Medical Device Innovation Consortium project report: Excessive Data Collection in Medical Device Clinical Trials

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This survey identified significant opportunities to reduce clinical trial complexity, data burden, and costs in the clinical trials enterprise for regulated medical devices.

According to these data:

- Studies required an average collection of 998 data points per participant.
- Over half (54.5%) of the study protocols required patient visits beyond the standard of care.
- Nearly 87% of central lab and 73% of adjunct committee costs were over $100,000 per study.

The clinical trial enterprise for medical devices has evolved significantly over the past 20 years as more sophisticated products have been designed and developed. These more sophisticated devices have created the need for more well-defined clinical data to support findings of reasonable safety and effectiveness for market entry. Additionally, clinical data collected in studies has expanded to meet reimbursement and other stakeholder needs, including sponsor research and development, and publications. These growing data requirements have led to an increase in trial costs and time. Clinical trials' growing complexity is inefficient, unsustainable, and may lead to delays in bringing important therapies to patients in need.

While clinical trial burden has been well characterized in the literature, it has mainly relied upon data from pharmaceutical and other non-device studies. The Medical Device Innovation Consortium (MDIC), the first public-private partnership created with the sole objective of advancing the regulatory science around the development and assessment of medical devices, designed a survey to characterize the data burden in medical device clinical trials. These findings will be used to guide further MDIC work in promoting the simplification of clinical trials for regulated medical devices to drive efficiency and maximize potential to more rapidly advance innovation for the benefit of patients and the healthcare system.

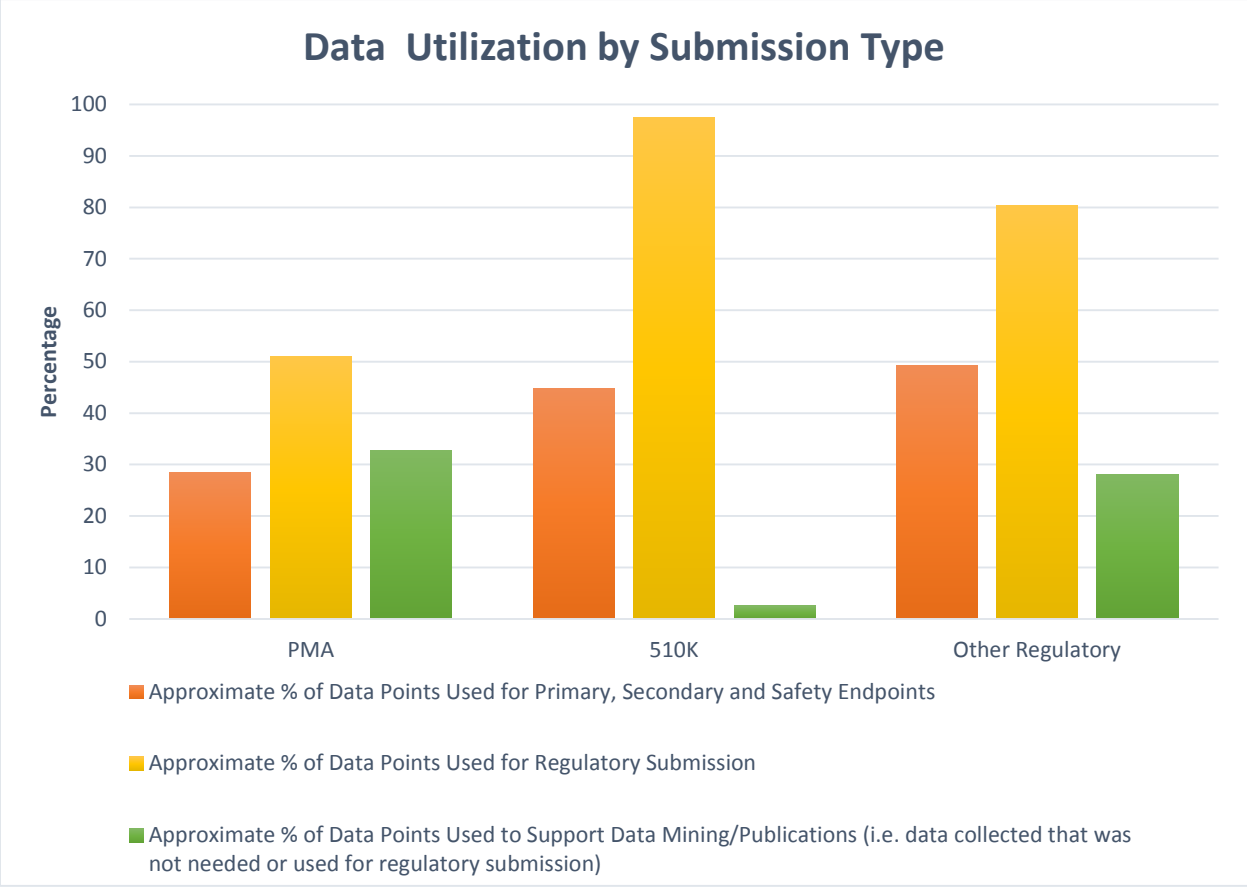
Approximately 30% of data points collected in Pivotal medical device clinical trials do not support core endpoints or regulatory submissions for marketing approval and may be considered to add time, money, and complexity to trials for little regulatory benefit (Table 1 & Figure 1).

- The study case report forms (CRFs) captured an average of 998 data points (range: 50 – 4450) per participant.
- With a mean of only 56.6% of data points being used in submissions, there is significant excess data capture.
- Critically evaluating the costs and benefits of additional data points beyond those to meet core study objectives will mitigate the potential for data scope creep and drive efficiencies in both cost and time.

Table 1: Utilization of Data

	Total Studies	Mean	Median
Number of investigative sites	22	33.7 (± 25.5)	26.5 (2.0, 100.0)
Number of study participants	22	310.3 (±399.6)	172.5 (18.0, 1850)
Number of data points per participant	21	998.1 (±1017)	581.0 (50.0, 4450)
Percent (%) of data points used for core endpoints: (1^o and 2^o efficacy and safety)	21	33.2 (±30.4)	17.0 (4.0, 90.0)
Percent (%) of data points used in regulatory submission for marketing approval	22	56.6 (±37.5)	75.0 (0.0, 100.0)
Percent (%) of data points used for other purposes (data mining/publication)	17	28.9 (±36.7)	10.0 (0.0, 100.0)

Figure 1: Data Utilization by Submission Type



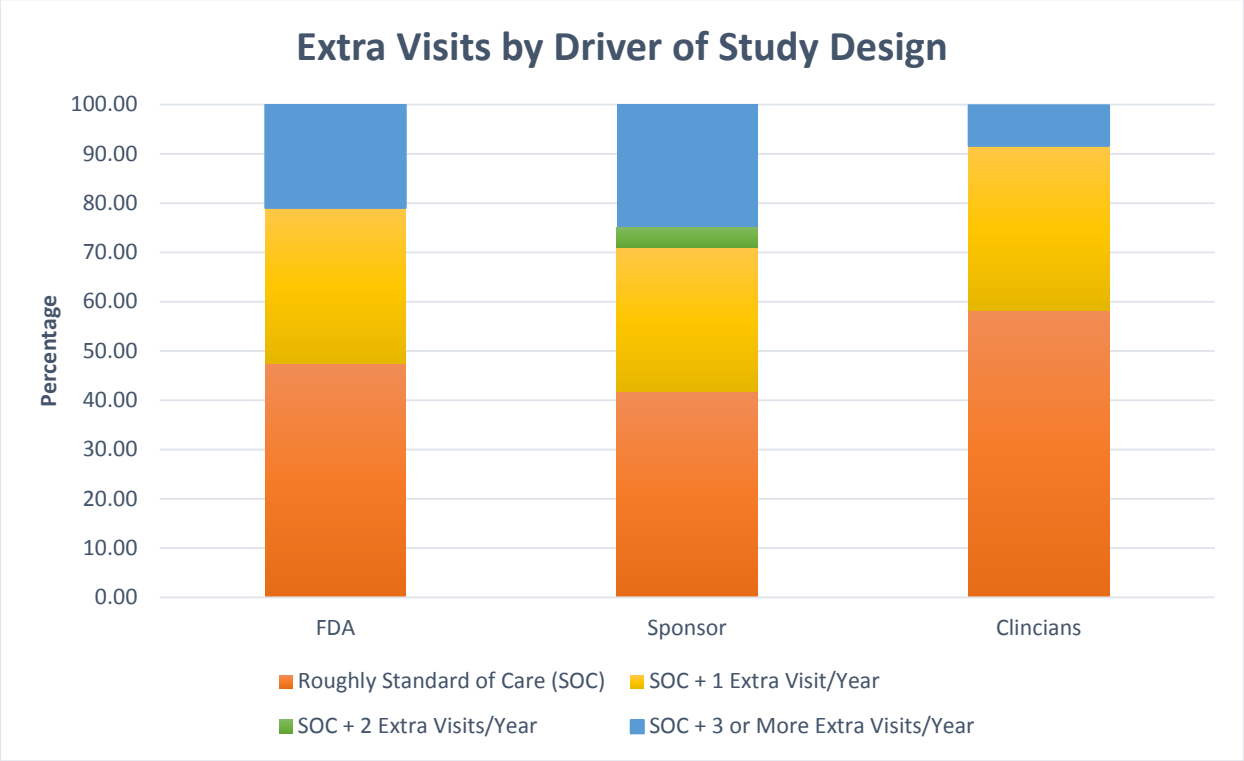
Aligning Pivotal clinical trial visits with standard of care drives efficiency and minimizes clinical site and study participant burden.

- Over half (54.5%) of study protocols required added visits beyond the standard of care (Table 2).
- Aligning study visit schedules with today's standard of care minimizes study costs, decreases burden on patients and research staff, and minimizes potential for missed study visits and associated data collection.
- When physicians are driving the study design there is a trend towards aligning the study visit schedule with standard of care visits (Figure 2).
- Sponsor-driven studies are those most likely to include visits beyond standard of care, with 58.3% of these studies having extra visits.

Table 2: Study Visit Schedule vs. Standard of Care

	Total Studies	**# (%)**
Roughly standard of care (SOC)	22	10 (45.5%)
SOC + 1 extra visit/year	22	7 (31.8%)
SOC + 2 extra visits/year	22	0 (0.0%)
SOC + 3 or more extra visits/year	22	5 (22.7 %)

Figure 2: Study Visit Schedule by Study Design Group



The use of adjunct committees and labs is common and can drive complexity and Pivotal trial costs.

- The majority of respondent trials utilized Central Labs, Clinical Event Committees (CECs), and/or Data Safety Monitoring Boards (DSMBs) (Table 3).
- Committees and core labs are major cost contributors to clinical trials, with the majority of trials utilizing these services having categorized their costs as greater than $100,000 each (Figures 3 & 4).
- Approximately 88% of central lab and 70% of adjunct committee costs were over $100,000 per study.
- Specific objectives and scope of work should be identified for selection and use of central lab or adjunct review committees (e.g., endpoint criteria are subjective; variability exists in local laboratory standards for specific test or procedure; adverse event relationship determination is complex and warrants adjudication to minimize bias).
- Only two of five studies costing less than $3 million used a CEC and/or DSMB. In contrast, 16 of 17 studies costing more than $3 million used a CEC or DSMB (Figure 4). Where CECs or DSMBs are necessary for a clinical trial, sponsors should plan their budgets accordingly.

Table 3: Use of External Central Lab(s) and/or Adjunct Committee(s) in Pivotal Trials

	Total Studies	# (%)
Use of Central Labs	22	18 (81.8%)
Use of Clinical Events Committee (CEC)	22	14 (63.6%)
Use of Data Safety Monitoring Board (DSMB)	22	15 (68.2%)

Figure 3: Count of Lab Costs Organized by Total Pivotal Trial Cost

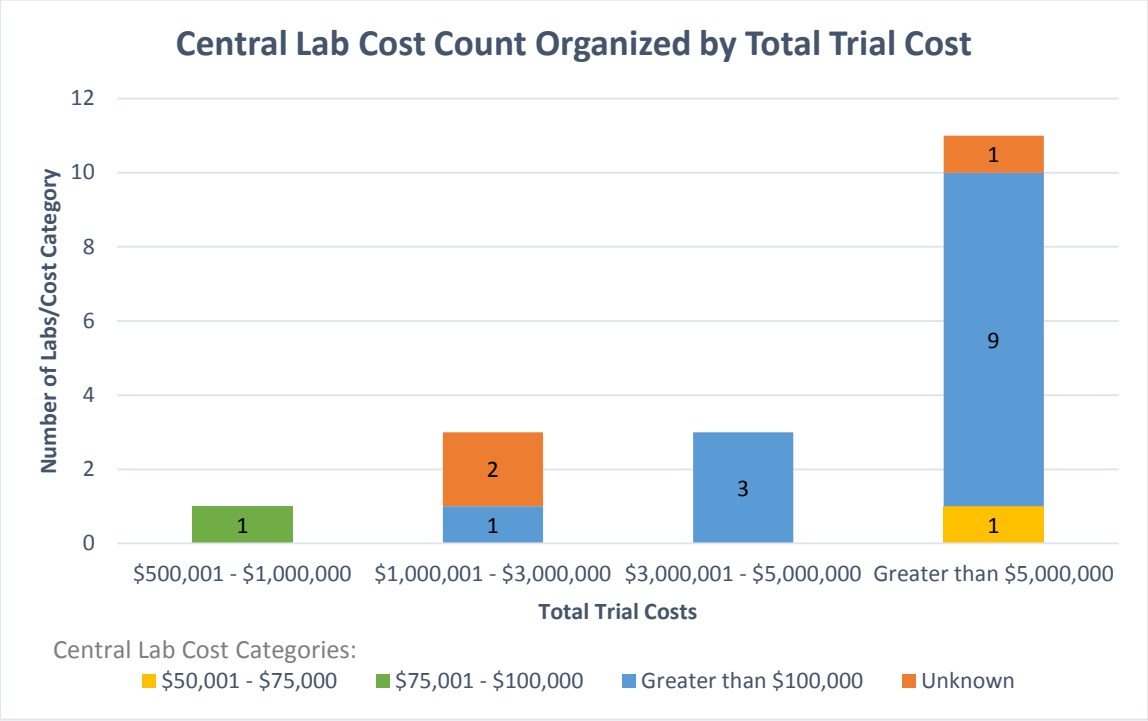
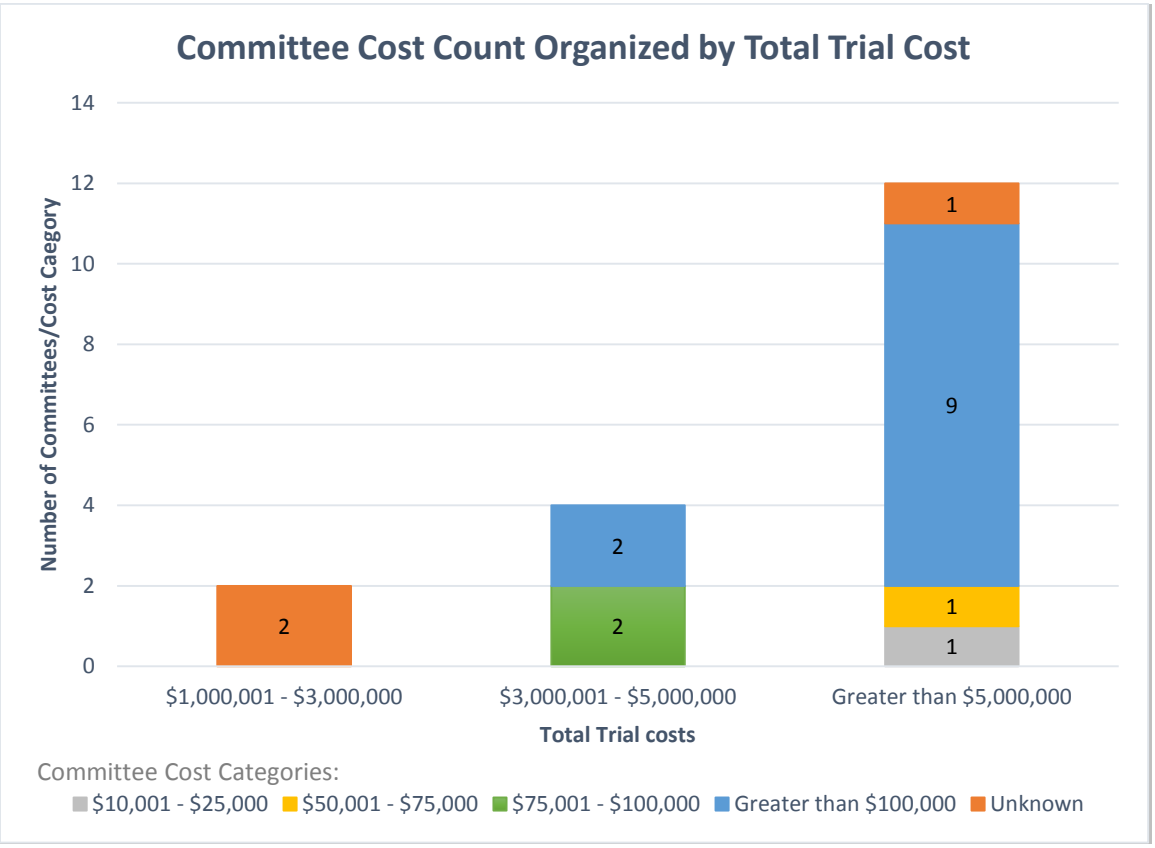


Figure 4: Count of Committee Costs Organized by Total Pivotal Trial Cost



MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM

Overview of the survey

The MDIC survey was conducted between August and November 2014. The web-based electronic survey was sent to a convenience sample of 24 MDIC-member medical device companies with requests to complete the survey for their three most recent clinical trials for products to be marketed in the United States. Survey questions covered study descriptors, amount and types of data collected, data review infrastructure, utilization of data for regulatory submissions and other purposes, and costs of data collection and review. Companies self-reported and self-classified all data on first submission and missing data were not queried.

Responses were received from 50% (12/24) of the companies surveyed, reporting on 22 pivotal clinical studies with enrollments between 2004 and 2014. The majority (71.4%) of the studies were designed and conducted in support of premarket approval (PMA) applications for Class III medical devices. Implantable devices composed the bulk (81%) of the surveyed products, however the sample also included non-implantable devices and diagnostics. While the products represented a broad range of therapeutic areas, approximately half (52.4%) were in cardiology. Forty-five percent of the studies were randomized (55% non-randomized), and 32% of the studies included European sites with < 10% in other geographies (Canada, Asia Pacific, Latin America, or Japan). Of note, 36% (8/22) of the pivotal trials had a planned interim analysis incorporated into the study design.

Funding sources for the companies reporting studies included 40.9% (9/22) public companies, 40.9% (9/22) private companies, and 18.2% (4/22) venture capital funded companies. Total study costs ranged from $100,000 to more than $5 million, with most, 77.3% (17/22) of the studies costing over $3 million.

Limitations

The survey team acknowledges several limitations to consider when interpreting these results. In addition to the limited sampling size (24), focus on members of MDIC, and percentage of survey respondents (50%), MDIC recognizes there are other potentially valid reasons for collecting data in the clinical trial (e.g., reimbursement requirements, marketing messaging). This survey focused on the regulatory needs as the clinical driver to the design and execution of the trials.

Next steps

The survey provides interesting data to use in assessing clinical trial design on a broader level. The MDIC Clinical Trial Innovation and Reform initiative envisions that clinical trial innovation has the potential to improve the safety and effectiveness of products being introduced into the market, reduce clinical trial cycle times and costs, and yield earlier access to beneficial innovative technologies for U.S. patients. While this sample is limited, the data we have gathered are an integral step on development of our Framework for Simplification of Clinical Trials in Regulated Medical Devices.

The main objective of the referenced framework is to advance health and healthcare by bringing important medical innovation forward through a more robust and efficient (cost, time, quality) clinical trial enterprise. The data gathered in this survey will help pave the way for a planned (1) Blueprint for Clinical Trials Simplification, and (2) an associated library of tools. These tools, along with robust engagement between regulators and industry, demonstrate the value of clinical trial innovation and change management to potentially shift the culture of clinical trials to a more efficient model of clinical trial design.

Acknowledgements

MDIC would like to thank the medical device companies who contributed data to the study. We would also like to thank MDIC member NAMSA for their valuable support collecting and analyzing the data.

Definitions

510(k) = "…a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device (21 CFR §807.92(a)(3)) that is not subject to premarket approval"[1].

Class III Medical Devices = ". . . those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury"[2].

Core Study Endpoints = data points that support primary and secondary efficacy, and safety endpoints.

Pivotal clinical study = study designed to support FDA market approval decisions.

PMA (Premarket approval) = ". . . the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices"[3].

1 https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=807.92

2 http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/premarketapprovalpma/

3 http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/premarketapprovalpma/