Paper DV03

Optimizing Clinical Trial Design with Real-Time Sample Size Calculation and Enrollment Projection: A Shiny Dashboard Solution

Dony Sabu, Genpro, Now part of Catalyst Clinical Research, Trivandrum, India
Sahalath K P, Genpro, Now part of Catalyst Clinical Research, Trivandrum, India
Vignesh V Gopal, Genpro, Now part of Catalyst Clinical Research, Trivandrum, India

ABSTRACT

The clinical trial design is a complex process that requires careful planning and decision to ensure the validity and reliability of the results. Determining the appropriate sample size and enrollment projections is a crucial component of trial design. Recent developments in using real-time data to optimize clinical trial data improve efficiency and reduce costs. This paper explores the potential of utilizing Shiny dashboards to optimize clinical trial design through real-time sample size calculation and enrollment projection. The dashboard will integrate the clinical trial database and provide users with real-time information on the expected number of participants and the required sample size. The ability to make more informed decisions using this tool can lead to a shorter overall timeline for completing the clinical trial. Furthermore, we discuss the scope of advanced interactive visualization of trial data, taking inputs such as the primary outcome measure, effect size, and expected dropout rate.

INTRODUCTION

Clinical trials are essential for evaluating and advancing medical treatments, medications, and interventions for humans. It ensures the safety and effectiveness of healthcare products and treatments before they are accessible to the public. For yielding a reliable result, sample size determination is an essential statistical consideration that is decisive for every study. Accurate enrollment projection is another prominent aspect that helps to ensure the trial is conducted efficiently and within the planned timeline. Incorporating real-time data and adaptive approaches for estimating these parameters provides benefits such as improved resource allocation, budget management, and quicker decision-making.

Clinical trial optimization involves an organized approach to enhance the efficiency and effectiveness of the trials. Shiny is an R package that enables the creation of interactive web applications for data visualization and analysis, through which we can explore the possibilities for optimizing clinical trials. In this paper, we present the idea of using a shiny dashboard that estimates the adjusted sample size and predicts the enrollment projection by taking real-time study inputs such as dropout rate, enrollment rate, etc. The dashboard will enable users to find reliable estimates of adjusted sample size, which is pivotal in optimizing the study design. The enrollment projection measures enrollment duration, and enrollment in a selected timeframe, which will enhance the overall pace of the study.

Advanced interactive visualization tools play a crucial role in harnessing data to make informed decisions and streamline the trial process, offering real-time insights into various aspects of the trial. This paper also depicts the scope for such an advanced visualization aspect in R shiny by taking inputs such as the primary outcome measures, effect size, and expected dropout rate into account.

APPLICATION LAYOUT

The OptimizeR application contains two modules, Sample Size Calculator and Enrollment Projection. The Sample Size Calculator defines the sample size and Enrollment Projection predicts the enrollment at the initial phase of the study. ***Figure 1.0*** represents the landing page of the application where the user can enter their credentials and log in to the shiny dashboard application.

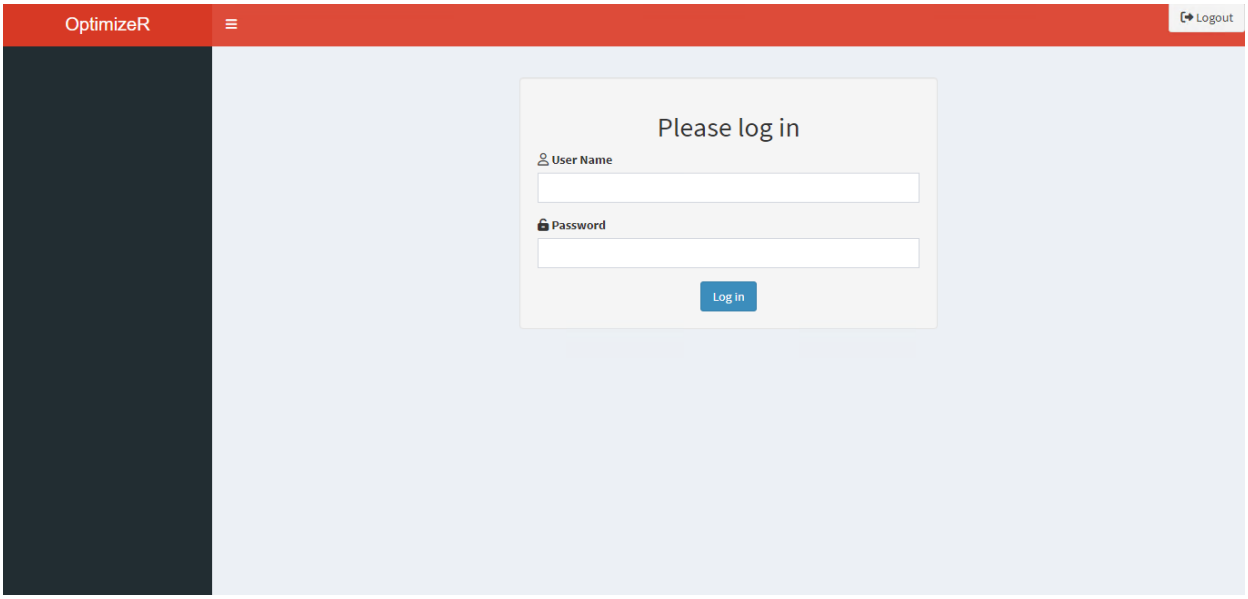

***Figure 1.0: Landing page of the application*.**

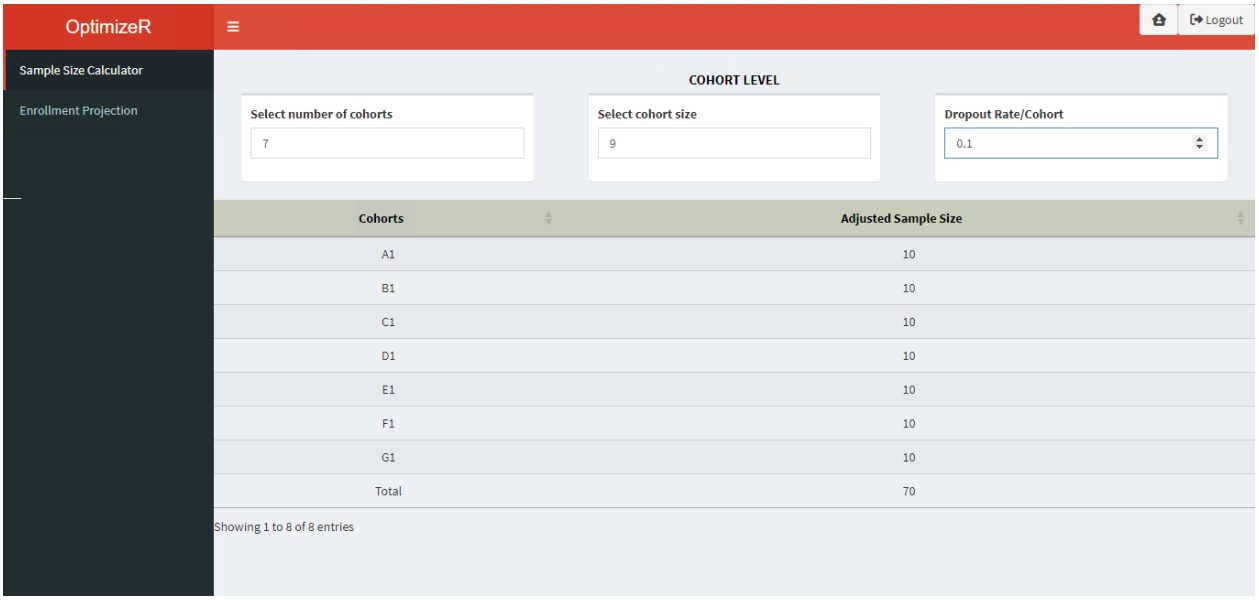

Figure 2.0: Sample size calculator

After logging into the application, both modules will be available in the left sidebar menu, as shown in ***Figure 2.0***. The Sample Size Calculator module will auto-select once logged in. The user needs to provide inputs such as the number of cohorts, cohort size, and dropout rate per cohort for the study. Then, as shown in ***Figure 2.0***, the adjusted sample size is calculated for a given dropout rate for each cohort based on the user's input. The final cohort size along with the total count is displayed in the data table.

Adjusted Sample Size Calculation is based on the following method.

$$N = n/(1-d)$$

Where, N = Number of subjects to be enrolled

n = Calculated sample size using power and effect sizes

d = Dropout rate

In ***Figure 2.1***, the enrollment projection tab is selected. This tab helps the user to compute the enrollment duration and the number of enrollments that can happen in a selected time frame. The enrolment duration is computed based on the enrolment rate, total number of sites, number of initial sites, number of sites active per month, and sample size.

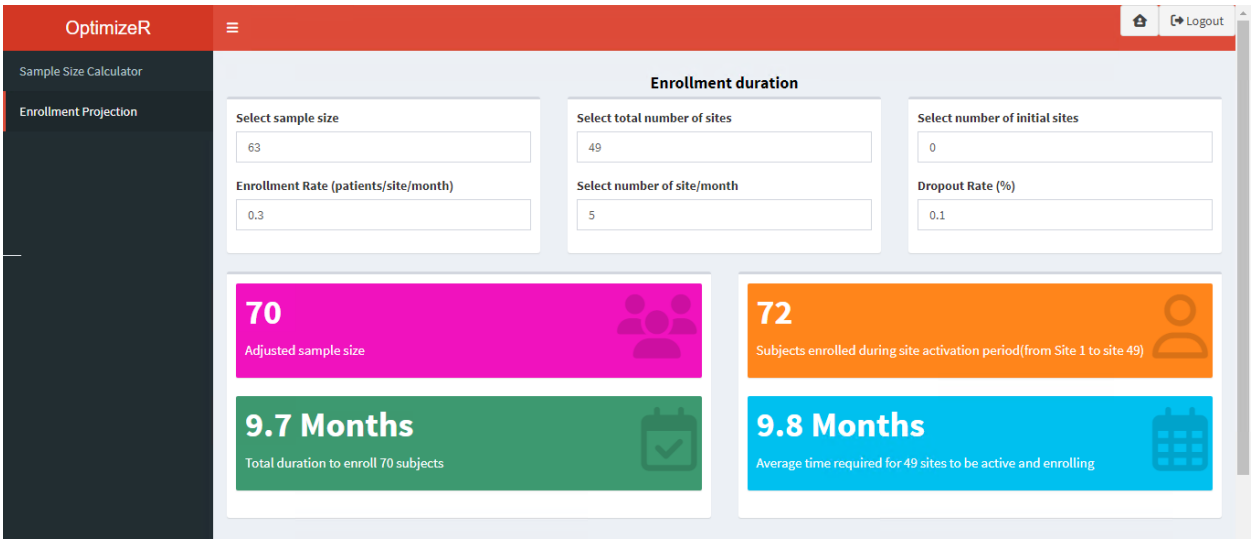

Figure 2.1 Enrollment Duration

The enrollment projection tab computes the adjusted sample size, total duration to enroll the subjects, the average time required for all sites to be active and enrolling, and the number of subjects that can be enrolled during the site activation period based on the enrollment rate (patient/sites/month). The site activation period is the amount of time it takes for all sites to be active and enroll. Enrollment throughout the site activation phase is also contingent on how many sites are active each month. Here, the total enrollment duration is the number of months required to enroll a specific number of subjects at a fixed enrollment rate and the number of sites active per month.

The tab also includes two calendar date inputs to provide the enrollment start date and reference date as shown in ***Figure 2.2.***

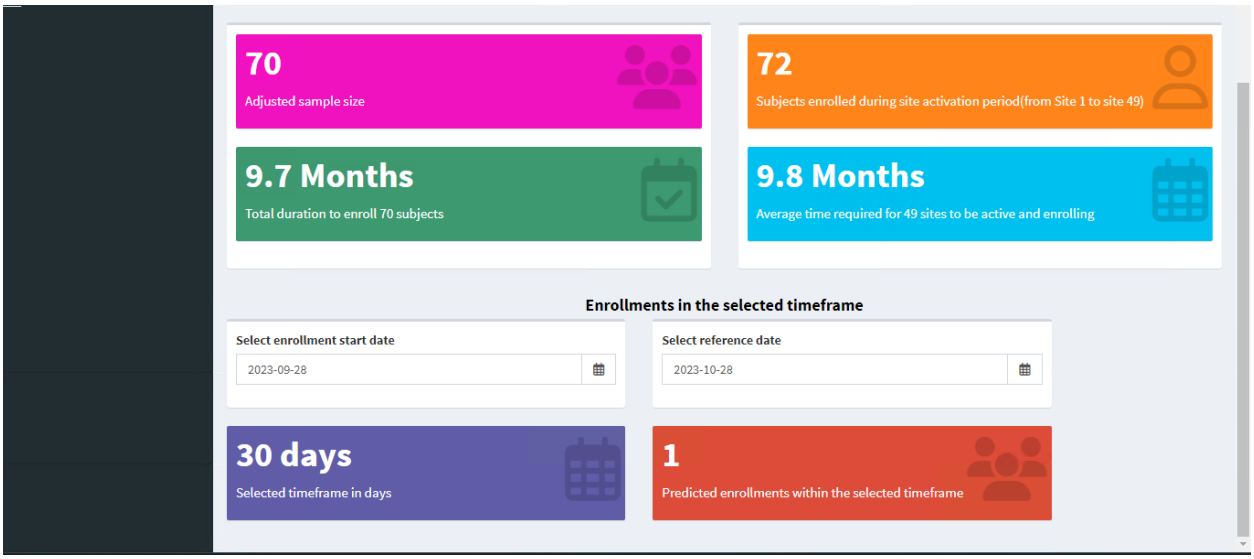

Figure 2.2 Enrollment in the selected timeframe

Predicted enrollments indicate the number of subjects that can be enrolled during the specified time frame, where the timeframe is the number of days between the enrolment start date and the reference date. The predicted enrollments are capped in such a way that they do not exceed the total number of subjects to be enrolled.

SCOPE OF ADVANCEMENT

Clinical trials generate vast amounts of data that are crucial for assessing treatment efficacy, safety, and overall trial progress. Advanced interactive visualization tools play a pivotal role in harnessing this data to make informed decisions and streamline the trial process. Such tools can offer a dynamic and user-friendly interface for stakeholders involved in clinical trials. In this paper, we discuss the scope of such an advanced interactive visualization using the shiny application. Considering trial inputs such as the primary outcome measure, effect size, and expected dropout rate into account, an interactive dashboard can provide real-time insights into various aspects of the trial.

For instance, an interactive dashboard that can display recruitment progress can help identify enrollment rates and potential recruitment challenges. Through such a dashboard, the stakeholders can establish enrollment goals and monitor how recruitment stacks up against expectations. Also, an interactive visualization of dropout rates over time through a dashboard allows trial managers to observe the efficacy of patient retention methods. By identifying trends in dropout rates, interventions can be implemented to improve patient engagement and reduce attrition. It is also possible through a dashboard to conduct treatment response tracking by displaying clinical outcomes, biomarker data, or patient-reported outcomes, through which a researcher can monitor trends and make timely adjustments based on treatment efficacy. Real-time safety data visualization also lies within the bounds of possibility, which can help assess the severity and frequency of adverse events and compare them across treatment arms.

Using Shiny, we can also develop an advanced visualization tool cum dashboard that can take key parameters of the trial into account and dynamically visualize various trial insights. Determination of the sample size in a trial is often based on the expected effect size of the primary outcome measure. As an advanced application of the dashboard discussed in this paper, it is feasible to update the same by incorporating primary outcome measures that can calculate sample size requirements specific to the trial's primary endpoint. This can ensure that the trial has sufficient statistical power to detect meaningful differences. Also, interactive visualization can allow users to input various effect sizes to assess their impact on sample size requirements. This flexibility enables trial designers to explore different scenarios and their consequences.

Interactive visualization tools can go beyond merely displaying data; they can provide real-time decision support by integrating the trial inputs. Users can conduct scenario analysis by adjusting the input parameters which allows for a comprehensive analysis of how these factors influence sample size and enrollment projections. Furthermore, it enables risk mitigation such as say, for instance, if enrollment is lagging projections, the tool can recommend strategies to enhance recruitment or extend the trial period. To cut the long story short by integrating sample size calculations and enrollment projections with actual data, such a visualization tool can assist in optimizing resource allocation.

CONCLUSION

The development of the Shiny application for optimizing clinical trial design using a sample size calculator and enrollment projection can be considered a significant advancement in the field of clinical trial data analysis. This application enables statisticians or clinicians to make informed decisions about study design, resource allocation, and project timelines by utilizing the capabilities of the Shiny framework. This application simplifies the process of computing the sample size for each cohort and estimates how long it will take to enroll the subjects. As we look to the future, the scope of evolving these applications is not limited. With Shiny, one can develop applications that can provide real-time insights into different aspects of trial adapting to evolving trial conditions, exploring different scenarios, and making real-time data-driven decisions. Thus, contributing to more efficient, cost-effective, and successful trials that can benefit both patients and the researchers.

REFERENCES

1. R Shiny, https://shiny.posit.co/r/getstarted/shiny-basics/lesson1/index.html
2. Shiny for R Gallery, https://shiny.posit.co/r/gallery/
3. https://www.appliedclinicaltrialsonline.com/view/improving-clinical-trial-enrollment-forecasts-using-sorm

ACKNOWLEDGMENTS

We gratefully acknowledge the support and input from Roshan Stanly (Manager – Clinical Data Analytics & Oncology, Genpro, Now part of Catalyst Clinical Research) and Denny Sebastian (Data Analyst II, Genpro, Now part of Catalyst Clinical Research).

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Author Name	: Dony Sabu
Company	: Genpro, Now part of Catalyst Clinical Research
Address	: Second Floor, Nila Building Technopark Campus
City / Postcode	: Thiruvananthapuram, Kerala – 695581
Work Phone	: +914717198600
Email	: dony.sabu@catalystcr.com
Web	: catalystcr.com

Co-Author Name	: Sahalath K P
Company	: Genpro, Now part of Catalyst Clinical Research
Address	: Second Floor, Nila Building Technopark Campus
City / Postcode	: Thiruvananthapuram, Kerala – 695581
Work Phone	: +914717198600
Email	: sahalath.kp@catalystcr.com
Web	: catalystcr.com

Co-Author Name	: Vignesh V Gopal
Company	: Genpro, Now part of Catalyst Clinical Research
Address	: Second Floor, Nila Building Technopark Campus
City / Postcode	: Thiruvananthapuram, Kerala – 695581
Work Phone	: +914717198600
Email	: vignesh.gopal@catalystcr.com
Web	: catalystcr.com