d) Decentralized Clinical Trials

The **Decentralized Clinical Trials (DCTs)** model is also referred as Site-Less or Virtual Study model. This study design places the patients at the center of the trial with the aim to limit or eliminate the need for patients to travel to an investigational site. This patient-centric model is likely the most disruptive for CDM especially when vastly decentralized (i.e. very few to no site visits). Data processing would be focused on data consolidation from diverse technologies and sources rather than data cleaning. So, CDM should proactively assess data mastering and data reconciliation keys across modalities. Additionally, a risk assessment tailored to DCT could allow the implementation of a pragmatic risk-based study execution approach to data processing.

In this context, traditional EDC is not applicable as all data are collected directly from the patients utilizing multiple eSource data collection modalities such as eCOA, Devices, Wearable, Sensors etc. All patient visits are either remote (i.e. Telemedicine) or conducted through home nursing. A pool of investigators may be available remotely to answer patient's emergencies. Figure 4 depicts an example of a visit schedule that a patient may follow in a fully Decentralized Clinical Trial. In this context, most of the traditional data cleaning processes are not applicable. Additionally, there are no site monitors to address data related issues on CDM's behalf. Due to the limitation of addressing data issues after collection, this model heavily relies on technologies collecting error free data with quality checking at the time of data collection. Lastly, CDM needs to wrangle and consolidate the data collected from the myriad of sources to enable the monitoring of data remotely. Pre-defined data handling strategies would be advisable to address illogical data (e.g. incompatible with life) since the source cannot be updated. CDM may also need to define a process to "disqualify and/or flag" such implausible data.

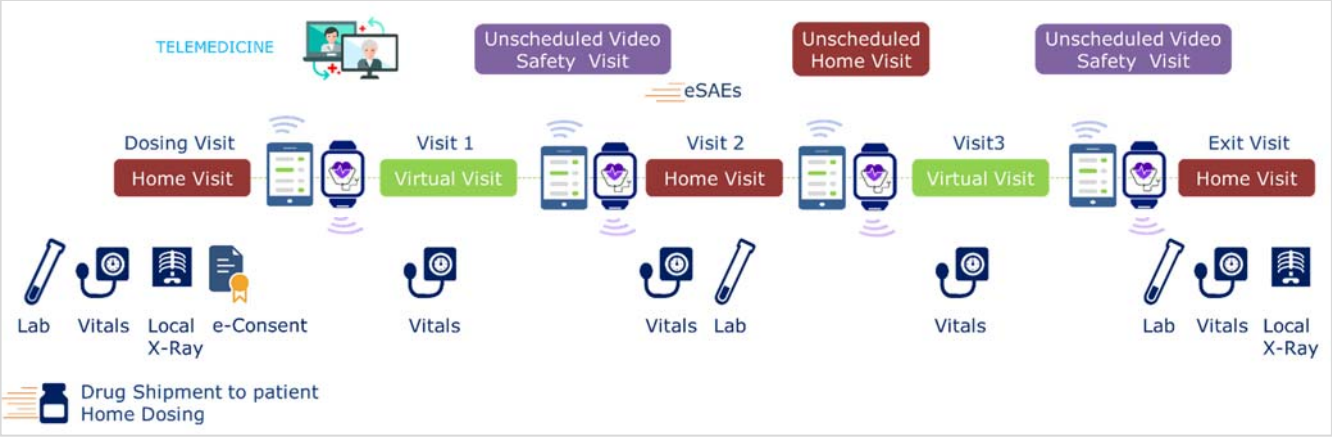

Fig 4. Example of design of a fully Patient Centric / Decentralized Clinical Trials

Today DCT is used in a limited number of clinical trials. Some indications are more appropriate than others. Some protocols requiring complex procedures (e.g. Implant Procedures) or necessitating large diagnostic equipment (e.g. MRI) would naturally not be implementable at patient's home.

Additionally, likely due to the immaturity of current technologies and risk aversion, many companies are only piloting some aspects of fully Decentralized Clinical Trials while keeping core visits and assessments at investigator sites (e.g. Dosing Visit and Exit visits). This may look simpler than a fully decentralized trial, but it is adding complexity by multiplying technologies, data sources and stakeholders. The set-up of such hybrid studies (i.e. partially decentralized) would require careful planning leading to the set-up of multiple systems with complex data flows and integrations.

e) Impact of emerging study designs on Clinical Data Management

These emerging and fast adopted study designs are leading to many data flow and study execution complexities that most CDM organizations are poorly equipped to handle today. The challenges are compounded by the lack of adaptive technologies and processes. Many data systems available on the market such as EDC, eCOA, CTMS and IxRS have been designed to handle traditional clinical trials and cannot rapidly adapt to design changes. Many cannot even implement multiple Schedules of Visits and Procedures. In that context, CDM needs to think critically to leverage available technologies, processes and work within the regulations to operationalize the clinical study protocol for data acquisition and management. It is important to anticipate all scenarios as early as possible in the process and proactively identify mitigation strategies. Per ICH E6 Rev. 2, mitigation strategies must include "*the design of efficient clinical trial protocols, **tools and procedures for data collection and processing**, as well as the collection of information that is essential to decision making*."[7]

This is requiring fundamental changes in skillsets, technologies and processes. CDM must lead the way for study teams to efficiently operationalize these new study designs. CDM must implement "fit for purpose" and "end to end" data strategies to prevent the critical risks introduced by the adoption of these innovative study designs.