**CLINICAL RESEARCH INFORMATICS**

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**ABSTRACT**

Clinical research informatics is currently evolving sub-domain of biomedical informatics that includes the use of informatics in discovery and application of new knowledge relating to health and disease. It includes the management of information related to clinical trials and also secondary research use of clinical data. Clinical research informatics (CRI) is a domain of transition and has attracted the attention of government, academic, and private sectors, as they have a significant scientific and financial interest in the conduct and outcomes of clinical research trials. Clinical researchers also face significant challenges with increasingly complex workflow and information management requirements. The access to effective and efficient information is important to solve the challenges faced in clinical research trials, therefore, there has been a rapid evolution of biomedical informatics tools and technologies specifically designed to address the clinical research information management requirements.

1. **INTRODUCTION**

Clinical research is fundamental to the generation of evidence that can in turn facilitate and improve in the quality of the human health. However, the conduct of design, execution, and analysis of clinical research is an inherently complex process. It includes information and resource-intensive endeavour, involving a broad variety of stakeholders, workflows, processes, data types, and computational resources [1].

Clinical informatics is study of application of information technology and informatics to deliver healthcare services. It is also referred to as health informatics or applied clinical informatics [2]. Currently researchers have explicitly focused on increasing the clinical research in the biomedical sector and to bring attention of the government, academic and private sectors and those who have significant scientific and financial interest towards the clinical research and related biomedical informatics activities or in the outcome of clinical trials and research [3-10]. These activities and initiatives have increased in significant emergence of a new sub-domain in biomedical informatics focused on clinical research, known as Clinical Research Informatics (CRI). CRI field is rapidly growing and has already brought significant improvements in the quality and efficiency of clinical research and trials [7, 11]. With the increase interest of researchers in CRI, it is emerging as a highly valued area of activity. This sub-domain also faces an increase in its scope and range of challenges and opportunities. Clinical Research Informatics involves the use of informatics in the discovery and management of new knowledge relating to health and disease. It includes management of information related to clinical trials and also involves informatics related to secondary research use of clinical data. Clinical research informatics and translational bioinformatics are the primary domains related to informatics activities to support translational research [12].

Clinical research is itself in a transition state. Clinical researcher’s faces significant and increasingly complex workflow and information management challenges. To solve these challenges, access to effective and efficient information is important in clinical research trials, therefore, there has been a rapid evolution of biomedical informatics tools and technologies specifically designed to address the clinical research information management requirements [12].

1. **CLINICAL RESEARCH INFORMATICS**
2. **Informatics**:

Informatics is the branch of science that deals with use of data, information and knowledge in improvement of human health and healthcare services.

1. **Health and Biomedical informatics**:

Health and Biomedical informatics involves application of principles of computer and information science to the advancement of life sciences research, health professions education, public health, and patient care. Biomedical informatics focuses on health information technologies (HIT), and uses of computer, cognitive, and social sciences. Health information technology permits advancement in healthcare by providing the methods and tools to set the knowledge in practical applications and practices.

1. **Clinical research**:

Clinical research is important for the advancement of medical science and public health. Conducting a clinical research is a complicated, resource intensive endeavour that comprised of a complex process and workflows including many multidisciplinary experts and information resources [2]. Efforts of such process on large scale to improve the clinical research capacity of biomedical sector have been able to brought attention of government, private sectors and academicians on the activities of clinical research and related biomedical informatics [3-10]. Such efforts have led to the emergence of a new sub-domain of biomedical informatics, which is mostly focused on clinical research activities and is referred to as Clinical Research Informatics (CRI). In the last five to ten years, CRI has evolved rapidly and has already enabled significant improvements in the quality and efficiency of clinical research [7, 11]. In 1997, the National Institute of Health (NIH) Director’s Panel issued the following 3-part definition of clinical research: Clinical research involves, “the range of studies and trials in human subjects that fall into the three sub-categories: (1) Patient-oriented research: Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Patient-oriented research includes: (a) mechanisms of human disease; (b) therapeutic interventions; (c) clinical trials, and (d) development of new technologies. (2) Epidemiologic and behavioural studies. (3) Outcomes research and health services research” [13, 14].

1. **Clinical research informatics (CRI):**

Embi and Payne, 2009, defined Clinical Research Informatics as the sub-domain of biomedical informatics concerned with the development, evaluation and application of informatics theory, methods and systems to improve the design and conduct of clinical research and to disseminate the knowledge gained [1]. Clinical research informatics also includes retrospective studies and prospective clinical trials. In such kind of studies, CRI aims for the development of methods and tools to support clinical researchers for reusing previously collected data or to collect new data in their own studies. The major area of focus of CRI is clinical data repositories and clinical trials data management systems [15].

With the evolution and rapid progress of Clinical research informatics (CRI), there is an extraordinary increase in scope and pace of clinical and translational research, which has brought attention of major funding programs such as that of National Institute of Health’s (NIH) Road map initiative [16]. One of the major goals of the NIH Road map includes programs to fundamentally reform the way in which organizations translate basic science discoveries into practicable therapies [6,16,17]. Clinical and Translational Science Award (CTSA) is among one of such program which is intended to transform the way in which academic health centers (AHCs) conduct and support clinical and translational science [5, 6,18]. As part of the national consortium of CTSA sites, efforts have been made to coordinate and develop a variety of CRI-focused development programs including data warehousing, clinical trials management and participant recruitment systems, collaborative team science tools, and integrative data “pipelining” and semantic harmonization platforms [18]. Like the Clinical and Translational Science Award (CTSA) program, there are many other significant efforts that are representative of CRI domain activities. Examples include: (1) the NCI’s Cancer Biomedical Informatics Grid (caBIG) initiative [3,4,7,8] (2) Various CRI focused standards and harmonization bodies such as the Clinical Data Interchange Standards Consortium (CDISC), Health Level 7 (HL7), and the Biomedical Research Integrated Domain Group (BRIDG) [19-22]; (3) The creation and growth of clinical trial data registries; [23-25] and (4) other NIH Road map initiatives such as the “re-engineering the clinical research enterprise” program which preceded the CTSA initiative and spawned the fundamental workflow and information management needs of the clinical research domain [16, 26, 27, 28]. Additionally, in the last ten years there has been the emergence of a growing body of literature describing central challenges to the national clinical research enterprise and the corresponding benefits that could result from addressing those challenges through, in part, effective integration of biomedical informatics and clinical/translational research workflows [5,8,11].

1. **APPLICATION OF INFORMATICS IN RESEARCH**
2. **Information needs and systems in the Clinical Research field:**

Clinical research involves collection of variety of data, information, and knowledge sources, and is a complicated set of complementary and overlapping workflows. Clinical research environment can be related to a number of critical information needs. Clinical research designs traverse the spectrum from passive or observational studies to interventional trials. The intervention may be as simple as administering a substance that is already found inside a human body and observing its change in the body (such as the amount of vitamin found in blood or urine) to a more complex intervention studies like administration of a preventive vaccine.

Data collection is critical in passive or observational studies to the proper performance of research. In interventional trials/ studies, it may become intense with the collection of clinical information occurring more frequently and involves data describing the intervention materials (example purity of a drug) and to data related to human (as study subject) and their response to the intervention under study. Clinical research endeavours exist on a spectrum of scientific activities that is commonly referred as clinical and translational research. Translational research involves a process by which basic science discoveries are used to design novel therapies. Such discoveries are then evaluated during clinical research studies, first pre-clinical and subsequently in clinical trial phases [7].

1. **Translational research**:

 National Institute of Health (NIH), defines Translational research, as covering two areas of translation. One is the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans. The second area of translation concerns research aimed at enhancing the adoption of best practices in the community. Cost-effectiveness of prevention and treatment strategies is also an important part of translational science [29].

1. **CHALLENGES AND BARRIER**

Many studies have informed that a lack of sufficient information technology infrastructure and tools, as well as a reliance on workflows defined by historical precedence rather than optimal operational strategies, account for hindrance to the convenient, effective, and resource efficient conduct of clinical research activities and trails [7]. The rapid progress of biomedical science and the need for advances in healthcare system demands that the conduct of clinical research be timely, efficient, and should yield high quality results [30, 31]. Hence, the importance of making the clinical care data available for the secondary use in support of clinical research has become a competitive need for clinical and research enterprises [31, 32]. Moreover, the increasing complexity of clinical research associated with challenges of regulatory requirements while conducting clinical studies have created further changes in the clinical research field, which includes a trend towards conducting clinical trials in community practice settings, as opposed to the historical norm of conducting such studies in large Academic Health Centers (AHCs) [26, 31]. The rapid growth and expansion of clinical research field has led stakeholders in the clinical research environment to acknowledge and call for system-levels solutions [14, 31].

Clinical research is itself a domain in transition and faces significant challenges in complex workflow and information management requirements. This clinical research field has brought increased attention of government, public sectors and academicians and also who have interest in significant scientific and financial interest in conduct of clinical research/ trails and management. With increase interest of researchers in this domain, the timely access to information that is effective and efficient to solution of the challenges faced is critical, and therefore, this has led to rapid evolution in biomedical informatics to develop tools and technologies, especially designed to address clinical research information management requirements [12]. New methods and tools for CRI systems have been developed in order to enable real-world evidence generation and optimize the lifecycle of clinical trials [33].

1. **ETHICAL ISSUES**

Ethicalstandards and public trust are major issues in Clinical research. There is a growing recognition and interest in the ethical development of health informatics research and innovation. The development of designing tool and technologies using artificial intelligence has gained maximum attention at present. There should be uniformity in ethical principles worldwide, as this is what most of the researchers in the research field need in order to be confident themselves and give confidence to others to follow ethical principles correctly. Many countries are publishing ethical principles, guidelines, or more formal legislation (like the European AI Act ) [34].

1. **LOOKING FORWARD**

CRI is an emerging and evolving sub-domain with increase in availability of literatures in various CRI topics such as data collection, information retrieval, designing methods and tools, planning management, and data analysis. In future researchers may develop more interesting tools and technologies which are effective for clinical trials and translational research that is more patient oriented and beneficial for a healthy lifestyle for human. Use of artificial intelligence may be encouraged in developing the tools and technologies and to make it accessible for the other researchers.Currently the most significant research efforts in CRI are focusing their research on data science with interest in the development and evolution of artificial intelligence algorithms based on more intensive use of real world data. Timely sharing of high-quality data and collaborative data analysis is very vital to inform policy decisions [35].

In future, CRI is expected to improve clinical research processes and facilities and will generate advances that can bring change fundamentally in the pace, direction, and effectiveness of the clinical research enterprise and discovery. Through CRI, biomedical advances, discovery, health care quality improvement, and the systematic generation of evidence will become easier, as advances in clinical informatics have already become in fostering the systematic application of evidence into health care practice [1].

1. **CONCLUSION**

Clinical research informatics (CRI) is emerging as a distinct sub-domain of biomedical informatics, and is one which is still maturing and altogether facing many challenges and opportunities. The conduct of clinical research is fundamental to the generation of evidence that can in turn facilitate improvements in the quality of human health. Data coordinating centers must have the facility of the clinical research informatics, frameworks and tools to support a wide variety of study designs, research questions, various domains for disease and patient populations, and data sources in clinical research. Framing various study design and implementation models for clinical research/ clinical trials faces many challenges, especially for identifying the optimal standards for medication data. In the CRI field, most significant efforts are made on research data science along with the development and evaluation of Artificial Intelligence (AI) algorithms based on intensive use of real-world data. Collaborative effort of data collection, data-sharing and data analysis worldwide is absolutely important to inform policy decisions.

The clinical research field is rapidly progressing and altogether facing challenges in significant workflow and information management. It has therefore gathered increased attention from the government, academic, private-sectors and funding agencies which are interested in the efforts of outcome of clinical study/ trials. This rapid progress explains CRI’s emergence as a distinct and highly valued sub-discipline of biomedical informatics. Part of the evolution of CRI can be credited to the extraordinary increase in the scope and pace of clinical and translational science research and development that has been catalyzed by a variety of funding and policy initiatives that seek to restructure the way in which government, public, and private sectors advance the basic science discoveries into practical therapies. CRI has emerged as a dynamic and relevant sub-domain of biomedical informatics, which provides a broad spectrum of research and development opportunities in context of both basic and applied informatics science.

**REFERENCES**:

[1] Payne P RO, Embi P J, Cimono J J. Clinical Research Informatics. E.H. Shortliffe, J.J. Cimino (eds.), Biomedical Informatics, 2014; 755-777 DOI 10.1007/978-1-4471-4474-8\_26, © Springer-Verlag London

[2] Peter J. Embi, MD, MS , Philip R. O. Payne, PhD, Clinical Research Informatics: Challenges, Opportunities and Definition for an Emerging Domain, Journal of the American Medical Informatics Association, Volume 16, Issue 3, May 2009, Pages 316–327.

[3] The cancer biomedical informatics grid (caBIG): Infrastructure and applications for a worldwide research community. Stud Health Technol Inform 2007;129(1):330 – 4

[4] Kakazu KK, Cheung LW, Lynne W. The cancer biomedical informatics grid (caBIG): Pioneering an expansive network of information and tools for collaborative cancer research. Hawaii Med J 2004 September;63(9):273–5

[5] Zerhouni EA. Translational and clinical science—Time for a new vision. N Engl J Med 2005 Oct 13;353(15):1621–3.

[6] Zerhouni EA. Clinical research at a crossroads: The NIH roadmap. J Investig Med 2006 May;54(4):171–3.

[7] Payne PR, Johnson SB, Starren JB, Tilson HH, Dowdy D. Breaking the translational barriers: The value of integrating biomedical informatics and translational research. J Investig Med 2005 May;53(4):192–200.

[8] Sung NS, Crowley WF, Jr, Genel M, et al. Central challenges facing the national clinical research enterprise. J Am Med Assoc 2003 Mar 12;289(10):1278 – 87.

[9] Oster S, Langella S, Hastings S, et al. caGrid 1.0: an enterprise Grid infrastructure for biomedical research. J Am Med Inform Assoc 2008 Mar–Apr;15(2):138 – 49

[10] Saltz J, Oster S, Hastings S, et al. CaGrid: Design and implementation of the Core Architecture of the Cancer Biomedical Informatics Grid, BioInformatics, 2006 Aug 1;22(15):1910 –16.

 [11] Chung TK, Kukafka R, Johnson SB. Reengineering clinical research with informatics. J Investig Med 2006 September;54(6): 327–33.

[12] Embi PJ, Payne PRO. Clinical Research Informatics: Challenges, Opportunities and Definition for an Emerging Domain. J Am Med Inform Assoc. 2009;16(3):316-327. DOI 10.1197/jamia.M3005.

[13] Glossary of Terms for Human Subjects Protection and Inclusion Issues, based on the 1997 Report of the NIH Director’s Panel on Clinical Research, entry: “clinical research”. [Accessed August 13, 2023].

[14] Ash, J. S., Anderson, N. R., & Tarczy- Hornoch, P. . People and organizational issues in research systems implementation. Journal of the American Medical Informatics Association, 2008;15 (3): 283–289.

[15] Solomonides A. Review of Clinical Research Informatics. Yearb Med Inform. 2020 Aug;29(1):193-202. doi: 10.1055/s-0040-1701988. Epub 2020 Aug 21.

[16] Zerhouni E. Medicine. The NIH Roadmap, Science, 2003 Oct 3;302(5642):63–72.

 [17] Zerhouni EA. US biomedical research: Basic, translational, and clinical sciences. J Am Med Assoc 2005 September 21;294(11): 1352– 8.

[18] CTSA. Clinical and translational science awards, 2008. Available at: http://www.ctsaweb.org/. Accessed 9/8/2023.

[19] Fridsma DB, Evans J, Hastak S, Mead CN. The BRIDG project: A technical report. J Am Med Inform Assoc 2008 Mar–Apr; 15(2):130 –7

[20] Kush RD, Helton E, Rockhold FW, Hardison CD. Electronic health records, medical research, and the tower of Babel. N Engl J Med 2008 Apr 17;358(16):1738 – 40.

[21] Richesson RL, Krischer J. Data standards in clinical research: Gaps, overlaps, challenges and future directions. J Am Med Inform Assoc 2007 Nov–Dec;14(6):687–96.

[22] Souza T, Kush R, Evans JP. Global clinical data interchange standards are here! Drug Discov Today 2007 Febr;12(3– 4):174 – 81.

[23] Ghersi D, Clarke M, Berlin J, et al. Reporting the findings of clinical trials: A discussion paper. Bull WHO 2008 Jun;86(6):492–3]

[24] Sim I. Trial registration for public trust: Making the case for medical devices. J Gen Intern Med 2008 Jan;23 Suppl 1:64 – 8

[25] Sim I, Chan AW, Gulmezoglu AM, Evans T, Pang T. Clinical trial registration: Transparency is the watchword. Lancet 2006 May 20;367(9523):1631–3.

[26] Khan SA, Kukafka R, Payne PR, Bigger JT, Johnson SB. A day in the life of a clinical research coordinator: Observations from community practice settings. Stud Health Technol Inform 2007; 129(1):247–51.

 [27] Boyd AD, Hunscher DA, Kramer AJ, et al. The “Honest Broker” method of integrating interdisciplinary research data. AMIA Annu Symp Proc 2005;902.

[28] Khan SA, Payne PR, Johnson SB, Bigger JT, Kukafka R. Modeling clinical trials workflow in community practice settings. AMIA Annu Symp Proc 2006:419 –23.

[29] National Institutes of Health. Definitions under Subsection 1 (Research Objectives), Section I (Funding Opportunity Description), Part II (Full Text of Announcement), of RFA-RM-07-007: Institutional Clinical and Translational Science Award (U54) Mar2007. [Accessed August 9th, 2023]

[30] Zerhouni EA. Clinical research at a crossroads: The NIH roadmap. J Investig Med 2006 May;54(4):171–3

[31] Research Rewired: Merging Care and Research Information to Improve Knowledge Discovery, Price Waterhouse Coopers, 2008

 [32] Westfall JM, Mold J, Fagnan L. Practice-based research—“Blue Highways” on the NIH roadmap. J Am Med Assoc 2007 Jan 24;297(4):403– 6.

[33] Daniel C, Kalra D. Clinical Research Informatics. IMIA Yearbook of Medical Informatics 2020. Pg 203-207

[34] Daniel C, Tannier X, Kalra D. Clinical Research Informatics. Yearb Med Inform. 2022 Aug;31(1):161-164. doi: 10.1055/s-0042-1742530. Epub 2022 Dec 4.

[35] Daniel C, Bellamine A, Kalra D. Key Contributions in Clinical Research Informatics. Yearb Med Inform 2021; 30(01):233-238. DOI: 10.1055/s-0041-1726514