Query Effectiveness in Light of Risk-based Monitoring (RBM)

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BACKGROUND

Query management is a standard process utilized by Data Management (DM) and Clinical Operations (ClinOps) for data cleaning. The resources and costs associated with query management are not trivial because querying is a long, multi-step process that involves many individuals at the sponsor company, Contract Research Organization (CRO) and investigational sites. Unfortunately, people in the trenches are only aware of the portion of the cost that comes from their individual contribution and are not trained to recognize the total cost associated with a query. This typically results in issuing multitudes of queries that have no impact on the study performance or conclusion, which then inflates the overall cost of studies. In order to reduce costs, can an "effective" query be differentiated from a "non-effective" query?

The Query Effectiveness Ratio (QER) is defined as the ratio of the number of queries leading to change divided by the total number of queries issued. This ratio is a viable metric for assessing the productivity of query management by highlighting the high-value queries that lead to data corrections, as a proportion of the total number of issued queries.

$$\text{Query Effectiveness Ratio (QER)} = \frac{\text{\# of data corrections}}{\text{Total \# of queries}}$$

In an earlier paper, we argued that reduced query effectiveness consumes many resources without notable returns on investment. Thus, we proposed more "intelligent" data management that requires judgement when issuing queries.[1] The suggested process is presented in Figure 1.

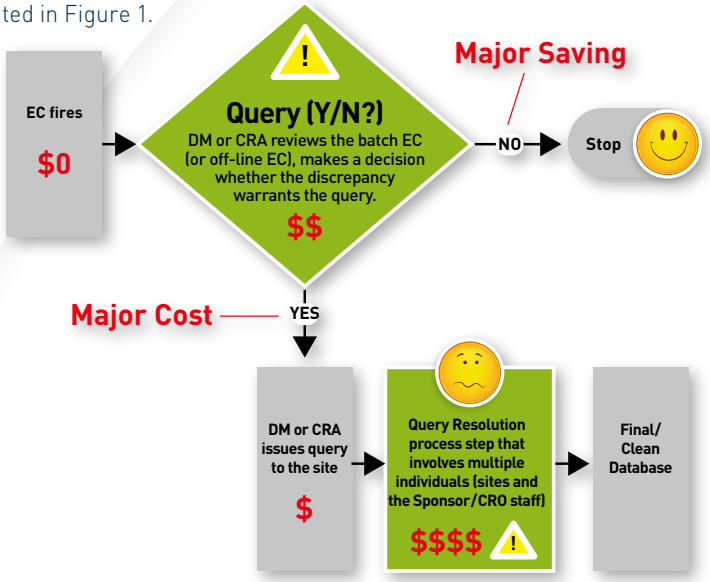

Figure 1. Query Management Process

In this paper, we take the previous discussion a step forward and propose industry-wide targets for query effectiveness metrics that will impact DM and ClinOps.

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EMPIRICAL EVIDENCE

QERs under 50% were observed in EDC studies and published in literature[2, 3, 4]. More specifically, 37% query effectiveness was reported by Mitchel[1], 44.5% was derived from Dillon and Zhao [3] and 38% was estimated by Tantsyura et al.[4]. This indicates that only 40% of queries across the industry lead to data corrections and 60% of queries result in no data changes. In a recent registrational Phase 3 Direct Data Entry study, we observed a slightly higher average QER 56%. The table below presents the detailed summary (by Form) of the Forms Entered, Queries Issued, Queries/Form (Ratio), Data Modifications and Query Effectiveness Ratio (queries leading to change %), per Form for the referenced study.

Table 1. Query Effectiveness Ratio (QER) (Color-coding: High QER, →75-100% QER are color coded green, medium QER, →20-75%, are color coded yellow and low QER, ←=20% are color-coded orange; NOTE: 5 forms had no queries associated with them; they are listed at the bottom the table and greyed out)

CRF	Forms Entered	Queries Issued	Queries / Form	# Resulted in Data Modification	QER (% of queries Leading to Change)
Migraine-Specific Quality of Life Questionnaire	774	15	1.9%	15	100.0%
Adverse Event Changes	97	1	1.0%	1	100.0%
Tobacco Use	903	4	0.4%	4	100.0%
Phone Contact	1259	5	0.4%	5	100.0%
HIT-6	774	2	0.3%	2	100.0%
Migraine Medical History	757	1	0.1%	1	100.0%
Self-Harm Supplement	4121	60	1.5%	57	95.0%
C-SSRS – Baseline/Screening Version & Since Last Visit	4128	54	1.3%	51	94.4%
Caffeine Use	900	9	1.0%	8	88.9%
Alcohol Use	903	12	1.3%	10	83.3%
Concomitant Medication	6930	365	5.3%	294	80.5%
Adverse Event	857	46	5.4%	31	67.4%
Screen Failure	500	15	3.0%	10	66.7%
Demographics	934	34	3.6%	22	64.7%
Subject Status	4248	60	1.4%	36	60.0%
Sitting Vital Signs	10122	99	1.0%	55	55.6%
Other Medical History	5397	128	2.4%	65	50.8%
Drug Administration	1192	40	3.4%	12	30.0%
Body Measurements	1384	45	3.3%	12	26.7%
Date of Visit	4298	372	8.7%	85	22.8%
Prior Migraine Prevention Therapy (Prophylaxis)	1016	27	2.7%	6	22.2%
Subject Summary Study Period III & Study Period IV	462	1	0.2%	0	0.0%
Subject Registration	936	2	0.2%	0	0.0%
Allergic / Hypersensitivity Reaction Follow-Up	6	0	0.0%	0	N/A
Follow-Up - Study Treatment Administration	410	0	0.0%	0	N/A
Nicotine Use	900	0	0.0%	0	N/A
Post-Study Follow-Up	63	0	0.0%	0	N/A
Self-Harm Follow-Up	25	0	0.0%	0	N/A
TOTAL or Average	**38207**	**1397**	**3.7%**	**782**	**56.0%**

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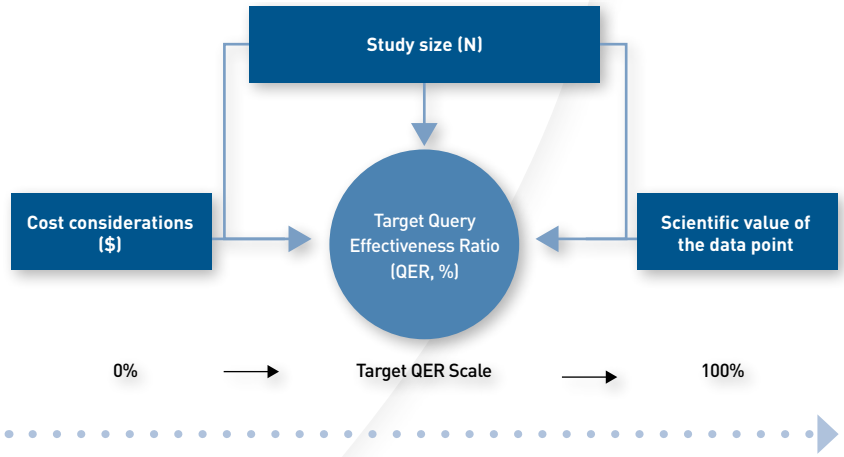
DISCUSSION

As Table 1 illustrates, some case report forms (color coded green) are characterized by above average QERs. For example, the Tobacco Use form had 4 queries issued and all 4 forms were subsequently modified (QER = 100%). Some other forms (color coded yellow) however are characterized by below "study average" QERs. As an example, the Body Measurements form was queried 45 times, which led to only 12 forms being modified and resulted in a QER of 26.7%. It can be hypothesized that the observed variability is partially due to the lack of monitoring of such a metric and absence of any reference or "target" QER that would prompt the study team towards a more intelligent and mindful approach to query issuance[1].

Question 1 - What should such a metric be? Should one expect that every query leads to a data correction, so QER = 100%? Such an idealistic expectation would mean that a query would not be issued unless a study team member was sure of the positive outcome of the query (necessary data correction) regardless of any doubt, suspicion and uncertainty surrounding each data discrepancy. Obviously, the QER = 100% ideal is unattainable given the amount of available information for the query issuer. These uncertainties cannot be completely removed from consideration, but can be handled via a risk-based or "probabilistic" approach.

Figure 2: QER Determining Considerations



Question 2 - Can a standard be established in the presence of so many moving parts? Is establishing such a standard even feasible with different scenarios, study types and so much uncertainty in general? We would like to propose leveraging a risk-based approach in establishing a Target QER. Since the scientific value of each data point is determined by its contribution to the primary or secondary study objectives, we suggest using a 3-tiered approach which is represented by the "Tier" column in Table 2 below. Study size is the second most important consideration in determining the Target QER since the diminishing impact of a study's size has been observed and reported. Our earlier works "demonstrated that data cleaning effectiveness is inversely related to study size and had an inferior impact on study results."[4, 5, 6] That is why we suggest considering the risks and QERs for small and large studies separately (as shown in Table 2). The increasing value and higher data quality (DQ) risk of each data point is associated with the higher "Tier" and smaller study size as demonstrated by the blue arrows. A higher DQ risk will justify the larger number of queries, lower QER and the higher cost associated with them as summarized in the Table 2.

1 The other contributing factor may include the lack of clear understanding of the case report form (CRF) that could be caused by unclear protocol, confusing CRF completion instructions or by insufficient training.

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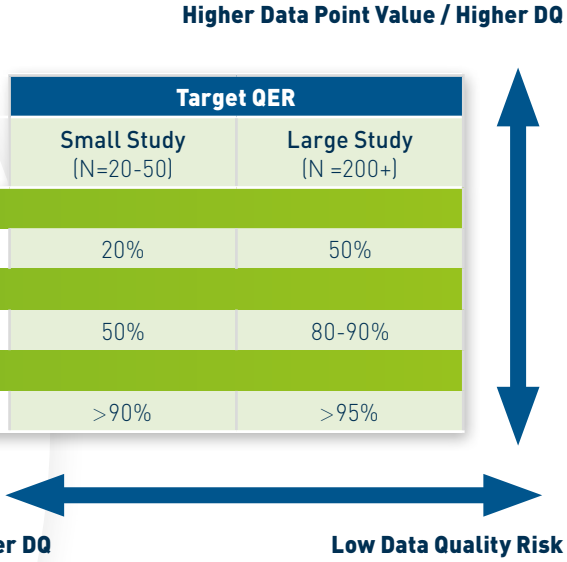
Table 2. Target Query Effectiveness

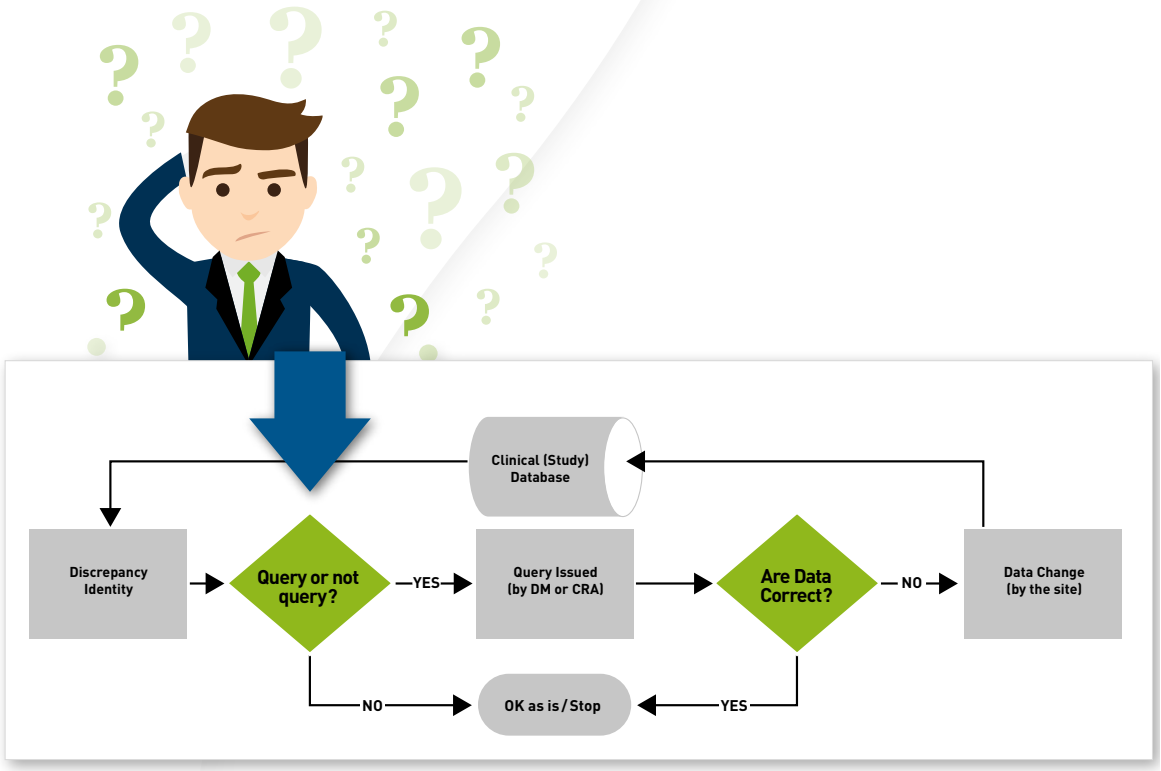
Tier	Description	Target QER: Small Study (N=20-50)	Target QER: Large Study (N =200+)
Tier #1.			
Critical data	Data points supporting primary study objectives	20%	50%
Tier #2.			
Secondary data	Data points supporting secondary study objectives	50%	80-90%
Tier #3.			
Auxiliary data	Not included in the analysis	>90%	>95%



Process Implications and Training

The final question - How can such an ideal state be achieved? The process change will come from first empowering DM and ClinOps to assess the impact of each (newly identified) discrepancy prior to issuing a query. In many cases, such a "stop-and-think" approach will lead to the decision to ignore the discrepancy and close it without issuing a query as demonstrated by the following process diagram in Figure 3.

Figure 3. Query Process: Not Every Discrepancy Deserves a Query



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Second, incentives and corporate policies should be adjusted so that the CROs or individual contributors are not paid (or otherwise rewarded) on a "per-query" basis. Mindless extra work is often perceived as pre-condition for "job security" and this mentality requires change too. Third, this evolutionary reduction in the number of queries is unlikely to occur on its own without a formal "change management" initiative coming from upper management supported by significant training. To take true advantage of the cost savings, training materials (that use real-life detailed scenarios and examples) should be developed and utilized. "Not Every Discrepancy Deserves a Query" is a seemingly simple concept, however, due to the conservative nature of our industry, training and implementation of this new approach will require time and effort. ■

CONCLUDING REMARKS

1. The current broad-brush approach to query management leads to unnecessary costs and operational delays. Thus, the elimination of low-value queries will inevitably lead to significant resource savings across the industry. An intelligent approach to query management requires a closer look at and monitoring of high-value queries (that lead to data corrections) versus low-value queries (that do not lead to data corrections). The Query Effectiveness Ratio (QER) is the best metric to achieve this goal. Consistent monitoring of the QER and, subsequently, establishing standards and benchmarks for the QER is the most practical and powerful path forward.
2. Currently reported QERs of 40% are clearly suboptimal. To reduce waste, the industry should strive to increase this ratio to 75-80%. If done properly this effort will not have a negative impact on data quality. These target levels of QER might be easier to achieve via direct data entry (DDE) or at the time of the subject encounter because a larger proportion of queries are addressed at the entry point via edit checks, which then results in a smaller proportion of discrepancies being unresolved and needing to be handled via manual queries.
3. This 75-80% target does not imply uniformity across all forms. The more critical the data point is and how large the study is are two main considerations. The QER for the "Critical data" (Tier 1) is expected to be lower than the overall target of 75-80%. The QER for the "Auxiliary data" (Tier 3) is expected to be higher close to 100%. DQ risk is higher for smaller studies and that is why a lower QER is more appropriate for them.
4. DM and ClinOps need to be empowered and trained to perform a "risk assessment" first, prior to issuing a query to save significant trial resources. This training needs to include knowledge of the protocol at the individual variable level, and the fundamental understanding that smaller study sizes result in a diminishing impact on the value of data cleaning.
5. In a few years, many of the queries that are routinely issued by study teams today will be widely recognized as unnecessary. With a new risk-based approach, risk assessments need to be performed during EVERY step of the data processing chain including during query management. The inevitable evolution of modern processes will lead to the reduction of waste in the system and produce larger numbers of new medicinal products with fewer resources.

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