



Life Sciences

White Paper

# Leveraging Emerging Technologies to Improve Patient Centricity in Clinical Trials

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The success of clinical trials is highly dependent on effective patient recruitment, engagement and protection of their rights. Patient participation in clinical trials is fundamental to the risk-benefit evaluation and overall safety profile of drugs under development. Data collected from subjects/patients during the course of a clinical trial is critical to determine the safety and efficacy of a drug. Since the patients in clinical trials are the ones who experience the effects of a drug, their contribution in the assessment of risks and benefits of the drug is remarkable. The process of gathering data from trial patients is heavily dependent on their participation and compliance during a clinical trial. Subsequent activities such as data processing and conclusions derived from the clinical trial are thus directly impacted by the nature and extent of patient participation. Today, the pharmaceutical industry faces many challenges related to patient participation and their involvement in the clinical development process. The aim of this paper is to provide an overview of emerging technologies to overcome these challenges in enhancing patient centricity.

*\*Note: The word 'subject' has been interchangeably used with the term 'patient' in this paper.*

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## Introduction

Clinical trials play a pivotal role in the lifecycle of drug development. Active participation by patients/human subjects in clinical research is one of the most critical factors for successful drug development. However, patient enrollment, retention, and compliance are among the biggest challenges in carrying out clinical trials swiftly and within budgets. It is imperative for patients to be process compliant in a trial, that is, among other things, meet all requirements of the study including following the clinical trial protocol, adhering to visit schedules, taking medication as per the instructions (for example, dosages and frequency), and reporting any side effects.

As per the International Conference on Harmonization – Good Clinical Practices (ICH-GCP) guidelines<sup>1</sup>, it is mandatory for the sponsors of clinical trials to ensure subject protection and data integrity. The quality and integrity of data in clinical trials can be highly influenced by patient reported outcomes (PRO), quality of patient care and satisfaction of patients with clinical trial participation.

As patient centricity is pivotal to patient recruitment and retention in clinical trials, companies involved in drug development such as pharmaceutical and biotech companies and their partners (for example, Site Management Organizations, Contract Research Organizations, and IT companies) try to introduce novel strategies to improve patient enrolment and satisfaction. This paper provides an overview of how emerging technologies can enhance patient centric approaches to overcome challenges that pharmaceutical companies face in the recruitment, retention and engagement of patients in clinical trials.

## Clinical Trials: Patient-related Challenges and Mitigation Strategies

Pharmaceutical companies are under tremendous pressure to introduce new drugs into the market faster to meet the needs of patients awaiting new drugs and/or enjoy a longer period of market exclusivity. Almost 80% of clinical trials fail to meet their initial patient enrollment milestones on time, resulting in delayed completion of clinical trials<sup>2</sup>. Pharmaceutical companies lose up to \$8 million in sales for each day of delay in getting a drug to the market<sup>2,3</sup>.

Lack of public awareness regarding available clinical trials and/or a poor perception of clinical research are among major reasons why only 8–10% of the general public have ever participated in a clinical trial<sup>3</sup>. Sponsors face overwhelming demands to increase the pool of volunteers for enrollment in clinical trials, have good recruitment and retention plans, improve communication channels, and provide user-friendly options for data collection and volunteer engagement. In addition to the significant role that the sponsors are required to play in enhancing

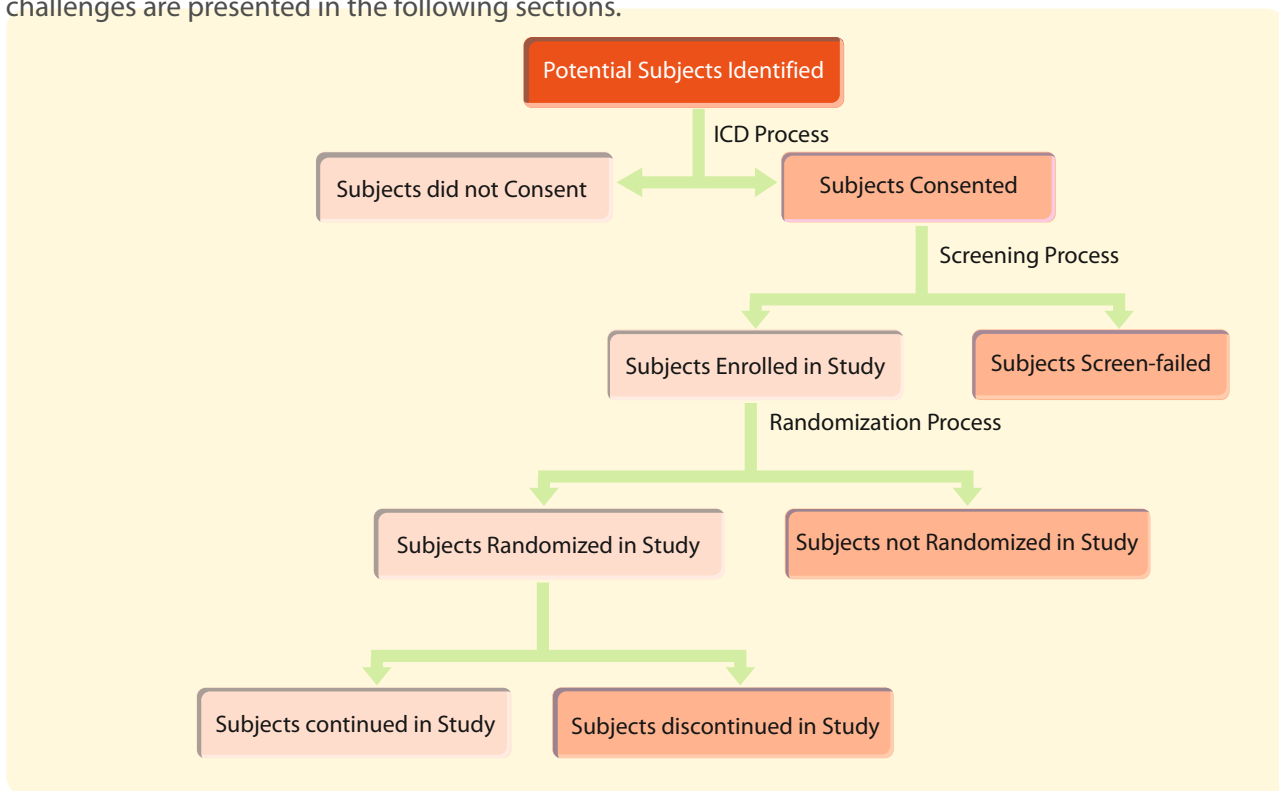
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[1] ICH- International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonized Tripartite Guideline, Guideline for Good Clinical Practice E6 (R1) (1996), accessed Aug 28, 2013, [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/Guidelines/Efficacy/E6\\_R1/Step4/E6\\_R1\\_Guideline.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1_Guideline.pdf)

[2] Cutting Edge Information, Web-based Patient Recruitment (WP211) (October 2005), accessed Aug 28, 2013, <http://www.cuttingedgeinfo.com/reports/white-papers/>

[3] Quintiles, Data driven subject recruitment to deliver qualified patients faster (2010), accessed Aug 28, 2013, <http://www.quintiles.com/library/white-papers/data-driven-patient-recruitment-to-deliver-qualified-patients-faster.pdf>

patient recruitment, physicians and more importantly the patients themselves drive the successful enrollment of adequate research participants and their retention through a research study. Figure 1 depicts the recruitment and attrition of subjects at various stages during a clinical trial. Major patient-related challenges in the successful completion of clinical trials and some of the strategies used to address these challenges are presented in the following sections.



**Figure 1 Subject recruitment and attrition at different stages in a clinical trial**

## Patient Recruitment

Successful recruitment of qualified investigators is important to ensure good patient enrollment. Strategies to recruit investigators include advertising, incentivizing, leveraging personal contact, and establishing a database of qualified and trained general physicians. Reluctance by investigators to enroll patients may result in reduced recruitment in clinical trials. Significant barriers to clinical trial participation are investigators' perceptions of clinical trials and their reluctance to enroll patients due to a variety of reasons, such as<sup>4,5</sup>:

- inadequate understanding of how clinical trials are conducted
- lack of awareness about relevant clinical trials
- hesitancy to refer a patient elsewhere to participate in a trial and thereby lose control of the patient's care

[4] Cancer Clinical Trials: The in-depth program (2001), accessed Aug 28, 2013, [http://myeloma.org/pdfs/NCI-InDepth\\_Book\\_m.pdf](http://myeloma.org/pdfs/NCI-InDepth_Book_m.pdf)

[5] SOCRA, Current Challenges in Clinical Trial Patient Recruitment and Enrollment (February 2004), accessed Aug 28, 2013, [https://www.socra.org/pdf/200402\\_Current\\_Challenges\\_Recruitment\\_Enrollment.pdf](https://www.socra.org/pdf/200402_Current_Challenges_Recruitment_Enrollment.pdf)

- belief that the treatment in clinical trials is not as good as standard therapy
- increased paperwork and administrative burden (for example, training staff) in referring and/or participating in a clinical trial
- the length and details of most clinical trial protocols

These barriers, including investigators' perception of clinical trial participation, can adequately be addressed:

- through increased industry sponsored educational programs for investigators
- by appropriately educating physicians that the authority to control the progress of patient care during study participation is retained by them and not by the sponsor company
- when sponsors share the administrative burden with the principal investigators in training the study staff

As pharmaceutical companies compete with each other to bring more novel drugs to the market, the volunteer patient pool is fast getting depleted. This adversely affects the successful completion of research studies and opportunities to save time and money. Traditional patient recruitment strategies such as physician referrals, advertising on TV and radio, and direct mailing of advertisements such as flyers to the general public, online registrations, and so on, have not proven to be very efficient in increasing patient recruitment. Inadequate knowledge about available treatment options, poor understanding of the risk and benefits of clinical trials, lack of awareness and access to clinical trials, fear and distrust or suspicions of research, lack of effective communication and cultural differences are among the many factors that contribute to the challenge of recruiting patients in clinical trials<sup>4,5</sup>.

To encourage patient recruitment, pharmaceutical companies reach out to potential participants through trusted organizations and maintain a relationship with them. They also create a support network for community physicians to encourage their involvement in clinical trials and drive patient referrals. These physicians and the sponsors educate potential participants about the importance of clinical trials and transparently address their questions about risks and benefits of participation to reduce their distrust in research. Today, pharmaceutical companies increasingly utilize social media for advertising and focus on direct two way communication with patients to enhance recruitment.

## Patient Retention

Retaining patients in clinical trials is equally challenging. Lengthy trials, complex trial designs, lack of motivation, unexpected risks, adverse events, poor communication of trial outcomes, delayed reimbursements for study costs to participating patients, and excessive travel to investigator sites can act as roadblocks to retaining patients.

Some strategies employed by sponsors or Contract Research Organizations (CROs) engaged in patient recruitment to enhance patient retention through the duration of a clinical trial include:

- sharing of complete information about the study so that screening of eligible patients is conducted effectively, and screen failure rates are low
- providing study information and educational material to patients in simplified format and language to ensure clear and explicit communication

- providing patient study packs, study guides, reminder cards or calendars, patient newsletters and patient appreciation items
- arranging transport for patients and providing assistance with diary completion

## Patient Compliance

Complex study designs, inconvenient schedules, a high frequency of dosing, invasive procedures, and adverse events often lead to non-adherence to treatment regimens and, consequently, to protocol violations and early patient withdrawals from clinical trials. Misunderstanding of prescription instructions, forgetfulness, and diminished faith in the drug's effectiveness also contribute to patient non-compliance. Among many other steps, sponsors undertake the following important measures to improve patient compliance to the study requirements:

- measure adherence to treatment through pill count
- provide patients with diaries to self-report outcomes
- replace packaging in bottles with blister packaging to act as a visual aid to help patients take their medication correctly
- introduce Radio-Frequency Identification (RFID)-enabled smart packaging to track delivery of correct dosage of medicine and prevent patients from consuming contraindicated medicine
- provide multilingual booklet labels for global trials

## Patient Engagement

The successful completion of clinical trials is often hampered by disconnect between sponsors and participating patients. Language or literacy barriers can also act as roadblocks to the continuance of some patients in a study. In addition, organizers find it challenging to keep track of patients participating in a trial. Some of the measures adopted by the industry in engaging fruitfully with the trial patients include:

- designing patient centric trials that seek to make study procedures simple and convenient for patients
- having frequent communication with patients, sharing the overall progress and outcomes of the study, keeping them aware of the ongoing progress of the trial and advising them on dos and dont's to be followed during participation in the study to increase patient satisfaction scores and compliance
- developing Frequently Asked Questions and sharing those with the patients through newsletters, providing patient help lines using qualified personnel, counseling and providing emotional support, and assisting with insurance and reimbursement queries



## Patient Driven Data Collection

Most trial patients find it cumbersome to record data in paper diaries provided to them to capture their health-related records. As incomplete data can lead to improper data analysis with serious implications, the industry is investing time and money to develop standardized tools for data collection of self-reported patient outcomes. Among multiple technology driven data collection modes for patients, some that have found better acceptability by both, the patients and the biopharmaceutical industry, include:

- handheld devices such as tablets, smartphones with touch screens
- apps downloaded on patients' phones
- Electronic Patient Reported Outcome (e-PRO) instruments such as e-diaries
- Interactive Response Technology (IRT) systems such as Interactive Voice/Web Response Systems (IVRS/IWRS)

## Emerging Technologies and New Possibilities

Technology plays an important role in introducing innovative methods to tackle some of the challenges related to patient participation and retention in clinical trials. Some of these barriers can be addressed by technologies such as social media, mobility and interactive response systems. A summary of how different technologies can be leveraged to resolve some of the key challenges in clinical trials is given in Table 1.

Challenge	Technology	Mitigation
Patient Recruitment	Social Media, Mobility	Patient recruitment can be enhanced by utilizing social media to reach out to potential research volunteers. Instant messaging systems and other mobility solutions can be utilized to educate potential participants about ongoing clinical trials and thereby enhance patient recruitment
Patient Retention	Social Media, Mobility, Remote Patient Monitoring, Virtual Trials, e-ICD	Patient retention is dependent on their satisfaction levels with the trial process, which can be improved through social media networking and using smartphones to keep patients informed; decreasing travel to research sites by providing patients with the convenience of being treated and monitored remotely; by conducting at-home clinical trials virtually by using e-tools such as mobility, electronic-Informed Consent Document (e-ICD) and remote monitoring
Patient Compliance	Mobility, Remote Patient Monitoring, e-PROs, IRT, e-ICD	Patient compliance can be enhanced by providing patients with easy networking tools, e-ICDs, user-friendly options for following study requirements, and remote monitoring of their health
Patient Engagement	Social Media, Mobility, IRT, Virtual Trials	Patient engagement enhances patient retention, which is possible by appropriately utilizing social media and mobility solutions for educating trial participants about the progress and outcomes of the study
Patient-Driven Data Collection	Remote Patient Monitoring, e-PROs, IRT	Patient data collection can be simplified and quality of the collected data can be enhanced by using user-friendly approaches such as e-PROs, IRTs, and remote patient monitoring systems

**Table 1 – Various technologies that can be leveraged in clinical trials to address patient related challenges**

## Social Media

Due to the easy availability and accessibility of the Internet, patients are increasingly using social networking sites (such as Facebook, Twitter, posts, and blogs) to access information about clinical trials. According to one survey, 52 million adults in the US have used the Internet to access health or medical information<sup>6</sup>.

The objective of having social networking in the pharmaceutical industry is:

- to build awareness about, diseases, trials, drugs, and side-effects of drugs
- to engage patients
- to understand recruitment feasibility
- to communicate about the successful completion of previous trials and new product launches
- to build a rapport with the patients and inspire trust

Social media leverages collaboration and communication, and facilitates listening to the voice of the customer to provide better healthcare options. Popular healthcare related websites such as WebMD, Yahoo Health, Medicine Net, Mayo Clinic, Everyday Health, and Drugs offer information related to diseases and drugs. Identifying trends in website access and statistical data analyses can help in sharing relevant information with intended patients only. Looking at the advantages of social media usage, pharmaceutical companies, within the ambit of applicable regulations and privacy laws, have launched their own portals to reach out to patients.

Integration of information from different sources is a recent trend utilized to extract useful knowledge from structured data or unstructured information by applying artificial intelligence or web semantics techniques. Information captured directly from patients is critical in judging the benefit of health interventions in chronic conditions. Various startup companies have come up with collaboration tools and listening platforms, some of which use Natural Language Processing (NLP) and artificial intelligence to identify trends on social media<sup>7</sup>.

Pharmaceutical companies are required to publish the synopses of protocols of their ongoing clinical trials and results of completed studies in clinical trial registries such as Clinical Trials.gov<sup>8</sup> and International Clinical Trials Registry Platform<sup>9</sup> (ICTRP). These registries serve as online repositories for patients seeking information on available trials to determine their suitability for enrollment. Online patient communities and social networking sites such as PatientsLikeMe, WeAre.U.s, NexCura, and 23andMe (for genetic testing) are opening up avenues for connecting with potential patients for recruitment in clinical trials<sup>10</sup>. Social media can further help save time by screening eligible patients using online screening tools that use specific questionnaires to identify suitable patients.

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[6] Pew Internet and American Life Project, *The online health care revolution: How the Web helps Americans take better care of themselves (2000)*, accessed Aug 28, 2013, <http://www.pewinternet.org/Reports/2000/The-Online-Health-Care-Revolution.aspx>

[7] FierceBiotechIT, *10 startups fuelling pharma in social media (June 2013)*, accessed Aug 28, 2013, <http://www.fiercebiotechit.com/special-reports/10-startups-fueling-pharma-social-media>

[8] Clinical Trials.gov, accessed Aug 28, 2013, <http://clinicaltrials.gov/>

[9] International Clinical Trials Registry Platform (World Health Organization), accessed Aug 28, 2013, [http://www.acronymfinder.com/International-Clinical-Trials-Registry-Platform-\(World-Health-Organization\)-\(ICTRP\).html](http://www.acronymfinder.com/International-Clinical-Trials-Registry-Platform-(World-Health-Organization)-(ICTRP).html)

[10] Life Science Leader, *Social media's impact on clinical trial enrollment*, accessed Aug 28, 2013, <http://www.lifescienceleader.com/magazine/past-issues3/item/3584-social-media%E2%80%99s-impact-on-clinical-trial-enrollment?list=n>

## Mobility

Effective communication among all stakeholders in clinical trials such as patients, investigators, site staff, sponsors, and CROs, helps in the successful completion of a trial within time and with reduced budgets. Today, the next generation communications solutions such as mobile devices (smart-phones and tablets) are being used for recruitment, retention, patient engagement, data capturing and maintaining compliance.

Mobility through voice and text messaging technology provides speedy and cost effective connectivity between patients and appropriate stakeholders in clinical trials. GPS enabled tablets or smartphones with interactive capabilities enable patients to locate nearby trial sites. For example, GlaxoSmithKline has developed an application for the iPhone that provides information on trial locations for 12 common cancers and easy access to ongoing cancer trials to oncologists and cancer patients. It lists trials by phase, gender, age, and study type, and provides a complete review of these trials accompanied by contact information and a visual map that shows the user the closest centers within a 500-mile radius<sup>10</sup>. Likewise, Novartis uses Clinical Trial Seek and My Net Manage mobile applications for smartphones that let patients use the phone's location data to search the National Institutes of Health (NIH) database for the availability of clinical trials in their areas<sup>11</sup>.

Patients who use mobile technology to register for participation in clinical trials can receive alerts about their recruitment status. Mobile solutions can also be used to send pre-screening eligibility questionnaires to potential patient volunteers, and share trial specific information and video clips to educate them about the benefits and risks of the trial. Depending on regulatory restrictions, investigator sites are increasingly using text messaging to engage in one-on-one and confidential interactions with patients and thereby help in improving patient recruitment, retention, and compliance in a cost-effective way. Use of cell phone technology by sponsors has shown an increase in the recruitment response rate to more than 30% as compared to the 5–10% response rate when using traditional patient recruitment methods such as physician referrals<sup>12</sup>. Patients can now easily express interest in registering and participating in ongoing trials by directly texting their queries or responses from mobile phones to a short code embedded in a traditional form of recruitment advertisement<sup>12</sup>.

Retaining enrolled patients in the trial is crucial for the successful completion of clinical trials. Mobility has enhanced direct patient communication, reduced the number of 'lost to follow up' patients, and increased retention. With proper regulatory approvals, there are several ways to use mobile technologies to assist with patient retention and study compliance. Messaging services are increasingly being used to send text, email, and deliver phone reminders on schedules dictated by patient preferences. Automated reminder call programs are used to achieve improved study compliance by helping deliver drug dosing instructions; assisting in maintaining drug schedules; and alerting patients about upcoming site visit schedules.

Mobility has simplified delivery mechanisms used for educating patients on multiple aspects of clinical trials and thus helps in driving compliance to the study requirements. For complex trials, sponsors and site staff can offer study support and educational material to patients via email, text or voice messaging. Likewise,

[10] Life Science Leader, *Social media's impact on clinical trial enrollment*, accessed Aug 28, 2013, <http://www.lifescienceleader.com/magazine/past-issues3/item/3584-social-media%E2%80%99s-impact-on-clinical-trial-enrollment?list=n>

[11] Novartis, *Putting Care in Patient's Hands*, accessed Aug 28, 2013, <http://www.novartis.com/newsroom/feature-stories/2013/07/putting-care-in-patients-hands.shtml>

[12] Drug Information Association, *DIA Global Forum*, 52-54, *The growth of cell phone technology in pharmaceutical industry (2009)*, accessed Aug 28, 2013, [http://exco.dojodigi.com/index.php/download\\_file/-/view/136](http://exco.dojodigi.com/index.php/download_file/-/view/136)

patients can communicate with the site staff to seek clarification on complex study-related issues and request immediate medical advice on adverse effects and/or any side effects, Through mobile solutions, patients can access information about health-related issues and treatment options and take charge of management and treatment of their diseases. Patients can leverage mobile solutions to request supplemental educational reminders or customized alerts for their appointments, laboratory tests, drug intake, and drug refills. Sweet Talk, a mobility-enabled program, was developed primarily to support diabetic patients between consecutive clinic visits via text messages sent to their mobile phones. Though the program was designed to send reminder messages, it has since been successfully used to recruit young patients in a diabetic trial. Sweet Talk also serves as an efficient medium for patients to submit data and questions to their diabetes care team; send requests for supplies; and seek confirmation on follow-up visits<sup>13</sup>.

## Remote Patient Monitoring

Mobile technology is used to bring about improvements in traditional forms of patient monitoring like monitoring through hardcopy diaries. Diaries delivered by utilizing mobile channels (for example, voice or email surveys) help patients to complete diaries promptly and more conveniently. Mobility plays a critical role in enabling remote monitoring of patients' health, data, and study compliance. Mobility enabled medical devices are designed to transmit captured data to an investigator in real-time and thereby alert staff if a patient needs urgent medical attention. For instance, Alere™ HealthPal, a highly mobile, cell phone-sized device automatically records and transmits readings from a patient's personal health monitoring equipments such as blood pressure monitors and/or glucose monitors. The data are immediately available to the patient's healthcare provider, and can be forwarded to an electronic health record, such as Microsoft's HealthVault<sup>14</sup>. This helps to provide timely information to medical (site) staff and improve patient management, and may also save the patient a few clinic visits. Pharmaceutical companies have now introduced technology enabled tools, such as Medication Event Monitoring System™ (MEMS), that record the time and date when a patient opens a pill box and removes a pill from a pack<sup>15</sup>, and thus help track compliance to study requirements.

In device trials, mobility can be used remotely to get continuous and real-time data from implantable medical devices equipped with sensors. For example, in diabetes where patients need to be monitored regularly for the highs and lows in blood glucose levels, devices such as glucometers include features to register the day, date, and time of data capture. Patients can use such devices at home wherein data is electronically captured and transferred to a database. Devices such as insulin pumps are equipped with technology enabled alert mechanisms that not only sense blood sugar levels of a patient in real-time, but also pump out the right amount of insulin as a remedial action. Such devices facilitate the monitoring of patients without intervention of medical staff, and save not only travel time but also enhance the patients' quality of life.

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[13] *J Med Internet Res.* 10(2): e20, Patients' engagement with "Sweet Talk" – A text messaging support system for young people with diabetes (Apr-Jun 2008), accessed Aug 28, 2013, [www.ncbi.nlm.nih.gov/pmc/articles/PMC2483928/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2483928/)

[14] PRNewswire, MedApps HealthPAL Connects to Microsoft HealthVault to Improve Patient Compliance and Lower Healthcare Costs, accessed Aug 28, 2013, <http://www.prnewswire.com/news-releases/medapps-healthpal-connects-to-microsoft-healthvault-to-improve-patient-compliance-and-lower-healthcare-costs-61823237.html>

[15] *Ther. Clin Risk Manag., September; 1(3): 189–199, The challenge of patient adherence (2005), accessed Aug 28, 2013, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1661624*  
*Perspect Clin Res. Patient-reported outcomes: A new era in clinical research Oct-Dec 2011. 2(4): 137–144, accessed Aug 28, 2013, www.ncbi.nlm.nih.gov/pmc/articles/PMC3227331*

## Electronic Patient Reported Outcome Data Capture Tools

Direct data capture is a proven cost effective measure to engage patients and improve retention. It provides patients with better access to healthcare and helps them manage their disease in a better manner. It significantly reduces patient burden, non-compliance, timelines and requirement of resources, and enhances data quality in clinical studies. Regulatory agencies now place more emphasis than ever before on ensuring patients' well-being and protection of their rights and privacy. These agencies also increasingly audit patient-reported data for validity and trustworthiness. Recent advances in technology support the development of highly specialized electronic data collection systems equipped with real-time patient-reported outcome acquisition and analyses tools. Electronic Patient Reported Outcome (e-PRO) instruments such as e-diaries are designed for patients to record and report well specified and reliable observations electronically. During the course of a clinical trial, patients can electronically report data on their health status such as improvement in symptoms, adverse events and other outcomes by using e-diaries instead of paper<sup>16</sup>. Besides allowing for safety monitoring and immediate treatment of patients and appropriate protocol adjustments, e-PRO data can be treated as primary efficacy or supportive data. e-PRO instruments help minimize data entry errors and missing information as compared to paper-based PRO systems, provide real time access to data, enable trigger alerts and notifications, and among other things, encourage patients to report sensitive information.

In 2004, NIH launched Patient Reported Outcomes Measurement Information System (PROMIS) and Assessment Center as dynamic tools to measure health outcomes from the patients, perspective. PROMIS provides efficient, reliable, and valid assessments of patients, self-reported health, and assists in disease management by identifying appropriate treatment plans<sup>17</sup>. Currently, PROMIS provides tools to improve the reporting and quantification of changes in PROs, such as pain, fatigue, physical functioning, emotional distress, and social role participation that have a major impact on the quality of life across a variety of chronic diseases such as cancer, congestive heart failure, depression, arthritis, and multiple sclerosis, as well as chronic pain conditions<sup>18</sup>. The objective of PROMIS is to create a psychometrically robust Computer-Adaptive Testing (CAT) system that allows administering of these outcomes. PROMIS also aims to create a publicly available system for clinical researchers to readily access data from the CAT system<sup>19</sup>. PROMIS tools are being adopted for use in clinical trials and translational research<sup>20</sup> and currently, 12 sites across the US use these tools in NIH-funded studies<sup>21</sup>.

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[16] *Perspect Clin Res. Patient-reported outcomes: A new era in clinical research* Oct-Dec 2011. 2(4): 137–144, accessed Aug 28, 2013, [www.ncbi.nlm.nih.gov/pmc/articles/PMC3227331](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3227331)

[17] *PROMIS – A dynamic tool that measure health outcomes from subject perspective*, accessed Aug 28, 2013, <http://www.nihpromis.org/about/overview>

[18] *PROMIS: Patient-Reported Outcomes Measurement Information System*, accessed Aug 28, 2013, <http://commonfund.nih.gov/Promis/overview.aspx>

[19] *PROMIS – A dynamic tool that measure health outcomes from subject perspective*, accessed Aug 28, 2013, <http://www.nihpromis.org/Software/DemonstrationSoftware/Demonstration>

[20] *NIH PROMIS Measure (2013)*, accessed Aug 28, 2013, <http://repository.academyhealth.org/cgi/viewcontent.cgi?article=1015&context=egems>

[21] *PROMIS – Active Studies*, accessed Aug 28, 2013, <http://www.nihpromis.org/about/activestudies>

## Interactive Response Technology

(IRT systems such as IVRS and IWRS are based on technology in which one uses a touch-tone telephone or the web to interact with a database by gathering information from or entering data into the database. IRT systems are widely utilized by the clinical trial and pharmaceutical industry to optimize drug availability at sites; maintain a record of the amount of pharmaceutical drugs dispensed, used, and returned to the sponsor; update dose titration, expiry date of drugs, and unblinding of trial participants to their treatment allocation; provide real-time data tracking for patient recruitment and patient history; and support efficient clinical trials data management<sup>22,23</sup>.

IVRS can be used for enrollment and efficient randomization of patients. As IVRS provides a centralized application and database, it can efficiently be used for global multi-centric trials by providing patients with automated access to trial information, translation facilities, 24x7 support, and use of PIN Security (for example, 4 digit pin). IVRS can also be leveraged- to educate and guide patients, much like virtual nurses, and enhance compliance. Patients can use it to improve their understanding of treatment so that they can actively participate in decisions concerning their healthcare<sup>23</sup>.

An integrated EDC/IRT approach is used to capture and maintain electronic patient reported outcomes or e-diaries<sup>24</sup>. These integrated solutions are used to securely collect quality of life and pharmacoeconomic data from patients, record patient diary information, collect post-marketing data for large studies, and complement disease management programs. In some neurological diseases such as schizophrenia, depression, phobias and other mental health disorders, patients are counseled through IVRS via auto-generated questions and solutions. Currently, IVRS therapy programs are being used in some medical disorders where self-help is imperative for the success of treatment or therapy<sup>23</sup>.

## E-Informed Consent

Informed consent is one of the primary ethical requirements underlying clinical research. The Informed Consent Documentation (ICD) process entails full disclosure and complete explanation of the pros and cons of a study to patients with different levels of reading abilities and understanding of medical terminology. The ICD process can be quite cumbersome if the clinical trial protocol undergoes multiple changes as it involves continuous tracking of changes, necessitating requests for patient consent at every stage of the version change in ICD.

Sponsors are increasingly seeking automated tools to employ electronic consent software to prepare detailed information packets that can serve to educate patients about planned procedures in a better and more robust way. With e-ICD process, participants do not have to commute to the research site and can review the consent form at their convenience, thereby enhancing their ability to make an informed decision.

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[22] EMEA, Reflection paper on the Use of Interactive Response Technologies (Interactive Voice/Web Response Systems) in Clinical Trials (August 2011), accessed Aug 28, 2013, [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2011/08/WC500110227.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/08/WC500110227.pdf)

[23] IVRS Development, IVRS for Self Care, accessed Aug 28, 2013, [http://www.ivrsdevelopment.com/ivrs\\_patient\\_self\\_care.htm](http://www.ivrsdevelopment.com/ivrs_patient_self_care.htm)

[24] Life Science Leader, The benefits of using integrated technology with clinical trials, accessed Aug 28, 2013, [http://www.lifescienceleader.com/magazine/past\\_issues3/item/3769-the-benefits-of-using-integrated-technology-with-clinical-trials?list=n](http://www.lifescienceleader.com/magazine/past_issues3/item/3769-the-benefits-of-using-integrated-technology-with-clinical-trials?list=n)



Mytrus, an innovative clinical technology and services company, has launched an iPad application that explains informed consent prior to clinical trial subject enrollment<sup>25</sup>. It is an online interactive consent system with options to read the ICD online or in printed form. Mytrus uses animation and other visual aids to simplify patient education and informed consent processes, thus streamlining patient enrollment process. Additionally, an interactive consent system (tablets such as iPads) can support automatic archiving of consent documentation independent of the enhanced consenting process<sup>26</sup>. Automation in ICD can thus improve efficiency and ensure subject satisfaction.

## Virtual Trials

Use of virtual trials in clinical research is one of the most challenging and highly patient centric technology-driven endeavors undertaken by the pharmaceutical industry. The Food and Drug Administration (FDA) recently approved a Pfizer Virtual Trial Pilot Study<sup>27</sup>, an all-electronic, home-based Phase IV study with an approved drug. Although the study was halted due to lack of participation, technology was not the limiting factor. Adoption of virtual trials in clinical research is a technological initiative to improve patients' convenience by minimizing the burden of visiting clinical sites. Virtual trials allow patients to participate remotely in clinical trials using smartphones and computers. The user-friendly approach of virtual trials has the potential to enhance:

- patient enrollment and retention
- patient engagement and compliance
- self-management of patients' healthcare
- drug dispensing and refills
- data capture and study data analysis

Despite the considerable benefits of virtual trials, some limitations and regulatory constraints have precluded its widespread use. Whereas the Pfizer pilot study<sup>27</sup> was a Phase IV study with a well established safety profile, virtual trials may pose some risk to the safety of patients in exploratory and confirmatory trials. Efforts are being made to refine available technology, increase public awareness about its advantages, and bring such technology to mainstream clinical trials through case by case assessment (for example, in behavioral studies).

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[25] Mytrus, Mytrus Rolls out Clinical Research Industry's First Subject-Friendly System for Informed Consent via iPad® Application (April 2012), accessed Aug 28, 2013, <http://www.mytrus.com/news/article/20120409-ipad-icd> (accessed August 28, 2013)

[26] PLoS ONE 8(3): e58603 Interactive Informed Consent: Randomized Comparison with Paper Consents (2013), accessed Aug 28, 2013, <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0058603>

[27] The Wall Street Journal, Health Industry, Clinical Drug Trial Via Phone, Computer (June 2011), accessed Aug 28, 2013, <http://online.wsj.com/article/SB10001424052702304432304576369840721708396.html>

# Technological Advances and Future Trends in Clinical Research

## Electronic Medical Records

Electronic Health Record (EHR) data offer significant opportunities for the advancement of medical research, the improvement of healthcare, and the advancement of patient safety, and enable clinical trials to be conducted more efficiently and cost effectively<sup>28</sup>. Health Level Seven® International (HL7) recently launched a collaborative effort with the National Cancer Institute to use HL7 Clinical Document Architecture (CDA®) in a unique way to connect clinical trial data to patients' EHRs. The Clinical Data Interchange Consortium (CDISC) has defined the use of EHRs to capture clinical trial data and incorporated it into an HL7 functional model<sup>29</sup>.

Patient-centered standard of care with relevant healthcare education can be established and delivered from the EHRs. Further, EHRs can be leveraged to educate patients about their healthcare. By accessing their EHR, patients can take responsibility for their health by identifying a core set of data relevant to their health status. EHRs can be valuable in removing communication barriers between the patient and physician, decreasing the occurrence of medical errors, and reducing overuse of the healthcare system (duplicate testing).

EHRs can be leveraged to improve speed and quality of the patient recruitment process. A readily accessible global health data repository in the form of EHR can help to identify relevant patients for clinical trials with diminished chances of screen failures, recruit sites in close proximity to the relevant patient population to improve recruitment chances, and enhance patient awareness of trials through their care provider. However, the development of this kind of a repository requires availability of health related data from different sources, standard formats for data collection, integration of different systems into one centralized system, intelligent querying mechanisms, and robust analytics. The pharmaceutical industry and healthcare organizations are looking for development of an interoperable platform that will allow re-use of data from EHRs for clinical research, in compliance with relevant legal, ethical, regulatory, privacy protection requirements and policies.

Nationwide Health Information Network (NHIN), led by the U.S. Department of Health and Human Services, is a "network of networks" that proposes to link regional Health Information Exchange systems to create a master exchange of health data<sup>30</sup>. Similar programs are under way in the United Kingdom, France, Singapore, and Austria, promising countrywide health records systems that cover the entire healthcare ecosystem. The Partnership to Advance Clinical Electronic Research (PACeR), a consortium of medical research centers, pharmaceutical firms, advocacy groups, and health IT organizations, aims to speed up clinical trials and make them less expensive by identifying potential patients more efficiently and enhancing protocol modeling and data collection<sup>31</sup>.

[28] *Electronic Health Records for Clinical Research*, accessed Oct7, 2013, <http://www.ehr4cr.eu/>

[29] HL7 International, *Adoption of HL7 CDA to Connect Clinical Trial Data, EHRs: Technology to Support Patient Care, Speed Process from "Bench to Bedside" (Feb 2011)*, accessed Aug 28, 2013, [http://www.hl7.org/documentcenter/public\\_temp\\_6BFC6086-1C23-BA17-0CFA86D3DECBD602/pressreleases/HL7\\_PRESS\\_20120221.pdf](http://www.hl7.org/documentcenter/public_temp_6BFC6086-1C23-BA17-0CFA86D3DECBD602/pressreleases/HL7_PRESS_20120221.pdf)

[30] *J Am Inform 17(3): 295-301, A Framework for evaluating the costs, effort, and value of nationwide health information exchange (2010)*, accessed Aug 28, 2013, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2995720/>



Moffitt Cancer Center in Tampa, Florida, in partnership with Oracle, has developed its Health and Research Informatics (HRI) platform and Oracle's data warehouse and analytics system has already enabled Moffitt to identify patients suitable for clinical trials much faster than in the past<sup>32</sup>. Danville, Pennsylvania-based Geisinger Health Plan, in a GlaxoSmithKline PLC-funded trial of a new cardiology drug, by using its database and EHRs, took just a few weeks to identify at least 5,300 patients who met at least 20 criteria for the trial and fit within the study's scope. It ended up mailing letters to 1,700 potential candidates, and eventually 101 out of 500 patients who called to show interest in the clinical trial were enrolled<sup>33</sup>.

## Cloud Computing and Big Data Analytics

The pharmaceutical industry is looking forward to generate significant value from patient related data available in varied forms (structured or unstructured), various volumes and velocities. A combination of new, smarter devices and robust data exchange will enable improvements in study designs and thereby greater efficiency in trial execution<sup>34</sup>. Integrated patient information in the form of Big Data can potentially be used to extract key details about patient-reported outcomes and predict future requirements. An analytics layer built on Big Data (a single source of standardized patient data) and supported by a cloud server such as Hadoop can be leveraged for better patient management. For instance, modeling on large scale human behavioral data using statistical and pattern recognition methods can provide insight into new therapies and treatments. It can bring value to a patient by offering them choices regarding their care and engage them in their own care. Optum Natural History of Disease (NHD), an analytics application, uses Big Data to identify early disease markers for life and cost saving interventions. The Big Data revolution can transform personalized medicine by providing a platform to map genetic and clinical data, and identify the right care for each patient<sup>35</sup>. Regulatory constraints such as data privacy and security need to be taken into consideration while implementing Big Data infrastructure. Trends, patterns, and outbreaks can be interpreted by researchers with the right tools or smart algorithms to predict risk and reshape strategies.

[31] FierceHealthcare, *Collaborative to speed clinical research and reduce costs* (2011), accessed Aug 28, 2013, <http://www.fiercehealthcare.com/press-releases/collaborative-speed-clinical-research-and-reduce-costs>

[32] InformationWeek Healthcare, *Oracle applications enable personalized cancer treatment* (Feb 2012), accessed Aug 28, 2013, <http://www.informationweek.com/healthcare/clinical-systems/oracle-applications-enable-personalized/232601067>

[33] FierceEMR, *Can EHRs give clinical trials an assist?* (Mar 2011), accessed Aug 28, 2013, <http://www.fierceemr.com/story/can-ehrs-give-clinical-trials-assist/2011-03-31#ixzz2d8NZjeaU>

[34] McKinsey and Company, *Insights and Publications, How big data can revolutionize pharmaceutical R&D?* (April 2013), accessed Aug 28, 2013, [http://www.mckinsey.com/insights/health\\_systems\\_and\\_services/how\\_big\\_data\\_can\\_revolutionize\\_pharmaceutical\\_r\\_and\\_d](http://www.mckinsey.com/insights/health_systems_and_services/how_big_data_can_revolutionize_pharmaceutical_r_and_d)

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## Summary

Patient centricity is a priority for all the stakeholders in clinical trials, including a proactive patient pool, healthcare providers, regulatory authorities, and biopharmaceutical industry and CROs. A patient centric approach to clinical research would include all actions that affect patients, from their recruitment through data analysis. Today, patients want to stay informed about drugs undergoing clinical trials and their safety and effectiveness profile. Regulatory authorities have introduced various programs to ensure that patient participation is incorporated in their decision making process. They encourage pharmaceutical companies to focus on the analysis of risk benefit ratios in both, pre-marketing and post-marketing stages, and transparently share information with patients.

In order to enhance patient centricity in clinical research, new technology driven initiatives are being undertaken to make clinical trial participation less burdensome for patients and increase efficiencies in conducting trials. IT companies contribute significantly to the commitment of pharmaceutical companies to ensure patient centricity in healthcare research. The conduct of clinical trials is poised to undergo a paradigm shift with the increased adoption of integrated technologies in mobility, data mining, and analytics. The explosion of social media has provided new avenues to the clinical trial industry to expand their outreach to patients and share information on ongoing research with the general public. The use of electronic methods to engage potential subjects has enhanced recruitment and retention of patients in clinical trials. To summarize, technology today plays a big role and promises to play an even bigger role in enhancing patients' knowledge of diseases, empowering them, reducing their burden, and aiding their participation in clinical trials efficiently and successfully.

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