Future Directions in Clinical Research Informatics

22

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Abstract

Given the rapid advances in biomedical science, the growth of the human population, and the escalating costs of health care, the need to accelerate the pace of biomedical discoveries and their translation into health-care practice will continue to grow. Indeed, the need for more efficient and effective support of clinical research to enable the development, evaluation, and implementation of cost-effective therapies is more important now than ever before. Furthermore, the fundamentally information-intensive nature of such clinical research endeavors and the growth in both health technology adoption and health-related data available for interventions and analytics beg for the solutions offered by CRI. As a result, the demand for informatics professionals who focus on the increasingly important field of clinical and translational research will increase. Despite the progress made to date, new models, tools, and approaches will be needed to fully leverage and mine these digital assets and improve CRI practice, and this innovation will continue to drive the field forward in the coming years.

Keywords

Clinical research informatics · Biomedical informatics · Translation research · Electronic health records · Future trends · US policy initiatives · Health IT infrastructure · Data analytics · Learning health systems · Evidence-generating medicine

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As evidenced by the production of the new edition of this book and reflected in its chapters, clinical research informatics (CRI) has clearly become established as a distinct and important biomedical informatics subdiscipline [1]. Given that clinical research is a complex, information- and resource-intensive endeavor, one comprised of a multitude of actors, workflows, processes, and information resources, this is not a surprise. As described throughout the text, the myriad stakeholders in CRI, and their roles in the health care, research, and informatics enterprises, are continually evolving, fueled by technological, scientific, and socioeconomic changes. The changing roles in health care and biomedical research bring new challenges for research conduct and coordination but also bring potential for new research efficiencies, more rapid translation of results to practice, and enhanced patient benefits as a result of increased transparency, more meaningful participation, and increased safety.

As Fig. 22.1 depicts, the pathway from biological discovery to public health impact (the phases of translational research) clearly is served by informatics applications and professionals working in the different subdomains of biomedical informatics. Given that all of these endeavors rely on data, information, and knowledge for their success, informatics approaches, theories, and resources have and will continue to be essential to driving advances from discovery to global health. Indeed, informatics issues are at the heart of realizing many of the goals for the research enterprise.

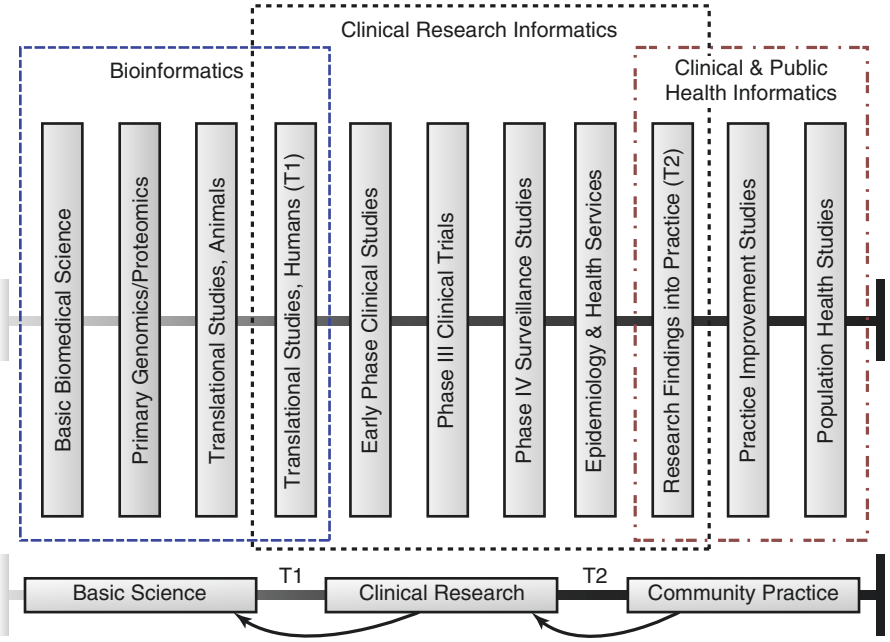

Fig. 22.1 Clinical and translational science spectrum research and informatics. This figure illustrates examples of research across the translational science spectrum and the relationships between CRI and the other subdomains of translational bioinformatics, clinical informatics, and public health informatics as applied to those efforts. (From Embi and Payne [1], with permission)

Initiatives, Policy, and Regulatory Trends in CRI

It should therefore come as no great surprise that recent years have seen the emergence of several national and international research initiatives, as well as policy and regulatory efforts focused on accelerating and improving clinical research capacity and capabilities. Indeed, a range of initiatives funded by US health and human service agencies are helping to advance the field. These include initiatives by the US National Institutes of Health (NIH), including important efforts related to the NIH Clinical and Translational Science Award (CTSA) [2, 3] programs, the establishment of visible and well-funded data science initiatives at NLM, and increased funding as a result of the twenty-first-century Cures Act toward the Cancer Moonshot and the evolution of the All of Us Research Program for advancing precision and personalized medicine.

In recent years, the CTSA program in particular has had fostered significant growth in both the practice and science of CRI and fostering professional development of CRI, given one of its major emphases the advancement of CRI, and the closely related domains of translational research informatics, translational bioinformatics, and biomedical data science efforts. Recent examples that are likely to play larger roles in the coming years, involved CRI activities that foster informatics innovations to support pragmatic and multi-site clinical research as well as recruitment innovations [4]. Other NIH activities advancing efforts related to "big data" and "data science" also have direct relevance to CRI [5, 6]. The growth of data science illustrated by the maturation of the Big Data to Knowledge (BD2K) awards the first phase designed to stimulate data-driven discovery via innovative methods, software, and training and more recently a second phase of awards designed to make the aforementioned products of research usable, discoverable, and broadly disseminated, embracing approaches that make biomedical data findable, accessible, interoperable, and reusable or "FAIR." Additionally, other CRI-related efforts led by institutes like the National Cancer Institute (NCI) [7–10] and National Library of Medicine [11, 12] will continue to advance work in the field. Beyond NIH, funders like the Agency for Healthcare Research and Quality (AHRQ) and the Patient-Centered Outcomes Research Institute (PCORI) are also driving advances in research data methods and techniques for CRI-related efforts, including comparative effectiveness and health services research [13–15].

In addition to such initiatives focused on advancing the science and practice of CRI, investments by institutions and by the government through the US Department of Health and Human Services (DHHS), the US Office of the National Coordinator for Health Information Technology (ONC), and the US Centers for Medicare and Medicaid Services (CMMS) have incentivized the adoption and "meaningful use" of electronic health records (EHRs). The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA) emphasizes the use of patient registries for quality measurement and reporting. The resultant widespread health IT infrastructure now in place, while initially focused primarily on improving patient care, is starting to enable interoperable infrastructure that is allowing for data reuse across research networks [16–18]. While initially separate efforts, recent efforts to translate between prevailing data models and adopt common interchange standards, as well as updates to

antiquated regulatory structures should enable increased interactions and enable more robust reuse of data and information from clinical care for public health and research improvements. A driving goal, to create and enable the learning health system, is now within reach, and early examples are coming online and more are likely to follow [19].

Creating Learning Health Systems Data and Knowledge Management, Evidence Generation, and Quality Improvement.

Just as biomedical informatics approaches and resources are essential to realizing the potential of such systems for enhancing clinical care, so too are CRI methods, theories, and tools critical to realizing the vision of a learning health system that enables systematic evidence generation and application via clinical practice [20]. Indeed, fully leveraging our health care and research investments to advance human health will require even more emphasis on making sense of the ever-increasing amounts of data generated through health care and research endeavors. It is work in the field of CRI that will enable and improve such research activities, from the translation of basic science discoveries to clinical trials to the leveraging of health-care data for population level science and health services research that enables its impact on care.

Importantly, these advances will continue to require increased effort not just to the development and management of technologies and platforms but also to the foundational science of CRI in an increasingly electronic world [21]. By facilitating all of the information-dense aspects of clinical research, population management, and quality improvement, CRI methods and resources will enable the conduct of increasingly pragmatic and rigorous research programs to generate new and impactful knowledge [22]. In fact, the now ubiquitous presence of EHRs will allow the systematic collection of essential data that will drive quality improvement research, outcomes research, clinical trials, comparative effectiveness research, and population level studies to a degree not heretofore feasible [23]. In addition to the technological and informatics underpinnings already mentioned, realizing this promise will require increased attention and efforts by experts focused on advancing the domain of CRI.

As depicted (Fig. 22.2), an informatics-enabled learning health system will enable the virtuous cycle of evidence generation and application, leveraging both real-world experiences and data, and applying increasingly computable knowledge artifacts in order to drive evidence-directed care and population management. Such a system will enable (a) the study of linkages from molecules to populations, (b) the development of tools and methods to enable evidence generation from real-world practice experience, (c) build bridges between health systems and research enterprises, and (d) enable the implementation and study of solutions to systematically improve health-care delivery.

Indeed, as the preceding chapters have also demonstrate, advances in CRI have already begun to enable significant improvements in the quality and efficiency of clinical research [24–26]. These have occurred through improvements in processes at the individual investigator level, through approaches and resources developed and implemented at the institutional level, and through mechanisms that have enabled and facilitated the endeavors' multicenter research consortia to drive team science. As research becomes increasingly global, initiatives like those mentioned above

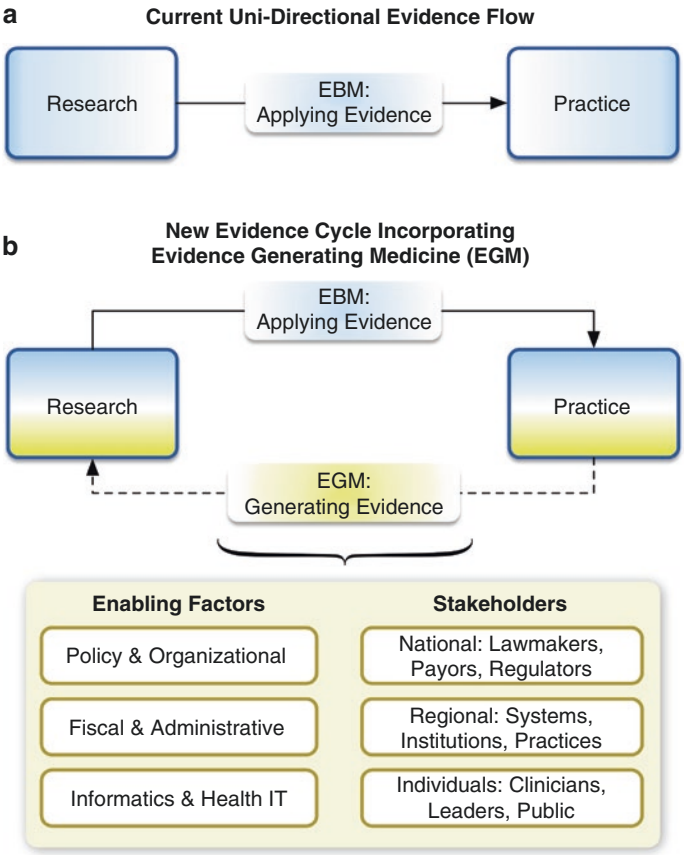

Fig. 22.2 Enabling a virtuous cycle of EBM and EGM is critical to realizing a learning health system, and there remain numerous enabling factors and key stakeholders that must be addressed and aligned to overcoming current challenges. (From Embi and Payne [20], reproduced with permission)

provide opportunities for collaboration and cooperation among CRI professionals across geographical, institutional, and virtual borders to identify common problems, solutions, and education and training needs. Increasingly, investigators and professionals engaged in these groups are explicitly self-identifying as CRI experts or practitioners, further evidence for the establishment of CRI as an important, respected, and distinct informatics subdiscipline.

Multidisciplinary Collaboration

CRI professionals come to the field from many disciplines and professional communities. In addition to the collaborations and professional development fostered by such initiatives as the CTSA mentioned above, there is also a growing role for

professional associations that can provide a professional home for those working in the maturing discipline. The American Medical Informatics Association (AMIA) is the most well-recognized such organization. Working groups focused on CRI within organizations like AMIA continue to see considerable growth in interest and attendance over the past decade. There has also been the emergence of operational professionals often referred to as chief research information officers (CRIOs) who are akin to CMIOs but focused on the research IT portfolios of academic health centers [27].

The past several years have also seen a growth in scientific conferences dedicated to CRI and the closely related informatics subdiscipline of translational bioinformatics (TBI). The main meeting hosted by AMIA has seen growing attendance and productivity among the informatics and clinical/translational research communities. In addition, journals like AMIA's *JAMIA*, *Applied Clinical Informatics*, and *JAMIA Open*, as well as other leading journals in the field, have also seen growth in CRI-focused publications. The importance of CRI has led to editorial board members with CRI expertise, and even journal space special issues are dedicated to important topics in CRI [28]. Given its growth, it is likely that journals specifically focused on this domain will emerge in the years to come. In addition, other important informatics groups and journal, such as International Medical Informatics Association (IMIA), and non-informatics associations and journals (e.g., DIA, The Society for Clinical Trials, Clinical Research Forum, and many other professional medical societies) also increasingly provide coverage and opportunities for professional collaboration among those working to advance CRI. Efforts like these continue foster the maturity and growth so critical to advancing the field.

Challenges and Opportunities

Despite these many advances, significant challenges and opportunities remain to be addressed if this relatively young discipline is to evolve and realize its full potential to accelerate and improve clinical and translational science. Indeed, as reported in 2009 by Embi and Payne, the challenges and opportunities facing CRI are myriad. In that manuscript, these were placed into 13 distinct categories that spanned multiple stakeholder groups (Fig. 22.3) [1].

This conceptualization of CRI activities includes those related to education and original (informatics) research, research support services and activities, and policy leadership. The stakeholders for all of these span the individual, institutional, and national levels and include those with clinical research as well as informatics perspectives and priorities. These broad groups of stakeholders and the wide range of diverse CRI activities should all be considered as the field evolves and as research agendas, educational and training efforts, and professional resources are developed.

One of the keys to enabling a learning health system is the ability to enable systematic evidence generation through practice. A key challenge today remains the now artificial but persistent paradigm that dictates clinical care and research

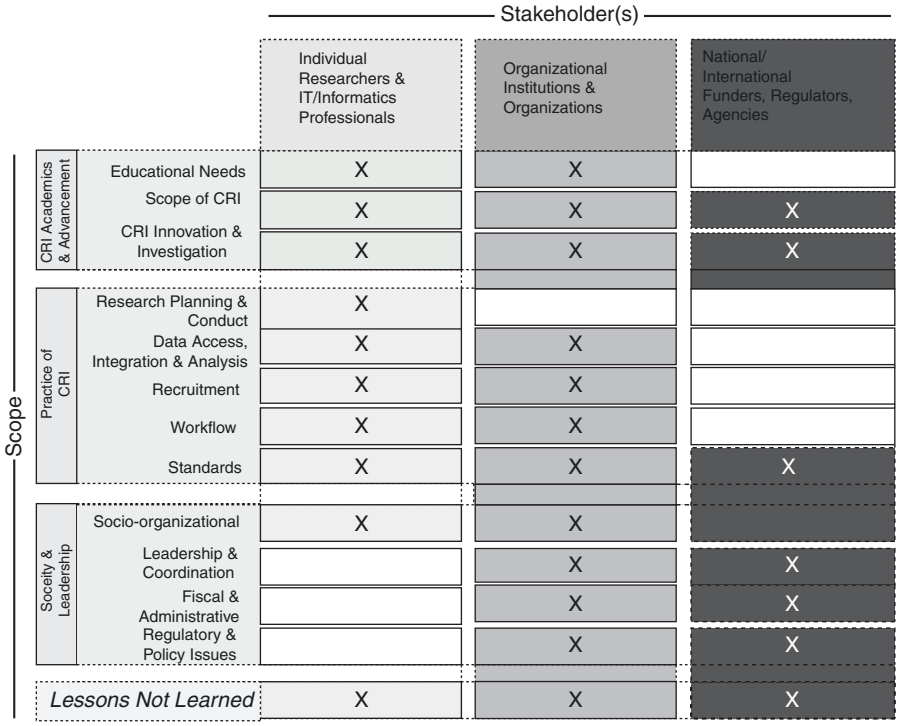

Fig. 22.3 Major challenges and opportunities facing CRI. This figure provides an overview of identified challenges and opportunities facing CRI, organized into higher-level groupings by scope, and applied across the groups of stakeholders to which they apply. (From Embi and Payne [1], with permission)

activities as distinct activities that are related only in the application of research evidence to practice, via evidence-based medicine [20]. Instead, CRI activities are increasingly demonstrating and creating environments that recognized a virtuous cycle of evidence generation and application, where "Evidence Generating Medicine" (EGM) paradigm is realized. As defined, EGM involves, "the systematic incorporation of research and quality improvement considerations into the organization and practice of healthcare to adavance biomedical science and thereby improve the health of individuals and populations" [20]. An EGM-enabled environment recognizes and supports the fact that (a) clinical care activities are not entirely distinct from research activities, (b) EGM must be enabled during practice to advance both research and care, (c) EGM activities are in fact ongoing, (d) advancing EGM is key to the desired EBM lifecycle, and (e) multiple enabling factors and stakeholders are essential to making this reality (Fig. 22.4) [20].

Another major challenge to be overcome in order to realize the promise of CRI is the need to address the severe shortage of professionals currently working to advance in the CRI domain. As with many biomedical informatics subdisciplines, training in CRI is and will remain interdisciplinary by nature, requiring the study of

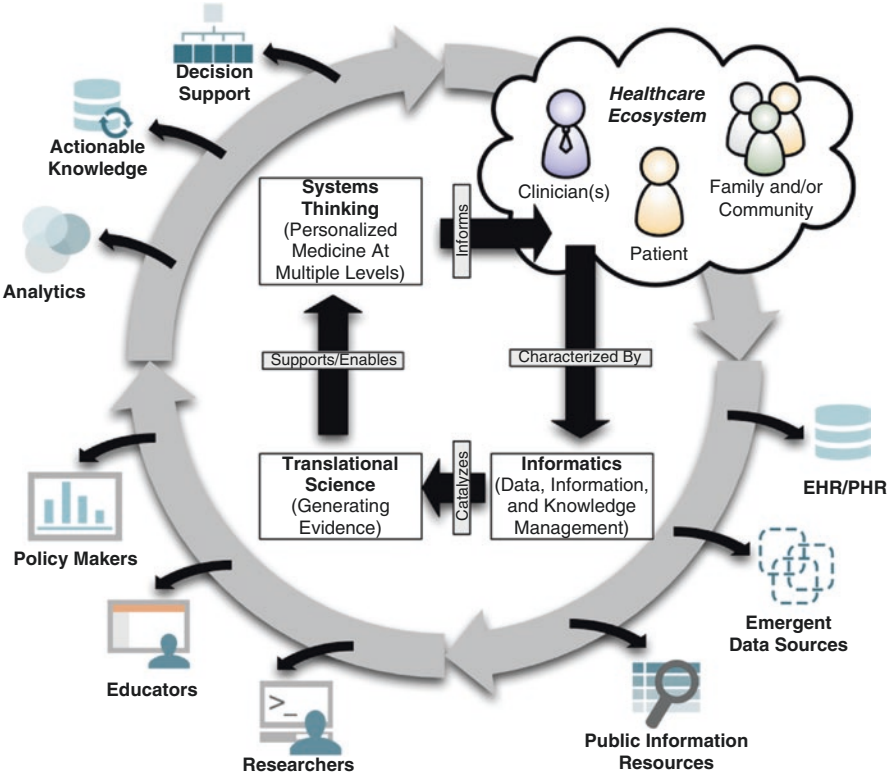

Fig. 22.4 Creating an informatics-enabled evidence-generating medicine (EGM) system: the virtuous cycle of evidence generation and application that fuels a learning health system. (From: Payne and Embi [29], reproduced with permission)

topics ranging from research methods and biostatistics, to regulatory and ethical issues in CRI to the fundamental informatics and IT topics essential to data management in biomedical science. As the content of this very book illustrates, the training needed to adequately equip trainees and professionals to address the complex and interdisciplinary nature of CRI demands the growth of programs focused specifically in this area.

Furthermore, while there is certainly a clear need for more technicians conversant in both clinical research and biomedical informatics to work in the CRI space, there remains a great need for scientific experts working to innovate and advance the methods and theories of the CRI domain. In recent years, the National Library of Medicine, which has long supported training and infrastructure development in health and biomedical informatics, recognized this need by clearly calling out clinical research informatics as a domain of interest for the fellowship training programs it supports. While most welcome and important, the availability of such training and education remains extremely limited. Significantly, more capacity in training and education programs focused on CRI will be needed to establish and grow the cadre

of professionals focused in this critical area if the goals set forth for the biomedical science and health-care enterprise are to be realized. This will require increased attention by sponsors and educational institutions.

In addition to training the professionals who will focus primarily in CRI to advance the domain, there is a major need to also educate current informaticians, clinical research investigators and staff, and institutional leaders concerning the theory and practice of CRI. Programs like AMIA's 10×10 initiative and tutorials at professional meetings offer examples like a course focused in CRI that help to meet such a need [30]. Such offerings help to ensure that those called upon to satisfy the CRI needs of our research enterprise are able to provide appropriate support for utilization of CRI-related methods or tools, including the allocation of appropriate resources to accomplish organizational aims.

As the workforce of CRI professionals grows, the field can be expected to mature further. While so much of the current effort of CRI is quite appropriately focused on the proverbial "low-hanging fruit" of overcoming the significant day-to-day IT challenges that plague our traditionally low-tech research enterprise, significant advances will ultimately come about through a recognition that biomedical informatics approaches are crucial centerpieces in the clinical research enterprise. Indeed, just as the relationship between clinical care and clinical research is increasingly being blurred as we move toward the realizing of a "learning health system," so too are there corollaries to be drawn between the current formative state of CRI and the experiences learned during the early decades of work in clinical informatics. Those working to lead advances in CRI would do well to heed the lessons learned from the clinical informatics experiences of years past. Future years can be expected to see CRI not only instrument, facilitate, and improve current clinical research processes, but advances can be expected to fundamentally change the pace, direction, and effectiveness of the clinical research enterprise and discovery. Toward that end, groups are already working to develop maturity models and deployment indices that can be used to measure and compare CRI infrastructures as to their level of maturity and ability to support the research enterprise [31]. Such measures of CRI maturity will only grow and become more useful to inform progress in the years to come. Guided by such measures, we should expect to see CRI efforts continue to improve, with consequent improvements to scientific discovery, healthcare quality, and real-world evidence generation as learning health systems continue to evolve and mature.

Conclusion

In conclusion, the future is bright for the domain of CRI. Given the rapid advances in biomedical discoveries, the growth of the human population, and the escalating costs of health care, there is an ever-increasing need for clinical research that will enable the testing and implementation of cost-effective therapies at the exclusion of those that are not. The fundamentally information-intensive nature of such clinical research endeavors begs for the solutions offered by CRI. As a result, the demand for informatics professionals who focus on the increasingly important field of clinical and

translational research will only grow. New models, tools, and approaches must continue to be developed to achieve this, and the resultant innovations are what will continue to drive the field forward in the coming years. It remains an exciting time to be working in this critically important area of informatics study and practice.

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