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Applying Risk Based Approach to Portfolio Management Chandi Kodthiwada, Comprehend Systems, Boston, US

ABSTRACT

With the recent recommendations and formal guidelines from regulatory bodies and a matured KRI library from Transclerate for Risk based approaches to Trial Monitoring, there has been a rise in development and application of Risk based approach to Trial Monitoring.

I present an evidence-based application of how we have broadened a risk-based approach to manage a portfolio of studies and in some cases proactively identify risk at a Portfolio, Study, Region, Investigator and Site levels

Some of the nuances we will go through the paper will include:

While discussing specifics on technology and how one could build and implement such a system, we will go through some business process one must go through to enable a system of this capability at scale:

1. Can we build a one size fits all risk model for any sponsor or therapeutic area?
2. Will this model need to be configurable? (If so, at which level?)
3. As a bonus, we will also look at how one could setup Risk based Performance alerts without having to rely on hard-coded thresholds

Introduction

I am going to start with a controversial take on how Programming or BI system-driven analytics has always underserved human interest in learning about patterns, trends or events of interest. The reason I believe this is not because I believe we have uncovered the fullest value of software driven Insights & workflows but because we have not fully developed a workflow on how humans typically would like to be informed about information. In my career of over a decade, I can argue the case for "we got our information delivery system (read: Dashboards) as a concept wrong from the early days of analytics"

To give you a simple example: For a typical question such as "How is the study doing?" - what we have been able to answer with is "here are the dashboards about Enrollment, Budgets and a handful other status-dashboards" and in most cases, we have left out the interpretation of encoded data signals to the human ("User")

In search of a better solution, what I have been able to do is look at other niche applications of better information delivery. Some of the ideas I have looked at included:

1. How eCommerce retailers such as Amazon, Nordstrom keep their customers informed about order, delivery and follow-up after delivery in simple, bite-sized information-based push alerts.
2. How financial industry and typical stock trading platforms such as Robinhood use a simplified Risk indicator to inform a rookie stock trader such as myself

What I have been able to conclude from my observations above:

1. I wasn't asked to look at an order status page and keep refreshing it to understand how my online orders were processed or when my merchandise would arrive (Although I could have if I wanted to!) instead they

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took an event-driven information delivery (in most cases a mobile push notification) that kept me informed about the process and when to expect within a 2-hour window!

2. Drawing similar conclusions from the stock trading experience, when I had built up a “Watchlist” (a potential list of companies I wanted to invest in.) The trading platform would keep an eye out for “interesting events” such as a drop or raise in the stock price by a certain percentage that would draw me to act/invest.

My overall observation is Event-driven analytics combined with a Smart ability to understand and comprehend “an event of interest” does a much better job of catering to the human interest about learning patterns, trends or “events of interest”.

Thankfully Event-driven Analytics has been around in the Analytics Industry for a while and current availability and cost of maintaining such infrastructure make the first half of this puzzle relatively easy. The second half (and the more relevant part to this audience) of the puzzle to applying similar concepts to Clinical Trial Industry was how to go about building a “Smart ability to understand and comprehend an event of interest”?

Applying Risk Based Approaches to Portfolio Management or Clinical Trial Operations:

In my search for documented processes of “Smart ability to identify Events of Interest”, I didn’t have to look farther than Transcelerate’s recommendations for Risk based Monitoring.

What I learned was the same way we can learn about the need for an On-site Trial Monitor visit, we can keep Rank/Score Performance, Milestone, Quality & Compliance and Risk aspects of Studies, Sites, Countries and/or Regions and have an algorithm-driven Risk Model at a Portfolio or a Drug Program level.

I have identified various risk elements that contribute to the above categories as below (not-exhaustive):

1. Performance
 1. Subject Enrollment
 2. Site Activation
 3. Budget Management
 4. Completed Subjects
2. Quality & Compliance:
 1. Training Completion (GCP, Study/Protocol etc.)
 2. Essential Document completion
 3. Trial Monitoring Visits
3. Risks:
 1. Time to Enter Complete, Verify & Lock eCRFs
 2. Protocol Deviations
 3. Volume of Adverse Events (or SAEs)
4. Timelines
 1. Milestones: On-time completion and documentation of Milestones at both Study & Site level
 2. Cycle times for Monitoring Visit Reports
 3. Cycle times to respond & close Queries

Classification of Risk:

An algorithm such as below enables a configurable risk model per Study, Site, Country and/or Region:

$$\text{Overall Risk at Study} = \sum_{i=1}^n (\text{Weight } i * \text{Risk Element } i) / n$$

The above formula creates a Total Risk Score at a Study which could further be categorized into simpler buckets such as low/medium/high or Red/Amber/Green at the Study level.

The same concept could be applied to learn about any entity involved in a Study as long as the metrics are tracked or data granularity allows for aggregation of Risk Elements at such level: For example if Performance & Timelines are collected at a Site level = it would enable us to measure Risk thereby create a “smart ability to identify events of interests” at Site, Country and/or Region.

The above formula allows for multiple ways to configure a risk model to account for variability each Sponsor, Study, Site, Region and/or Country bring to the Study:

1. To accommodate various risk models: The weighted averages for Risk elements allow for configuring a specific behavior as sensitive/critical, average or low value risk behavior
2. Risk Appetite may also change based on Phase, Therapeutic Area or Type of Study: So, the eventual classification of an Entity (Portfolio/Study/Site etc.) is totally up to another configurable classification

Case

When (Overall Risk Score at a Study) > X then “Red”

When (Overall Risk Score at a Study) > Y and (Overall Risk Score at a Study) <= X then “Amber”

Else “Green”

Conclusion

The above algorithm is rudimentary and can cater to a much complex, much more configurable Risk Modeling and can enable a smarter way to identify a potential event of interest.

Some capabilities to consider:

1. A seamless centralized way to aggregate data from various clinical trial sources such as EDC, CTMS, Payments, Project Management systems
2. An event-driven analytics capability that can alert and inform an end User
3. Provide a workflow for collaboration of multiple functional roles post insight-detection

A platform with capabilities listed above can enable an entirely new way of informing users, enabling proactivity in monitoring, preempting certain Insights thereby bringing best of both worlds of Risk Management & Event driven Insight delivery to help enable a paradigm shift to managing Portfolios.

REFERENCES

1. Transclerate Risk Based Monitoring: <https://www.transcleratebiopharmainc.com/initiatives/risk-based-monitoring/>

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CONTACT INFORMATION

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

Chandi Kodthiwada
Comprehend Systems
Boston
chandi@kodthiwada.com
<http://kodthiwada.com/chandi>
twitter: @_chandi

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