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Review Article

Integration of clinical research and medical care, slow but continuing effective future

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ABSTRACT

The demarcation between research and medical practice appears partly blurred as they often coexist together while still having significant differences between them. The prospective complete merger still seems to have a bright future that could benefit humankind. The goal of medical practice is to provide the diagnosis, palliative or curative therapy, preventative therapy and the term "research" is recognized as a pursuit to investigate a hypothesis and pull conclusions to develop the theory or contribute to generalizable knowledge. A clinical trial is usually described as a clinical research study protocol with certain objectives and steps to accomplish those objectives. Integrating evidence-based medicine in medical practice requires combining patient-targeted treatment and research and overcoming all possible methodological, organizational, and cultural challenges while integrating the teaching healthcare system.

Keywords: Patient-centered medicine, Evidence-based medicine, Good clinical practice, Patient-oriented research, International council on harmonization, Belmont report

INTRODUCTION

Although the objective, goal, and method for the conduct of medical practice and clinical research vary, they are still similar in many aspects and overlap. The similarities between them rest on the clinical judgment, clinical evaluation, and various associated factors, and the differences lay in the elements, duration of treatment, strict protocol binding requirements such as treatment regimen, study procedure, etc. Even though the desirable outcome of the objective is welcomed in both cases, the purpose and need for outcome could be well predicted and promising in medical care, whereas in clinical research, it is nonguaranteed or unpredictable due to the experimental nature of the treatment. Since both practices could be time demanding, it is challenging for the physician to provide an additional equal amount of time to research due to the busy clinic schedule.[1,2] Hence, these practices grew as independent entities of interest despite having many common elements. The fundamental objective of the research, when implemented in medical practice upon its approval, is to produce the output, which could help researchers in making a difference in a patient's life, whereas the objective of a medical course is to take care of well-being. Advanced healthcare systems and continuing advances in the medical discipline are emerging along with the advancement of technology, reflecting its impact on many levels. The increasing survival of patients with critical illnesses in the past few decades became a reality due to the advancements in medical science saving people's lives worldwide.

These advancements and positive changes in medicine also contribute toward increasing the ambitious conjunction of these two entities. Clinical research is advancing the goal of the new therapy development on the platform of routine medical treatment. Some of the advancements in clinical research are patient-focused; the emergence of comparative effectiveness research, real-world evidence, development of patient-focused outcome

research institutes, increasing utilization of patient-reported outcomes assessments, for example, quality of life questionnaires, functional status, or patient satisfaction surveys etc.[3-5] The healthcare system also includes the traditional features from the clinical research, such as, establishment of standards and protocols to implement good clinical practice principles. The increasing laws and regulations are protecting stakeholders in healthcare practices, such as routinely collected patient's informed consent, advancement of information technologies, transition of paper medical records into electronic health records. Additional rules and regulations such as HIPAA, not only benefiting the systematic analyzation of patient's data for the better treatment options but also protecting patients, health care providers and reflecting its further usage in the area of clinical research.[6]

As any other development comes with pros and cons, this development also comes along with some barriers, such as ethical, cultural, methodological challenges. These challenges require further review and resolution to enhance the full of merger of clinical research and clinical practice.

Following is the elaboration of differences between clinical research and clinical practice.

CLINICAL RESEARCH: EVIDENCE-BASED RESEARCH

In clinical research, per the study objective and the requirement research site successively enroll research participants. The trial's objective could be to study the efficacy and safety of a new therapy or to study new indications for an already existing approved therapy with the intention of benefiting the patients.

Finance and concept are sponsored by pharmaceuticals or by government agencies. Study treatment is usually restricted, duration varies per individual study protocol, typically study treatment requires patients and researchers to sign the informed consent unless regulatory authorities grant a waiver. Study protocol described study assessments, including periodical study visits and various study procedures. In United States the regulatory authority food and drug administration (FDA), governs clinical research conduct, and the IRB approves study protocol, informed consent document, patient-facing material, etc. Study treatment interventions could include studying a new drug, device, or test product which is considered unproved and not confirmed as safe or efficacious for the intended use. The concept is considered confidential intellectual property. After the clinical trial is complete, study data is analyzed using a statistical approach before it can be submitted to the FDA, study results are published in medical journals. Investigators must have knowledge and experience of working with ICH-GCP guidelines for human research. Investigators must delegate qualified staff to conduct the clinical trials.

The study protocol and its specific requirements may differ from the standard of care even though clinical judgment for the patient's safety remains the same.

MEDICAL TREATMENT: PATIENT-CENTRIC RESEARCH

Projected to benefit the individual patient with an existing approved therapy. Self funded or supported by charities. Treatment duration depends on the patients' need to resolve or reduce the severity of the medical condition. Periodic health checkups could includes various exam slabs, investigational procedures, according to the standard of care. The system is guided by legal and professional standards such as informed consent process, peer review, and the state board of medical practice. The approved drug, device, and test products are considered the safe and effective standard of care treatment options, and their information is available on the therapy patient package insert for the public. HIPAA prohibits disclosing protected health information, including treatment effects, to the public. A licensed physician qualified to practice medicine or specialty medicine is needed to conduct medical practice.[7]

Developments of ethical principles for clinical research

History demonstrated that scientific research, although provided extensive benefits to the society, it also put forth some tormenting ethical concerns. The abuse of camp prisoners enrolled in the reserarch as the study participants during Second World War necessitated the adjudication of involved physicians and scientists, and it gave birth to the Nuremberg Code. The Nuremberg code was originated to ensure the ethical conduct of human clinical research, and ultimately, it became the paradigm of many future regulations. To resolve the ethical problems in human research, the Belmont Report was established on September 30, 1978. It declares basic ethical principles and guidelines of three core values described ahead.

Borders between medical practice and research

Basic ethical principles include respect, beneficence, and justice for study participants. Applications include study subjects' informed consent, evaluation of risks and benefits for study subjects, and selection of study subjects.

Part A-Borders between practices and research: The objective of healthcare is to set up a diagnosis of medical conditions and provide preventative or curative treatment options for patients. The term "research" indicates a pursuit with an objective and a set of procedures intended to examine a hypothesis and produce a result that can

establish generalizable knowledge.[8] Society and medical practice should support the development of major innovations. To guide the researchers in their work, current clinical research codes include general and specific rules but often appear inadequate and difficult to interpret or apply for complex, conflicting situations. Even though broader moral principles are accommodated, they still may not be helpful in many ethical problems. Hence, these principles must be widened to protect all entities and serve the patients.[9] The merging of evidence-based medicine in medical practice requires assessments, modification, and acclimatization of principles such as informed consent, beneficence, autonomy, and voluntariness. But the most important is to update and spread the knowledge and concept of clinical research among healthcare workers, patients, and the public, and have the clinical research studies as an additional arm available for the patients in healthcare practice. However, this ambition requires reassessment and evaluation of the following ethical principles along with some of the challenges we will discuss ahead.

Informed consent: The current nature of the informed consent document is extensive; it contains pertaining clinical study-related formation in much complex and regulatory language, which makes the information difficult to understand for the patient. Even though the purpose of ICF is to provide correct, detailed, and relevant information to the patients so that they can make unbiased decisions to enroll or not to enroll in the research study, due to the complex nature of the ICF language, it apprehends the patients. In addition to that, the current ICF format appears to protect the physician more than the patients. Most importantly, many patients refused to participate in the trial due to the word "experimental" which refers to "research" described in the informed consent document.[10,11]

Autonomy (sovereignty and independence): This is one of the ethical principles for clinical research conduct. Researchers conducting studies usually decide which trial is suited for the subject. Instead, patients should have the independence to decide which trial they want to participate in, and the patients need to be informed about all the suitable clinical trials available for them to consider.[12]

Clinical equipoise: A state of clinical equipoise is tough to obtain in clinical trials in situations such as placebo-controlled clinical trials, new drug trials with a comparable commercialized drug when a different patient responds heterogeneously to the same treatment, and when patients have preferences for various available treatments options, etc. Currently, the doctrine of clinical equipoise exists from scientific and physician perspectives. "Patient equipoise" from the patient's perspective should also be included to accommodate the principles of respect and justice.[13,14]

Beneficence: Patients' sound understanding and acknowledgment of the meaning of beneficence is necessary. To achieve this value, two universal altruistic guidelines have been described: (1) Do not harm; (2) Amplify medicine's possible benefits and reduce possible harm. In general, in the case of scientific development, there is an obligation to acknowledge the benefits, risks, and associated knowledge that could be the outcome of the enhancement of innovative therapeutic, psychotherapeutics, and social practices.[15]

Voluntariness: Well-informed information to the study subject must be followed by well-confirmed acceptance of voluntariness without coercion, undue influence, and rapid decision. To contribute to the betterment of society, this ethical principle is not only applicable to patients for their contribution to research, but it should also be applicable to physicians, all healthcare workers, and the public. This feature can be created via an integrated teaching healthcare system while continuously emphasizing and spreading knowledge and education about clinical research, learning about the drug development process, and its impact on healthcare. It can also remove misunderstandings and reduce biases about experimental medicine among patients, healthcare workers, and the public, thereby obliterating the demarcation between clinical research and clinical care.

METHODOLOGICAL CHALLENGES AND POSSIBLE SOLUTIONS

Evidence-based medicine emphasizes the collection of data, the analysis of common factors, the evaluation of the intervention effectiveness in average patients, generalization, and implementation of results. Randomized controlled trials have become the core of evidence-based medicine. Patient-centered medicine focuses on individual patients by providing the best available treatment under the umbrella of clinical practice while considering the patient's objectives, preferences, values, and economic resources. The advancement of patient-centered medicine (PCM) demands the growth of patient-oriented research and emphasis on factors such as the detection of the best treatment option, detailed individualized data, and evaluation of exemptions and irregularities.[16-18]

Vigilant singular surveillance is the basis for patient-orientated research. Both EBM and PCM combination establish knowledge and maximize healthcare outcomes of patients today and tomorrow. Combining such individual observations into clinical research contributes to patient-orientated research, even though it is not classified as supreme evidence. and it is supported by the research methodology development to assess its crucial role, and it can promptly alter the clinical practice.[19,20] The commonly used electronic medical records help to locate individual symptoms and related alterations as unique findings so the associated factors can be analyzed, and doctors can be alerted to monitor such key

symptoms. In addition, electronic health records can also identify and screen the types and subgroups of patients according to associated medical conditions and risk factors and assess which interventions were applied and how it was applied to these patients.[21,22]

On discovering the first antidepressant, Khun's described the importance of the precise observation of patients as a supreme value. Randomized clinical trials are logically stimulating, as stated by Dr. Crofton, the Medical Research Council Member, and that's so true. There are additional reasons to call RCT intellectually challenging, which are conducted to locate and evaluate the precise observations, it provides detailed reasons for the treatment failures and learns from them to achieve complete success, for example, the successful treatment of pulmonary tuberculosis after several failures.[23]

Observational studies and pragmatic clinical trials are the chief methods to carry out comparative effectiveness research and to generate real-world data. Patient clinical databases and registries are used in observational studies and real-world platforms in pragmatic clinical trials.

Pragmatic trials, as the name suggests, are practicable as they are planned to practically examine the long-term effectiveness of the intervention for its successful implementation in daily care. It includes broad, inclusive criteria and diverse patient populations receiving treatment in healthcare systems while engaging patients and providers, collecting data, and interpreting results in real-world settings. Pragmatic trials have been aiding healthcare systems and providers for decades, for example, polio vaccine studies 1950s, early studies of the acute treatment for heart attack 1980s and 1990s, etc. The trial results concentrated on issues and data suitable for making decisions, which showed a faster demonstration of real-world treatment success.[24,25]

Randomized database studies could be an effective way to coalesce the vital assets of registry trials and randomized controlled trials. The single-patient trial is another method to rule out the best option between new and existing treatments for an individual patient.[26]

As described earlier, due to the current nature of the informed consent form it is repelling rather than enhancing the patient's participation in the clinical trial. Therefore, this ethical and methodological challenge requires updating the informed consent form and related requirements. The informed consent form needs to be in a simplistic, easily understandable language, protecting the patients and providing them with all possible approved and non-approved treatment options available for study-specific indication. It will then allow the patient to decide what they want from all the available options. At present, it is the healthcare provider who decides which trial is going to be good for the patients, and it is presented to the patient accordingly.

The current informed consent process should be more transparent regarding study subjects' protection in case of injury caused due to their participation in the clinical trials or caused during their clinical trial participation. Clinical trial participation-related injury should be completely covered by the study sponsor or the subject's health insurance without financially burdening the participants.

The major cultural challenge that has been facing the field is how to recruit and retain qualified clinical research professionals. Other challenges are staffing turnover and associated factors such as a competitive job market, lucrative job opportunities, staff burnout due to the fast-paced, extensive detail nature of the clinical trial, insufficient funding to support the research framework, temporary funded nature of the research roles, insufficient processes for clinical research training, lack of tenure and promotion metrics for clinical researchers, the busy work schedule of clinicians and lack of sufficient time to include in the research responsibilities, and the promotion of evidence-based medical practice.

Suggestions to remove challenges

The need for clinical research coursework and related experience should be a mandatory part of the medical school curriculum. Increased aid for health services research, observational studies, and comparative trials of new and approved treatments, well-supported investigator-initiated trials to promote the clinical and scientific interest of the researchers, promoting research to evaluate the impact of racial, gender, socioeconomic, cultural disparities in healthcare utilization and associated healthcare outcomes, promoting clinical researchers by providing them incentives in the form of tuition fees for clinical research courses and helping them attend clinical research meetings, and educational workshops, awards for great performance, creating lucrative and competitive salary packages.

Lifestyle and behavioral modification can help patients and the public obtain good health and quality of life. Surmounting organizational and methodical challenges is crucial for the successful melding of clinical research and medical practice. However, the most critical element to expedite the integration of these two systems is to overcome the cultural challenge. and it can be possible by developing various measures to reevaluate how researchers, clinicians, healthcare workers, the public, and, most importantly, patients understand research and its impact on health.

CONCLUSION

The advancement in healthcare motivates the best utilization of direct or indirect entities, factors, and practices, such as clinical research and clinical care. While the margins between these two entities continue to blur, globally they appear to have a bright future, proving

beneficial to humankind. Clinical research is improving the evaluation of efficacy in real-world scenarios while respecting patients' perspectives, their preferences, and the best utilization of the available resources and shifting its focus toward patient-orientated research. The standard of care medicine accommodates the key elements of research such as informed consent, electronic health records, applications of advanced information technologies, and shifting its focus toward patient-centered medicine. The successful future of the drug development process requires the merging of evidence-based medicines and assessments and observation of patient-centered medicine, overcoming of several ethical, methodological, and organizational challenges, the development of a combined education health system, which can produce valuable knowledge for the betterment of patients at present and in the future.

To achieve a full merger of clinical research and clinical practice, both these practices should progress to patient-oriented informed consent, patients' autonomy, patient equipoise, and utilization of risk-based ethical vigilance for the patients. The requirement for altruism-based research is not only applicable to the patients, but it is also expected from the physician, healthcare workers, and the public so as to develop respect, appreciation, and cherish the advanced equipment of research and medicine for the betterment of society. From a methodological challenges perspective, clinical research should progress towards patient-orientated research, which includes careful observations and its usefulness. Research should be practically incorporated into daily medical practice by implementing single-patient trials, randomized database trials, and practical trials while using decision aids tools and electronic health records. These implementations may reduce the efforts of comparative effectiveness research and hasten the development and implementation of new knowledge for the patients.

The effective merger of medical research and clinical care will need the removal of organizational and operational challenges by establishing an acceptable financial structuring, a system for improving and developing patient-centered medical education and counseling, patient-centered outcomes, collecting data about beneficial effects, incorporating education health system and the required elements to expedite the transformation.

However, the most crucial element to expedite the integration of these two systems is overcoming cultural challenges, which can be possible by developing various ways to reevaluate how researchers, clinicians, healthcare managers, the public, and, most importantly, patients understand research, and its impact the on health. At the same time, study sponsors should create better ways to design and implement affordable, innovative, efficacious study protocols so that inventions can be produced in a cost-effective way by accommodating clinical research in routine practice in parallel.

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