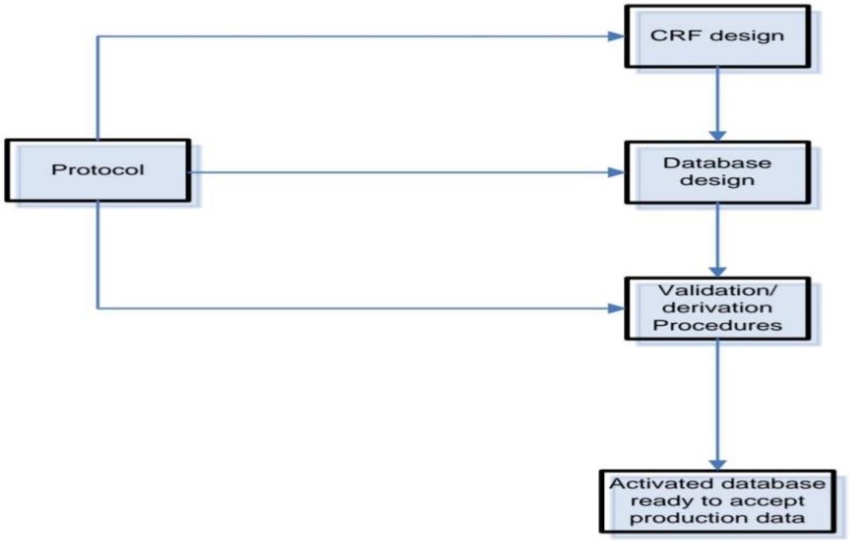
• Electronic Archival

• Database Transfer

CDM Process Overview[5]**:**



Study Start Up Process Review[5]**:**



Case Report Form (CRF):

A case repot form can be electronic or a paper based system and isgenerally abbreviated as CRF. It is widely used tool by the sponsor for thecollection of the data from the patients participating in a clinical trial.The data regarding the participation of a patient in a clinical trial isdocumented in the case report forms which also includes the adverseevents. The CRF is usually developed by the sponsor to collect the datathat would be required for testing the hypothesis in a clinical trial or itcan also be used for answering a plethora of questions regarding theclinical testing [6]. The size of the CRF varies from a snapshot of hand-written pages regarding the physical condition of the patients or hun-dreds of pages of electronically captured data that has been collected as a result of the trial carry out for over a timeperiod of weeks or months. Also,the CRF accurately depicts or provides detailed information about the protocol referred for the clinical trial. A sponsor also holds the duty ofmanaging the production of the results gained by the trial and monitoring the collected data.[6]

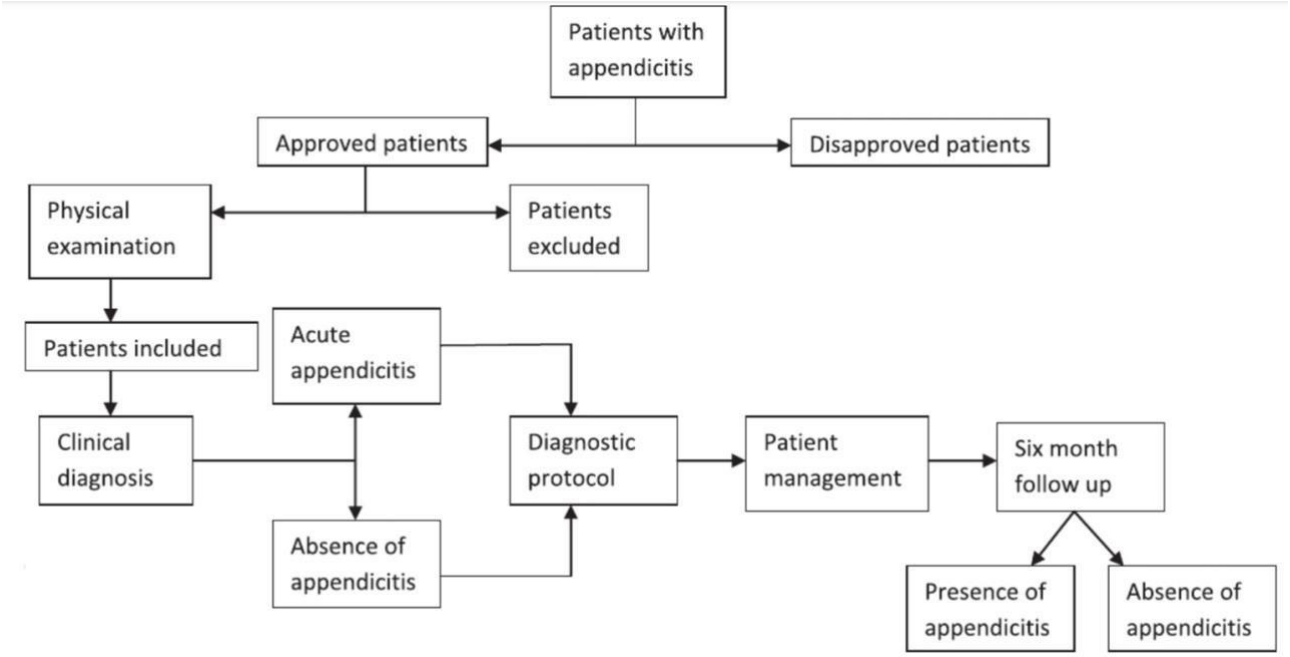
CRF Design/Review:

A representation of the study as outlined in the protocol is made (including CRF completion guidelines if necessary). Thus a final protocol needs to be available before this exertion can beinitiated.CRF design generally takes about three rounds First draft (rough without detail but correct content), alternate draft (as good as we can get it) and final interpretation. We need input from our guarantor to correct draft performances and to authorize the final interpretation[5].

Screening of patients having non-distressing appendicitis is observedfor participation in clinical studies is depicted.After that, thepatients are approved and disapproved for the Clinical Data Managementis based on several factors one of these given in the flow chart is preg-nancy. Further, after the selection of the patients the physical examina-tion of the patients is also done and again on this basis the selectivityprocess of patients is achieved.After the physical examination, selectedpatients are then sent for the clinical diagnosis to check absence orpresence of acute appendicitis. Probing further the patients are diagnosedand managed and a follow

up for six months is performed of the patients.At the end they are sent for the observation at the expert panel to checkwhether the patients suffer from appendicitis or not.

Screening of patients suffering from acute appendicitis for participation in clinical studies:



Data Management:

Data accession is generally appertained to as that contrivance that's used to attain the data from the clinical trial without any elision from the set of rules that are given to conduct the trial. The quality of the data acquires depends entirely upon the quality of the instrument used to acquiredata.Therefore, the design, quality assurance and development of similar aninstrument must be given consummate significance.

Collection or acquisi-tion of the clinical data may be brought by using colorful technicalitiesthat may include but not inescapably be limited to paper forms, interac-tive voice response systems, electronic or paper medical proceedings, central web grounded systems or electronic data prisoner systems. For theproper reference of these systems the ICH guidelines on good clinicalpractices use the term “Case Report Form” which is employed for theeminence and uprightness of the data [7].

The CRF should be started during the development of the protocol asit assures the reservations that the data collection or accession is position- headed and practicable. In discrepancy, numerous a times the CRF is developedafter the development and blessing of the protocol. At this point, anydata points that are undesirable need emendations and corrections. WhenCRF and protocols are premeditated concomitantly, the collaborationsprovide the parties with imperative judgment. Main focus should bespecified on what data

should be unworried or acquired and how the datashould fulfill the protocol of the study. A statistical arrangement can beregarded as a lead as to what data points can be considered essential forthe clinical study. If non material data is collected it may negatively affectthe quality of the data by out- putting point rookies sweats from vitalfactors.It's thus, significant to declare that the crucial variables should bedefined or given previous to the development of the CRF. One of the systemsthat is used for data accession is explained below [8].

Data redundancy is generally used to assess data validity when otherpractical forms of data collection aren't available. When redundancy isused to validate the data, the confines are generally attained via sov-ereign coffers. Data that's recorded via same quantum shouldn't becollected in further than one place or further than formerly as this would createsuperfluous work for the exploration point and would develop the bear-ment to check the moldabilities between the two data situations. Also, if thedata is to be participated to develop an end point, the original data mustn't becollected further than formerly. Only one out of the two that's the raw data orthe accession made by the raw data must be collected and generally rawdata is preferred. The spare data may also beget logical in- density say; point variations in the computation system can beget in- density. Therefore, the raw material should be used to calculate theaverage in the first algorithm and the average collected should be utilizedfor alternate algorithm. Until the thickness in the data is developed, boththe algorithms can produce variable results [7,8].

With the position of moxie new improvements in data store house, miningand and linking ways are observed this, programs and events as respects todata insulation must be reevaluated. Data sequestration can be defined as thestandards governing the bastion of private data. Particular data isreferred to as the information related to the study subject which leads tothe recognition of the exploration subject either unswervingly or in aroundabout way. Exemplifications of private particular data include patientnames, address, initials, inheritable law etc.

The ICH Guideline for Good Clinical Practice countries, " The confidenti-ality of records that could identify subjects should be defended, esteeming theprivacy and confidentiality rules in agreement with applicable nonsupervisory.[9]

Tools and formats of various clinical data management system:

S No.	Clinical Data Management System	Tools under Focus	Raw Data Format
1.	REDCap	Electronic Data Capturing (EDC)	Case Report Forms
2.	XNAT	EDC and neuroimaging tool	ECAT (electronic catalogue), zip files, Analize
3.	NeuroMAT NE S	data repository for electrophysiology and EDC	Matlab files, NEO objects, EEG (electroencephalography) raw data
4.	G – node	Electrophysiological tool	g-node data API, Matlab, NIX
5.	OpenElectrophy	Electrophysiological tool	NEO objects
6.	LORIS	Neuroimaging tool and EDC	NIfTi (neuroimaging informatics technology initiative), FreeSurfe, MEG (magnetoencephalography), EXCEL/CVS files
7.	CARMEN	Electrophysiological tool	txt, csv, XML, NDF, Matlab files

Data Collection:

Data collection is done in the CRF in the form of either a paper or an electronic interpretation. In the traditional system, paper CRFs were used to collect data responses which were also restated to the database by the means of data entry done in- house. The stuffing of the paper CRF is done by the investigator according to the guidelines given for the completion of CRF. In the electronic systems of CDM the nominee or the investigator is primarily logged in to the system and the data is directly entered in the site. In this system, the probability of crimes is lower and the discrepancies can be managed fluently[15]. Pharmaceutical companies need a reduction in the time for medicine development processes which is achieved by enhancing the speed of processes that are involved therefore; utmost of the companies conclude fore-CRF.

Data Entry:

Data entry is done according to the guidelines handed. This is relevant only in the case of paper CRF. Also, double entry can be performed when the data in entered by two different drivers collectively. The entry entered by the alternate person helps in resolution and validation by depicting the dictation mistake and disagreement caused by the undecipherable data. Also, it has been plant that a double data entry helps in achieving a cleaner database than a single entry. Also, studies show that the double data entry ensures better uniformity with paper CRF and also there are a lower number of mistake [10,11].

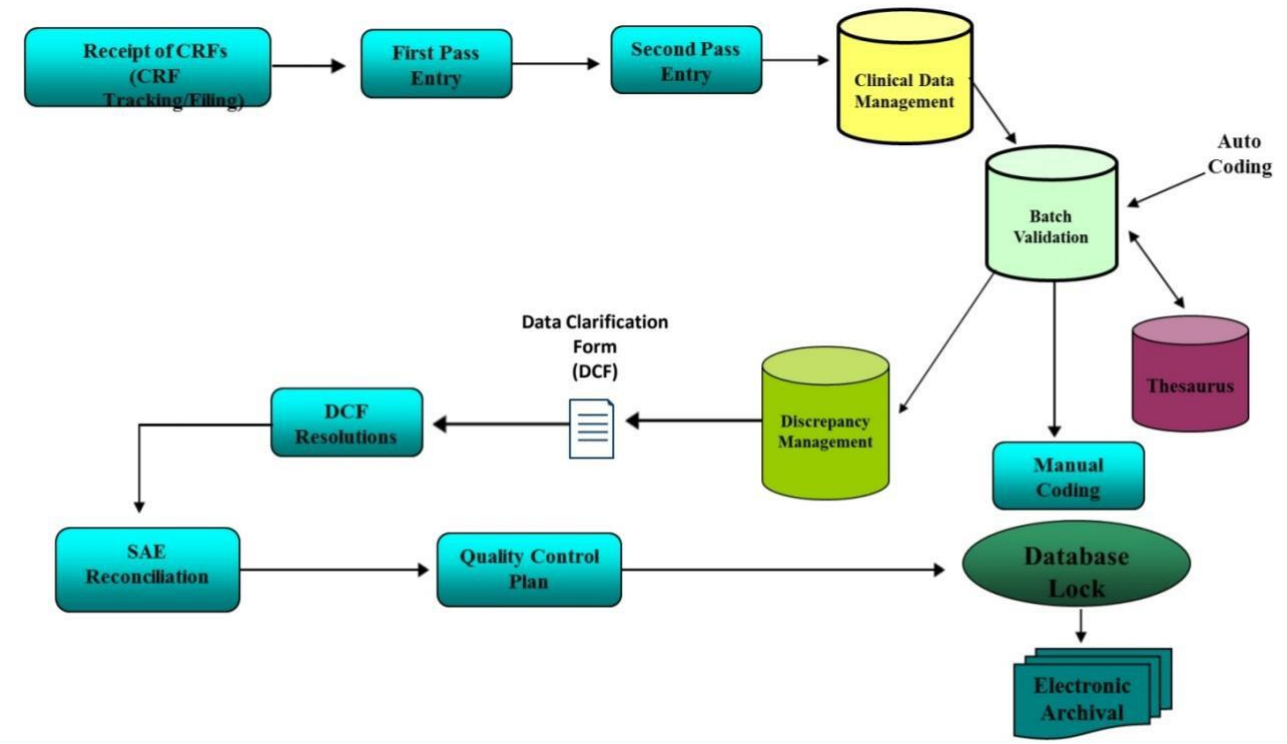
Data Validation:

Test of the confirmation of the data according to the protocol mentioned is known as the data confirmation. The disagreement bedded in the database entry are linked to insure data validity. The programs are published according to the logical circumstances mentioned in the data confirmation plan. These programs are primarily checked with replica data that contain disagreement. Disagreement are defined as the data points that fail to pass the confirmation check. These disagreement may arise due to the missing data, inconsistent data, range checks and diversions from protocol. Data confirmation is done constantly in the case ofe-CRF. In vestigators also resolve the issues after logging into the system. During the course of CDM the quality control of the data is checked at regular intervals. When there are disagreement in the data they will be high lighted in the system and in the Data Explanation Forms. Data Explanation Forms are the documents that contain dubieties that pertain to the linked disagreement [18].

Database locking:

The final data confirmation is done after a proper quality check and assurance. If there are no disagreement establish the datasets are perfected with the statistician. Before locking the database all the operation of data activities should be completed. This is assured as the database can not be altered in any manner after locking. Once the stakeholders authorize the database locking, the data is locked and the clean data is extracted [11].

Data Managment Workflow [5]**:**



Clinical data management softwares:

All the associations analogous as the medical, disquisition, bio technology and medicinals are getting advantaged from clinical trial software. These softwares support all the aspects of a clinical trial starting from conscription to the submission of the study and archiving the study. These softwares can be used for small phase 1 trials and also for large studies with thousands of contenders. There are a variety of softwares that are available for the operation of data and are thus called clinical data operation systems or softwares. In the case of multi centric systems or trials these softwares play a vital part as they have the capability to handle large amounts of data. Utmost of these softwares in pharmaceutical sedulity are marketable but some of the softwares are also available as open source tools. There are a variety of softwares that are used as CDM softwares in apothecary some of them are ORACLE CLINICAL, MACRO, RAVE, CLINTRIAL,

eClinicalSuite, EZ entry and so on. These softwares are more or less similar in their functionality and can't offer a great advantage over one another. The disbenefit of these softwares is that they are precious and the orga nizations need to acquire a refined Information Technology commu nications to serve. These were the marketable tools that are available as softwares for medicinals. Among the open source tools some of the software tools are OpenClinica, Trial IDB, openCDMS and PhosCo. They are open source and are available as free of cost and are as good as their marketable counterparts. They can be easily downloaded from their websites as they are open source softwares. Some of the advantages offered by these clinical data operation softwares are that they accelerate the timeline of the study and also control cost of the study, they have the capability of furnishing ac curate prognostications for the clinical trial, they enable a robust modeling of the program, grease netting, scheduling, recruiting, help croakers, automatically adjust for foreign exchange rates and so on. Details of certain of softwares are bandied further in this review[15,17]

S.No.	Software	Organization	Key features
1.	SAS Clinical Software	SAS Solutions	• Single integrated platforms • Speeds up and automates repeatable processes. • Ensures use of standards and analyses structure and content of the data. • Automated data quality, integration and compliance with industrial standards.
2.	COGNOS 8 Business Intelligence Software	COGNOS	• Multilingual reporting in formats such as PDF, HTML, XML, Excel and CSV. • Data reporting in compliance with CFR 21, PDMA, state marketing regulations, HIPPA, PDMA, FDA and ANDA processes. • Improved resource allocation • Return of results only at summary level.
3.	Symetric Software	Symetric Sciences	• Fully integrated and extended data dictionary • Designed ergonomically • Classification of missing data • Built-in CRF tracking and query management. • Designed for rapid prototype application. • Expanded Audit Trial • Full set of review and reporting tools • PC based and have full graphical user interface
4.	Akaza's OPENCLINICA Software	Akaza Research	• Clinical research by study protocol • Support for sharing resources • Dynamic generation of web-based CRFs • Management of longitudinal data • Flexible data export/import tools • Compliance with HIPPA privacy and security guidelines • Robust and scalable technology
5.	SigmaSoft's DMSYS Software	SigmaSoft International	• Fully validated and compliant with FDA • Easy study set up • Easy data entry screen • High speed platform for rapid data cleaning • Sophisticated error management • User validation package • High quality and timely training
6.	Progeny Clinical Software	Progeny Software, LLC	• Draw and manages pedigrees quickly • Manage and assign samples to the individuals • Import/export data and imports pedigrees • Integration with Lab and LIMS • Multiple database collection • Create custom reports
7.	EZ-Entry	EpiData system software	• Simple syntax to set up e-CRFs • Entry of data with checkout theory. • Checking of data after double input
8.	Oracle Clinical software	Oracle	• Easy transition from paper to EDC • CRF in an annotated form • Easy to read study data • Increased audit trials • Addresses all the four phases of the clinical trial • Faster implementation • Productive marketing • Higher return on investment
9.	TCS CLIN E2E Software	Tata Consultancy Services	• Addresses all the four phases of the clinical trial • Captures EDC that is integrated with sponsor and other sites. • Study templates are created • In accordance with the standards mentioned in CFR 21 part 11.

1. Oracle clinical software:

Oracle software has been used by the experts since 30 times as it handed information with a loyal, defended and incorporated technology. Oracle software has been developed by the association mystic itself and mystic spends further than US$ 30 million over the exploration and development annually. Colorful advantages offered by the mystic software include the effective platoon work, briskly perpetration, productive marketing and advanced return on investment. This software was developed on the base of expansive experience of hundreds of or ganizations that conducted clinical trials [15,18]. Further than clinical trials have been conducted by using Oracle clinical by further than 200 associations dealing with biotechnological and pharmaceutical products. Crucial features of the software include

Best of breed clinical data management and remote data prisoner services.

- Easy transition from paper to electronic data prisoner of the trials data. Annotated CRF.
- Enhancement inrandomization.Built-in test atmosphere
- Increased inspection trials to insure artificial compliance
- Easy to read study data.

2.SAS clinical software:

SAS Clinical Software is software that's run by the SAS result for Life Lores association. It's one of the leading companies in the world. There are 44000 spots available in around 109 countries. There are no redundant charges for specialized support and professed telephone and indeed for online specialized support. Time to vend new medicines is reduced by clinical data integration. Through this software system crimes are canceled and new curatives for marketing are generated.

SAS association has designed the software on the base that each medicine that's to be retailed has incomparable requirements. Therefore this software addresses these requirements in the form a portfolio which drives efficaciousness throughout the colorful stages of the medicine lifecycle starting from dis covery development, commercialization and beyond [17]. Colorful functions that are performed by the software are:

- Simple and intertwined platforms that lets one access and manage the data from a wide range of sources which include CDMS, EDCetc.
- It helps in the robotization and discovery of different processes to reduce home supplication.
- Proper use of norms is assured by the proper use of the data.. With the help of SAS data integration is managed and automated and the quality of data in compliance with the artificial norms is achieved therefore, precious coffers can be released to work upon more complex subjects thus, it helps in saving time.

3.Symetric software

Symetric software has been developed by symmetric life lores association which is a cost-effective system for the purpose of clinical trial data collection and management which completely abides by the inter public norms and has a proper customer base each over the world. Various organizations in which Symetric Sciences has a membership are:

- The society for clinical trials
- Drug Information Association
- The American Statistical Association. The International Biometric Society
- The Association for Clinical Data Management
- The Regulatory Affairs Professional Society

This software provides a detailed understanding of day-to-day re quirements for the workflow processes that are involved in clinical data management beginning from set of the database, quality control of the data and final export [17,18]. Various functionalities with which the software has been loaded are:

- Fully integrated processes with elongated data dictionary
- Full discrepancy management
- Classification of the missing data with the help of special codes
- Interactive double-data entry verification
- CRF tracking functions and query management
- Rapid prototype application development
- Module available in compressed form which minimizes disk storage

Artificial Intelligence(AI):

Artificial Intelligence is the general thing that we want to achieve. For illustration, we want algorithms suitable to reproduce what a human would do in specific situations. We can definesub-goals under this general thing, like having algorithms being suitable to reuse images (field of computer vision) or having algorithms suitable to reuse mortal textbook (field of natural language processing). But this does n't say anything about the way to achieve these pretensions[12].

Artificial intelligence (AI) generally applies to compu-tational technologies that emulate mechanisms supported by mortal intelligence, similar as study, deep literacy, adaption, engagement, and sensitive understanding [13,14]. Some bias can execute a part that generally involves mortal interpretation and decision-

mak-ing. These ways have an interdisciplinary approach and can be applied to different fields, similar as drug and health. AI has been involved in medi-cine since as early as the 1950s, when croakers made the first attempts to ameliorate their judgments using computer- backed programs [16]. Interest and advances in medical AI operations have surged in recent times due to the mainly enhanced computing power of ultramodern computers and the vast quantum of digital data available for collection and utilisation. AI is gradu- supporter changing medical practice. There are several AI operations in drug that can be used in a variety of medical fields, similar as clinical, individual, rehabilita-tive, surgical, and prophetic practices. Another critical area of drug where AI is making an impact is clini-cal decision- timber and complaint opinion. AI tech-nologies can ingest, assay, and report large volumes of data across different modalities to descry complaint and companion clinical opinions.

Role Of Artificial Intelligence(AI) In Healthcare:

Serving from the topical dendrogram, researchers will give a development model grounded on four applicable variables [19,20]. AI has been a disruptive invention in healthcare. With its sophisticated algorithms and several uses, AI has supported croakers and medical professionals in the disciplines of health information systems, geocoding health data, epidemic and syndromic surveillance, prophetic modelling and decision support and medical imaging [14,21,22,23]. Likewise, the researchers considered the bibliometric analysis to identify fourmacro-variables dominant in the field and used them as authors'keywords. ahead, the followingsub-sections aim to explain the debate on uses in healthcare for AI methodologies

Conclusion:

Pharmaceutical companies have an adding demand of fast- track medicine development process wherein the elaboration of CDM is of lesser concern which in agreement to the nonsupervisory authorities as they put quality systems to insure high quality data generation in medicine evaluation process. To meet the eventuality in this area a shift has been made from paper grounded data management systems to electronic data operation systems. Therefore, all the developments that have been made on the technological front have impacted appreciatively on the CDM processes and systems which have led to the development of encouraging results on the quality and speed of the data that has been generated. Data quality is bettered by the CDM professionals by assuring standards. CDM therefore, should be estimated by the standards being followed and the processes and styles being enforced. The leading challenges from the perspective of regulations are the chronicity of the process of data management and the proper development of regulations to find the protocols that are demanded to be followed. The biggest chain from artificial point of view is the planning and prosecution of data management systems .Despite of all the challenges faced CDM is getting a standard grounded clinical exploration reality by balancing prospects and constraints in the being systems which are taken in by the developments in technology and demands of the business .Nowadays Artificial intelligence (AI) plays an important part in clinical data management.

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