A system dynamics analysis to determine willingness to wait and pay for inclusion of data standards in clinical research

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Abstract

The objective of this study was to evaluate the value of the extra time and cost required for different levels of data standards implementation and the likelihood of researchers to comply with these different levels. Since we believe that the cost and time necessary for data standard implementation can change over time, System Dynamics (SD) analysis was used to investigate how these variables interact and influence the data standard adoption by clinical researchers. Three levels of data standards implementation were defined trough a focus group with four clinical research investigators. Brazilian and American investigators responded to an online questionnaire with possible scenarios regarding options for standards implementation, and choose one of two options presented in each scenario. A random effects ordered probit model was used to estimate the effect of cost and time on investigators willingness to adehere to data standards.A preference for low cost and fast implementation time standards was observed, and investigators were more likely to incur costs than to accept a time delay in project start-up. The SD analysis indicated that initially there are extra time and cost necessary to clinical studycstandardization,however, over time a there is a decrease in cost and time.

Background

Information technology adoption is increasing by the medical community, and the patient´s health care records that used to be collected in different locations and both in paper and eletronic sources, are now gathered in the Eletronic Medical Records (EMR) (Dean, Lam et al. 2009). Besides the potential benefits for patients and providers, such as fewer medical errors and improved quality (Hanna 2005), there are also benefits for health care researchers, such as allowing the understanding of clinical practice and assessing outcomes (Dean, Lam et al. 2009). However, there are some obstacles impairing the achievement of these benefits. While there is a standardized system for coding diagnosis and procedure, medical terminology and clinical data such as labels for laboratory tests and units of measurement are not always standardized and therefore are not easily accessible in discrete fields within the EMR (Dean, Lam et al. 2009).

In the academic research scenario there has also been an attempt to automate the clinical trial process and decrease the use of multi-part paper case report forms leading to an increasing use of electronic data capture (EDC) tools. However, such adoption demonstrates a slow rate, and such tools are being used in only ~30% of clinical studies, with many of those still keeping a paper back-up component (Kush, Bai et al. 2007). Also, these tools still need to be improved, since many of them are not ready to connect or share data, with other applications within the clinical trial process (Kush 2007).

Thereby, millions of biomedical research datasets are generated every year with the potential to yield critical information affecting the way we practice healthcare but this potential is often not realized, because different datasets typically use different ‘term’ definitions (Karp 1995), which prevents them from being combined into larger datasets. Term definitions refer to definitions of variables in a database. Large integrated datasets

are crucial because they have the statistical power necessary confidently to generalize findings from a sample to the population.

Data become much easier to handle if variables are referred to by the same term across different database (Bodenreider and Stevens 2006). Data standards provide a rigorous description of data representation (Chalmers 2006), allowing cooperation between researchers through the exchange of ideas and data (Lee, McDonald et al. 2009). Consistency in variable naming not only aids the integration of databases but also their analysis. This ensures compatibility across different clinical studies. The concept of standardized data includes the specification of data fields (variables) as well as value sets (codes) that encode data within these fields (Richesson and Krischer 2007). Despite their crucial importance, up to now data standards are not extensively used in clinical research (Kush, Helton et al. 2008).

Although the reasons for this lack of compliance are not clear, the cost and time-intensive nature of data standards implementation could be responsible. A study with primary care practices showed that despite of the fact that many participants could list motivation and antecipated benefits related to data sharing, such as savings from improved coding, more efficient workflow for anciliarry staff (eg. laboratory results can be sent directly to patient´s practice EMR) and even altruistic goal to improve public health, costs were identifyed as a great barrier to health information exchange (Fontaine, Zink et al. 2010), and could be a factor related to the lack of compliance to data standards. However, it has been demonstrated that data standards implementation in the industrial setting, can save not only money, but also time in the long term, when standards implementation occur in the startup stage (Rozwell, Kush et al. 2007).

In the initial phase of the study, time and funding are required for the implementation of data standards. Despite the fact that this investment will repay in the long term, it is feasible to believe that researchers would be less likely to make the effort to standardize their CRFs or EMRs. Nevertheless, the lack of quantification prevents an adequate modelling of the minimum level of maturity required for widespread adherence among clinical researchers.

The economic aspects of using data standards from the perspective of bio-pharmaceutical companies, technology providers and contract research organizations has previously been studied (Rozwell, Kush et al. 2007). To date, however, there has been no investigation of clinical researchers' willingness to spend the additional money and time needed for implementing data standards. Therefore, the objective of this study was to evaluate the value of extra time and cost required for different levels of data standards maturity and the corresponding likelihood of researchers complying with data standards.

Methods

Study sample

A list of ten investigators from the Hospital Alemao Oswaldo Cruz, Brazil, and eighteen from Duke University Hospital, USA, was obtained from the administration department of each of these institutions. Professional clinical researchers who have participated in at least one multi-site clinical trial participated in this study. Investigators were contacted by email and invited to respond to an online questionnaire offered through DADOS-Survey (Shah, Jacobs et al. 2006), a web application specifically designed for conducting surveys that is compliant with international survey guidelines (Eysenbach 2004). Because the survey was anonymous, the project was exempt from informed consent, nevertheless, approval from the Institutional Review Board was obtained from both participating institutions.

Attributes and levels

The study began with a slide presentation on data standards implementation for all study participants. The presentation explained the advantages of data standards such as the ability to merge data from the current study with other studies or administrative data as well as the limitations of data standards which included increased cost and time for project completion. Participants were presented with different examples of cost and time necessary for study initiation using data standards, along with three possible implementation levels for data standards, namely lite, intermediate and full (Table 2). Lite implementation level was defined as one involving low cost, faster implementation time and a low level of standardization. Intermediate implementation was defined as having mid-range cost, time for completion and a greater level of standardization. Full implementation was defined as one with high cost, slower rate of completion and the highest level of standardization.
Since the implementation of data standards can involve different steps, there is no consensus regarding the value of average time and cost spent on implementation of data standards for different types of clinical research studies. Therefore, we formed a focus group with four clinical research investigators, who agreed through a Delphi method (Linstone and Turoff 1975) on time and dollar values that would be reasonable for the implementation of data standards in a medium-sized study. All investigators had experience with at least four previous clinical registries and at least one experience of participating in data standard implementation. After three rounds of a Delphi survey the values (presented in Table 1) were agreed upon by all but one panel member (who disagreed on the amount of time for the full protocol).

Twenty different data standard implementation scenarios were identified for analysis (Table 2) after those that might generate contradiction were discounted. This arrangement resembled that of a conjoint analysis, but since only a small sample of researchers was available no modelling was performed. Instead, descriptive analysis was conducted so that it could be fed into the SD model. Study participants were presented with these possible scenarios and were asked to choose one of two option s presented in each scenario which they would consider implementing for one of the clinical trials that they usually performed (constituting the average trial size and complexity for the group).

Once the participants had completed the surveys, data were extracted by the project

coordinator and only questionnaires that were internally consistent were selected for statistical analysis.

Statistical analysis

In order to estimate the effect of cost and time on investigators' willingness to adhere to data standards for their CRFs, we used a random effects ordered probit model (Agresti 2007), using change from current scenario as the dependent variable. In each model, we created dummy variables for the level of standards implementation (intermediate=1, full=2), additional cost of study (US$10,000, $40,000 for American researchers or R$5,000, R$10,000 for Brazilian researchers. We included both currencies to allow for comparison between the data collection conducted in Brazil and the US), additional time before initiation of study (one or four additional months for starting a study).

Modelling

Despite the fact that the implementation time and cost stand to increase when data standards are used in a study, we believe that these variables can interact over time, leading to a modification in the overall behavior of a system and is commonly referred to as dynamic behavior. For example inflow and outflow of water from a bathtub results in the generation of dynamic behavior over a period of time (figure 1). We used System Dynamics (SD) analysis to investigate the behavior of variables like implementation time and cost over time. SD is a set of tools to help us understand and predict how systems (complex systems) behave over time (2009). It is graphically represented by stocks (boxes), flows (thick arrows) and causal diagrams (thin arrows). A stock represents elements that can be measured and accumulated, and it is regulated by the flows. A flow determines the rate of influx to or efflux from the stock. Any other elements that influence the system are represented as a variable and their relationship with other elements are represented by causal diagrams. The SD model (Sterman 2000) was used to demonstrate the relationship between degrees of standardization, cost of standardization, and time required to start the study. The model was created with the program Vensim PLE for Windows 5.9c (2010).

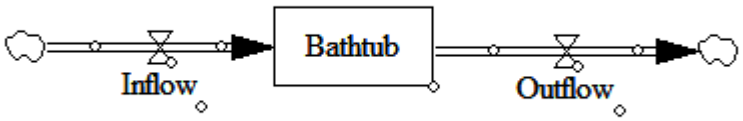

Figure 1: Illustration of dynamic behavior

Despite of the fact that applying and using data standards to clinical studies can bring many advantages that could encourage researchers to adopt their implementation, there are also many drawbacks related to them that could inhibit their use. From the survey, we observed that an increase in cost and time to start a study are unwanted aspects related to the use of data standards. Based on this, we wanted to investigate how these variables, plus the increase in the number of standardized case report forms accumulated by a researcher could

interact and behave over time, creating a new situation that could change the researchers perception about the standards implementation problem. Since SD is a set of tools used in order to help understanding of complex systems, we chose to use this strategy to help identify and explain the complex behavior related to the use of data standards, by unveiling the complexity that is behind the its structure. We believe that by learning about the behavior of this complex system, the advantages and drawnbacks related the adoption of using data standards can be identifyed and presented to researchers, so they can make an informed decision related to this subject.

Results

Probability of response

Results from the probability of response in relation to cost indicated a preference for free (definitely lite) standards, with increasing probabilities for both intermediate and full standards as they are progressively implemented at the low, medium and high levels. This relationship, however, was only significant for the full implementation vis-à-vis lite implementation ($p< 0.001$) but not vis-à-vis intermediate implementation ($p=0.228$) (Table 3).

The results for probabilities in relation to time response also show a preference for free alternatives (definitely lite), although this relationship was not statistically significant for the comparisons against either intermediate or full standards ($p = 0.116$ and 0.496 respectively) (Table 4).

Policy model

In our model we assume that the progressive accumulation of standards for a given field will progressively decrease the cost and time required to implement a given standard level. We describe here the behaviour of three variables (number of uniform datasets, implementation cost and implementation time) for a hypothetical period of five years. We normalized degree of standardization, cost of standardization, and time required to start the study on a scale from 1 to 10, with individual beta coefficients being derived from the regression model using the normalized variables.
The general idea behind the model is that the implementation of data standards will generate uniform datasets which integrate different databases, making it possible for the researcher to work with bigger databases. This will generate better research and better publications, creating the desire for more uniform datasets, which in turn will lead to the implementation of data standards. That causal relationship between the variables of the system is called a loop. In this case, the loop leads to the growth of the system, so it is known as a reinforcing loop, and is represented by the letter R in Figure 2.

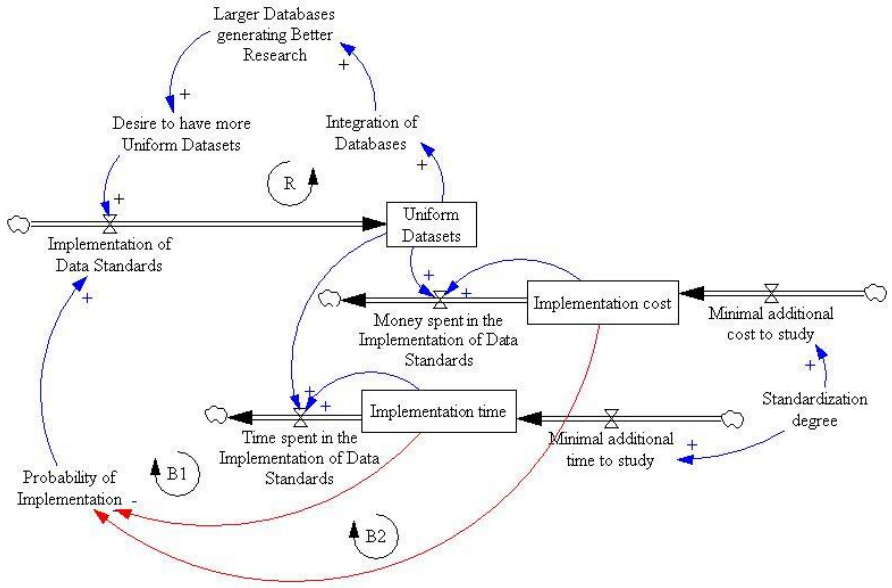

Figure 2: System Dynamics Model

If we were working with a system composed of a reinforcing loop only, the growth of the system would be exponential. In a real scenario, however, the implementation cost and time tend to act negatively in the whole process of standards implementation, as demonstrated by our results, leading us to the balancing loops B1 and B2. The first balancing loop (B1) represents the limitation in the implementation of data standards caused by the additional time needed before the study start-up with data standards. As it is a limitation, it will act negatively in the probability of implementation. Note that there is a causal relationship (represented by the arrows) within the number of uniform datasets and the time spent in the implementation. This relationship will lead to lower implementation over time in the function of the number of uniform datasets.
The second balancing loop (B2) represents the limitation in the implementation of data standards caused by the extra costs of conducting a study with data standards. Here again there is a causal relationship within the implementation cost and the number of uniform datasets, leading to lower costs over time depending on the number of datasets. In both balancing loops (B1 and B2), the standardization degree will always generate some additional resource (time or money) to be consumed by the study.

In Figure 3, the behavior of the variables "number of uniform datasets" and "time" and "cost" necessary for standardization where analyzed over time. This analysis showed that, the number of uniform datasets (green line), tends to show slow growth initially and then is a little more aggressive in terms of the function of time and cost. The second variable, additional cost to the study (red line), drops drastically in the first six months because of the implementation of the initial datasets, and continues dropping all the time. The same occurs with the variable behaviour of time (blue line); first a drastic drop, and then continuous dropping.

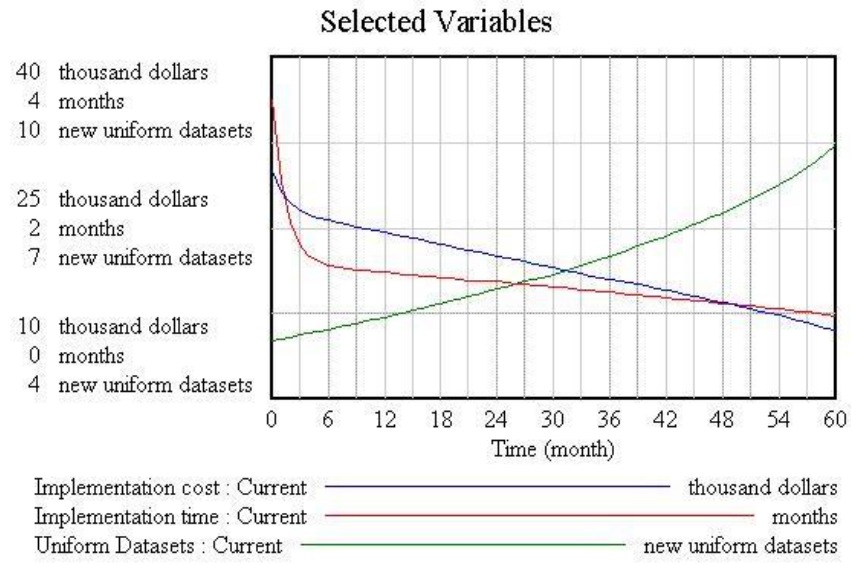

Figure 3: Simulation

Discussion

In the present study, whenever possible a researcher would prefer to implement the lowest possible level of standards that would make them minimally compliant. They also indicate that his/her preference is for a free alternative rather than a more expensive one. This reflects the fact that increased expenditure and time needed to implement data standards for a study are perceived as a barrier by the researchers. Considering the fact that many research projects rely on limited funding, this result could be expected. One interesting result, however, was that researchers prefer to pay rather than to delay the beginning of the project. Therefore, when the implementation of data standards is perceived as delaying the start-up of a project, they might be rejected.

Given the growth of clinical research and the increasing volume of data, standards that facilitate the sharing, transformation and reuse of data are critical for maximizing the knowledge that can be gained from data (Richesson and Krischer 2007) and help in developing priceless repositories of knowledge (Bleicher, Kubick et al. 2007). In the industrial setting, the implementation of standards in the case report form development stage of a clinical tria, enhances data quality and facilitates communication between team members or partners (Adams 2001; Kush, Bai et al. 2007). The most widely recognized advantages of industrial data standards are cost and time savings. For example, a standard implemented at the beginning of a study gives greater returns on investment and can result in 60% of resource savings (Kush 2007) for a single clinical research study and 80% in the start-up stage (Rozwell, Kush et al. 2007). Industry-wide standards are efficient and effective in assessing the safety of new therapies (Kush 2007). According to the Institute of Medicine, the use of standards helps in reducing expenditures by 20 to 30 % in healthcare administration and also yields a cost reduction of 35% in the pharmaceutical industry

(Corrigan, Institute of Medicine (U.S.). Committee on Rapid Advance Demonstration Projects: Health Care Finance and Delivery Systems. et al. 2003).

In the industrial use case, implementation of standards also has also proven to have a time-saving benefit in the execution of research. Data organized in different databases and stored in different formats are difficult to gather and thus delay research activities (Kush, Alschuler et al. 2007). The use of standards can help shorten the time needed to complete clinical trials by as much as one year (McCourt, Harrington et al. 2007). Sponsors have also been motivated to adopt standards to realize considerable time savings in the research processes (Bleicher, Kubick et al. 2007). When data standards are used there is a definite reduction in the time required to create CRF and the database, perform audit checks, clean data, programme tables, lock database after last subject visit, train new employees and conduct regulatory reviews (Rozwell, Kush et al. 2006).

Clinical Data Acquisition Standards Harmonization (CDASH) is aimed at standardizing the structure of a study's data and meta-data, and promises significantly to expedite clinical studies as well as the exchange of data between sponsors and other participants in the process. An analysis by Gartner Inc (2010) indicated that when standards are implemented in the CRF development stage of a clinical study, there can be significant time and cost savings (Adams 2001). According to a collaboration between the Clinical Data Interchange Standards Consortium (CDISC) and the Health Information Management Systems Society (HIMSS), the process of enabling the data to be entered only once to satisfy both the patient healthcare record and clinical research protocol requirements will save cost and time as well as enhance data quality (Kush 2007).

All the studies cited above indicate savings of time and cost obtained in an industrial setting. To the best of our knowledge, until now estimates of the amount of time and/or money necessary for the implementation of data standards in an academic environment have not been available. Since this sort of research can count on a reduced budget and personnel compared with research developed by a big pharmaceutical company, such information must be provided to researchers so they can evaluate the adoption of standards in their context. In the present study, the time and cost necessary for implementing data standards were analyzed from the perspective of academic research; the research rather than the social perspective was taken, whereas CDISC took the industrial perspective and predicted cost savings in the long run, when standards are implemented upfront the studdy (Kush, Bai et al. 2007; Rozwell, Kush et al. 2007). The objective of the survey preformed in this study was to provide clinical researchers a parameter of cost and time necessary to standardize a clinical trial in the initicial phase of the study.

To our knowledge, the SD analysis has not been used until the present moment to analyze the use of data standards by clinical researchers. The SD analysis of the variables "number of uniform datasets", "implementation cost" and "implementation time" indicated initially that both the extra time and cost necessary to implement data standards in the initial phase clinical study can act as a limitation to their implementation. However, over time, as there is a increase in the number of uniform datasets accumulated by the researcher, leading to a decrease in cost and time necessary for standardization. It is important to notice that the information from the SD analysis, that the cost and time necessary for data standards use

decrese over time in the clinical research setting, was not available to the researchers at the moment they were asked to choose between the levels of standardization. However, researchers were informed of the advantages of using data standards. This could be a limitation of the present study, since it is possible that researchers would make a different selection regarding the level of standardization if they were presented with these information, and should be considered in future studies. Another litimation from the present study is that the small sample size precluded further analysis.

Given the difficulty to quantify most of the elements involved in this complex system, we created a very simple model in order to help the better understanding of the relationship of the elements cost and time that are necessary for data standards implementation. In this way, we would like to point out that the SD model and simulations are not intended to work as a forecast, and the simulations were created for hypothetical scenarios. While the developed model may be useful to explain why the standardization is important, further studies are necesary in order to better understand this problem.

In this study, the values of the time and money needed to implement data standards were based on a consensus among researchers; nevertheless, variations could occur. The amount of money defining each level (lite, intermediate or low) was defined in different currencies (American dollars for American researchers and Brazilian reais for Brazilian researchers) and only numerical values were used to determine the levels of standardization (lite, intermediate, full). For the statistical analysis, different currencies were not considered, but only the levels of standardization, so this should not have influenced the results.

The focus of the present work was to investigate the cost and willingness of data standards implementation in a clinical trial design study, when the researcher does not have the prior intention of using this data for research collaboration. In this respect, it is important to have in mind that if the costs associated with study standardization will differ when this process is developed prior to the openning of the study or after it is complete. Also, the motivation to standardize a study when the researcher foresees the colaboration and data sharing with another group is definatly different from what we observed in our results, since we did not used this framework on the survey. Lastly, our results are also probably not suitable for generalizing aspects to other clinical research design, for example, when the standards is a component of the (required) submission of research data associated with publication.

Before making the decision between these levels of standardization, researchers were informed of the advantages of using data standards (i.e. sharing and reuse of data) in their study.It should be borne in mind that owing to the competitive scientific research environment and the historical culture of not sharing data, this is not a common practice among researchers (Campbell, Weissman et al. 2000). In addition, many researchers are afraid that their findings could be stolen or misused when data are shared (Birnholtz and Bietz 2003).

Despite of the fact that the investigation of this psychological aspect was not part of the objectives of this study, we believe that in order to expand the use of data standards in the scientific community, these aspects must be considered and addressed. Lastly, we emphasize that the advantages of research standardization, and most important, the concept that despite of the initial investment necessary, researchers will actually gain time and save money as they acummulate a greater number of starndardized studies must be clear in the research community if researchers intend to take full advantage of research data.

Conclusions

In the light of the above results, we believe that the identification of time and cost factors will allow for customization of different approaches depending on the researcher's priorities. It will also allow research policy organizations to match their data standardization policies better with the expectations of researchers. Since the rise in time and cost of starting a study were important factors that persuaded the researchers not to use data standards, future studies should create mechanisms to decrease time and cost associated with standardization processes, thus facilitating its implementation. Other mechanisms should be created to increase the personal benefit of individual researchers so that they have additional benefits in using standards; for example, they might encourage publications of studies in which data standards were implemented or data sharing from multiple research groups was used. Meta-data sharing should be encouraged since this will enhance data reuse and therefore will indirectly encourage standardization, which in turn will produce critical information benefiting healthcare research.

Competing Interests

The authors have no competing interests.

Authors' contributions

LC wrote parts of the manuscript and reviewed it for intellectual content.
GZ created the SD model, wrote parts of the manuscript and reviewed it for intellectual content.
AZ wrote parts of the manuscript and reviewed it for intellectual content.
JS wrote parts of the manuscript, reviewed the manuscript for intellectual content.
EC participated in the development of study design and reviewed the manuscript for intellectual content.
MN participated in the development of study design and reviewed the manuscript for intellectual content.
GK was responsible for data collection and wrote parts of the manuscript.
RP conceived the study, participated in its design and coordination and helped to draft the manuscript.
All authors read and approved the final manuscript.

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Table 1: Time and money parameters for defining the different levels of implementation

Attributes	Levels
Additional cost of study	no additional cost, $10,000, $40,000 for US or R$5,000, R$20,000 for Brazil
Standards implementation	LITE, INTERMEDIATE, FULL
Additional time before initiation of study	no additional time, 1 month, 4 months

Table 2: The 20 possible scenarios of data standard implementation presented to the participants in the study. Participants were asked to choose one from two possible data standard implementation levels.

	(A) Current Standards Implementation		(B) Alternative Standards Implementation
choice 1	LITE	OR	INTERMEDIATE
choice 2	LITE	OR	INTERMEDIATE
choice 3	LITE	OR	INTERMEDIATE
choice 4	LITE	OR	FULL
choice 5	LITE	OR	FULL
choice 6	LITE	OR	FULL
choice 7	LITE	OR	FULL
choice 8	LITE	OR	INTERMEDIATE
choice 9	LITE	OR	INTERMEDIATE
choice 10	LITE	OR	INTERMEDIATE
choice 11	LITE	OR	INTERMEDIATE
choice 12	LITE	OR	FULL
choice 13	LITE	OR	FULL
choice 14	LITE	OR	FULL
choice 15	LITE	OR	INTERMEDIATE
choice 16	LITE	OR	INTERMEDIATE
choice 17	LITE	OR	INTERMEDIATE
choice 18	LITE	OR	FULL
choice 19	LITE	OR	FULL

choice 20	LITE	OR	FULL

*Time measure in months and money measure in American dollars for American researchers and in Brazilian reais for Brazilian researchers.

Table 3: Probabilities in relation to cost response

	STANDARDS IMPLEMENTATION					
	INTERMEDIATE			FULL		
	LOW	MEDIUM	HIGH	LOW	MEDIUM	HIGH
DEFINITELY LITE	0.2690	0.2871	0.2999	0.1944	0.2728	0.3152
PROBABLY LITE	0.2980	0.2801	0.2579	0.2297	0.2319	0.1871
DEFINITELY INTERMEDIATE	0.0739	0.0641	0.0548			
PROBABLY INTERMEDIATE	0.1623	0.1341	0.1101			
DEFINITELY FULL				0.1318	0.1037	0.0679
PROBABLY FULL				0.3419	0.2048	0.000

Table 4: Probabilities in relation to time response

	PROPOSAL					
	INTERMEDIATE			FULL		
	FAST	MEDIUM	SLOW	FAST	MEDIUM	SLOW
DEFINITELY LITE	0.2738	0.2927	0.3048	0.2906	0.2850	0.2784
PROBABLY LITE	0.2929	0.2726	0.2476	0.1957	0.2010	0.2057
DEFINITELY INTERMEDIATE	0.0723	0.0618	0.0519			
PROBABLY INTERMEDIATE	0.1595	0.1294	0.1042			
DEFINITELY FULL				0.0829	0.0875	0.0921
PROBABLY FULL				0.1673	0.1809	0.1955

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