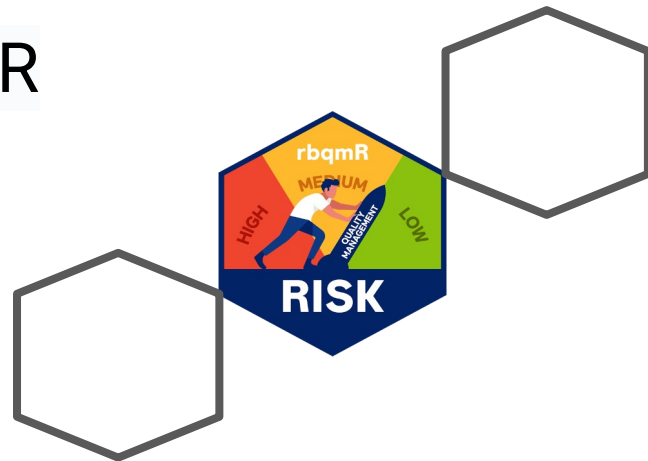


AR05

R you ready to join the RBQM revolution

Introducing rbqmR



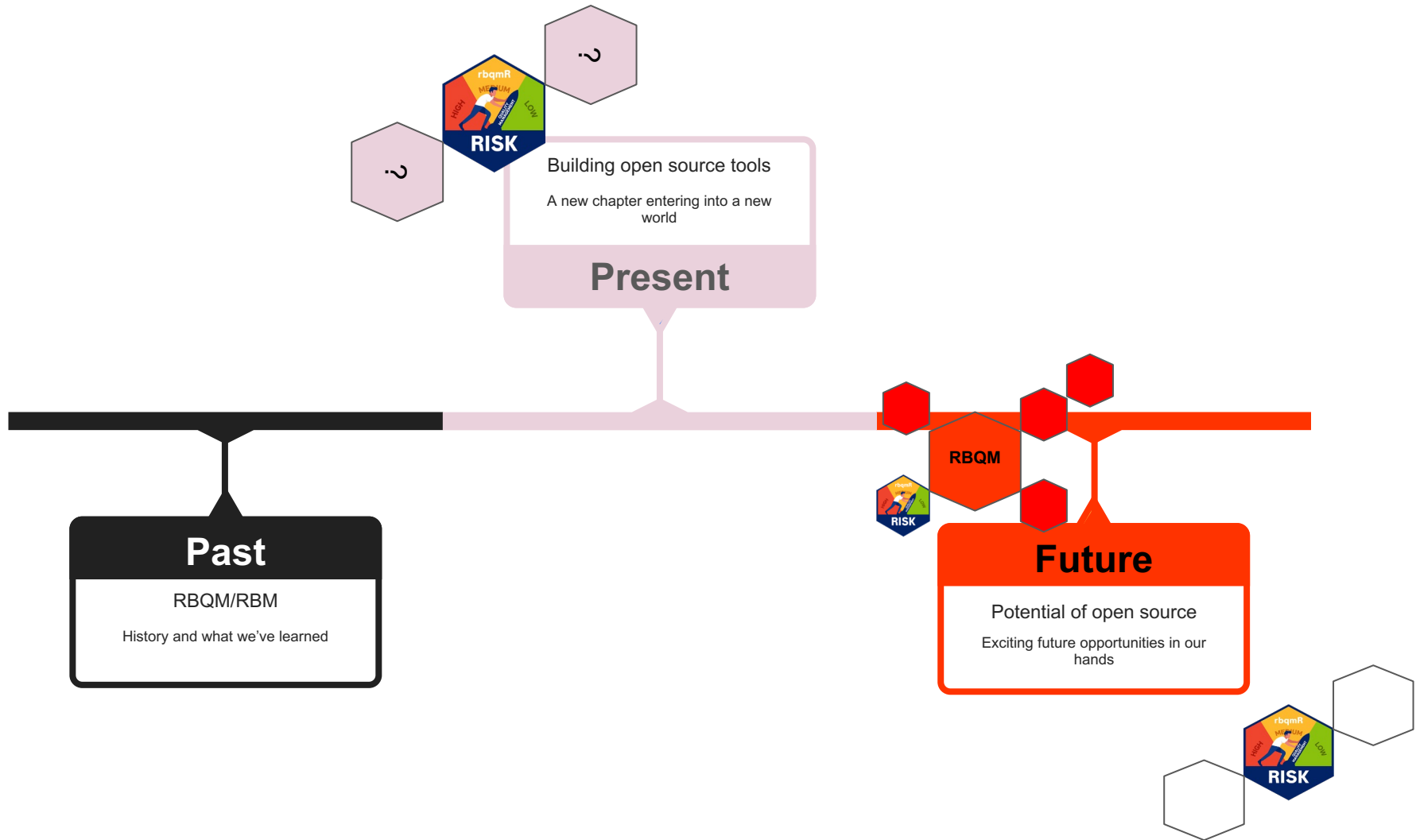


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It began with ICH GCP...



The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) requirements for data collection and review, briefly summarised in the following points:

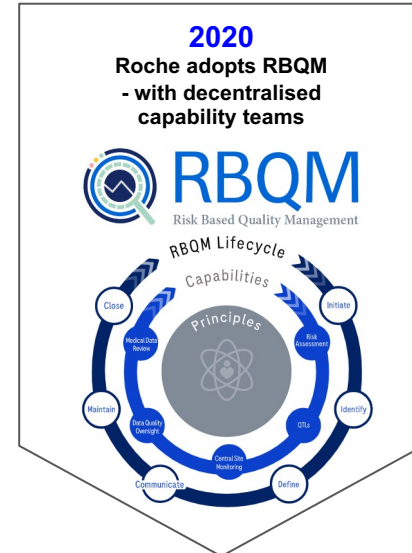
- [E6 R2](#): “The methods used to assure and control the quality of the trial should be proportionate to the risks inherent in the trial and the importance of the information collected.”
- [E6 R3](#): “The sponsor should adopt a proportionate and risk-based approach to quality management... identifying those factors that are likely to have a meaningful impact on participant’s rights, safety and well-being and the reliability of the results”
- [E8 R1](#): “Having a risk-based approach to quality management is an ICH recommendation advocated by Regulatory Bodies. Clinical trials should follow a Quality by Design approach



And so came interpretation and implementation...

2016
E6 R2

2016
Roche adopts
Statistical
Monitoring



Past

RBQM/RBM

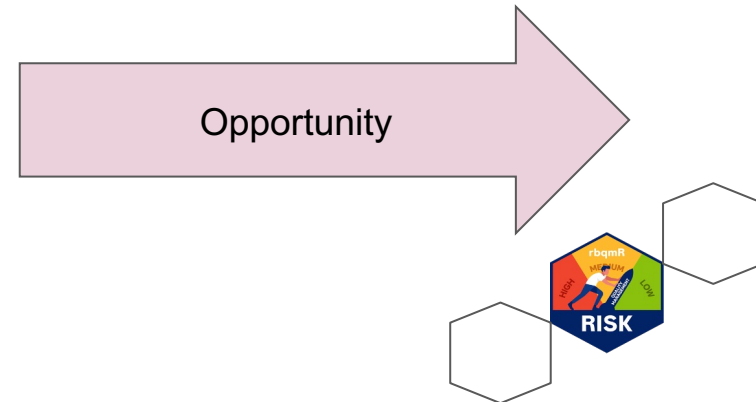
History and what we've learned

Challenging adoption and change management



Tools, Methodologies, approaches
developed successfully (but in isolation)

Tools tend to be a “**black box**”



What are QTLs?

A level, threshold, or value associated with a parameter which is critical to quality. QTLs are set for risks identified at the trial level. A deviation from a threshold during the conduct of the trial may indicate a systematic issue that could impact participants' safety or reliability of trial results (Bhagat et al, 2021)

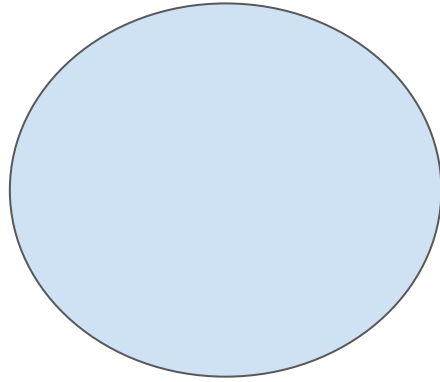
At Roche, we've identified some common risks across trials and developed methodology to monitor them, the risks being; Adverse Events; Serious Adverse Events; Baseline Protocol Deviations; Ongoing Protocol Deviations

Ideally we want to detect, mitigate and learn from any breaches, improve patient safety, see more cost effectiveness in running trials and importantly for data science, improve data quality and thus the reliability of trial results.

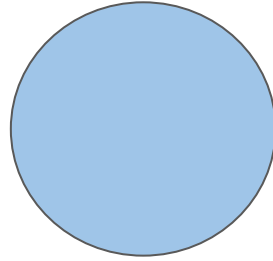


Open Source, InnerSource, Or just develop something that works...

(What's the difference between the strategies?)



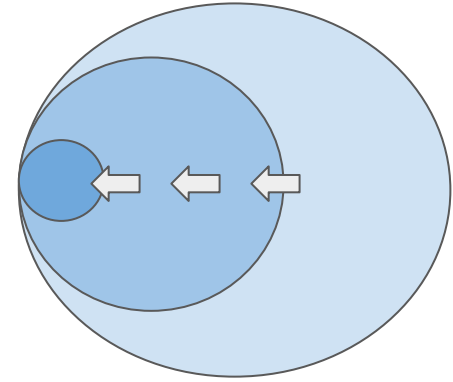
One time programming



InnerSource



Open Source



Current in-house solution

The most common risks across Roche trials were identified and some methodology developed in order to monitor them, for specific event types:

- the rate of adverse events (AEs)
- the rate of serious adverse events (SAEs)
- proportion of patients with baseline protocol deviations (BPD)
- the rate of ongoing protocol deviations (OPD).

Bayesian methods were used, with an MCMC (Markov Chain Monte Carlo) poisson model fit to AEs, SAEs and OPD rates and an MCMC binomial model fit to BPD proportions.

Code is rigid and very dependent on data being exact format (SDTM structure)



Introducing rbqmR...

(<https://openpharma.github.io/rbqmR/main/>)



Created and developed by:

John Kirkpatrick (Senior Principal Statistical Scientist), Roche

QTL Capability Owner:

Chris Wells (Principal Clinical Data Specialist/Biostatistician), Roche



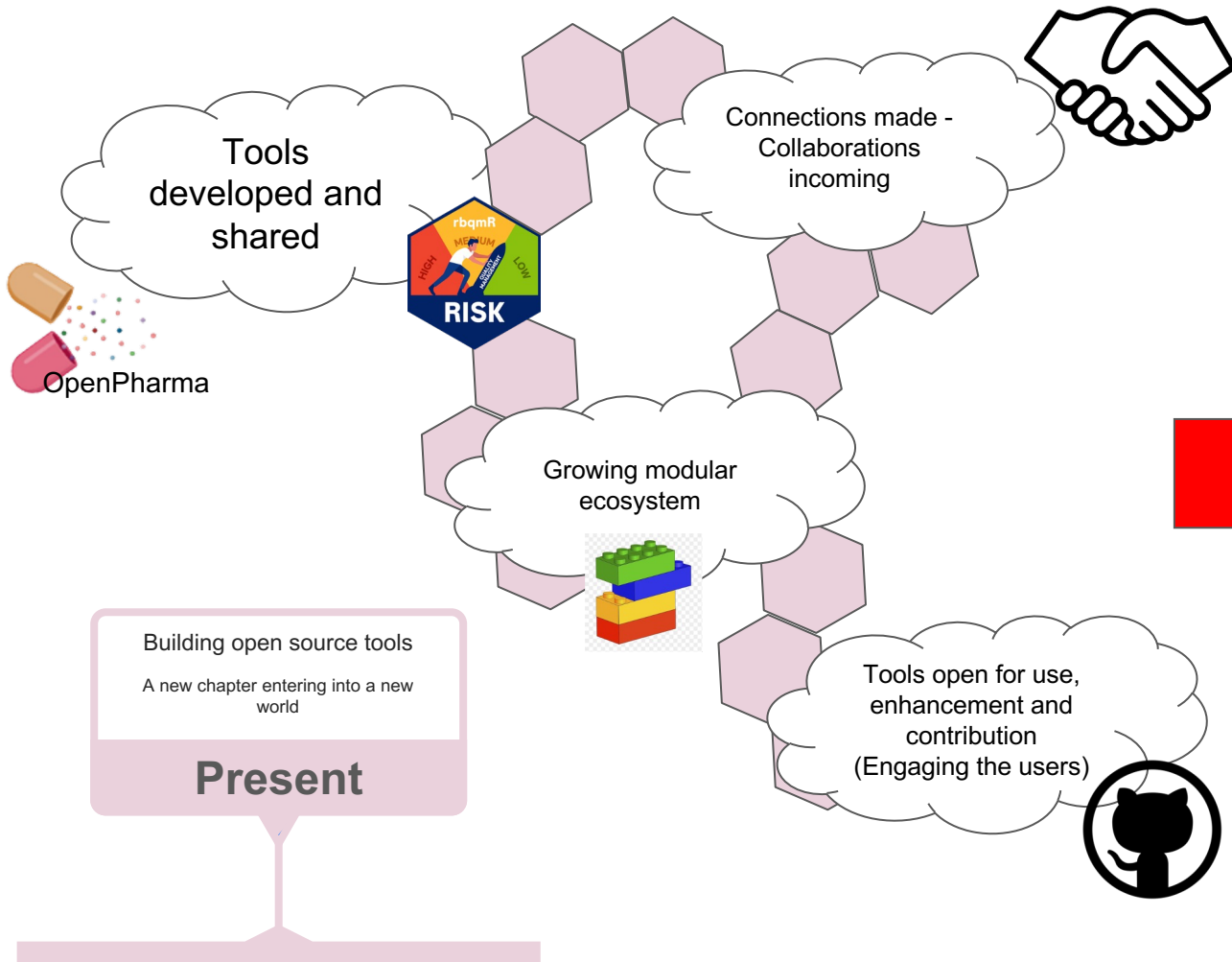
rbqmR Overview

<https://github.com/openpharma/rbqmR>

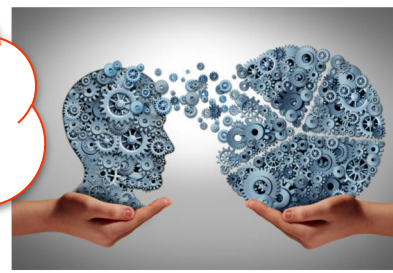
Hosted in OpenPharma, rbqmR takes what was previously implemented internally at Roche but applies it with a broader scope, the idea being that the existing methods can be implemented on data types not yet being monitored

Built with flexibility in mind around tidyverse principals and easier to QC





contribute co-
create
collaborate



Future

Potential of open source
Exciting future opportunities in our
hands

Industry
alignment and
standardization

Reduce
waste, re-use
and recycle



References

Bhagat R, Bojarski L, Chevalier S, Görtz DR, Le Meignen S, Makowski M, Nadolny P, Pillwein M, Suprin M, Turri S. Quality Tolerance Limits: Framework for Successful Implementation in Clinical Development. *Ther Innov Regul Sci*. 2021 Mar;55(2):251-261. doi: 10.1007/s43441-020-00209-0. Epub 2020 Sep 3. PMID: 32885397; PMCID: PMC7864825.

Gilbert, SA. 2020. "Implementing Quality Tolerance Limits at a Large Pharmaceutical Company." PharmaSUG.

