Investigator Council presents: Insights

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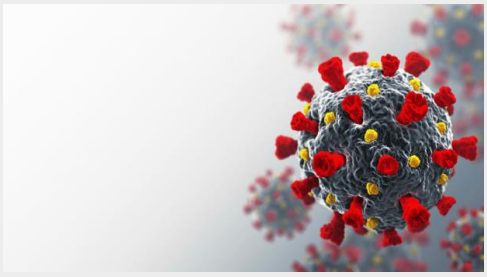
- International Clinical Trials Day (ICTD) 2020
- National Guidelines for Ethics Committees Reviewing Biomedical & Health Research During COVID-19 Pandemic (April 2020) - https://www.icmr.gov.in/pdf/covid/techdoc/EC_Guidance_COVID19_06052020.pdf
- Changing Trends in COVID-19 Era : Changing Trends in way Clinical Trials are conducted, General Perspective of Audit trends
- Recommended Best practices while resuming patient and trial management
- Investigator's Column: Telemedicine in Clinical Research - 5 Solutions for the Pandemic Era

INTERNATIONAL CLINICAL TRIALS DAY

Commemoration of the first controlled clinical trial promotes increased awareness of the important work clinical trials do today by raising clinical trial awareness and honoring clinical research professionals and patients across the globe that make scientific advances and new therapies possible.

RESEARCH THAT MATTERS

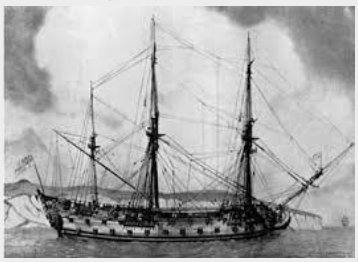
There is a very good reason for celebrating Clinical Trials Day this year, on May 20, with all the efforts put in by the healthcare fraternity to manage the corona virus situation and also to find a potential cure for this pandemic. In 2005, International Clinical Trials Day was launched to commemorate the very first controlled clinical trial in 1747. The purpose of this day, which has expanded into an awareness week in many parts of the world, is to remind the public of the importance in participating in clinical research while recognizing the dedicated professionals that make the research possible.



How it All Started: The First Clinical Trial

Scurvy has been a fatal ailment that would cause gum deterioration, open sores and ultimately death for sailors, for as long as humans had embarked on long sea journeys; some sources claim that across history, millions of sailors have succumbed to the disease. James Lind was a Scottish surgeon serving aboard the British gun ship HMS Salisbury when 12 of his fellow sailors showed signs of scurvy. Seeking to prove a theory that the putrefaction of the body could be prevented with acids, he divided the sailors into six groups – each receiving a different dietary supplement. The groups were treated with cider, diluted sulfuric acid, vinegar, sea water, an expectorant, and two oranges and a lemon.

The experiment began on May 20, 1747 and within days, despite running out of citrus fruit, the men treated with oranges and lemons recovered and returned to active duty – the only sailors to show any improvement. While no modern ethics Committee would approve Lind's experiment today (there was no control group), this is generally regarded as the first controlled clinical trial. The trial conditions were standardized for his subjects-kept under similar conditions, fed the same diet aside from the supplements.



Where We Are Today

Several centuries after the first clinical trial, modern medicine has come a long way in testing the efficacy, safety, side effects and more. Controlled clinical trials have resulted in virtually

almost all advances in modern medicine and treatment and are the global standard for the development of new therapies today.

Despite the known benefits of clinical trials, there are obstacles to research even today. Clinical trials are under-enrolled and difficult to fill. Available data suggests that only a small percent of the population have ever participated in a clinical trial, with the greatest cause being lack of awareness. Evidence suggests that the public has never or rarely considered clinical trials as an option, including patients suffering from a chronic or rare condition have only participated in trials at a very low rate when compared to disease incidence in our country.

So together as part of this community, let's spread the good word to increase awareness of research among the general population and encourage participation in clinical trials for the betterment of mankind.

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NATIONAL GUIDELINES FOR ETHICS COMMITTEES REVIEWING BIOMEDICAL & HEALTH RESEARCH DURING COVID-19 PANDEMIC

In the ongoing COVID-19 pandemic situation, research has to take the front stage in order to tackle the novel challenges that have come to the fore in an unprecedented manner. Hence, Indian Council of Medical Research (ICMR) has released a set of Guidelines in April 2020 for the Ethics Committees involved in the review of Biomedical and Health Research projects during COVID-19 Pandemic to ensure continuity of critical research activities.

Some of the salient features of these guidelines include:

- Maintaining Privacy and Confidentiality
- Community Engagement
- Storage of Biological Material and Datasets
- Public Health and Socio-behavioral Research
- Ethical Review Procedures to prioritize trials on urgency basis
- Decisions regarding ongoing studies
- Review of new non-COVID Research
- Innovative and secure consenting procedures (LAR, eConsent, Consent Waiver)
- Inclusion of COVID-19 patients under vulnerable category
- Consideration for psychological needs and mental health of persons tested positive for COVID-19, their families and health care workers
- Provision for electronic submission and review of research proposals

For a detailed review of the guidelines, please refer to the guidance document via below link: https://www.icmr.gov.in/pdf/covid/techdoc/EC_Guidance_COVID19_06052020.pdf

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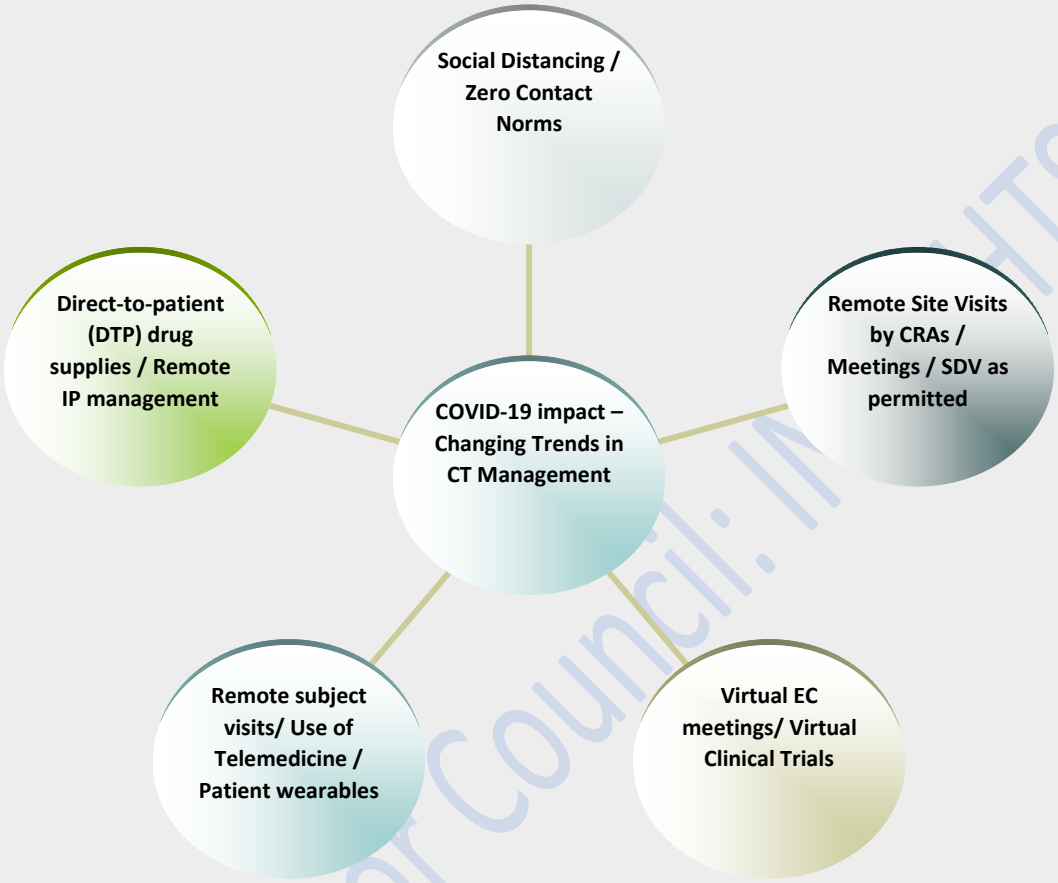
CHANGING TRENDS IN COVID-19 ERA

1. Changing Trends in way Clinical Trials are conducted:



2. General Perspective on Audit Trends:

We are currently living in a world of increasing uncertainty due to the global spread of COVID-19 which has resulted in many restrictions. This crisis has changed the way Life Science companies approach working practices within the research world which can sway in many directions. However, medical fraternity, clinical researchers, support staff and Regulators have been resilient in adapting to these challenges and are forced to look for new solutions that allow them to ensure business continuity and efficient patient protection. No matter what the situation is, all regulators are clear on one thing: **COMPLIANCE!** It is always obligatory to maintain compliance with applicable regulations while ensuring that patient's rights, safety, and wellbeing are always protected.

To accommodate these testing times, many sponsors (and even regulators) are looking at new ways to conduct Quality Assurance audits without being physically present on site. Most sponsors and consultancies are coming up with a solution of remote audits. Although, the concept of 'remote audit' was always into existence, it has now become more evident and

acceptable. There are number of variants of remote auditing and new technologies help to facilitate remote review.

Few examples of remote audits include:

- Remote system audit of Contract Research Organisation
- Remote clinical database review
- Remote assessment of investigator site
- Remote computer system compliance audit
- Remote laboratory audit (central as well as local)
- Remote safety monitoring audit

If your sponsor decides to conduct remote audit of your facility, please contact them to understand what is expected of you. Remote audits have its limitations but are acceptable in times like this.
Remember, no matter the situation, it is always important to maintain adequate oversight of your trial and its related compliance. Remote audit helps you to keep that oversight and may soon become the new norm of auditing.

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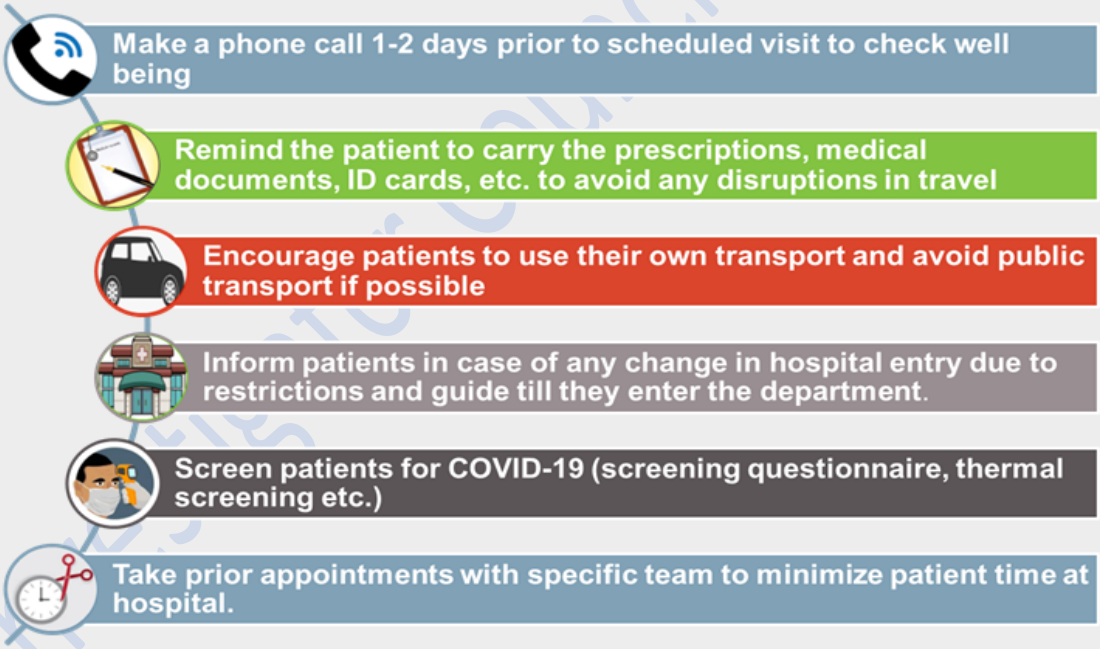
RECOMMENDED BEST PRACTICES WHILE RESUMING PATIENT AND TRIAL MANAGEMENT



INVESTIGATOR'S COLUMN

Telemedicine in Clinical Research: 5 Solutions for the Pandemic Era

Clinical research has never been more important in human history. As the world stands still with no clear treatment in sight for the COVID19 pandemic it is imperative that anecdotal medicine gives way to time tested evidence based clinical trials-based decision making. Despite the apparent hopelessness of the situation there is an uprising of innovation, collaboration and creativity that is fueling our rapid journey to end the pandemic. In the meantime, we must go back to the basics of research and validate solutions for safety, efficacy and reliability. The SARS-CoV-2 virus is just another virus. Granted it has multiple manifestations of disease and seems to create new pathophysiologic inroads everyday. Yet it is a virus and mankind has learnt to overcome or coexist with many other similar creations of nature. The treatment of the COVID19 syndrome will need a concerted effort to systematically test the most relevant techniques for the maximum benefit with the least side effects at a cost that will not bankrupt economies any further.
There is light at the end of the tunnel. As of May 12,2020, there were 1358 registered research studies on clinicaltrials.gov. There has been a rapid rise in the number of ideas and the geographic distribution has also been widespread. Good clinical research needs a good protocol executed flawlessly by a committed team. We may consider funding to be the backbone of research but in my opinion, it is the individual researcher and their team which has discipline and an attention to detail that is crucial. There are no shortcuts. Most good research is meticulous, appropriately paced and transparent. It is this process that is also the most challenging. The need for a clinical research coordinator and a research organization cannot be understated. The workflows that have developed so far are important foundations for progress in clinical research in India.

The COVID19 pandemic has thrown open former barriers in many ways. Translational work is now being contemplated to move from the bedside to the bench. Social experiments at a population level are ongoing. People have turned citizen scientists and are documenting in vivid detail their health status and the impact of COVID19. Designers and makers are creating parts and tools within days using 3D printing instead of the usual prolonged timelines.
One specific area that can be immediately implemented and result in efficient as well as cost effective outcomes is the use of remote technology. Here are five solutions that can transform how clinical research is done. There is absolutely a continued need for close monitoring of all facets of the clinical trial and research process. In fact, there is now an opportunity to remove redundant, time consuming expensive old templates and look afresh at how research can benefit from the use of telemedicine systems.

1. **Recruitment:** The use of social media to advertise a clinical trial as well as engage interested participants is almost a necessity today. Potential trial participants can be interviewed and given an opportunity to ask questions and have a detailed informed consent process that can be moderated and recorded. Group discussions with several trial members as well as with many potential enrollees can be done simultaneously. The savings in time spent without traveling, money saved and the impact on carbon savings to the environment are likely quite large. Just as verification of identity is crucial for banking and telemedicine, the same safeguards can be put in place.
2. **Education:** The role of the investigator is critical to the success of a trial. The reality is that most researchers are busy clinicians who may have several responsibilities. It will help to rapidly create content to educate and engage with the investigator team. Even at planning stages it may be faster to have a five-minute conversation to ascertain feasibility rather than wait weeks for a piece of paper to return with vague details. Likewise all staff involved and even patients can be educated on the basis of the trial as well as the logistics and integral regulatory components.

3. **Ethical Committee/Institutional Review Board Meetings:** Scheduling a meeting with a diverse set of individuals has always been difficult and with the current physical distancing it is even more complex. Our days have been upended with a variety of responsibilities ranging from running the home to managing your institutional department as well as dealing with a variety of crises triggered by manpower and material shortages. It is important to have a clear agenda as well as a reasonable number of study protocols that need to be reviewed in any of these meetings. However, given the challenges these days it may be necessary to move to more frequent shorter meetings. The upside is that more protocols can be evaluated in a shorter timeframe and important research especially related to COVID19 can be fast tracked. The meetings can be done using institution specific video conferencing software with appropriate security features and recorded also.

4. **Subject monitoring:** Many trials in progress have been challenged by the lack of travel capacity for many subjects. Although strictly speaking there should be no restrictions in their movement as it is a medically essential service the reality is that many patients and subjects have been reluctant to come to hospital settings. The situation may change as the lockdown eases and travel becomes widespread. In the meantime, several aspects of patient monitoring can be continued by phone and it will be possible to minimize the time needed to physically evaluate a subject to the bare necessity. This will improve efficiency in turnaround time for data but may need extra hands to help with the changed workflow. Convenience in timing of visits will be a major advantage for all stakeholders. The use of portable biomedical devices can be helpful in several ways to capture vital signs as an example.

5. **Collaborative research efficiency:** Multicenter trials are necessary to balance bias in geographic disease prevalence and management styles. Likewise, given many trial locations, collaboration is easier with multiple meetings to clarify processes. Instead of having large gatherings of investigators in various locations it would be easier to have online meetings. The appropriate compensation for time and effort can be built into the structure of such engagements and the savings in boarding, lodging and travel can be enormous.

In summary, the use of telemedicine techniques and remote technology can transform how research is done. The pandemic will be controlled through the sustained efforts of the research community and will require collaboration, communication and compassion. At the heart of all that we do is the need and the innate desire to improve human health and that reality must never be forgotten in the whirlwind of meetings, paperwork and deadlines. Remote technology will transform how clinical research is done, for good.

Further Reading:

https://social.eyeforpharma.com/clinical/telemedicine-future-clinical-trials
https://hitconsultant.net/2019/06/20/medable-launches-telemedicine-solution-virtual-clinical-trials/#.XrrNcRMzbEY
https://www.europeanpharmaceuticalreview.com/news/75996/telemedicine-clinical-trials/

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