Community-Based Clinical Trials — The New "Virtual"

Long recruitment timelines and under-performing sites are the most frequently discussed topics in the clinical trials sector. With actual recruitment timelines double the planned expectations, at least 39% of sites under-enroll and 11% of sites fail to enroll a single patient[1], new technological advances are often heralded as holding the answer to these problems.

In this world of pressure to digitize the way we work in the pharmaceutical industry – from investors, the C-suite, and from our customers — it is important to separate the hype from the useful. The recent surge in interest surrounding "virtual trials" represents both an opportunity and a risk. The opportunity is that some of the digital tools will be truly helpful and the risk is that some of them will not provide any advantage and yet carry significant cost and safety risks. Of course, digital tools exist in every niche of the trial sector, but this article will only look at those that allow clinical trial visits to be moved from the investigator site into the community — usually the patient's own home — examining how to maximize the innovation already driving improvements in the clinical trials sector and to marry it with the new digital tools to create additional benefits.

Today's Reality

In the last three decades we have seen some key developments that have added value in this area. Some of those digital tools that relate to the patient are below.

- EDC
- IXRS
- Social Media Patient Identification Tools and Advertising
- Electronic Medical Records
- Electronic Informed Consent
- ePRO
- eSource

Coupled with this has been a decade long development of the concept of community-based clinical trials driven by MRN and similar companies that has moved clinical trial visits out of hospitals to patients' homes, thereby reducing the trial burden on the patient. This subsequently boosts recruitment and retention by reducing the estimated 60% of patients who decline to participate in trials and the 20% or more who drop-out after randomization.[2] This is a people-based solution focusing on the combination of the need for medical activities to be done face to face, the technical knowledge of highly trained health care professionals (HCP), and patients' desire for professional and human care during their illness.

What Are the New Technologies and How Do They Combine?

The fusion of EDC and ePRO has created eCOA (electronic clinical outcomes assessments), integrating the various forms of digital patient data into a single platform. This allows the simultaneous, up-front development of all digital capture tools in a trial, eliminating the need for integration at a later stage.

eSource is also taking hold. This is not strictly new — EDC and ePRO systems have had an eSource definition right from the start — but the area was crying out for clarification by regulators and pharma companies as the common practice of using paper and digital systems in parallel was unnecessarily generating huge workloads in source data verification (SDV). Eliminating that step has great cost advantages in trials and is a core benefit of eSource efforts.

eConsent is also gaining traction with 66% of the top 50 pharma companies considering its use[3]. Allowing patients more time to review and consider information before consenting can improve both enrollment and retention as patients are better informed.

Newer entrants to the trial sector utilize technology already embeded in our daily lives. If a wearable device can link to your phone, it can route biometric data straight to a clinical outcomes database. The talking head tech is also commonplace today — like skype — and is creating a virtual consultation, linking patients to their HCPs while being geographically far apart. The same goes for more medically technical equipment which can be linked to a phone — at present these are mostly aimed at vital signs (weight, pulse, temperature, etc.) but the ability to build these data links into many pieces of equipment will lead to an explosion of types of data that can be collected from devices the patient uses on their own or under direction from a nurse.

The value proposition of all these technologies exactly parallels MRN's Home Trial Support (HTS) solutions, they allow patients to be seen in the community and thus reduce the burden of site visits on the patient. This speeds up trials and makes them more acceptable experiences for patients, a key outcome as sponsors lose approximately $1.3 million in prescription sales for each day that a drug is delayed.[4] However, trials that suit these solutions are quite different. Those that suit virtual designs can be characterized as "low touch" and those that suit HTS are "high touch," as shown in diagram 1. Choosing which trial design to opt for is not straightforward.

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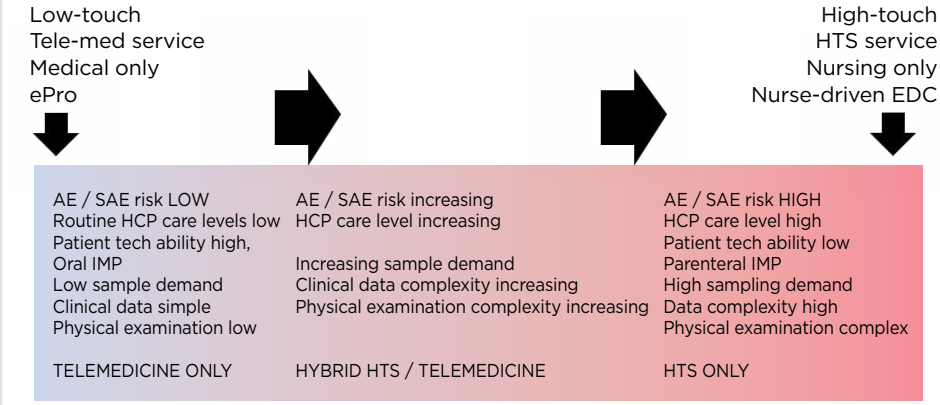
Limitations of This Polarized Approach

Setting up trials as virtual or "HTS only" has limitations. Clinical research is by its nature, risky. A totally virtual design is only going to be medically sensible in a small percentage of very safe trials. Patients and physicians will make these judgments when participating in trials and if they are not comfortable, they won't take part. An HTS study however is often much more intense — they can be in any phases of drug trial and indeed at MRN we specialize in complex drug administration using mostly parenteral administration and complex health assessments, with safety managed by choosing the right time to go into the community and the right visits to

Spectrum of Low-Touch to High-Touch Trials (diagram 1)



do in the community. The down side is that HTS cannot cover all visits, as some of them require specialist data collection from medical equipment or from experts only available at the hospital sites.

The implication is that we should not force any given trial into one of these theoretical profiles, but instead combine them under a unifying concept of a "community-based clinical trial." Within this concept we can then envisage different visit types:

- Virtual visits — using technology alone in the patient's home
- Site visits — where the patient still needs to go to the site
- Home Trial Support visits – where the patient is seen by a nurse in the home

This is the so called "hybrid" model — a merge of digital, community-based HCP, and traditional site solutions to get the best recruitment and retention result in any given trial.

What Are the Advantages of the Hybrid Concept?

The hybrid model — correctly designed — achieves the best of both worlds. Most trials can benefit, most visits can be done in the community, and the type of data collected spans a much broader spectrum.

The trick then is in deciding the visit distribution, which of the three types of visit do we want and at what time point in the protocol design. Applying the high- and low-touch spectrum concept to visits instead of the whole trial can maximize the community component with small adjustment to visit activities.

Implementation — Realizing the Benefits

Setting up a hybrid model can be done today. The technology is available — although much is still untested within clinical research — and the nursing service has been around for over a decade, showing low risk and high return. If implemented, the trial becomes more patient-centric, increasing recruitment and retention and decreasing the number of sites needed. The balance between these is of course key; fewer sites reduces cost, but if you keep the site numbers the same, all with an increased recruitment rate, you get to market faster. Exactly what balance you pick is very dependent on your appetite for risk and budgets.

Let's look at some numbers. For a standard Phase 3 trial, HTS alone has the ability to reduce the number of required sites by 5% to 20% based on improved retention rates. In addition, the impact on consenting improves recruitment rates by a factor of 1.5 to 2.0., all of which essentially keeps the clinical trial budget neutral. If however, the recruitment period was kept constant, this would equate to a 48% reduction in site numbers and reduced budgets.

Used in conjunction with digital solutions already on the market (EHR search tools, eConsent, ePRO, and telemedicine) and based on published and estimated assessments of the impact of these solutions (for example, a 2014 report by Eastern Research Group notes that the use of a EHR clinical trial alert system — CTA — resulted in a 28% increase in identification of eligible patients and a subsequent doubling of monthly enrollment rates[5]), the required number of trial sites could reduce by as much as 60% as each site is able to find, recruit, enroll, and keep a higher number of patients. Alternatively, this could be traded for an increase in speed and limited or zero reduction in site numbers. Details of our model can be made available on request.

Conclusion

The means to move clinical trials into the community is already available with nursing services, and is being enhanced by digital tools that will allow more visits to be done outside the site. This can both reduce site numbers and speed up the trial. However, the drive to a fully virtual design is possibly more hype than practical or indeed valuable, as value of achieving such dramatic site numbers reductions when you could have further speed up in recruitment instead, is dubious, especially when you consider the medical safety issues introduced which would reduce the number of studies to which it could be applied dramatically. Hybrid is the way to go. PV

Editor's Notes:

[1] *Mary Jo Lamberti PhD, Senior Research Fellow and Kenneth Getz, MBA, Director of Sponsored Research Programs and Research Associate Professor. Profiles of New Approaches to Improving the efficiency and performance of pharmaceutical drug development. TUFTS Centre for the Study of Drug Development White Paper Page 2.*

[2] *Emerging Clinical Trial Recruitment Benchmark Metrics: The Recruitment Funnel Analysis by Beth Harper, President, Clinical Performance Partners, Inc (CPP) and Gen Lei President, Pharmaceutical Pipeline Enhancement Strategies (PhESi). Parexel Statistical Sourcebook 2016/2017*

[3] *Lindsay McNair, MD, MPH, MSB, WIRB-Copernicus Group; Antony Costello, Mytrus, Inc; Charlotte Crowder, MPH, WIRB-Copernicus Group. Electronic Informed Consent: A New Industry Standard*

[4] *Karyn Korieth and Annick Anderson. 'Today's Fastest, Most Efficient Drug Developers: A 2014 Assessment' CenterWatch Monthly, September 2014*

[5] *Eastern Research Group, Inc. Examination of clinical trial costs and barriers to drug development, Eastern Research Group, July 2014. Page 63*