

## CLINICAL TRIALS IN AMERICAN MEDICAL COLLEGES: PRACTICAL ASPECT OF INNOVATION ACTIVITY

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### Summary

The article covers clinical trials as a type of clinical research in American medical colleges that develop innovation activity. Predominantly such clinical trials deal with oncology, neurology, ophthalmology, traumatology, pediatrics, pulmonology, and so on. To reach the aim of the article, there are the following methods as content-analysis of information concerning clinical trials from U.S. state websites and official ones of American medical colleges and a descriptive method – to give clear and accessible data on the mentioned problem. Moreover, the authors focus on clinical trials at Yale University, Johns Hopkins University School of Medicine, Stanford University School of Medicine, University of California Irvine School of Medicine, Keck School of Medicine of the University of Southern California, etc. These educational establishments attempt to find out effective and safe ways to preserve and restore health using the latest developments in science and technology. Besides, today they strive to meet effectively modern social challenges among which there is COVID-19.

**Keywords:** American medical education, innovation, clinical research, science, technology, social challenges, health, diseases.

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### 1. Introduction

American medical colleges always provided future specialists with both theoretical and practical knowledge because there was no medicine only with theory. The 1960s marked the new way of how better to advance medical competences. The direction dealt with clinical research.

Thus, according to the Association of American Medical Colleges, “medical schools and major teaching hospitals – in partnership with the National Institutes of Health, other federal agencies, foundations, and the pharmaceutical and biotechnology industries – are uniquely responsible for providing both the institutional support and the rigorous training necessary to conduct high quality, hypothesis-driven clinical research and to nurture physician-scientists equipped to exploit scientific opportunities” (*Clinical research, n.d.*).

In this context, we consider highlighting clinical trials as a type of clinical research in some American medical colleges. Many clinical trials take place in medical colleges of U.S. universities. It is worth mentioning that these institutions of higher education carry out clinical

trials in various fields of medical science (for example, oncology, neurology, cardiology, ophthalmology, psychiatry, traumatology, dentistry, gastroenterology, pulmonology, allergy, etc.). However, our attention will be focused on those that mostly deal with innovation trends, since innovation activity is an integral part of modern education. To reach our aim, we will use content-analysis of information concerning clinical trials from U.S. state websites and official ones of American medical colleges and a descriptive method – to give clear and accessible data on the mentioned problem.

## 2. Clinical trials as innovation activity in American medical colleges

Stanford University School of Medicine is currently conducting clinical trials of two innovative products. There are “Virtual Reality Glove for Hand and Arm Rehabilitation After Stroke” (vREHAB) and a program for virtual reality rehabilitation “Smartphone App for Head and Neck Cancer Control and Patient Support”.

The first mentioned clinical trial is designed for three years – from October 2018 till December 2021. It is a randomized, controlled trial that consists of three phases and aims to evaluate the safety, ease of use, and effectiveness of the device Neofect RAPAEEL Smart Glove that may promote restoration of hand and arm function in the acute and subacute period after a stroke or acute cerebral infarction compared with standard therapy. The trial intends to find out (i) the impact of using a virtual reality glove on functional recovery in addition to conventional rehabilitation methods; (ii) the feasibility of increasing the dose of rehabilitation effects in patients with acute stroke with a virtual reality glove; (iii) the impact of using a virtual reality glove on quality of life. As for the participants, they may be sick, 18 years and older, of all sexes (*ClinicalTrials.gov. Virtual Reality Glove..., 2018*).

The second clinical trial aims to examine the advantages of the mobile application in patients receiving head and neck radiation exposure. The mobile application allows a person to improve the program of preventive exercises and increase the frequency of these exercises to improve swallowing function during treatment. To participate in this clinical trial, the volunteer must correspond to the following criteria (i) age  $\geq 18$  years; (ii) fluent English; (iii) ability to give informed consent; (iv) presence of newly diagnosed non-metastatic cancer of the head and neck: mouth, oropharynx, nasopharynx, hypopharynx, and larynx, which require bilateral irradiation of the neck. Besides, there may be patients who have unknown primary head and neck cancer with a nodular disease requiring bilateral irradiation as well as patients with previously untreated head and neck cancer who need a course of radiation therapy with a prescribed dose of 60 Gy or more; (v) ability of a smartphone or tablet based on Android or Apple iOS to be consistent with the application; (vi) stable Internet connection (*ClinicalTrials.gov. Validation of Smartphone..., 2019*).

Johns Hopkins University School of Medicine conducts several innovative clinical trials, including “Patient Response to Immunotherapy Using Spliceosome Mutational Markers” (PRISMM); “Virtual Reality During Procedures in Pediatric Patients”; “Design and Clinical Evaluation of a Smartphone-based Low Vision Enhancement System”; “Environmental Localization Mapping and Guidance for Visual Prosthesis Users”; “Neural Correlates of Hypoalgesia Driven by Observation”, etc. (*ClinicTrials.gov, 2020*).

A clinical trial “Patient Response to Immunotherapy Using Spliceosome Mutational Markers” aims to determine the response frequency of patients with advanced or metastatic breast cancer who have a specific genetic tumor mutation (SF3B1 mutation) to available immunotherapy (*ClinicalTrials.gov. Patient Response to..., 2020*).

Testing the effectiveness of using virtual reality during pain-inducing medical procedures in pediatric patients at the pediatric emergency department is the goal of another clinical trial at Johns Hopkins University School of Medicine. According to the description of this clinical trial, pediatric ambulances and hospitals are frustrating and painful to pediatric patients and their families. Children of all ages are admitted to the emergency department with a wide range of diseases, many of which require medical intervention. As a rule, the psychological support of young patients varies from non-intervention to soothing conversations. To solve this problem, researchers at Johns Hopkins University School of Medicine have proposed an innovative method of increasing comfort during such procedures – non-invasive virtual reality (VR) therapy, which is a promising means of distraction during various medical procedures (*ClinicalTrials.gov. Virtual Reality During Procedures...*, 2018).

The next clinical trial conducted by Johns Hopkins University School of Medicine involves testing the effectiveness and detection of adverse side effects of a virtual biopsy telescope and a virtual projection screen in a new low vision enhancement system (LVES) with a wide field of view compared to existing devices using vision enhancement technology. Also, trial results will help to obtain quality information from patients, and to evaluate the functionality of the system, optimize its functions and operations (*ClinicalTrials.gov. Design and Clinical Evaluation...*, 2018).

The clinical trial “Environmental Localization Mapping and Guidance for Visual Prosthesis Users” is based on the hypothesis that navigation for users of retinal prostheses can be significantly improved by including spatial localization and mapping (SLAM) and object recognition technology which transmits information about the environment through a retinal prosthesis and auditory feedback. This plan to study how effectively SLAM technology allows the visual prosthesis system to build a map of the user’s environment and find it on this map. Testing of this technology is expected both with those (i) who have normal vision, (ii) who have to wear a virtual reality headset, and (iii) who have retinal prostheses (Argus II). (*ClinicalTrials.gov. Environmental Localization...*, 2020).

The innovation of a clinical trial “Neural Correlates of Hypoalgesia Driven by Observation” is to rethink the effect of placebo and to activate in the brain the mechanisms of reducing pain sensitivity. The placebo effect has been ambiguous among health problems at least for two centuries. On the one hand, placebo has traditionally been used as a control in clinical trials to correct prejudice, and the placebo response is seen as an effect to be considered when accurately measuring the treatment effectiveness. On the other hand, there is scientific evidence that the placebo effect triggers central nervous as well as peripheral physiological mechanisms that affect the perception of pain and its clinical symptoms and significantly modulate the response to pain therapies. Thus, the placebo effect has been transformed from a challenge for clinical trials to a resource that initiates pain reduction based on endogenous mechanisms that can be activated in the brain and promote hypoalgesia, self-healing, and well-being. The above is relevant for chronic diseases with acute pain, given the fact that, for example, users of chronic opioids die within about two and a half years after getting the first opioid drug for the treatment of acute pain (*ClinicalTrials.gov. Neural Correlates...*, 2019).

The general hypothesis of this clinical trial is that observation-based learning affects the nervous modulation of pain and the cognitive system, including processes related to mentalization (the ability to cognitively perceive the mental states of others), empathy (the ability to share emotional experiences), and benefit expectation. The task of the clinical trial is to determine the brain mechanisms of observation-induced analgesia by mapping the brain via tracking changes in blood oxygenation and brain vibration activity. Outcomes will allow researchers to conclude

about the location and degree of neurobiological activation that underlies the observation-induced hypoalgesia. For this purpose, innovative experiments have been introduced, using such diagnostic means as functional magnetic resonance imaging (fMRI), electroencephalography (EEG), as well as combined EEG-fMRI (*ClinicalTrials.gov. Neural Correlates...*, 2019).

Researchers from the University of California Irvine School of Medicine have completed a clinical trial to test the effectiveness of “Twitter-enabled Mobile Messaging for Smoking Relapse Prevention” (*ClinicalTrials.gov. Twitter-enabled...*, 2012).

A clinical trial to test the effectiveness of Twitter-enabled Mobile Messaging for Smoking Relapse Prevention was during 2012 – 2014 and covered three phases. In phase I (N = 40), the researchers tested and improved the protocol that included smoking cessation and relapse prevention through the creation of two virtual groups on Twitter, which included volunteers who had expressed a desire to give up smoking, and the sending messages of appropriate content to participants of the interactive clinical trial. In phase II (N = 160), a randomized controlled trial of the treatment protocol developed in phase I was performed in two groups (experimental and control). In phase III (N = 80), some groups on Twitter wishing to give up smoking were involved and various interventions were tested (*ClinicalTrials.gov. Twitter-enabled...*, 2012).

The results of the trial, covered in many publications (*Pechmann et al., 2015; Pechmann et al., 2017*) confirmed the effectiveness of the proposed method for treating smoking dependence and relapse prevention.

Molecular diagnostics is a priority area of clinical research at the Virginia Commonwealth University School of Medicine. Its mission is to provide high quality and cost-effective services in molecular pathology to improve patient care, education, and research. The vision of the Virginia Commonwealth University School of Medicine is to become the U.S. leading pathology department in biomedical research, health education, and the innovative application of science and technology to diagnose and manage human disease (*VCU. Virginia Commonwealth University, 2020*).

This medical school specializes in molecular diagnostic testing in the following areas: hereditary disorders; infectious disease; hematopathology; coagulation; pharmacogenetics; alpha and beta testing of new diagnostic products in vitro; evaluation of analytical characteristics of the effectiveness of new diagnostic products in vitro.

Besides, we consider it crucial to emphasize that a separate area of innovative clinical trials of all U.S. medical colleges is finding the effective ways of COVID-19 treatment and its prevention.

Thus, Keck School of Medicine of the University of Southern California is a participant of the national project “ACTIV-2: A Study for Outpatients With COVID-19”, which examines the safety and efficacy of various drugs while the COVID-19 treatment in outpatients. The ACTIV project, which means “Accelerating COVID-19 Therapeutic Interventions and Vaccines”, gathers both private organizations and government agencies to coordinate strategies and accelerate the advancement of the most effective treatments and vaccines against coronavirus disease. As part of this project, in October 2020, there was phase III beginning of a clinical trial aimed at testing the efficacy and safety of a monoclonal antibody drug known as LY-CoV555. Monoclonal antibodies are synthetic variants of antibodies that the body produces naturally under the influence of SARS-CoV-2. When taken during the early stages of COVID-19, these antibodies can prevent replication and spread of the virus (*USC enrolling for phase 3...*, 2020).

Johns Hopkins University School of Medicine is also the center for clinical trials under the national ACTIV-2 project, participating in the testing of the drug LY-CoV555. Moreover, researchers from the mentioned medical school report on the determination of drug treatment that could potentially reduce the risk of death from the cytokine storm, the most serious complication of COVID-19. Prazosin, an FDA-approved alpha-blocker that relaxes blood vessels, may focus on a hyperinflammatory process that disproportionately affects the elderly with underlying diseases and increases the risk of death during COVID-19 infection. Thus, its preventive use for the treatment of hyperinflammation of the lungs and other organs associated with COVID-19 may reduce mortality among the most vulnerable segments of the population (*Johns Hopkins Medicine, 2020*).

In March 2020, the Commonwealth Medical School of Virginia developed its COVID-19 test for inpatients during a pilot program. The internal test significantly reduces the waiting time for results, which helps reduce the risk of COVID-19 infection in the community. Access to testing during the pilot phase is open primarily to patients who require hospitalization and have severe symptoms of COVID-19 (*Novak, 2020*).

Stanford University School of Medicine conducts clinical trials “COVID-19: Pediatric Research Immune Network on SARS-CoV-2 and MIS-C” and “Anti-thrombotics for Adults Hospitalized With COVID-19 (ACTIV-4)”.

The main objectives of the clinical trial “COVID-19: Immune Network of Pediatric Studies for SARS-CoV-2 and MIS-C” are (i) the determination of the proportion of children with SARS-CoV-2 associated with death, re-hospitalization, or major complications after SARS-CoV-2 infection and/or multisystem inflammatory syndrome in children (MIS-C); (ii) the detection of immunological mechanisms and immune features associated with the disease spectrum and the subsequent clinical course during the year of observation (*Stanford Medicine. Clinical Trials. COVID-19..., 2020*).

A clinical trial of antithrombotic agents for adults hospitalized with COVID-19 is a randomized open-label study on an adaptive platform to compare the efficacy of antithrombotic agents for the prevention of adverse effects in patients with COVID-19 (*Stanford Medicine. Clinical Trials. Anti-thrombotics for..., 2020*).

Note that researchers at U.S. medical colleges are studying not only the efficacy and safety of COVID-19 drugs and its complications but also the long-term health effects of people who have had this disease.

For that purpose, in cooperation with other American universities, Yale University is implementing Innovative Support for Patients with SARS COV-2 Infections Registry – INSPIRE, funded by the Centers for Disease Control and Prevention. The project will monitor 4,800 people over two years to evaluate delayed infection outcomes for different age groups in the following areas: health, current clinical events, physical and mental functions, including neurocognitive functions and fatigue. INSPIRE participants must register on the Hugo Health platform, a medical data system, that takes into account the right of individuals defined under the Health Insurance Portability and Accountability Act (HIPAA) to access their medical information and collect medical data on their behalf while maintaining the highest degree of confidentiality. Such a system allows the collection of the necessary large-scale data. Recruitment of volunteers to participate in the INSPIRE clinical trial began on December 1, 2020. The project envisages enrollment of 3,600 people who have had COVID-19 and 1,200 people who are not ill in the control group. The major research method should be a survey that will not require participants to see a physician (*New COVID-19 Study..., 2020*).

### 3. Conclusions

Thus, we can state that clinical trials belong to the innovation activity of American medical colleges. The leaders, who actively use innovations within clinical trials, are Yale University, Johns Hopkins University School of Medicine, Stanford University School of Medicine, University of California Irvine School of Medicine, Keck School of Medicine of the University of Southern California, and so on. They focus on finding both effective and safe ways and means to preserve and restore health using the latest developments in science and technology. Besides, their main aim is to meet effectively modern social challenges among which there is COVID-19.

As for research prospects, there is a necessity to find out features of engineering and design within the innovation activity of U.S. medical colleges.

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