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Cost-effectiveness of health research study participant recruitment strategies: A systematic review

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Abstract

Background: A large fraction of the cost of conducting clinical trials is allocated to recruitment of participants. A synthesis of findings from studies that evaluate the cost and effectiveness of different recruitment strategies will inform investigators in designing cost-efficient clinical trials.

Purpose: To systematically identify, assess, and synthesize evidence from published comparisons of the cost and yield of strategies for recruitment of participants to health research studies.

Methods: We included randomized studies in which two or more strategies for recruitment of participants had been compared. We focused our economic evaluation on studies that randomized participants to different recruitment strategies.

Results: We identified 10 randomized studies that compared recruitment strategies, including monetary incentives (cash or prize), direct contact (letters or telephone call), and medical referral strategies. Only two of the 10 studies compared strategies for recruiting participants to clinical trials. We found that allocating additional resources to recruit participants using monetary incentives or direct contact yielded between 4% and 23% additional participants compared to using neither strategy. For medical referral, recruitment of prostate cancer patients by nurses was cost-saving compared to recruitment by consultant urologists. For all underlying study designs, monetary incentives cost more than direct contact with potential participants, with a median incremental cost per recruitment ratio of Int$72 (Int$—International dollar, a theoretical unit of currency) for monetary incentive strategy compared to Int$28 for direct contact strategy. Only monetary incentives and source of referral were evaluated for recruiting participants into clinical trials.

Limitations: We did not review studies that presented non-monetary cost or lost opportunity cost. We did not adjust for the number of study recruitment sites or the study duration in our economic evaluation analysis.

Conclusions: Systematic and explicit reporting of cost and effectiveness of recruitment strategies from randomized comparisons is required to aid investigators to select cost-efficient strategies for recruiting participants to health research studies including clinical trials.

Keywords

Cost of conducting health research studies, recruitment, economic evaluation, recruitment effectiveness, clinical trial efficiency

Introduction

A large fraction of the cost of conducting health research studies, including clinical trials, lies in the recruitment of participants.[1–3] Maximizing recruitment and ensuring high follow-up rates in clinical trials with minimal expenditure are important financially, ethically, and statistically (i.e. to obtain adequate statistical power for hypothesis testing or adequate precision).[4] In economics and operations research, efficiency is described as a set of structures and processes that aim to achieve high performance at minimal cost.[5–7] In the

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context of the design and conduct of clinical trials, we consider efficiency as the minimal cost to carry out a trial while still achieving satisfactory statistical power.

Approaches to improving the operational efficiency of clinical trials and approaches to enhancing clinical trial designs, study start-up, data quality, and adverse event reporting have been discussed in the literature.[8] It is critical to employ design strategies that minimize costs while maintaining adequate power.[9–11] More formally, cost-effectiveness models can be built to examine the trade-offs between cost and benefits of different methods for conducting a clinical trial while optimizing statistical power.[12]

Recruiting participants to health research studies is resource intensive and has been recognized as a challenge by many investigators.[13] Recruitment strategies can be broadly categorized as direct contact (e.g. telephone call to potential participants), community outreach, mass media, referrals, and incentives (e.g. cash or gift card to reimburse participants' time).[14] Systematic reviews of strategies to recruit participants to research studies have been performed, but those reviews focused on the effectiveness of the strategies and did not report the cost of recruitment.[15–18] Some recruitment strategies may be more efficient than others, but cost more. The objective of this study was systematically to identify, assess, and synthesize findings from randomized studies that compared different recruitment strategies on the effectiveness and cost of recruitment.

Methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines to report our systematic review.[19]

Criteria for selecting studies

We included randomized controlled trials (RCTs) that had compared two or more operational processes, defined as strategies for recruiting participants into health research studies. To be eligible, a study must have reported monetary cost directly related to operational processes (recruitment of participants). We excluded studies that reported cost only in a non-monetary form or cost unrelated to participant recruitment, such as the cost to attend clinic for medical services (e.g. cost for national immunization programs or annual mammography examinations).

Search strategy

We searched PubMed (1950–2010), the *Cochrane Library* (2010, Issue 4) which includes the Cochrane Methodology Register and the Cochrane Central Register of Controlled Trials (CENTRAL), Current Index to Statistics–Extended Database (CIS-ED) (1967–2009), EMBASE (1980–2010), and ISI Web of Science (1900–2010) using a search strategy developed by L.H. and reviewed by a medical informationist. We also handsearched references of included studies, and contacted experts at the Johns Hopkins Center for Clinical Trials for any additional potentially eligible studies. We completed the search in August 2011. We used various terms related to study design, recruitment of participants, cost, and power. The complete search strategies are available in the web supplemental section (S1, which also includes a parallel search for studies examining strategies for participant retention).

Data collection and analysis

Study selection process. Pairs of authors (L.H., S.H.L., B.J., T.L., and S.S.V.) independently screened each abstract and reviewed full text of relevant abstracts resulting from the electronic search. We resolved disagreements by consensus or by arbitration by a third person.

Data extraction. For data on the underlying research study and the relationships of the authors' affiliations and funding institutions, L.H. performed the initial data extraction, which was verified by S.H.L. or B.J. For data on operational processes and quality assessment, L.H., S.H.L., and B.J. performed independent data extraction. We resolved disagreements through discussion. We made up to three attempts to contact the primary authors for additional information or missing data on the costs of recruitment.

In this review, expanding on Silagy's taxonomy, we classified recruitment strategies into the following categories: medical referral, community outreach, mass media, direct contact, personal referral, incentives, registry, and other.[14] Medical referral refers to health professionals inviting participants to the study. Community outreach involves mobilizing the community to promote the study at local fairs, churches, or community organized events. Mass media refers to using public service announcements and advertisements to inform potential participants about the study. Direct contact involves mailing, telephoning, or emailing potential participants. Personal referral includes word of mouth referral by friends and family to the study. Incentives include cash or prizes to compensate for the participants' time in the study. The registry category refers to the use of clinical databases to identify potential participants for the study. Examples of approaches classified as "other" include recruitment at the worksite or use of multiple recruitment approaches.

Assessment of the risk of bias of included studies. We examined the method of randomization, allocation concealment, reporting of blinding to the operational

processes, analysis by "intention to treat," comparability of clinical recruitment site, methods for dealing with missing data, and definition of the operational process and outcome of the recruitment efforts.[20]

Analysis. We conducted a cost-effectiveness analysis and calculated incremental cost-effectiveness ratios (ICERs) for each study. Equation (1) is the formula for computing the ICER:

$$\text{ICER} = \frac{\text{Cost of Strategy B} - \text{Cost of Strategy A}}{\text{Recruitment ratio of Strategy B} - \text{Recruitment ratio of Strategy A}} \quad (1)$$

The ICER is the effect of changing the recruitment strategy and the additional cost incurred compared to the less costly and less effective approach. The incremental cost is the difference between the total cost per eligible participant for strategy B and the total cost per eligible participant for strategy A. Strategy A was defined as the least costly and least effective strategy reported in the study. Strategy B was the comparator. In our analyses, the least costly and least effective strategy was usually the group assigned to no additional operational process. We used the total cost per eligible participant to normalize our incremental cost, specifically for studies that had a randomization ratio other than 1:1.

We used the number of participants recruited (screened) over the number randomized (eligible) or contacted as a measure of effectiveness of the strategies. The effectiveness was determined by the recruitment ratio. The incremental recruitment ratio is the difference between the recruitment ratio for strategy B and the recruitment ratio for strategy A. We referred ICER as the incremental cost per recruitment ratio. We conducted an expansion path analysis, based on the ICER, to identify the most cost-effective strategies. We used the cost-effectiveness threshold as a metric to assist investigators to choose among different strategies for recruitment of participants. The cost-effectiveness threshold value, which is undefined for operational process research, would be the value that investigators are willing to pay to recruit an additional participant into the study.

We first presented cost in the unit in which it was reported. We then adjusted for inflation to 2009 national currency using the consumer price index for each country. For studies that did not report the cost year, we assumed that the cost year was 2 years prior to the publication date on the assumption that it takes on average 2 years after study completion to publish an article in a peer-reviewed journal.[21] We converted the national currency to the international dollar (Int$) using the purchasing power parity (PPP) index.[22] The Int$ is a theoretical unit, which allows us to compare across countries the cost of conducting the study and to report the cost for all studies using a common unit. The PPP index is the number of units of a country's currency needed to purchase the same amount of goods or services in the domestic market as the US dollar would buy in the United States.[22]

Data management. We used Endnote® version X.0.2 to store the bibliographic citations from the search and QUOSA® Information Manager[23] to retrieve the full-text articles. We abstracted and entered data to a Microsoft Access® 2007 database developed specifically for this study. We used Stata® version 10.1 to analyze the data and to obtain key statistics and Microsoft Excel® 2007 for the cost-effectiveness analysis.

Results

Search

We identified 4819 unique citations and excluded 4366 after screening the titles and abstracts. Of the 453 titles and abstracts we attempted to review the full-text for further evaluation, the full-text reports were not available for nine titles and abstracts. We excluded 434 full-text reports for the following reasons: commentary/reviews (n = 62), no operational comparator (n = 252), no cost comparator (n = 73), and no randomization of operational processes reported (n = 47). In total, we included 10 studies in this review[24–33] (see Figure 1). Only 2 of the 10 studies[25,29] were conducted to evaluate recruitment methods to clinical trials of interventions.

Overall description

The primary diseases studied in the included reports were prostate cancer, smoking cessation, breast cancer, ocular disorder, and abnormal pregnancy. Five (50%) studies enrolled both male and female participants, one (10%) study enrolled only male participants, and three (30%) studies recruited only female participants. Nine (90%) studies enrolled only adults, and one study (10%) recruited children. Three (30%) studies received funding from academic institutions, two (20%) studies received funding from government agencies, two (20%) studies received funding from pharmaceutical companies, and one (10%) study received both academic institution and government agency funding. A majority of the studies were conducted in the United States (60%). Other study locations were Australia (30%) and Canada (10%).

The 10 included studies reported a total of 29 strategies for recruitment. Cost data came from retrospective review of the financial budgets. Table 1 provides a summary of the characteristics of the studies that randomized recruitment strategies. The overall recruitment duration ranged between 2 and 24 months. The median number of participants randomized was 443 (interquartile range

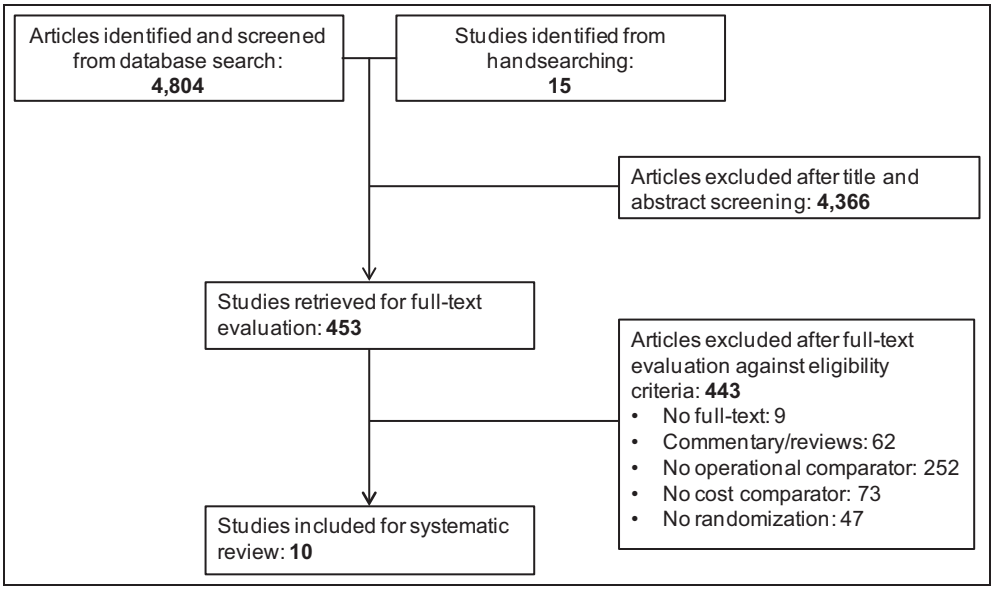

Figure 1. Flow diagram for study selection.

[IQR]: 331–900). The median number of participants who responded to the recruitment strategies was 177 (IQR: 104–483). Two to five strategies were compared in each of the included studies.

Quality assessment of the included studies

Of the 10 studies that randomized operational processes, only three studies reported the method for randomization. Our assessments of the risk of bias associated with features of the study designs can be found in the web supplemental section (Table S2). None of the studies described allocation concealment, blinding of the investigator, or methods for handling missing data. Three (30%) studies described an "intention to treat" analysis, and three (30%) studies discussed comparability of the clinical recruitment sites. The definitions of the operational processes and cost measures were reported explicitly in all studies.

Economic evaluation of strategies in the randomized studies

Six (60%) studies, including one conducted in the context of recruitment to a clinical trial,[29] assessed monetary incentives to recruit participants into the study. Three (30%) studies implemented different methods of direct contact, and one (10%) study[25] compared nurses with consultant urologists for recruiting participants to a clinical trial. Table 2 presents the cost-effectiveness results.

The median ICER for the six studies assessing monetary incentives was Int$72. The median ICER for the three direct contact studies was Int$28. The study populations for the six studies which evaluated monetary incentives were adolescents enrolled into a trial of a smoking cessation program,[29] pharmacists,[31] enrollees of health plans,[32] and physicians.[26,33] The investigators compared incremental cash value to either no incentive or an incentive of lesser amount. Providing vouchers to pharmacists yielded the highest cost (Int$88). The incremental cost per recruitment ratio was Int$466 for the voucher group compared to no voucher.

In the trial of a smoking cessation program,[29] the $200 prize was less cost-effective compared to the $2 incentive. An extended cost expansion analysis was conducted for the $2 incentive and the $15 incentive. The ICER was Int$13 for the $2 incentive group to enroll an additional individual into the smoking cessation study compared to the no incentive strategy, and the ICER was Int$123 for the $15 incentive group to recruit an additional person into the study compared to the $2 incentive group.

The study of medical referral that compared nurses and consultant urologists with respect to recruitment of participants to a clinical trial[25] demonstrated that having consultant urologists recruit male participants with prostate cancer into the study was more costly and less effective compared to nurses.

In a study about enrolling members of a health plan,[32] the $5 incentive group had an ICER of Int$53 compared to the $2 incentive group. For the study to recruit general physicians, the $20 incentive group was dominated because it was more costly and less effective compared to the $10 incentive group.

In another study recruiting general internists and family practitioners,[26] the $10 incentive had an ICER of Int$72 compared to the $5 incentive group. For the study recruiting female cosmetologists,[27] it was less expensive and more effective to enclose $1 in the

Table 1. Characteristics of randomized studies that evaluated recruitment strategies.

Ref.	Year	Underlying study design	Topic of study	Types of recruitment strategies	Overall recruitment period (in months)	N strategies compared
Donovan et al.[25]	2003	Clinical trial	Prostate cancer	Medical referral	24	2
Martinson et al.[29]	2000	Clinical trial	Smoking cessation	Monetary incentives	2	4
Page et al.[30]	2006	Observational study	Breast cancer screening	Direct contacts	3	4
Livingston et al.[28]	1994	Observational study	Ocular disorder	Direct contacts	3	2
Choi et al.[24]	1990	Survey	Abnormal pregnancy	Direct contacts	NR	5
Paul et al.[31]	2005	Survey	Smoking cessation	Monetary incentives	NR	2
Shaw et al.[32]	2001	Survey	General health	Monetary incentives	NR	2
VanGeest et al.[33]	2001	Survey	Physician response	Monetary incentives	NR	3
Halpern et al.[26]	2002	Survey	Physician response	Monetary incentives	NR	2
John and Savitz[27]	1994	Survey	Pregnancy and women health	Monetary incentives	3	3

NR: not reported.

envelope containing the letter of invitation compared to no incentive.

For the three studies that chose direct contact to recruit participants,[24,28,30] the median ICER was Int$28. These studies reached out to a general group of women,[30] nurses,[24] and the general public dwelling in Melbourne.[28] Postal mail and interviews were used to recruit participants. The doorstep interview had a response rate greater than 50% with a total cost of Int$7037.[28] The ICER for the doorstep interview was Int$57, which is the additional cost to implement the doorstep interview compared to telephone interview per unit increase in recruitment ratio. In the study that used different postage stamps, the large stamp had an ICER of Int$0.10.[24] For another study using mail to recruit participants, sending out two letters was less expensive and more effective compared to the one letter plus a telephone call at 6 weeks.[30]

We found that investing additional resources to recruit participants yielded between 4% and 23% additional participants recruited compared to no additional recruitment strategies. However, in two studies,[29,33] the $200 prize and the $20 incentive were eliminated from consideration as a cost-effective strategy because they had higher ICERs and were more costly and less effective compared to the $2 incentive and $10 incentive, respectively.

Discussion

Our systematic review synthesizes the existing evidence from randomized comparisons of recruitment strategies to reduce costs while achieving the target sample size based on the statistical power needed for a study. Only three strategies (monetary incentives, direct contact, and medical referral) had been assessed for recruitment of participants to randomized clinical trials. Based on the ICERs calculated for each study, we found that monetary incentives, in general, cost more than the direct contact and medical referral strategies.

Across all underlying study designs, monetary incentives increased the responses among the participants compared to no incentives but at an additional expense. Investigators who have a short time frame to recruit participants and an adequate budget may consider using monetary incentives as a strategy. Increasing monetary incentives showed diminishing returns on the response or recruitment rate. That is, the cost-effectiveness diminished as incentives increased beyond a certain point. The trade-off that the health research study investigator faces is whether to offer a small incentive to recruit more participants or to prolong the duration for recruitment and incur the costs to maintain the recruitment sites. It should be noted that policies in some countries[34] and at some institutions prohibit monetary incentives apart from

Table 2. Cost-effectiveness analysis for randomized studies.

Ref.	Strategies evaluated	Year	Currency	Duration of recruitment (in months)	N people randomized	N people responded	Recruitment ratio	Int$	Cost per randomized[a]	Cost per responded[b]	Incremental cost per recruitment ratio
Monetary incentives (N = 6)											
Martinson et al.[29]	No incentive	2008	USD	2	1050	483	0.46	5332	5.08	11.04	
	$200 prize	2008	USD	2	1050	589	0.56	7339	6.99	12.46	18.94
	$2	2008	USD	2	1050	650	0.62	7439	7.09	11.45	1.65
	$15	2008	USD	2	1050	721	0.69	16185	15.41	22.45	123.18
Paul et al.[31]	No voucher	2003	USD	NR	331	177	0.53	0	0.00	0.00	
	Voucher	2003	USD	NR	334	220	0.66	19269	57.69	87.59	465.49
Shaw et al.[32]	$2	2001	USD	NR	900	590	0.66	5708	6.34	9.67	
	$5	2001	USD	NR	900	649	0.72	8829	9.81	13.60	52.89
VanGeest et al.[33]	$5	1999	USD	NR	292	176	0.60	3805	13.03	21.62	
	$20	1999	USD	NR	291	189	0.65	9349	32.13	49.47	408.51
	$10	1999	USD	NR	290	198	0.68	5103	17.60	25.77	−436.67
Halpern et al.[26]	$5	2000	USD	NR	700	354	0.51	5398	7.71	15.25	
	$10	2000	USD	NR	500	293	0.59	6746	13.49	23.02	71.99
John and Savitz[27]	No incentive	1988	USD	3	443	327	0.74	1915	4.32	5.86	
	$1 enclosed with 2nd mailing	1988	USD	3	4315	3385	0.78	14979	3.47	4.43	−18.40
	$1 enclosed with first mailing	1988	USD	3	2791	2257	0.81	12443	4.46	5.51	40.79
Direct contact (N = 3)											
Choi et al.[24]	No stamp	1998	USD	NR	400	104	0.26	372	0.93	3.58	
	Business reply stamp	1998	USD	NR	400	132	0.33	443	1.11	3.36	2.53
	Metered stamp	1998	USD	NR	400	149	0.37	577	1.44	3.87	7.87
	Small regular stamp	1998	USD	NR	400	159	0.40	585	1.46	3.68	0.80
	Large stamp	1998	USD	NR	400	173	0.43	586	1.47	3.39	0.10
Livingston et al.[28]	Telephone interview	1992	AUD	3	216	86	0.40	4500	20.83	52.33	
	Doorstep interview	1992	AUD	3	256	132	0.52	7037	27.49	53.31	56.66
Page et al.[30]	No intervention	2004	AUD	3	788	11	0.01	0	0.00	0.00	
	One letter	2004	AUD	3	786	43	0.05	0	0.00	0.00	
	One letter plus phone call at six weeks	2004	AUD	3	785	61	0.08	1106	1.41	18.14	61.28
	Two letters	2004	AUD	3	785	67	0.09	503	0.64	7.51	−100.51
Medical referral (N = 1)											
Donovan et al.[25]	Nurse	2001	GBP	24	75	61	0.81	3772	50.29	61.83	
	Consultant urologist	2001	GBP	24	75	53	0.71	3897	51.96	73.53	−15.71

USD: US dollar; AUD: Australian dollar; GBP: Great Britain Pound; NR: not reported.

[a]The cost per randomized is calculated by dividing the cost (Int$) by the number of people randomized.

[b]The cost per responded is calculated by dividing the cost (Int$) by the number of people responded.

reimbursement for time and expenses directly associated with study participation.

Our findings on monetary incentives as a strategy to increase enrollment are supported by other studies. Giuffrida and Torgerson[35] investigated financial incentives to enhance patient compliance and found that financial incentives may improve patients' compliance to medical treatment. In a systematic review by Treweek et al.,[15] the authors reported that participants' willingness to participate in the study increased with payments. In another study, lottery-style incentives did not increase complete response rates to postal questionnaires[36] which suggests that in addition to providing financial incentive, multiple factors affect recruitment.

We were unable to compare directly monetary incentives and direct contact strategies because the studies evaluating these strategies were conducted with different objectives. The two strategies may be effective for different reasons to different people; monetary incentives may be appealing to younger potential participants because of the financial reward, but others may prefer direct contact strategies that provide human interaction.

Limitations

The unit for comparison in this review was the monetary cost presented in standardized currency. We did not account for indirect costs such as overhead cost that may have been incurred by the investigators but not reported in the included studies. We did not include studies that presented non-monetary cost or lost opportunity cost. We did not adjust for the number of study recruitment sites in our cost calculation or measurement for effectiveness. Higher cost of recruitment could be associated with having multiple sites for recruitment. We did not account for the study duration in our cost-effectiveness analysis. Finally, we did not explicitly distinguish between studies on recruiting participants for surveys versus other health research studies. We considered both types of studies to have the common goal of collecting data from participants.

We were unable to determine which recruitment strategies meet an acceptable cost-effectiveness threshold because an acceptable threshold value has yet to be defined. The heterogeneity in the included studies precluded us from identifying a specific threshold to which incentives are cost-effective or a particularly cost-effective strategy for recruitment.

Conclusion

Our findings highlight the need for further research focused on comparing different strategies for recruitment of participants to clinical trials, disseminating the findings, and using them to design cost-efficient trials. Currently, methodological investigations to compare different recruitment strategies are often low on the list of priorities for researchers and sponsors. Among the 10 included studies, only two studies[25,29] reported recruitment strategies to clinical trials. In addition, recommendations for standardized reporting of cost-effectiveness findings from RCTs on the cost of conducting clinical trials can ensure appropriate design of future trials through sharing of best practices. Furthermore, standardized reporting could minimize potential biases which may influence the credibility of the findings as observed in our risk of bias assessment. Appropriate choices of recruitment strategies during trial design could lead to cost-efficient clinical trials, but comparative data from RCTs are needed to inform choices. Thus, investigators proposing to conduct clinical trials should be encouraged to include in their proposals a discussion on cost-effectiveness of the recruitment strategies they plan to adopt in the trial, perhaps by imposing such a requirement at funding agencies.

Monetary incentives, direct contact, and medical referral are cost-effective strategies for recruiting participants to health research studies with a variety of designs. Recommendations for standardized reporting of findings from methodological studies on cost-effectiveness of strategies for recruitment, retention, and follow-up of trial participants and a central resource to host the findings from such studies are necessary to support investigators to design high-quality, cost-efficient health research studies including clinical trials.

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Declaration of conflicting interests

No author reported any conflict of interest.

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