Use of Company Historical Data in Design of Medical Devices

16.1 INTRODUCTION

Database Auditing is one of the major issues in information security. Lack of data auditing leads the business applications to the lost trail of business processes. To cope with auditing, historical data or temporal database is needed in order to track operations and actors of the operation with the time. Valid and transaction times are two major timestamps in temporal database.

Information System, IS, and Information Retrieval, IR, have been defined and adopted into the practices since the beginning of digital revolution. While information has been used for business processes, information security emerged in term of authentication and authorization.

A large proportion of clinical trials involve the comparison of a novel treatment to an existing control arm, either a placebo or a standard of care. While often the control arm stands on its own within a trial, with parameter estimates for the control group. Often, one or more clinical trials have been conducted involving the control arm. In theory, bringing this existing information into the current trial holds the promise of more efficient trial design. Such trials may be smaller, and/or unequal randomization may be used to place proportionately more subjects on the experimental treatment arm in a study, potentially increasing the relative amount of information both on the efficacy and safety of the current novel treatment, as well as on secondary endpoints. In clinical practice, expected results are based on the current set of historical studies, and it makes statistical sense to capitalize on this historical data whenever possible.

In practice, methods for borrowing historical information, and the ramifications of these methods, are less well understood in terms of benefits, effects, and regulatory ramifications.

Potentially, the incorporation of quality external information allows for reduced mean square error (MSE), increased power, and reduced type I error within the current trial. In contrast, should the historical data be inconsistent with current trial control arm data, there is a potential for bias and inflated type I error. The relative weights of these risks depend on the phase of development.

(BSWG), which was formed in 2011 and includes representatives from industry, regulatory agencies, and academia, with the vision to ensure that Bayesian methods are well understood, accepted more broadly, and appropriately utilized to improve decision making and enhance patient outcomes.

We specifically emphasize the idea of 'dynamic borrowing' in the approaches considered. It is important that any method for historical borrowing recognizes when the current data appear to be inconsistent with the historical data. We expect variation in the actual parameters from study to study. These may be due to slightly differing patient populations, site locations, improvements in secondary aspects of treatment in the time between the historical and control data, and so forth. A method that incorporates dynamic borrowing borrows most when the current data are consistent with historical data and borrows least when the current data are inconsistent.

Typically, an agent is explored in many clinical trials over the course of several years, in situations analogous to the study we want to undertake. We expect there to be some variation in the response rates for our drug across these studies.

Thus, fundamentally the historical data can either help or hurt depending on the relationship between the past data and the current parameter. Some methods are more robust to drift than others, and we try to illustrate which methods are the most robust. After assessing the possible benefits and risks, the user must assess whether the benefits exceed the risks, an assessment that should include the likelihood of their occurrence.

16.2 AUDITING

Auditing a change to a management system such as accounting, performance, and software, has been well defined and proctored to improve the quality. One of the major sources of auditing is data where auditor can find the errors and misuses. Lately, data, itself, is audited for its movement to identify malicious behavior, maintain data quality, and improve system performance proposed a framework for auditing the changes to a database system with the retention policies. The declarative rules for expressing retentions, semantics for audit query answers, and performance of audit query under retention restrictions were demonstrated.

16.3 HISTORICAL DATA

One key success of auditing is to be able to track the change on the trail of who made the changed, what operation of the modification, and when it happen. The first two trails can be manipulated in relational model while the last trail requires temporal characteristics to handle.

Two different types of time are considered when recording the history of information; valid time and transaction time. suggested that valid and transaction times should guarantee no information loss in any circumstantial transactions. suggested that the transaction time is needed to satisfy the data mining.

16.4 HISTORICAL DESIGN FOR AUDITING ON RELATIONAL DATABASES

Historical data can be modeled in Relational Database, RDB, in several techniques such as separated tables for history records, transaction logs, and multi-dimension data using XML. Creating a separated table for historical data of each relational table is a straight forward solution with minimum design complexities while the transaction logs must cross-check data from the data dictionary. Both solutions require no change to the

original relational tables. Without additional tables, XML columns can be added to the original table with the background of XPATH, XQUERY, and SQL/XML for the data retrieval.

16.4.1 Row-based Auditing

This technique creates a separated table for each relational table to maintain historical data. The table, also, includes both static data and historical data. The static data remains unchanged such as data of birth or rare to change such as name. For the historical data, only the last-updated values are maintained in the operational table.

16.4.2 Column-Based Auditing

The column-based auditing solves the redundancy of the row-based auditing. This auditing table does not include the static columns such as date of birth and hired date of an employee. Data in historical column of auditing table are stored only the changed value except the primary key, such as ID, which is used to reference its operational table. The historical query on auditing is less complex than row-based auditing. So, it is likely to execute faster.

16.4.3 Log-Table Auditing

Log tables have been used for transaction management in the relational database for a long time. Due to the nature of transaction that needs to know operation, data, and time of execution, log tables can be utilized for the auditing purpose too.

16.5 Methods of borrowing

We consider six methods for incorporating the historical data, the first two acting as ‘fence posts’ for understanding our three main historical borrowing methods. We also consider single arm trials, as these are also a form of historical borrowing in that

typically the threshold for success (e.g., a null hypothesis response probability) is determined after looking at historical data. The six methods are as follows:

1. Separate—we ignore the historical data. This would be viewed as a 'standard analysis'. Here, we would continue with equal randomization on the current treatment and control, with no incorporation of the historical information. We perform a Fisher exact test.
2. Pooling—suppose we perform equal randomization in the current trial, but we pool the historical subjects with the current control subjects. One could combine pooling with unequal randomization, but we are attempting to maintain an equal number of treatment subjects for all methods. We perform a Fisher exact test but here pool the historical information as if they had been control observations in the current trial.
3. Single arm trial—while somewhat unusual for these sample sizes, many single arm trials are conducted that look at historical data (often with sample sizes less than our 100 historical subjects) to create a performance criterion that must be beaten in the current study.
4. Test-then-pool—pooling presents an obvious difficulty in that a priori we may not be sure our historical data are sufficiently similar to our current control arm (our efforts in reviewing the literature notwithstanding). We would like a way to avoid pooling in situations where the current control arm appears to be different from the historical data.
5. Power priors—the power prior assigns a 'weight' to the historical data some-where in between the pooling (weight=1) and separate analyses (weight=0). Thus, the historical data are incorporated to a degree into the current analysis.
6. Hierarchical modeling—in a hierarchical model, we assume a distribution across studies (here the current and historical controls) with an explicit parameter τ measuring the variation across studies.

16.5.1 Comparison of pooling, separate, and single arm trials

We tend to think of the separate and 'pooled' analyses as fence-posts in that they represent the extremes of borrowing. Intriguingly, a single arm trial represents a further extreme of borrowing in that we typically use the historical data to construct a performance criterion.

16.5.2 Test-then-pool

A difficulty in the pooled (and single arm) examples is the dramatic type I error inflation. This is a result of 'static borrowing' in that the pooled analysis always borrows the complete historical dataset.

In test-then-pool, we first perform a hypothesis test of equal rates between the current and historical control subjects. If this hypothesis is not rejected, we use the pooled analysis. If the null hypothesis of equality is rejected, we perform the separate analysis. This results in an 'all or nothing' approach, using one of the extremes of borrowing.

16.5.3 Power priors

The power prior is a useful class of informative priors for historical borrowing. Here, we focus on the particulars of applying the power prior to the binomial dataset.

Given that we may have differences between the historical studies and the current control arm beyond simple sampling error (if that were the only discrepancy, pooling would be appropriate), one option is to down weight the historical data, treating the historical data as if it had the same observed rate but with a smaller sample size.

16.5.4 Comparison of methods

The previous sections have focused on each method (single arm trials, test-then-pool, power priors, and hierarchical modeling), demonstrating how user controlled

parameters can affect the borrowing behavior of each method. Here, we make a brief comparison of the methods against each other.

16.6 EXTENSIONS FROM THE LITERATURE

There have been many extensions to the models demonstrated thus far. For example, exchangeability between historical studies and current studies in the hierarchical model may be a concern. Extensions include the addition of covariates, multiple historical controls or multiple clinical sites, and adaptive randomization using historical controls.

16.6.1 Multiple historical controls

Multiple historical controls entail multiple power parameters in the power prior model and a more complicated relationship between the commensurability parameter and the between-study variance from the hierarchical model.