



Remote Health Monitoring in Clinical Trial using Machine Learning Techniques: A Conceptual Framework

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Abstract

Monitoring any process is crucial and very necessary, this is to ensure that standard protocols and procedures are strictly adhered to, monitoring clinical trials is not an exception. It is one of the most crucial processes that should be monitored because human subjects are involved. In trying to monitor clinical trial, information and communication technology techniques can be deployed to facilitate the process and hence improve accuracy. This research formulates a new conceptual framework for monitoring clinical trial using Support Vector Machine and Artificial Neural Network classifiers with physiological datasets from a wearable device. The proposed framework prototype consists of data collection module, data transmission module, and data analysis and prediction module. The data analytic and prediction module is the core section of the proposed framework tailored with data analysis. These datasets are preprocessed and transformed and then used to train and test the system, through different experimental analysis including bagging Support Vector Machine (SVM) and Artificial Neural Network (ANN). The outcome of the analysis presents classification into three different categories, such as fit, unfit, and undecided participants. These various classifications are used to determine if a participant should be allowed to continue in the trial or not. This research provides a framework that is useful in monitoring clinical trial remotely, thereby informing the decision-making process of the research team.

Keywords Clinical trial · Framework · Monitoring · Physiological data · Wearable device

1 Introduction

Clinical trials are research designed to evaluate new ways to enhance treatments and quality of life of people with

different types of diseases. Results from clinical trial, help to develop new drugs, new diagnostic tools, and new clinical procedures. It can also spur new questions for research, which can lead to discovery for understanding certain diseases better. All drugs and medical devices in use today are possible because patients or volunteers made themselves available for clinical trial. [1]. It is a research designed for volunteers who receive investigational treatments under close supervision of doctors, nurses, social workers, or other health care research professionals. Clinical trial looks at new ways to prevent, detect, control, or treat disease. There are four major stakeholders involved in clinical trial research; these are trial sponsors, volunteer patients, the government agency, and the research team [1]. Clinical trial helps the research team to ascertain if a new therapy, treatment, or medical device is safe and effective before approval by the government agency such as the ethical board. Different age

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range, races, ethnicities, and genders can participate in clinical trial, and this must be with the individual's physicians' consent [1]. Modern Information and Communication Technology can be applied in industries, including healthcare and drug development. Technological innovations offer the potential to improve efficiency and productivity using innovative outcomes, increased patient engagement, reduced patient burden, and improved trial management [2]. The use of ICT in healthcare can never be overemphasized since it has been used to deliver healthcare services, patients' location notwithstanding. ICT enables patients' remote access to doctors and caregivers when the need arises; also, patients can have access to their normal routine checkups remotely using ICT. With the fast-increasing aging population, disabled patients' remote monitoring enables them to access timely healthcare services when needed. Due to rapid development in ICT, accessibility of real-time monitoring of the health status of patients living in remote areas can be enhanced, unlike the traditional remote monitoring system where fixed telephone lines were in use, there could be delay due to busy or network failure; hence patients' access to doctors or healthcare givers in an emergency situation has been compromised [3]. The aim of monitoring clinical trial is to protect human subjects participating in the trial: ensuring that data accuracy is maintained throughout the clinical trial research and to ensure that the research protocols and regulatory requirements are strictly adhered to [4]. Machine learning (ML) is an aspect of artificial intelligence that learns from a training dataset or a model to predict future datasets. Machine learning can be classified into supervised and unsupervised machine learning techniques. Supervised learning builds a model by learning from labeled training datasets, while unsupervised learning learns features from unlabeled training datasets [5]. One of the advantages of ML techniques is the ability to detect hidden patterns from big and complex data sets [6].

Machine learning is a technique that can be deployed in making predictions and decisions, based on similarities in what is being analyzed to what has previously been observed. Machine learning algorithms are constantly learning and updating its rules without external intervention. These algorithms give clinicians a better understanding of the diagnosis. The data points that fall outside the range that is considered to be the standard value for a particular parameter in this case blood pressure, heart rate, body temperature etc. is done by giving explanatory meaning to generated patterns for physiological parameters obtained, thereby eliminating false alarm [7]. Machine learning techniques can help to improve health care delivery using mathematical physiological models and modelling expert-based opinions to inform clinical decision-making. The application of machine learning algorithms in health care can reduce the

time spent by the patients in hospital hence reduce mortality rate [7]. Support Vector Machine (SVM) and Artificial Neural Network (ANN) are machine learning techniques used to learn patterns from transformed data, and it is used to model the system. These results are extracted to get the clinical data points for participants' health records, the data points are aggregated to develop the clinical data profile for each participant. The clinical profile of the participants is used to discover and evaluate participants' cohorts and populations [6].

The emergence of technology has introduced wearable devices in healthcare. Internet of Things (IoT) is a system that integrates physical objects, software, and hardware to communicate with each other. Population increase, limited healthcare resources, and increase in medical costs has made IoT-based technologies necessary to solve challenges in healthcare. IoT has several applications in healthcare, ranging from remote monitoring to smart sensors and medical device integration. Internet-of-things has made healthcare smart by integrating smart wearable medical devices used to monitor patient health status in real time. These wearables devices are capable of overseeing health and wellness of a patient and sending biofeedback to a hub in real time. Mobile health can be said to be the application of mobile monitoring devices in medical and public healthcare [8]. It offers a very fast way of gathering health associated data remotely. With the aid of these mobile monitoring devices, data can be transmitted to the database server for analysis and decision making by the medical practitioners [8].

Also, it is worthy to know that the advent of mobile telecommunication and wireless devices has improved clinical trial in monitoring patients and volunteers participating in any intervention. Basic body parameters such as heart rate, body temperature, blood pressure, diet, psychological state, as well as data associated with physical body exercise, can be tracked using wearable devices with embedded sensors which can also be called fitness trackers. These wireless fitness activity trackers can enhance the accuracy of data collected from patients and volunteers, hence hasten patient recovery [9]. Clinical trial research can take advantage of the advancement in electronic technology in the design and execution of clinical trial research instead of the conventional face-to-face approach that was used initially in the recruitment, delivery of interventions, data collection, and retention of clinical trial participants [10]. Using conventional approach in clinical trial research is one of the causes of very long duration in the time taken in clinical trial research, but with the introduction of electronic technology, clinical trial process improves hence minimizing the time spent in clinical trial research. [10].

There are some misconceptions about clinical trial, most people who may want to participate in clinical trials do not

have medical personnel to explain some of the medical terminologies, insurance policy involved, as well as the processes involved in the trial. These misunderstandings might lead to suspicion that will hinder future medical interactions if they are not well addressed. The modalities involved in clinical trials need to be made open to the public who may wish to participate in any intervention [11]. Techniques used to monitor data quality in clinical trials are also not efficient enough, hence there is lack of data verification, there is therefore the need to monitor the quality of data generated from the wearable devices [11].

This paper is structured into four major sections. Section 1, gives a brief introduction about the concept of clinical, reasons for clinical trial and its importance. The introduction of information communication technology in clinical trial to enhance the process hence make it more effective, through the application of wearable sensors. Section 2, dwells on literature reviews on existing articles on clinical trial. Section 3, describes the proposed conceptual framework, how it will be used to monitor COVID 19 clinical trial participants, parameters that will be used for prediction, the algorithm for prediction and the final outcome, which classify each trial participants, hence enhance informed decision making for the clinicians. The authors conclude the work in Sect. 4 by summarizing the importance of clinical trial to determine the efficacy and safety of any medical products under consideration for safety since human life is involved and critical.

2 Related works

This section presents a review of the research work done in monitoring patient health status. A remote patient monitoring system by [8] was used to remotely monitor elderly patients suffering from chronic diseases using digital technology facilitated by wireless sensor networks. The system was used to collect physiological signs from patients using a wearable sensor, the collected data is transmitted to the hospital server where the doctors and nurses can access for analysis, hence used to determine the health status of the patient. Knowledge of the medical personals such as the medical doctors and nurses are transferred into the system, such as standard body physiological parameters and symptoms of some chronic diseases such as diabetics, high blood pressure, asthma etc. is used to monitor the patient, to determine the health status of the patient using ensemble classifier. Using Java JADE by [3], an agents-based software for developing a framework used for patient health monitoring, the agents in the framework consist of the following: diagnostic agent, physician agent, user agent, resource agent, knowledge-based data service and external services.

The diagnostic agent is made up of the computer system, data analysis engine and patients cell phones. Its main function is to analyze collected physiological data from the electronic device. The physician agent is used for authenticating medical personnel's profile before granting them access to monitor patients' health status. The user agent is the access control mechanism that authenticate the patients before the physician agent can be enabled. While the resource agent secures and grant access to the software resources needed by the medical personnel. The knowledge-based data service agent is responsible for collecting and transmitting patients' physiological signs to the database, as well as maintaining monitoring process. External services facilitate patients to physician interaction. A model for early prediction of patient outcome using artificial neural networks (ANN) was developed by Johnson et al. [12]. This model was used to detect complex dependencies between clinical variables available and to investigate intervention effects on patients treated with targeted temperature management. Results from the trial were later subjected to sensitivity analyses in post hoc analyses and sub studies and the pooled dataset analyzed. The emergence of technology has introduced wearable devices in healthcare industry, with the introduction of Internet-of-things, healthcare is now becoming smarter by integrating smart wearable medical devices for monitoring patient physiological health status in real-time remotely, virtual clinical visits, Mobile health, and E-health. Due to the rapid development of technology, establishments may be reluctant to oblige to a single technology for improved signal detection because future technologies may prove to be better [13]. The widespread use of mobile devices, cloud computing, and the Internet of things has made the use of wearables devices in clinical trials readily available. Hence researchers can develop applications that can be used to interconnect specific devices and the Internet. Wearable devices are becoming prolific because of their computing, communicating, and sensing capability [13]. In the past decade, most clinical trial and health care institutions rely on traditional methods of monitoring participants' health, which are not able to meet participant requirements, and are not efficient enough. The traditional patient monitoring system deployed the use of ancient telecommunication network to connect participants to the health monitoring system. There is a need to introduce information communication technology to make up for the lapses created by the traditional methods hence, computational tools can be used to facilitate participants' health monitoring in real-time, the location notwithstanding [14]. The use of computational techniques enhances patients' routine checkups rather than frequent visits to the hospital or health care centers [15]. Su et al. [3] designed a remote patient monitoring system that automatically triggers an alarm system whenever it detects

any abnormality in patients. With the introduction of sensor technologies and fast Internet access, real-time monitoring is made possible [13]. Clinical trial is said to be successful if the set goals for participant recruitment are achieved which of course could impact on the financial, scientific, policy and ethics of the research [16]. Literature has revealed that about 19% of registered clinical trials were terminated mid-way due to lack of participants' recruitment and retention policy. It is worthy to know that about 86% of clinical trial research has never met its participants' recruitment goals within the trial duration which has led to prolong period than the initial planned duration for the trial research. Although clinical trial researchers have tried to solve the issues of participants' recruitment and retention in the past decades, but the challenge persists [16]. Hence [16] designed a framework that describe a strategic trial feasibility, site selection, trial design, protocol development, and good communication between the researcher and participants all through the research process. The application of wearables sensors in clinical trials enable real-time feedback and remote monitoring of both patients and volunteers participating in clinical trials. This has helped to improve doctor's effectiveness, increase patient safety, lessen mental-health issues, revolutionize physical examination, and save time and cost for the patient [17]. The application of artificial intelligence (AI) technique in clinical trial helps to alleviate the burden on the cost of clinical trial research which has persisted in the past decade [14]. Before a drug could pass through the stages of clinical trial and getting to the market, it takes a long time, between ten to fifteen years, therefore increasing the cost of clinical trial research [14]. It is worthy to know that out of every ten trials, only one has successfully reached its completion stage due to the long duration of clinical trial research [14]. Wearable device is used to capture physiological data from the participants, and the captured data is transferred to the database sever [17]. Smartwatch data collection system is made up of two main systems: proprietary and third-party systems developed by De Arriba-Perez et al. [18], data is collected using the wearable device and smartphone, the data is transmitted via a wireless network to the computer for analysis. The proprietary system consists of the wearable devices, smartphones and cloud services, while programs for the wearable devices, smartphones and computers are developed by programmer to perform specific functions that make up the third-party system.

3 Proposed monitoring framework

Figure 1 is a proposed framework that can be used to monitor clinical trial for the treatment of COVID-19, using a wearable device to capture physiological datasets such as

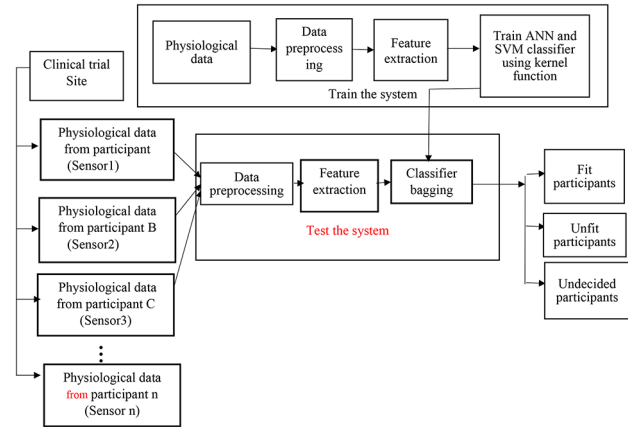


Fig. 1 Proposed Clinical Trial Monitoring Framework

Blood Pressure, Blood Oxygen Saturation level, Electrocardiogram, Respiration Rate, Heart Rate and Respiration Rate visibility from the clinical trial participants. These physiological datasets are transferred through a wireless network to the proposed monitoring system where the prediction analysis is done. This analysis informs the decision-making process of the clinicians. Support Vector Machine (SVM) and Artificial Neural Network (ANN) algorithms are used for data classification and prediction analysis to provide insight and discovery into the clinical trial datasets. Clinicians can access safety signals with the use of links or graphs, as well as access to reviews. Any abnormality in the physiological data of the trial participants can easily be accessed hence, investigators and clinicians can easily take decision based on the analyzed data if a participant should either continue in the trial or not.

Table 1 List of parameters to be captured by the wearable device

Physiological signs	Standard physiological signs measurement	Initial par-clinical trial participants data sets	clinical trial data sets (readings from the wearable device)
Temperature (Temp)	36.5–37.5 °C (97.7–99.5 °F)	Not available (N/A)	Not available (N/A)
Heart rate (HR)	60 to 100 bpm (bits per second)	N/A	N/A
Electrocardiogram (ECG)	25 mm/sec	N/A	N/A
Respiration rate (RR)	12 to 16 breaths per minute	N/A	N/A
Blood Oxygen Saturation (SpO ₂)	80 and 100 millimeters of mercury (mm Hg)	N/A	N/A
Blood pressure (BP)	120/80 millimeters of mercury (“mm or Hg”)	N/A	N/A

These physiological datasets are preprocessed and transformed to a feature set that is used to train the classifiers. Data from the wearable device are transmitted through a wireless communication network to the database for remote access. Emergency occurs when the physiological sign of the patients is reading above or less than the normal range as shown in Table 1.

The collected data from the wearable device is preprocessed to remove noise and outlier using principal component analysis and transformed into useful information for the classifier algorithm (Support Vector Machine and Artificial Neural Network). Machine learning algorithm such as Support Vector Machine and Artificial Neural Network are used for data classification [19]. They are used to instantly identify anomalies and potential points of failure thereby enabling informed decision-making in real time. These algorithms are designed to translate raw data into signals based on the parameters they have been programmed to analyze. The generated signals are presented in a human-readable form such as visualizations and actionable workflow.

The essence of pre-processing data from the wearable device (Biobeat) is to check for missing values, noisy data as well as data inconsistency. Data pre-processing is the preparation of the collected datasets for final training set before feeding the data into the algorithm (SVM and ANN) for execution. It involves data cleansing, instance selection, data normalization and transformation. It is removal of any unwanted datasets that is not related to the problem that is been solved. The pre-processed datasets are divided into two, eighty percent (80%) is used as a training dataset while the remaining twenty percent (20%) is used as a testing dataset. Feature Extraction is the process of representing the pre-processed datasets for further analysis. The essence of Feature Extraction is to reduce the number of features in the physiological datasets by creating new features from the existing physiological datasets.

Feature Extraction is applied to the pre-processed datasets to prevent the machine learning algorithms (SVM/ANN) from overfitting, hence speed up the training process and improve the accuracy of the machine learning algorithms. Bagging is used to reduce variance within noisy datasets. Classifier Bagging is an ensemble technique [20] used for classifying test datasets from trial participants by introducing randomization into its construction procedure and then making an ensemble out of it. Bagging classifier is an ensemble meta-estimator that fits base classifiers each on random subsets of the original dataset and then aggregate their individual predictions either by voting or by averaging to form a final prediction. Each base classifier is trained in parallel with a training set which is generated by randomly drawing, with replacement, N examples (or data) from the original training dataset – where N is less than the size of the

original training set. Training set for each of the base classifiers is independent of each other. Many of the original data may be repeated in the resulting training set.

This conceptual framework being proposed to be used for monitoring COVID-19 patients in clinical trial is somewhat new and different from already existing ML frameworks in the following ways:

- i. This work uses a unique device (Biobeat) for data collection. This is done remotely, considering the risk involved with collecting data directly from COVID-19 patients [21]. Biobeat is a new device that has been proven to be very efficient.
- ii. The proposed wearable device can collect about six physiological data, while most other wearable devices collect lesser number of body physiological data. Invariably, some other researcher employs more than one device for data capturing thereby creating data synchronization and comparative analysis issues. This work improves on existing research by the engagement of one device for optimal capturing six different body physiological data.
- iii. Most clinical trials are carried out on-site but our study attempts to improve the current practice by considering remote monitoring of clinical trial for COVID-19 patients. To the best of our knowledge there's no known or existing clinical trial that is designed to use Biobeat remotely to monitor COVID-19 patients by collecting data from trial participants. This becomes a major contribution in health care monitoring for COVID-19 patient.
- iv. This remote human health monitoring will enable quick intervention in case of adverse effects of drug outcome on clinical trials for COVID-19 patients who volunteered themselves to be used for COVID-19 clinical trial.

4 Conclusions

Clinical trial is considered as the gold standard technique for measuring the efficacy and safety of new drugs and other healthcare interventions [22]. As a result of the occurrence of chronic diseases, such as high blood pressure, cardiovascular disorders, diabetes etc. affecting many lives around the world, there is a demand to provide a solid foundation for developing wearable Internet of things technologies to deploy large-scale wearable sensors that are networked with remote medical infrastructure to increase the treatment outcomes' efficacy and effectiveness. Health workers, care givers, researchers, physicians etc. can accurately monitor volunteers and patients' reactions to a newly discovered

medication remotely using wearables devices, and this can enhance the participant quality of life [13]. In the light of the challenging issues of total monitoring of clinical trials on-site by ethical boards and regulatory government agencies, our proposed framework forms the basis of remote human health monitoring to ensure quick intervention in case of adverse effects of outcome of clinical trials involving COVID- 19 participants’.

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Code Availability (Not applicable)

Declarations

Conflicts of interest/Competing interests There is there is no conflict of interest.

Ethics approval Not applicable

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Consent for publication All authors approve and gave their consent for the submission and publication of the manuscript.

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