RESEARCH NOTE

PROBABILITY MODEL OF DECISION MAKING FOR SUCCESSFUL TRANSPLANTATION OF NON-CADAVERIC ORGANS

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Abstract Mathematical modeling based on a probabilistic approach for making decisions for organ transplantation can be successfully employed in cases when the choice of decisions can affect the results produced. In this study, the minimum probability of success required for organ transplantion in case of multi-donors is determined. The governing equations are constructed in terms of probabilities and some other factors like quality adjusted life-years (QALYs) of recipients, donors, expected knowledge gain, medical benefit and expected fame of surgeon. The analytical results are obtained by solving equations and illustrated numerically.

Keywords Mathematical Modeling, Organ Transplantation, Decision-Making, Probability, Quality-Adjusted Life Years (QALYs), Multi-Donors

چکیده مسئله تصمیم گیری در رابطه با جایگزین کردن یک سازمان را در نظر بگیرید. این مسئله در حالت انتخاب در تصمیم گیری بر روی نتایج حاصله اثر می‌گذارد و از طریق مدل سازی احتمالی قابل حل است. در این مقاله، حداقل احتمال برای جایگزینی با موقعیت سازمان در حالتی که هبه کنندگان متعدد وجود داشته باشد، محاسبه گردیده است. معادلات حاکم در این مسئله بر حسب احتمال بعضی از فاکتورهای مهم مانند طول عمر تنظیمی کیفیت (QALY) مشتریان، هبه کنندگان، میانگین دانش حاصل شده، مواهب پزشکی به دست آمده و شهرت انتظاری جراحان ساخته شده اند. نهایتا" نتایج تحلیلی از حل معادلات به دست آمده و سپس به صورت عددی نشان داده شده است.

1. INTRODUCTION

The mathematical modelling of organ transplantation has attracted researchers working in the area of Biomathematics. Transplantation of an organ is a process by which the damaged sections of the tissues are removed and are implanted by taking the same from healthy adult donors. The successful experimental transplantation of non-cadaveric organs such as livers, lungs, hearts etc. is uncertain in medical science so far. The transplantation depends on both the patient's (recipient) and donors' health before the transplantation, expected health of both after and the degree of willingness of the donors, and the expertise of the surgeon. If family members, donors and friends show strong emotions towards performing transplantation, then the surgeon must do so for the gain of knowledge , earning of money and fame, despite of high risk of failure. A few researchers have developed mathematical models quantifying the decision making process of organ transplantation.

The main purpose of the present investigation is to obtain minimum probability of success of the operation by developing a probabilistic model for the non-cadaveric organ transplantation decision-making problem. It is worthwhile to briefly review the earlier works done in this field. Israil and Yechiali [1] formulated a time dependent stopping problem and applied it to live organ transplants. Ahn and Hornberger [2] studied the problem of a cadaveric kidney transplant allocation process. Bleichrodt and Quiggin [3] analyzed life-cycle preferences over consumption and health and made a cost analysis. Sculpher et al. [4] developed a model on cost-effectiveness in practical decisions for transplantation. Howard [5] answered the reason as to why do transplant surgeons turn down organs by developing a scientific opinion in this regard. Karnonn [6] developed decision-modeling techniques for the evaluation of health care and used the Markov process to simulate the results. Groen et al. [7] explored the relationship between diagnosis and the cost-effectiveness and cost-utility of lung transplantation and suggested that there was considerable variation in cost-effectiveness and, to a lesser degree, in cost-utility between the different diagnostic categories. These variations are due to the differences in survival and quality of life with and/or without a lung transplantation. Philips et al. [8] analyzed the modeling of decision-making on health technique assessment. Roth et al. [9] explained, experimentally, various points of caution for the transplantation of kidneys. Levy [10] formulated a non-cadaveric organ transplantation decision-making model and derived the probability of success for transplantation of non-cadaveric organs. No model has been proposed before Levy that considered the well being of donors and medical knowledge gain. Gardiner et al. [11] formulated a stochastic model of patient health and cost outcomes. They used a continuous time-finite state non-homogeneous Markov process to describe the occurrence of events regarding the patient. In practice, sometimes more than one donor is needed. We extend Levy's work [10] by incorporating more than one donor, money gain and fame of the surgeon. These factors also play significant roles in the decision making process for such transplantations. Through this investigation, the minimum probability of success for non-cadaveric organ transplantation when more than one donor shows interest in saving the life of a patient, is obtained. The rest of the study is organized in the following way. In Section 2, we describe a model in terms of the surgeon's overall concern. The governing equations are constructed in Section 3. In Section 4, decision making and minimum probability of success are derived. The numerical illustrations are given in Section 5. Finally, in Section 6, the conclusions are drawn.

2. MODEL DESCRIPTION

In a non-cadaveric organ transplantation process, there are three main stakeholders (i) recipient, (ii) donor(s) and (iii) surgeon; except the family members, friends and relatives of both the recipient and the donor. The success of the operation depends mainly on the condition of the two. It is also well known that a surgeon's self esteem is at stake and therefore his best practice prevails during an operation.

For the mathematical formulation of the model, we use the following notations:

n =	Number of donors
U^S =	Surgeon's overall concern
U^R =	Recipient's life time well being
U_0^R =	Pre-operation level of recipient
U_{post}^R =	Post-operation level of recipient
U^{D_i} =	ith donor's life time well being
$U_0^{D_i}$ =	Pre-operation level of ith donor
$U_{post}^{D_i}$ =	Post-operation level of ith donor
ΔK^S =	Knowledge gained by the surgeon
ΔM^S =	Money gained by the surgeon
F^S =	Fame gained by the surgeon
Q_0^R =	Pre-transplantation quality-adjusted life years of recipient
$Q_0^{D_i}$ =	Pre-transplantation quality-adjusted life years of ith donor
δ_i =	Surgeon's degree of concern for ith donors' well being relative to surgeon's degree of concern for recipient's well being

δ_K = Surgeon’s degree of interest in gaining knowledge relative to surgeon’s degree of concern for recipient’s well being.

δ_M = Surgeon’s interest in money relative to surgeon’s degree of concern for recipient’s well being.

g_R = The rate of increase in the recipient’s quality adjusted life years during successful operation,

δ_R = The rate of decrease in the recipient’s quality adjusted life years when operation fails,

δ_{D_i} = The rate of decrease in the quality adjusted life years of ith donors due to operation

p_1 = The probability of successful transplantation

p_2 = The probability that there is no change in the condition of recipient after transplantation

p_3 = The probability of failure of operation

p_{min} = Required minimum probability of success

β_{R_i} = The recipient’s degree of concern for the quality adjusted life years of i^{th} donor relative to his/her own.

β_{D_i} = Degree of concern of i^{th} donor for quality adjusted life years of recipient relative to their own

In the decision making process for transplantation, the surgeon is concerned with the well being of the recipient, donors, knowledge gain, money and fame. The surgeon’s concern can be formulated by involving all these factors as

$$U^S = U^R + \sum_{i=1}^{n} \delta_i U^{D_i} + \delta_k \Delta K^S + \delta_m \Delta M^S + F^S \quad (1)$$

If δ_i = 1, the surgeon is not biased; he has equal care for the donor and recipient. If δ_k = 1, the surgeon’s interest towards gain knowledge and the surgeon’s degree of concern for the recipient’s well being are equal. δ_k > 1 shows that the surgeon is more interested in learning by doing. δ_m > 1 indicates that the surgeon’s interest is more in the money making aspect than the recipient’s well being.

The lifetime well being of the recipient and donors are measured in quality adjusted life years (QALYs). The value of the medical knowledge gained from the transplantation (ΔK^S) is measured as expected contributions to the quality adjusted life years of the future recipient and donors. Money contributes in developing the medical industry in terms of the infra structure that enhances the quality adjusted life years for future recipient and donors.

3. THE ANALYSIS

Since the outcome of the recipient’s operation is uncertain i.e. it may result in one of the three states (i) successful operation that means it improves the condition of the recipient (ii) no change in the condition of the recipient and (iii) failure of the operation that cause deterioration in the condition of the recipient and may be fatal. The recipient’s post transplantation life time well-being is denoted by

$$U^R_{Post} = \begin{cases} \left[(1+g_R)Q_0^R + \sum_{i=1}^{n} \beta_{R_i}(1-\delta_{D_i})Q_0^{D_i}\right]p_1, \\ \text{when operation is successful;} \\ \left[Q_0^R + \sum_{i=1}^{n} \beta_{R_i}(1-\delta_{D_i})Q_0^{D_i}\right]p_2, \\ \text{when no change in recipient's condition;} \\ \left[(1+\delta_R)Q_0^R + \sum_{i=1}^{n} \beta_{R_i}(1-\delta_{D_i})Q_0^{D_i}\right]p_3, \\ \text{when operation is failure.} \end{cases} \qquad (2)$$

and

$$\sum_{i=1}^{3} p_i = 1$$

If β_{R_i} = 1, recipient is selfish and he cares only for himself and not for i^th (i = 1,2,3,…,n) donor. If β_{R_i} = 1, he cares equally for ith donor and himself.

The recipient's expected post operation well being is given by

$$E\left(U_{post}^{R} \right) = \left[(1+g_R)p_1 + (1-\delta_R)p_3 + p_2\right]Q_0^R + \sum_{i=1}^{n} \beta_{R_i}[(1-\delta_{D_i})p_1 + (1-\delta_{D_i})p_2 + (1-\delta_{D_i})p_3]Q_0^{D_i} \qquad (3)$$

The recipient's pre-operation well being is

$$U_0^R = Q_0^R + \sum_{i=1}^{n} \beta_{R_i} Q_0^{D_i}$$

Expected improvement in QALYs of the recipient is given by

$$E\left(U_{post}^{R} \right) - U_0^R = \left[(g_R + \delta_R)p_1 + \delta_R\, p_2 - \delta_R\right]Q_0^R - \sum_{i=1}^{n} \beta_{R_i}\delta_{D_i} Q_0^{D_i} \qquad (4)$$

Distribution for the donors' post operation life time well being is given by

$$U_{Post}^{D_i} = \begin{cases} \left[(1-\delta_{D_i})Q_0^{D_i} + \beta_{D_i}(1+g_R)Q_0^R\right]p_1, & \text{when operation is successful;} \\ \left[(1-\delta_{D_i})Q_0^{D_i} + \beta_{D_i}Q_0^R\right]p_2, & \text{when no change in recipient's condition;} \\ \left[(1-\delta_{D_i})Q_0^{D_i} + \beta_{D_i}(1-\delta_R)Q_0^R\right]p_3, & \text{when operation is failure.} \end{cases} \qquad (5)$$

Expected post-operation lifetime well being of i^th (i = 1,2,3,…) donor is given by

$$E\left(U_{post}^{D_i} \right) = \left[(1-\delta_{D_i})p_1 + (1-\delta_{D_i})p_2 + (1-\delta_{D_i})p_3\right]Q_0^{D_i} + \beta_{D_i}\left[(1+g_R)p_1 + (1-\delta_R)p_3 + p_2\right]Q_0^R \qquad (6)$$

When β_{D_i} > 1, the i^th donor cares more for QALYs of recipient.

The pre operation well being of i^th (i = 1, 2, 3, …) donor is

$$U_0^{D_i} = Q_0^{D_i} - \beta_{D_i} Q_0^R$$

Expected change in QALYs of i^th donors is

$$E\left(U_{post}^{D_i} \right) - U_0^{D_i} = \beta_{D_i}\left[(g_R + \delta_R)p_1 + \delta_R p_2 - \delta_R\right]Q_0^R - \delta_{D_i} Q_0^{D_i} \qquad (7)$$

4. DECISION-MAKING AND MINIMUM PROBABILITY OF SUCCESS

A surgeon can be either in favour of the transplantation or against it; depending upon the health and mental status of the recipient and donors. However apart from these factors, he is also concerned with knowledge enhancement, monetary gain, his reputation, etc. For making a decision to perform the operation, the risk neutrality is assumed for the transplantation outcome. A risk neutral surgeon will favour transplantation after taking consent from the donors and recipient. For the success of the operation,

$$U^S = E\left(U_{post}^{S} \right) - U_0^S > 0$$

Hence from Equation 1, we get

$$U^{R} + \sum_{i=1}^{n} \delta_i U^{D_i} + \delta_k \Delta K^{S} + \delta_m \Delta M^{S} + F^{S} > 0 \tag{8}$$

Therefore

$$\left\{\left[(g_R + \delta_R)p_1 + \delta_R p_2 - \delta_R\right]Q_0^{R} - \sum_{i=1}^{n} \beta_{R_i}\delta_{D_i} Q_0^{D_i}\right\} + \sum_{i=1}^{n} \delta_i \{\beta_{D_i}\left[(g_R + \delta_R)p_1 + \delta_R p_2 - \delta_R\right] Q_0^{R} - \delta_{D_i} Q_0^{D_i}\} + \delta_k \Delta K^{S} + \delta_m \Delta M^{S} + F^{S} > 0 \tag{9}$$

Now we will find the probability of success of the operation. Here we assume that there is very low probability of no change in the condition of the recipient as noticed from previous experiments in various health care centres. Thus substituting $p_2 = 0$ in 9, we obtain the expression

$$\left\{\left[(g_R + \delta_R)p_1 - \delta_R\right]Q_0^{R} - \sum_{i=1}^{n} \beta_{R_i}\delta_{D_i} Q_0^{D_i}\right\} + \sum_{i=1}^{n} \delta_i \{\beta_{D_i}\left[(g_R + \delta_R)p_1 - \delta_R\right] Q_0^{R} - \delta_{D_i} Q_0^{D_i}\} + \delta_k \Delta K^{S} + \delta_m \Delta M^{S} + F^{S} > 0$$

or

$$p_1 > \frac{\left[\sum_{i=i}^{n} (\beta_{R_i} + \delta_i)\delta_{D_i} Q_0^{D_i}\right]}{\left(1 + \sum_{i=1}^{n} \delta_i \beta_{D_i}\right)(g_R + \delta_R)Q_0^{R}} + \frac{\left(1 + \sum_{i=1}^{n} \delta_i \beta_{D_i}\right)\delta_R Q_0^{R} - \delta_k \Delta K^{S} - \delta_m \Delta M^{S} - F^{S}}{\left(1 + \sum_{i=1}^{n} \delta_i \beta_{D_i}\right)(g_R + \delta_R)Q_0^{R}} \cong p_{min} \tag{10}$$

The right hand side of the above Equation gives the critical value of probability of success. The probability of success should be higher than this critical probability. We call this critical probability as minimum probability of success (p_{min}). If the probability of success is higher than this probability, then the surgeon, donors and recipient will give comment to perform the operation. Therefore

$$p_{min} = \frac{\delta_R}{(g_R + \delta_R)} + \frac{\sum_{i=i}^{n} (\beta_{R_i} + \delta_i)\delta_{D_i} Q_0^{D_i}}{\left(1 + \sum_{i=1}^{n} \delta_i \beta_{D_i}\right)(g_R + \delta_R)Q_0^{R}} - \frac{\delta_k \Delta K^{S}}{\left(1 + \sum_{i=1}^{n} \delta_i \beta_{D_i}\right)(g_R + \delta_R)Q_0^{R}} - \frac{\delta_m \Delta M^{S}}{\left(1 + \sum_{i=1}^{n} \delta_i \beta_{D_i}\right)(g_R + \delta_R)Q_0^{R}} - F^{M} \tag{11}$$

Now we examine the effects of different terms of Equation 11 and other parameters on the minimum required probability of success of the operation as follows:

(a) if we assume that there is no change in the quality adjusted life years of ith donor due to the operation (i.e. $\delta_{D_i} = 0$) then learning by experimenting on human patients is totally prohibited; the money part and fame of the surgeon are of little concern for the surgeon in comparison to the surgeon's degree of concern for the recipient. In this situation, only first term of R. H. S. in Equation 11 represents minimum probability of success for transplantation of non-cadaveric organs. It indicates that the minimum probability of success declines as the rate of increase in the quality adjusted life years of recipient rises in case of a successful transplantation and vise versa in case of the failure of operation.

(b) The second term on the right hand side of Equation 11 shows the effect of ith donor-recipient quality adjusted life years ratio on required minimum probability of success. This probability rises on the raising of the ratio. The parameters given in this term can affect this ratio remarkably.

The following factors increase the i^{th} donor-recipient quality adjusted life years ratio at minimum probability:

- When $\beta_{R_i}\beta_{D_i} < 1$, (i) the rate of decrease in quality adjusted life years of i^{th} donor due to operation, (ii) the recipient's degree of concern for i^{th} donor's quality adjusted life years and (iii) the surgeon's degree of concern for i^{th} donor's quality adjusted life years relative to the surgeon's degree of concern for quality adjusted life years of recipient (i.e. donor and recipient are selfish).

Following factors lower this ratio:

- When $\beta_{R_i}\beta_{D_i} < 1$, (i) the expected rate of increase in the quality adjusted life years of recipient following a successful operation, (ii) the expected rate of decrease in the quality adjusted life years of the recipient following the failure of the operation, (iii) i^{th} donor's degree of concern for the well being of recipient and (iv) surgeon's degree of concern for i^{th} donor's quality adjusted life years relative to the surgeon's degree of concern for quality adjusted life years of the recipient (i.e. donor and recipient are not selfish).

(c) The third term describes the ratio of knowledge gain and pre-operation quality adjusted life years of the recipient. Minimum probability declines with this ratio of knowledge gain and pre-operation quality adjusted life years of the recipient increases. This ratio for minimum probability is raised by the surgeon's interest of learning by doing relative to surgeon's degree of concern for the recipient' s well being and is decreased by the following parameters (i) the expected rate of increase in the quality adjusted life years of the recipient following the successful operation, (ii) the expected rate of decrease in the quality adjusted life years of the recipient following the failure of the operation, (iii) i^{th} donor's degree of concern for the well being of the recipient and (iv) the surgeon's degree of concern for i^{th} donor's quality adjusted life years relative to the surgeon's degree of concern for the quality adjusted life years of recipient.

(d) The fourth term of Equation 11 predicts that the minimum probability of success is decreased by the ratio of the value of money gain from the operation to pre-operation quality adjusted life years of the recipient. This ratio is raised by the surgeon's interest of making money relative to the surgeon's degree of concern for recipient's lifetime well being. It is decreased by the following factors (i) the expected rate of increase in the quality adjusted life years of the recipient following a successful operation, (ii) the expected rate of decrease in the quality adjusted life years of the recipient following the failure of the operation, (iii) i^{th} donor's degree of concern for the well being of the recipient and (iv) the surgeon's degree of concern for i^{th} donor's quality adjusted life years relative to the surgeon's degree of concern for quality adjusted life years of the recipient. In view of the last term, the required minimum probability of success for transplantation of non-cadaveric organs reduces.

5. NUMERICAL RESULTS

In this section, numerical results for the minimum probability of success for transplantation of non-cadaveric organs are calculated for fixed default parameters as follows:

$Q_0^R = 1$, $Q_0^{D_i} = 50$, $\Delta K^S = 10$, $\Delta M^S = 1$, $\delta_i = 1$(i = 1, 2, 3), $\delta_K = 1$, $\delta_M = 1$, $g_R = 10$, $\delta_R = 0.75$, $\delta_{D_i} = 0.2$(i = 1,2,3), $\beta_R = 1$ $\beta_D = 1$, $F^M = 0.001$.

We consider the illustration of three donors and obtain the required minimum probability of success (p_1) for the transplantation of a non-cadaveric organ as 0.4874. Then if p > = 0.4874, then the surgeon agrees to perform the operation. The effects of different parameters on required minimum probability of success are summarized in the Tables 1-4.

From Table 1, when $\delta_i = 0.1$ (i = 1,2,3), it is clear that the required minimum probability of success for transplantation of non-cadaveric organs strongly decreases as quality-adjusted life years of the recipient increases and the minimum probability increases as quality-adjusted life years

TABLE 1. Minimum Probability for Different Values of Q_0^R and $Q_0^{D_i}$.

$Q_0^{D_i}$	40	40	40	50	50	50	60	60	60
Q_0^R	$\delta_i = 0.5$	$\delta_i = 1$	$\delta_i = 1.5$	$\delta_i = 0.5$	$\delta_i = 1$	$\delta_i = 1.5$	$\delta_i = 0.5$	$\delta_i = 1$	$\delta_i = 1.5$
0.8	0.1462	0.3594	0.4873	0.3788	0.5926	0.7199	0.6114	0.8245	0.9520
1	0.1307	0.3013	0.4036	0.3168	0.4873	0.5896	0.5028	0.6732	0.7759
1.2	0.1204	0.2625	0.3478	0.2254	0.4176	0.5028	0.4305	0.5726	0.6579
1.5	0.1101	0.2238	0.2920	0.2341	0.3478	0.4160	0.3581	0.4718	0.5400

TABLE 2. Minimum Probabilities for Different Values of ΔK^S and δ_K.

δ_K \ ΔK^S	40	50	60
0.5	0.8362	0.7194	0.6036
0.8	0.7664	0.5003	0.3943
1	0.7199	0.4873	0.2548
1.2	0.6734	0.3943	0.1152
1.5	0.6036	0.2548	0.0001

TABLE 3. Minimum Probability for Different Values of ΔM^S and δ_K.

δ_K \ ΔM^S	40	50	60
0.5	0.5222	0.5106	0.4990
0.8	0.5152	0.4966	0.4780
1	0.5106	0.4873	0.4641
1.2	0.5059	0.4780	0.4501
1.5	0.4990	0.4641	0.4292

of ith donor increases. Apparently the lower values of p_{min}, motivates the surgeon to hope for a successful operation. Thus we conclude that this probability is lower at the early stage of damage of the organ than at later stage. When $\delta_i = 0.5$ (i = 1,2,3), the surgeon is biased and he cares more for quality-adjusted life years of the recipient as compared to ith donor. In this case also, the minimum probability of decision for successful transplantation decreases on increasing the quality-adjusted life years of the recipient and it increases as quality-adjusted life years of ith donor increases. Same trends are noticed when $\delta_i = 1.5$; the surgeon is more interested in the quality-adjusted life years of ith donor than that of the recipient. We conclude that the required minimum probability of success (p_1) for transplantation of non-cadaveric organs decreases as the surgeon' s degree of concern for life time well being of ith donor relative to the surgeon' s degree of concern for life time well being of the recipient decreases.

In Table 2, required minimum probability of success (p_1) for the transplantation of non-cadaveric organs is calculated for different values of ΔK^S and ΔM^S. We observe that the minimum probability declines for both cases when ΔK^S and δ_K increase. The same trends can be seen in Table 3; the required minimum probability lowers on increasing ΔM^S and δ_M.

Table 4 shows that the required minimum probability of success for transplantation of non-cadaveric organ strongly decreases when g_R increases. The minimum probability remarkably increases on slight increment in the rate of decrease in the quality adjusted life years of the recipient (δ_{D_i}) in the case of failure of the operation and increases on increasing, β_R. Required probability decreases as β_D increases. In particular when the operation fails (i.e. $\delta_R = 1$), then the combined sum of the QALYs of 3 donors is mathematically equal to 150 and the effect of this combined sum is seen on the knowledge gain and money gain. In this case the knowledge gain and money gain for future recipients and donors increases up to 51 and 41 quality adjusted life years for the three donors respectively.

6. CONCLUSION

In this paper, we have derived expression for the required minimum probability for decision making in view of success for transplantation of non-cadaveric organs based on the surgeon's concern about the recipient, donors and himself. In an ideal case, the recipient and donors may not be selfish and have the feeling of altruism for each other. The surgeon may show equal interest towards the quality adjusted life years of the recipient, donors and other factors like knowledge gain, money making, and fame; in such situations, the required minimum probability of success may play a vital role. On the basis of this minimum probability, the surgeon, recipient and donors cooperatively make a decision to go ahead with performing the operation. The minimum probability of success for different cases is obtained to find out the effect of parameters on it. Analytically the increasing ratio of the values of expected knowledge gain and money gain stemming from the operation to the recipient's pre-operation quality adjusted life years reduces this probability of success. It is noticed, based on numerical experiments that the number of donors' involvement enhances the quality-adjusted life years of knowledge gain and money gain even if the operation fails. The minimum probability of success is lower in the early stages of development of the transplantation.

TABLE 4. Minimum Probability for Different Values of Different Parameters.

Parameters	Low Level	Medium Level	High Level	Effect
g_R	5	10	20	
p_{min}	0.99120	0.4874	0.2520	Strong decline
δ_R	0.5	0.75	1	
p_{min}	0.4751	0.4874	0.4990	Slight increment
δ_D	0.1	0.2	0.3	
p_{min}	0.0222	0.4874	0.9524	Strong increment
β_{Ri}	0.5	1	1.5	
p_{min}	0.2548	0.4874	0.7199	Increase
β_{Di}	0.5	1	1.5	
p_{min}	0.6264	0.4874	0.4036	Decrease

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