

Quantifying the impact of protocol design on enrollment and dropout rates in breast cancer clinical trials



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Background

- Clinical trial enrollment can fail due to overly complex protocol design
- Procedures that may be logistically challenging or introduce higher risk, can affect trial enrollment and retention

Example scenario: “If I ran my phase 2 breast cancer trial with a protocol including 2 PET Scans, 4 MRIs, 10 blood draws, etc., what would Medidata predict for my enrollment rate?”

Protocol design, such as procedure requirements and frequency, had measurable impact on clinical trial enrollment and retention

Results

% change in Enrollment Rate (N protocols=13)

FEATURE	MEAN	SD	DIRECTION
Symptom and Functional Assessment Questionnaires	-41.1	14.8	▼ negative
Comprehensive Eye Examination and Assessment	-28.7	21.8	▼ negative
Surgical Pathology Examinations	-11.7	19.0	▼ negative
Combined PET Imaging Procedures	-10.7	10.7	▼ negative
Immune checkpoint protein testing	-8.1	9.8	▼ negative
Brief Cardiovascular Exam	+41.8	37.6	▲ positive
Non-invasive Clinical Assessment Scales	+22.8	55.2	▲ positive
Ki-67 (MIB-1) IHC	+16.4	14.3	▲ positive
Respiratory Symptom Assessment Questionnaires	+12.6	6.1	▲ positive
Non-invasive Clinical Assessments	+6.7	8.5	▲ positive

Acknowledgements

We would like to thank all the clinical trial participants and researchers who contributed their generous time and experiences to this research. For any inquiries, please contact: sheila.diamond@3ds.com

% change in Dropout Rate (N protocols=13)

FEATURE	MEAN	SD	DIRECTION
Symptom and Functional Assessment Questionnaires	-55.4	17.3	▲ positive
Bone Density and Imaging Procedures	-35.6	21.2	▲ positive
Patient and Physician Assessment Scales	-23.6	24.2	▲ positive
Monocytes IHC	-23.0	19.3	▲ positive
Vital Signs Monitoring and Physical Examinations	-22.0	30.6	▲ positive
Electrical Activity Monitoring Procedures	+451.9	688.8	▼ negative
Stereotactic Radiosurgery Procedures	+127.4	197.5	▼ negative
Diagnostic Imaging of Bones and Extremities	+60.1	93.2	▼ negative
Follow-Up Physical Exam Only, Routine	+52.7	97.4	▼ negative
Cancer-Specific Quality of Life Questionnaires	+28.1	86.8	▼ negative

Discussion

- These findings provide an opportunity to optimize a protocol by finding a balance between enrollment and retention
- In 13 breast cancer protocols, procedure importance depended on overall content of the protocol, accounting for other aspects of the protocol like phase, other procedures and their frequencies
- Enrollment rate is affected by both screening procedures and overall frequency of clinical activities
- Dropout rate is affected by type of procedure and frequency
- Some procedures vary on how they impact the protocol design, and integrating clinical subject matter expertise can help find a proper balance

Future Directions

Incorporating inclusion/exclusion criteria into the model can further address some barriers to recruitment given their overall effect on enrollment rate

Methods

- Sourced aggregated, anonymized Medidata Clinical Cloud® data from trials conducted between 2010-2023
- 285 breast cancer protocols were used to train a model, to predict enrollment rate and dropout rate
- Input features were clinical procedures and frequency of the procedures as included in the protocol design
- Clinical procedures were grouped into relevant clusters for modeling, e.g. multiple imaging procedures would fall under one general cluster of imaging procedures
- Feature impact was assessed by increasing the frequency of each procedure by 1, holding all other procedures constant and measuring the resulting percentage change in outcome