RAPID PATIENT RECRUITMENT

WHY DO STUDIES OVERRUN THEIR TIMELINES?

Clinical trial conduct is inherently inefficient, plagued as it is by hurdles which are difficult to control, such as regulatory and ethics approval processes, budget and contract negotiations, and the need to recruit patients and collect data through third parties.

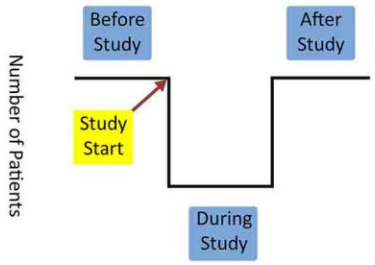
In 2007 only 7% (USA) to 18% (Europe) of studies were completed on schedule. The delay was greater than 1 month in 41% (Latin America) to 70% (USA) of studies (*CenterWatch 2007*).

In the USA 57% of delays were due to slow patient recruitment and enrollment, and to protocol amendments (*Thomson CenterWatch 2007*).

Typically 30% of investigators recruit no patients or just one patient.

The number of patients predicted by investigators typically plummets by up to 90% at the start of a study (*attributed to Dr Louis Lasagna*).

Lasagna's Law



"The number of patients available to join a trial drops by 90% the day a trial begins. They re-appear as soon as the study is over."

Yet, in this morass of uncertainty there is concrete information that can significantly reduce protocol amendments and patient recruitment times and which is available to all. Most, however, overlook real data in favour of predictions by investigators about patient numbers that everyone knows to be wrong.

There are numerous approaches to patient recruitment strategy, many expensive and complicated. It may be necessary to use these approaches, but in all cases the most effective primary approach is to carry out the following three steps, each of which is based on real data about patient availability.

1. PROTOCOL FEASIBILITY: DO THE PER PROTOCOL PATIENTS ACTUALLY EXIST?

- The primary purpose is to validate the protocol and avoid amendments and non-recruitment.
- A protocol-specific, detailed, specific questionnaire, including the inclusion and exclusion criteria and the schedule of visits, assessments & procedures is compiled.
- Patient records are checked against this questionnaire in person, face-to face with the investigator.
- Sample from all types of sites likely to recruit patients; number sampled depends on size of study.

2. SITE SELECTION: DO THE SITES YOU INTEND TO USE HAVE THE PATIENTS?

- This is the same process as used for feasibility, but now conducted at all potential sites.
- All aspects of site suitability are examined; emphasis here is on availability of patients.
- Documented proof of a sufficient number of suitable patients is required for a site to be included.

3. INDIVIDUAL PATIENT IDENTIFICATION: CAN THIS BE DONE IN ADVANCE?

The process depends on the type of disease being studied:

A. Chronic, pre-existing diseases

- Since these patients exist, it is be possible to identify and consent most, if not all, patients before the start of the study
- Rate of enrolment limited only by investigator resource

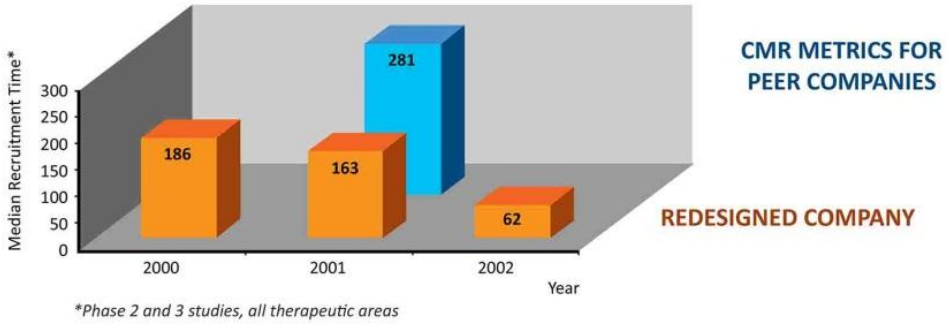
B. Newly diagnosed, acute or acute on chronic diseases

- The same process applies
- The exact frequency with which actual relevant patients are seen by the investigator is determined
- Only investigators who see these patients at a well-defined, pre-determined frequency are included.

THE PROOF IS IN THE OUTCOME

CASE STUDY 1: Large, top 10, multinational pharmaceutical company

Application of the approach described overleaf resulted in a 67% reduction in median recruitment time globally over two years. In this analysis, all Phase 2 and Phase 3 studies in all therapeutic areas are included.

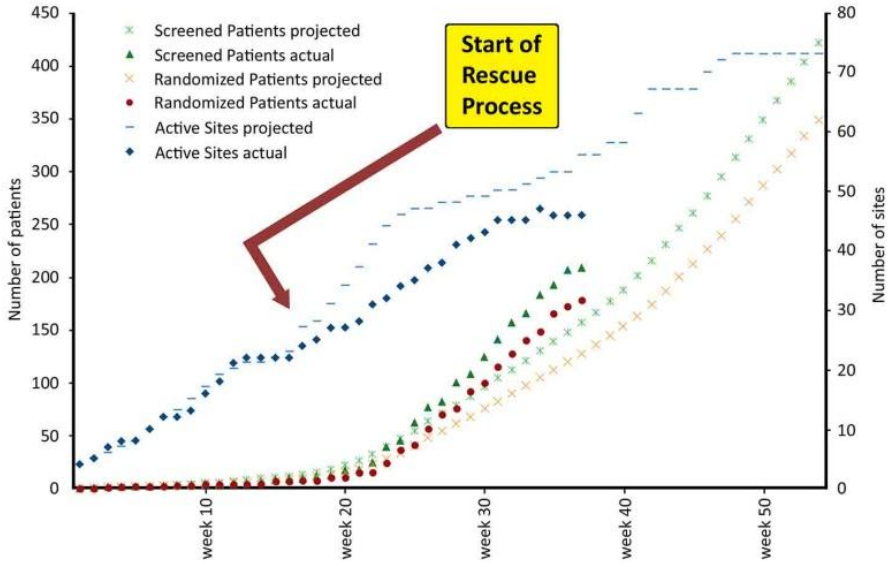


*Phase 2 and 3 studies, all therapeutic areas

Effect of protocol feasibility and patient selection: 67% Reduction in Recruitment Time

CASE STUDY 2: Rescue of single study in small biotech company

The company was suffering from poor patient recruitment over several months, despite activation of over 25 sites. Application of the approach described overleaf to existing sites, and to some new sites, resulted in immediate increase in patient recruitment and to an on-time completion of the study.



Rescuing a non-recruiting study