Comparative Cost Outcomes Analysis between Coronary Artery Bypass Graft Surgery Versus Drug Eluting Coronary Artery Stenting

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ABSTRACT

With the recent advent of the drug eluting stent as a possible alternative for coronary artery bypass graft (CABG) surgery, the economics of cardiac healthcare have shifted dramatically. Many doctors are now electing to send their patients to an invasive cardiologist for cardiac catheterization rather than for open heart surgery. However, the debate continues as to whether stenting is a viable alternative to open heart surgery. This study seeks to approach this problem with an economic analysis of the comparative cost-effectiveness of the two procedures. Using a variety of statistical techniques including conventional mean differences tests and linear probability models, we test the relative effectiveness of the different treatment options.

INTRODUCTION

Innovations in healthcare are implemented in order to accomplish one of two things: (1) to improve the quality of treatment; (2) to lower the costs of treating an ailment. In medicine, the cost of treatment options often remains a taboo topic when deciding what is best for the patient, but economists realize that treatment costs are highly intertwined with the real value of a prescribed treatment option. The marginal effectiveness of one treatment option over another should also factor in a measure of price to determine its net "worth." Seeing that treatment costs are not solely confined to the price of the procedure itself, but also to hospital care costs, which often account for up to 44% of the total price of treatment, the cost-effectiveness of a treatment is closely tied to technology innovation that reduces patient recovery time, drug usage, and a number of other post operative metrics (Polverejan, Gardiner, Bradley, Holmes-Rovner, and Rovner, 2003). The analysis in this paper seeks to determine the cost-effectiveness of two popular treatment options for surgical revascularization: the traditional coronary artery bypass graft (CABG) versus the recently developed drug-eluting stent.

BACKGROUND

Development of Thought

With the increasingly profit-driven nature of the medical industry, the press often publicizes the conflict of interest between the motivation of an industry to make money and healthcare's mission to improve lives. In a recent issue of BusinessWeek, it

was expressed that critics of the aforementioned conflict believe that these financial interests influence treatment decisions for the patient (Weintraub, Feb. 6 2006).

Therefore, it is becoming more important that the treatment methods and practices of the healthcare industry are evaluated with not only a traditional scientific approach, but also with an economic eye. What is the best cost-effective treatment option for the patient? Are additional costs of one treatment over another legitimately justified when looking at marginal outcomes? An econometric statistical analysis seeks to answer these questions, whereas a traditional biostatistics methodology may not. For these reasons, this paper is not only timely to the current state of healthcare, but also unique in its approach to the problem of healthcare evaluation.

A Brief History of Cardiac Healthcare

For over two decades, the Coronary Artery Bypass Graft (CABG) has been considered the "gold standard" procedure for the treatment of ischemic heart disease, a condition where the heart does not receive enough blood due to a blockage of a coronary artery. Over the past twenty years, the innovations and improvements in CABG surgery techniques have been numerous and well-studied.

One of the original studies relating to cardiac healthcare was the Framingham Heart Study conducted by the National Heart Institute in 1948. The study looked at the probable causes of coronary vessel disease (CVD) in 5,209 people. The study enrolled more participants in 1971 and carried out its third, most recent, stage in 2002. Over the course of the study, it was found that major CVD risk factors include high blood

pressure, high cholesterol, smoking, obesity, diabetes, and physical inactivity (Cupples, 2003). This study introduced the fundamental variables of interest in the evaluation of heart health, and many of the factors found in the Framingham study are still used today as predictors of heart disease.

Soon after, *The Journal of Thoracic and Cardiovascular Surgery* published one of the first analyses of the effectiveness of logged attempts at bypass surgery (Wisoff, Hartstein, Aintablian, and Hamby, 1975). The study was a simple analysis of mortalities in an initial observational study of 200 CABG patients. This study presented initial evaluation of surgery success and complications based on demographic characteristics such as age, sex, weight, and race. Early studies such as this one set the parameters for measuring cardiac infarction and surgical outcomes.

Advancement of Cardiac Care, Introduction of the Stent

More recently, the availability of long term data has made the effectiveness of CABG surgery easier to track in patients. As a consequence, key variables contributing to better outcomes in open heart surgery have been identified. Various studies over the past decade have confirmed the improving success rates of open heart surgery. This improvement can be attributed to a number of factors including a better understanding of pre and post operative care, improvement in technology, and procedural advancements. For example, Magee, et al. (2001) found that patients undergoing CABG surgery without the use of a bypass device ("off-pump"), have fewer post-operative complications and a significantly shorter length of stay (Magee et al., 2001). Other

research which further demonstrates this improving understanding of CABG surgery includes studies performed by Seccareccia (2005) in which the importance of assessing center and physician-specific risk was highlighted. Studies by Kobayashi, et al (2005) and Williams et al (2005) also demonstrate a trend towards better managed cardiac bypass surgery with lowering mortality and complications rates.

Due to falling mortality rates, decreased complications, and better post-operative care of CABG surgery, few viable alternatives were considered before sending a patient to the operating table. However, in the past decade, the introduction of the cardiac stent has changed this trend, and more doctors are choosing to send patients for percutaneous coronary intervention (PCI)[1], a minimally invasive procedure for less severe cases of cardiac ischemia. Due to the relative newness of the introduction of the stent, longer-term follow up could not be performed until recently in order to gauge the comparative effectiveness of PCI versus CABG surgery. In May of 2005, University of Albany researchers published a study that concluded that CABG produced higher adjusted rates of long-term survival than stenting (Hannan, Racz, Walford, Jones, Ryan, Bennett, Culliford, Isom, Gold, Rose, 2005). It seemed that the stent's viability was greatly limited by the fact that arteries returned to their blocked state after a few years of stent implantation. This finding was confirmed in European studies by the SoS Investigators, (2002) as well as by an Argentinean research group published in *The Journal of the American College of Cardiology* (Rodriguez et al., 2001).

[1] Percutaneous Transluminal Coronary Angioplasty (or PTCA) is a type of PCI surgery in which a balloon catheter is used to reshape the blocked or collapsed vessel. Additionally, a stent may be used with PTCA, as is the case in this study, in order to hold the shape of the vessel.

In 1997, a team of researchers from the Stanford School of Medicine published a study that used medical care costs and a quality of life measure to compare randomization to either coronary angioplasty or coronary bypass grafting (Hlatky et al.). The study concluded that CABG remained the optimal choice in terms of quality of life after three year follow up measures. Furthermore, coronary angioplasty was shown to have a lower five-year cost than bypass surgery only for patients who have two-vessel coronary disease. Even though the cost of angioplasty is 65% of the cost of CABG surgery, it is surprising that the lower cost is only justified in a very limited subsection of the study population. In fact, the study found that the five year cost associated with angioplasty was 95% the cost of surgery, and additionally, CABG produced better results for most patients, especially those with diabetes. These results were further reinforced in more recent studies that were able to look at longer-term outcomes. Thus, there was a need for innovation in the PCI procedure for it to become a viable alternative to CABG surgery instead of a "short-run" fix for a problem.

The Drug Eluting Stent

It was not until the mid 1990s that the drug-eluting stent was introduced for clinical trial. Consequently, while there is a prolific collection of studies on CABG effectiveness, the availability of long term data and published literature on drug-eluting stents are relatively limited. With the introduction of the drug-eluting stent, the comparative cost effectiveness of the CABG is again under question. In a study comparing drug-eluting versus bare metal stents, Van Hout, et al., have determined that

the cost-effectiveness of drug-eluting stents is inline with the increased cost of the device and procedure (2005). This finding sets the stage for a comparison of two gold-standard procedures for cardiac revascularization: the CABG versus the drug-eluting stent, and I perform this in the analysis that follows.

METHODS

Data Sample

A non-randomized sample of 1,253 patients assigned to coronary artery bypass graft and 3,099 patients assigned to angioplasty with drug eluting stent formed the basis of our sample. The patients were observed for approximately an 18-month period from February of 2004 to August of 2005. The database was assembled from a Dallas physicians' group of cardiac surgeons and cardiologists who performed the procedures in various facilities in the Dallas-Fort Worth Metroplex. Six, twelve, and eighteen month follow-up were available for 96.1%, 96.4%, and 58.6% of the patients, respectively. Incidences of re-hospitalization, mortality, and current medications were recorded over this period (see **Appendix A**). Due to the relative lower response rate of the 18 month follow-up, this paper will focus on 6 and 12 month follow-up statistics in assessing the longer-term viability of the two procedures.

The data collection forms (attached as **Appendices B** and **C**) were a slightly modified and abridged version of the traditional Society of Thoracic Surgeons (STS) data

form[2]. Because the sample is non-randomized, an observational, econometric approach is taken in analyzing the statistics. In this approach, we use linear probability models (LPM) and ordinary least squares (OLS) regressions to estimate the marginal probability of an adverse event occurring in catheterizations relative to CABGs.

LPM and OLS analyses take into account a variety of inherent differences and pre-existing conditions of each sample in order to create an accurate model based on the dependent variables in question. OLS minimizes the square of the differences between measurements of the dependent variable in question in order to estimate a slope and intercept relating an outcome measure and independent variable. OLS makes four key assumptions:

1. Linearity: $E(u_i \mid X_i) = 0$, where u_i is the expected value of the sample and X_i is the specific regressor
2. All observations are independently and identically distributed (*iid*)
3. u_i and X_i have non-zero and finite fourth moments

   $0 < E(X_i^4) < \infty$ and $0 < E(u_i^4) < \infty$
4. There is no perfect multicolinearity between regressors (the included regressors cannot be expressed as a linear combination of other included regressors)

The linear probability model (LPM) can be thought of as a simplified case of OLS that is used for binary (0,1) variables such as mortality. In LPM, the coefficients measure the increased probability of the independent variable due to a unit change of the

[2] The Society of Thoracic Surgeons is a not-for-profit group that sets standards for clinical research practices in the field of cardiac surgery.

independent variable changing. The data analysis software that was used for this paper automatically took into account whether the dependent variable was continuous or binary. *Logit* and *Probit* regressions, which force probabilities to lie between zero and one by basing estimates off of the cumulative distribution function, were not used in this study because the problem of probability estimates greater than one was not an issue.

As a baseline for comparision, a white-male undergoing CABG surgery was used. The LPM and OLS models use this baseline in order to produce probability measures to quantify differences due to a variety of characteristics such as race, gender, and surgery type.

The overall analysis of the data will be broken down into three components,

1) A differences-in-means analysis which compares attributes of the two samples (sex, weight, pre-diseased vessels, etc) and tests for significance in the differences via a standard t-test.
2) Linear probability and ordinary least squares (OLS) modeling to regress the dependent variables (mortality, length of stay, complications, etc) against key independent variables (procedure type, demographics, pre-existing conditions, etc.)
3) A cost-measure analysis in which averages for length-of-stay, medicine, and treatment costs are used to weight the probabilities found in part two of the analysis. A difference of significance levels will then be used on these weighted-

averages to measure whether one procedure is significantly more "cost effective" than the other.

RESULTS AND DISCUSSION

In order to perform a comparative analysis on the two groups of patients, first the pre-operative attributes of the respective groups were compared. The patient groups were found to be significantly different in terms of the number of drugs before surgery, the presence of diabetes, whether the patients are current smokers or have smoked in the past, the ejection fraction, the number of diseased vessels, and number of previous interventions **(see Table 1)**. Differences observed are most likely due to the fact that the study population was not randomized. Based on the number of diseased vessels and ejection fraction (EF), the surgeon decided which treatment was best for the patient. As a general rule, patients with three or more diseased vessels and a lower ejection fraction qualified for CABG, while those with less than three vessels and a relatively higher ejection fraction were sent for catheterization. Therefore, major sources of bias in the sample seem to stem from selection mechanisms used by the doctors.

Additionally, the results presented in Table 1 suggest that smokers, whether current or past, are more likely to undergo CABG surgery. Surprisingly, patients receiving stents evidence significantly higher levels or pre-surgery drugs. This may be because these patients are often treatable through solely drug therapy up to the point of operation whereas the CABG patients are not.

[TABLE 1 ABOUT HERE]

Post-Surgery Outcomes and Regressions

Four variables were used immediately post-operatively to compare the short-term success of stent versus CABG patients: mortality, the number of drugs prescribed post-operatively, the number of operative complications, and the length of stay. While it is difficult to gauge the full breadth of a treatment's success within only a few hours of surgery, measures of drug usage and the length of stay gave some insight into the quality of life of the patient immediately after surgery. The underlying assumption here is that a patient is better off if he or she is required to take less drugs post operatively because most drugs have associated side-effects and financial costs which contribute to a lower quality of life[3].

Surveying a simple comparison of means (summarized in **Table 2**), post-operative drug usage, operative complications, and length of stay are all significantly lower for cardiac catheterization. Mortality is also lower for stent patients, but the result is only marginally significant (t-stat = -1.55). However, these results are expected and not out of the ordinary since the CABG is a highly invasive procedure with known increased risks of infection, bleeding, and other complications. Despite this, a somewhat interesting finding is that the quantity of drugs prescribed to a patient *at discharge* is significantly less for CABG patients. This result may be explained by the fact that many of the CABG surgeries performed by the particular surgery group were off-pump

[3] The idea of quantifying drugs as an outcome measure is unique to this paper and is not readily found in previously published studies comparing cardiac procedures.

operations[4] that do not require the patient to take a blood thinning agent after the procedure.

[TABLE 2 ABOUT HERE]

In order to gain a more accurate view of the impact of procedure type on the four outcome variables, we perform a series of regressions that are summarized in **Table 3**. These regressions simply measure the level of impact that a given independent variable has on the outcome variable in question. In this preliminary regression, we find that stent patients stay approximately 4.6 days less than CABG patients, are nearly .6% less likely to lose their lives in the procedure, and have approximately a quarter less complications than a CABG patient. However, CABG patients take on average .725 drugs less than a typical stent patient at discharge. These results are all in line with the findings in the means comparison analysis. The only difference is that a linear probability model allows us to quantify the differences more concretely.

[TABLE 3 ABOUT HERE]

However, in order to ensure that the results observed in the simple regressions are not simply due to differences in pre-existing conditions between the two patient groups, we run regressions including various pre-condition variables. These more comprehensive results are reported in **Tables 4** through **8**.

[TABLE 4(a) ABOUT HERE]
[TABLE 4(b) ABOUT HERE]
[TABLE 4(c) ABOUT HERE]

[4] An off-pump procedure is an open heart surgery that does not use an external bypass device and the surgeon operates on a beating heart.

We see a number of interesting finding in the comprehensive mortality regression presented in Table 4(a). First, the relationship between surgery type and mortality becomes statistically significant (t-value of 2.14 versus 1.55). This is peculiar because we would expect that after accounting for the fact that the CABG population is initially sicker (e.g. more diseased vessels, lower ejection fraction), one might expect that there would be less of a difference in the mortality rates for the two procedures. However, this is not the case. Further, we find that African Americans tend to do worse in terms of overall mortality than other races and Hispanics tend to do better. While the significance of these variables is marginal, it indicates that tailoring treatment according to demographic characteristics may be warranted. Additionally, in **Table 4(b)** we can see that mortality of African Americans is higher regardless of treatment type. However, as stated in the analysis of **Table 4(c)**, African Americans are more likely to be diabetic, which could influence the group's negative rate of survival.

Tables 5(a) through **5(c)** assess the length of hospital stay in terms of a variety of explanatory variables. Looking at the regression of the pre-condition variables on the length of stay, one can see that Asians and females tend to have a longer length of hospital stay than other groups. Females on average stay one half of a day longer while Asians stay 2.5 days longer on average. However, when we test the CABG and stent groups separately in **Tables 5(b) and (c)**, we find that the results are only significant for CABG. In fact, women actually perform significantly *better* in the catheterization

scenario, which leads us to believe that women and Asians undergoing CABG require extra care and precautions than other groups.

The third outcome measure that we analyze is operative complications. These results are presented in **Table 6(a)**. Much like the observations on length of stay, females are 3.7% more likely to experience operative complications than men. However, if we only assess females receiving the stent (**Table 6(b)**), we find that they experience approximately 4% fewer complications. These results imply that many of the observed complications are coming from women receiving CABG surgery. Here, again, the implication is that doctors might want to consider gender when assigning patients to various treatment options.

Finally, the comprehensive regression analyses of drug usage post surgery and at discharge are presented in **Tables 7** and **8.** The results in these tables are not surprising. We expect catheterization patients to be prescribed more cardiac drugs at discharge because they came in taking more cardiac drugs, and doctors probably feel that it will be beneficial for the patient to stay on these drugs for some indefinite time period. It is somewhat interesting that Hispanic patients receive more drugs at discharge. However this result is only marginally significant and could be caused by any number of factors including higher medication usage by Hispanics before surgery or a higher presence of diabetes in Hispanics. We see the opposite trend in black patients immediately post operatively (**Table 7**), but again, this finding is only marginally significant.
This is similar to the case in Hispanics who are prescribed more drugs at discharge, but this result is also borderline significant (**Table 8**).

[TABLE 7 ABOUT HERE]

[TABLE 8 ABOUT HERE]

[TABLE 9 ABOUT HERE]

Six and Twelve-Month Outcomes and Regressions

At six and twelve months, the surprising observation is that the initial outcomes that favor catheterization begin to equilibrate and even overturn to favor CABG in some areas. At six months, PTCA patients were shown to be taking significantly more cardiac medications including significantly more adenosine diphosphate receptor antagonists (or ADP drugs), which implies that many of the PTCA patients may have been experiencing arterial blocking at their stents. Additionally, a significantly greater number of PTCA patients were sent for additional stents (3.55% versus 2.08%) or bypass surgery (1.49% versus 0.08%) than the initial CABG group. It is also important to note that of the cath patients receiving CABGs or additional catheterizations, the majority received treatment on the same vessel in which their DES was installed. Seeing that these re-operations were significantly greater for DES patients than CABG patients, important questions arise as to the effectiveness of cardiac stenting as a replacement for bypass surgery, even with drug eluting stents.

[TABLE 11 ABOUT HERE]

This is not to imply that stenting procedures did not have their merits at the six month mark. Patients receiving DES were prescribed less beta blockers and reported less re-hospitalizations after surgery. However, this value includes incidences of both

cardiac and non-cardiac emergencies. Therefore, the observation is not wholly specific to the analysis presented here. Recall that the original population of CABG patients had more incidences of diabetes and were in generally poorer health than the stent patient pool.

[TABLE 12 ABOUT HERE]

At the twelve month follow up, we observe a decrease in the number of significant adverse events for PTCA. However, PTCA patients still are taking more cardiac medications at this point and have more occurrences of re-stenting than CABG patients. While more CABG patients are on Beta Blockers at the year mark, more PTCA patients are also taking ADP medications. The reason for the decrease in adverse events at twelve months is most likely due to the fact that patients who had adverse events or needed re-intervention were treated in the zero to six month period after their initial surgery.

Cost Comparisons of Treatment Groups

[TABLE 12 ABOUT HERE]

Differences in costs are calculated based on a probability-weighted system; the chance of the event occurring is multiplied by the cost of its occurrence. For initial adverse events, the cost of the occurrence is included in the hospital costs for the different procedures. It is interesting to note that although the six and twelve month measures without cost factors detailed in the previous section suggest that CABG remains to be the gold standard, after incorporating a variety of cost measures into the

analysis, the one-year cost of CABG surgery is $10,662.40 higher than that of stenting. The primary reason for this difference is that the occurrence of measured adverse outcomes (e.g. re-catheterization or re-CABG) is characterized by very low probabilities in both study groups. Thus, they did not significantly detract from the additional initial cost of the CABG surgery. Even though CABG surgery had lower associated follow-up medication costs and lower occurrence of re-intervention, the percentage difference of these two factors was not large enough to drive down the overall cost of the procedure. However, It is also important to note, that this study did not factor in the economic opportunity costs of a longer length of stay and increased physical strain associated with CABG surgery. These subjective factors are difficult to quantify. They may affect the patient's treatment decision, and may further bias the decision in favor of the stent[5].

[5] Additionally, a shortcoming of the analysis proposed is that it does not factor in follow-up costs of doctor visits over the six and twelve month periods.

CONCLUSION

The analysis in this paper highlights the important of including cost in gauging the effectiveness of one procedure over another. Traditionally, researchers have waned away from incorporating monetary weights in medical studies. In reality, costs can be a decisive factor for many patients in choosing between two treatment options. Two important findings of this study include,

1. Demographics may be important to consider when choosing between cardiac treatments, especially for females and African Americans
2. CABG surgery provided better results at six and twelve months in terms of the occurrence of adverse events. However, when cost measures were applied, these marginally better results did not translate to cost savings for the patient.

In comparing a highly invasive procedure with a minimally invasive one, longer-term studies provide valuable insight into the true effectiveness of a procedure. This is because by the very nature of a highly invasive procedure, we expect to see more short term adverse events than minimally invasive ones. Therefore, eighteen and twenty-four month studies on the data set used in this study may reveal different findings than the six and twelve month analysis here. Additionally, randomized studies incorporating measures of utility, patient quality of life, and opportunity cost measures can be valuable to physicians choosing between catheterization and CABG surgery.

TABLES AND APPENDICES

BIBLIOGRAPHY

Cupples, L., Yang, Q., & Demissie, S. (2003). Description of the Framingham Heart Study data for Genetic Analysis Workshop. *BMC Genetics*, *4,* 1-3.

Fenwick, E., Claxton, K., & Sculpher, M. (2001). Representing uncertainty: The role of cost-effectiveness acceptability curves. *Health Economics*, *10,* 779-787.

Hannan, E. L., Racz, M., Walford, G., Jones, R., Ryan, T., Bennett, E., Cullifod, A., Isorn, W., Gold, J., Rose, E. (2005). Long-Term Outcomes of Coronary-Artery Bypass Grafting versus Stent Implantation. *The New England Journal of Medicine*, *352*, 2174-2183.

.

Hlatky, M.A, Rogers, W., Johnstone, I, Boothroyd, D., Brooks, M., Pitt, B., Reeder, G., Ryan, T., Smith, H., Whitlow, P., Wiens, R., Mark, D. (1997). Medical Care Costs and Quality of Life after Randomization to Coronary Angioplasty or Coronary Bypass Surgery. *The New England Journal of Medicine, 336*, 92-99.

Kobayashi, J, Tashiro, T., Ochi, M., Yaku, H., Watanabe, G., Satoh, T., Tagusari, O., Nakajima, H., Kitamura, S. (2005). Early outcome of a randomized comparison of off-pump and on-pump multiple arterial coronary revascularization. *Circulation, 112,* 1338-43.

Magee, M., Dewey, T., Acuff, T., Edgerton, J., Hebeler, J., Prince, S., Mack, M. (2001). Influences of diabetes on mortality and morbidity: off-pump coronary artery bypass grafting versus coronary artery bypass grafting with cardiopulmonary bypass. *The Annals of Thoracic surgery*, *72*, 776-781.

Polverejan, E., Gardiner, J., Bradley, C., Holmes-Rovner, M., Rovner, D. (2003). Estimating mean hospital cost as a function of length of stay and patient characteristics. *Health Economics*, *12*, 935-947.

Rodriguez, A., Bernardi, V., Navia, J., Baldi, J., Grinfeld, L, Martinez, J., Vogel, D., Grinfeld, R., Delacasa, A., Garrido, M., Oliveri, R., Mele, E., Palacios, I., O'Niell, W. (2001). Argentine Randomized Study: Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients With Multiple-Vessel Disease (ERACI II): 30-Day and One-Year Follow-up Results. *The Journal of the American College of Cardiology,* 37. 51-58.

Seccareccia, F. Perucci, C., D'Errigo, P., Arca, M., Fusco, D., Rosato, S., Greco, D. (2006). The Italian CABG Outcome Study: short-term outcomes in patients with coronary artery bypass graft surgery. *European Journal of Cardio-thoracic Surgery*, *26,* 56-64.

SoS Investigators. (2002). Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. *Lancet, 360*, 965-970.

Van Hout, B., Serruys, P., Lemos, P., Brand, M., Es, G-A., Lindenboom, W., Morice, M., (2005). One year cost effectiveness of sirolimus eluting stents. *Heart, 91*, 507-512.

Weintraub, Arlene. (2006). Should Doctors Own Hospitals? *BusinessWeek*, 63-64.

Williams, M., Muhlbaier, L., Schroder, J., Hata, J., Peterson, E., Smith, P., Landolfo, K., Messier, R., Davis, R., Milano, C. (2005). Risk-adjusted short- and long-term outcomes for on-pump versus off-pump coronary artery bypass surgery. *Circulation*, *112*, 1366-70.

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