

a) Adaptive Study Design

In its simplest form, **adaptive design** may consist of combining study phases into one protocol (Phase I/II, Phase II/III). However, its true intent is to use data collected in the earlier stages of the study to adapt its design moving forward in accordance with pre-specified rules defined in the study protocol. Examples of adaptations include changes to the dose regimen, study arms, sample size, sub-populations and study duration. Adaptations may apply to new patients being enrolled or all patients retrospectively. In some cases, the outcome of data reviews could result in stopping the study.

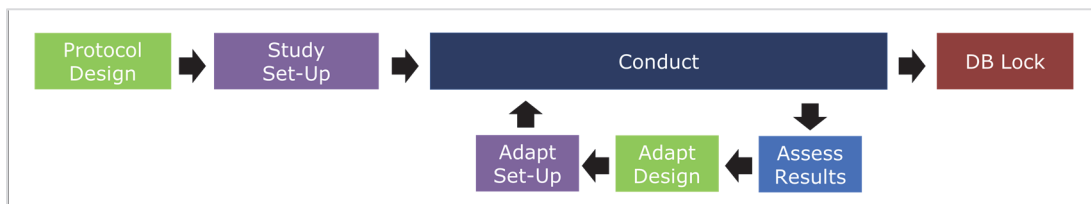


Fig 2. Adaptive Study Design

Theoretically, Adaptive Design applies to all clinical development phases (i.e. Phase I through IV) and all types of studies. In reality, the current limitations of the traditional clinical development processes and technologies are restricting its adoption due to their lack of flexibility. As an example, most IxRS systems cannot change treatment arms, dose and/or block allocations without going through lengthy programming changes. As a consideration to cope with these many adaptation scenarios, CDM may proactively pre-program all possible adaptations defined in the protocol before study start. This seemingly “proactive” approach would however require designing all data collection tools including IxRS with every complex branching logic which risks extending study initiation cycle times. As an alternative, CDM could minimize the risk to start-up timelines as well as optimize the design of the data collection methods by applying a risk-based study execution (a.k.a. RBx) approach and only pre-program the most likely adaptations. However, it is still possible that data reviewed during the study leads to unanticipated adaptations. In these cases, it may become necessary to put the study on hold until these systems are updated.

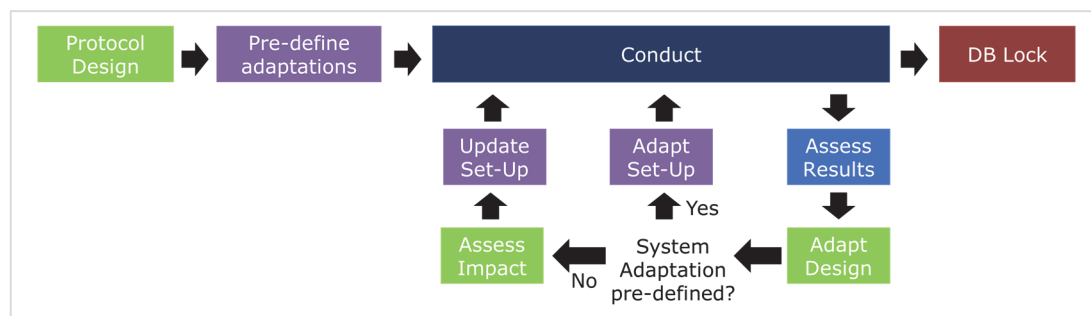


Fig 3. Example of workaround to processes and systems limitation

Overall, the study and data flow set-up of adaptive design protocols require a deep understanding of the strengths and weaknesses of the processes and systems to anticipate adaptations. CDM needs to lead the study team in assessing how to implement data collection tools allowing patients, sites or countries to follow different Schedule of Visits and Procedures.