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Avoided Costs and Economic Benefits Associated with Sponsored Clinical Trials

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ABSTRACT

The benefits associated with randomized clinical trials (RCTs) for patients, investigators, and sponsors are well known. However, little has been done to estimate the economic benefits related to sponsoring a RCT. Herein, a methodological analysis is proposed to assess the economic benefits and cost-savings of a RCT, namely the trial avoided costs (TAC). The TAC was considered to be cost-saving for the investigational medicinal product (IMP) (i.e., the drug adverted cost) and the diagnostic tests (i.e., procedure adverted cost) in a RCT. This tool is potentially helpful in understanding the financial impact of RCTS on healthcare institutions and provides the opportunity to invest budgets in other resources (i.e., core facilities, research infrastructure, human resources) that can increase the quality of clinical research.

BACKGROUND

Clinical trials are a potential source of information about costs and outcomes for a new treatment or healthcare program. Consequently, a growing number of economic evaluations are carried out alongside clinical trials [1, 2] and have become an increasingly important tool for healthcare systems to make decisions, as well as for regulatory authorities and in negotiating drug prices [3,4].

Different types of economic assessments are used to evaluate and compare the costs and outcomes of a new treatment or healthcare intervention, which can contribute to reducing the costs and burden of diseases for the healthcare system [5].

Sponsored randomized clinical trials (RCT) have significant implications for developing new therapeutic drugs and improving public healthcare [6]. For example, a patient can be administered a new treatment that is free of charge before it becomes fully accessible or when no alternative is available [7]. In this regard, the medicinal product can be provided or reimbursed by the sponsor during the period between the end of the trial and approval of marketing authorization. In addition, some protocols have an open-label extension phase (i.e., expanded access program) that assess the drug's long-term safety and efficacy [8, 9], which allows the patient to continue the new treatment until commercial availability.

Evidence from benefits associated with carrying out a sponsored RCT for patients (i.e., access to a new therapy), investigators (i.e., opportunity to contribute to the advancement of medical research), and sponsor (i.e., marketing authorization) is well known. Although cost analyses and budgets for conducting a clinical trial are widely documented [2, 10], little has been done to estimate the economic benefits in terms of costs avoided during a clinical trial [11 - 14].

Thus, the main purpose of the present article is to propose a methodological analysis of cost-savings in conducting a sponsored RCT, which demonstrates economic benefits not only for patients, but also, as a consequence, for the healthcare institution.

METHODS

To determine the cost savings in carrying out an RCT, we considered the trial avoided costs (TAC) as the cost-savings associated with the investigational medicinal product (IMP), including any active comparators supplied by the sponsor and the costs of diagnostic tests (i.e., laboratory tests, imaging).

For each RCT, we identified the IMP and/or the comparator (i.e., active control or placebo), the dose administered per patient, treatment period (days), and number of patients enrolled. In a double-blind RCT, when there was no difference between subjects who received the IMP or placebo, all subjects enrolled were considered.

The ex-factory price (i.e., the price set at the level of a manufacturer) of the IMP (including active comparators and standard of care) was used to calculate the unit cost. For a study drug administered orally, the unit cost was calculated by dividing the total cost by the number of the tablets. If the study drug was administered by infusion, the unit cost was the number of vials administered during treatment. When no price was available, the price considered was the price of the active comparator or the therapeutic standard of care.

As a result, the drug avoided cost (DAC) per trial was calculated as the product of the unit cost (P), the number of tablets administered per day (or the number of vials administered in the treatment period) (D), duration of treatment (days) (T), and the number of patients enrolled (n).

$$DAC = P \times D \times T \times n$$

As an example, a randomized placebo-control trial that investigated the efficacy of the drug ALFA was considered. The treatment dose was 2.5 mg three times daily for 12 weeks. The DAC was obtained by multiplying the unit cost of ALFA (P= 89.98 €) by the number of tablets administered per day (D= 3), days of treatment (T= 84 days), and number of patients enrolled (n= 5). Thus, the total DAC for the trial was 113,374.80 € **(Table 1).**

For randomized, placebo-controlled, double-blind studies, it was impossible to differentiate patients who received the investigational drug or placebo. Therefore, all patients enrolled in the study were

considered. In the case that the investigational drug was not authorized for marketing, the standard of care was taken into consideration for the analysis as if the trial was not carried out (Table 1). For an RCT that assessed combination therapy or compared two drugs, the DAC was the sum of the single DAC for each drug **(Table 1)**.

To evaluate the procedure avoided cost (PAC), we identified the clinical visits and diagnostic tests performed and the frequency of visits according to the protocol. As an example, we considered a protocol that assessed the effect of a planned screening visit and six visits every two weeks for the duration of the study. Screening visits involved clinical laboratory tests, electrocardiogram (ECG), echocardiography, and high-resolution computerized tomography (CT) scan; each clinical visit involved laboratory tests and ECG. In particular, clinical laboratory tests evaluated several parameters, as well as hematology (i.e. hemoglobin, hematocrit, platelet count, white blood cell count), coagulation (i.e. PTT, PTT-INR), blood chemistry (i.e. sodium, potassium, albumin, urea, total bilirubin, total protein, alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), and creatinine), as well as other markers (i.e. pregnancy test, cystatin C) **(Table 2)**.

The TAC for each protocol was obtained by the sum of DAC and PAC.

Table 1. Drug avoided cost evaluation for clinical trials

STUDY DESIGN	INVESTIGATIONAL DRUG (comparator)	DOSE (No. tablets per day)	COST/day (€)	TREATMENT PERIOD (days)	PATIENTS ENROLLED (N)	DRUG AVOIDED COST (€)
IDRA Randomized placebo-controlled	**ALFA**	3	89.98	84	5	113,374.80
LIRA Randomized Placebo-controlled	LAMBDA (beta)	2	160.74	83	3	80,048.52
LIRA_OLE Extension Open-label	LAMBDA (beta)	1	80.37	1034	3	249,307.74
ORIONE Randomized Combination therapy vs. monotherapy	**SIGMA+TAU**	2	85.74 (sigma) 54.15 (tau)	35	4	19,584.60

The drugs in bold had marketing authorization prior to the clinical trial. If the investigational drug was not authorized, the standard of care was considered for drug-avoided cost analysis.

Table 2. Diagnostic avoided costs evaluated per patient when enrolled in a clinical trial.

DIAGNOSTIC PROCEDURES	FREQUENCY	COSTS PER TEST (€)	TOTAL COSTS (€)
BLOOD SAMPLE			
Hematology	All study visits		
Hemoglobin (Hb)	7	10.60	74.2
Hematocrit	7	3.30	23.1
Platelet count	7	4.00	28
White blood cell count	7	1.95	13.65
Coagulation test	All study visits		
PTT	7	2.50	17.5
PT-INR	7	2.90	20.3
Chemistry	All study visits		
Sodium	7	2.80	19.6
Potassium	7	2.80	19.6
Serum albumin	7	2.60	18.2
Urea	7	1.70	11.9
Total bilirubin	7	1.70	11.9
total protein	7	6.00	42
AST	7	2.90	20.3
ALT	7	2.90	20.3
GGT	7	2.60	18.2
Creatinine	7	2.60	18.2
Other	All study visits		
β- HCG in serum	7	3.70	25.9
NT-proBNT	7	9.1	63.7
ECG	All study visits		
	7	11.6	81.2
Echocardiography	Screening visit		
	1	77	77
High-resolution CT scan	Screening visit		
	1	86.3	86.3

Total per patient = € 711.05

DISCUSSION

Despite the high costs of running a clinical trial, pharmaceutical companies are willing to spend substantial resources in bringing a new drug to market, which has the potential to resolve a chronic disease, increase survival, and improve the quality of life [15, 16].

Moreover, in many clinical areas in which significant pharmaceutical expenses or no other treatment options exist, participating in a clinical trial

becomes an opportunity for both patients and the healthcare organization as it can reduce hospital expenditures. The sponsor covers all costs associated with treatment (i.e., the investigational drug, the standard of care therapy when an active comparator is considered), and represents a major source of cost savings.

The cost savings, and therefore the economic benefits, are often underestimated or are not taken into account. Our study aims to provide a methodological analysis that can estimate the cost savings associated with a clinical trial, which demonstrated economic benefits for patients and healthcare institutions. Estimation of the TAC may be a helpful tool in better understanding the economic benefits for healthcare institutions. Moreover, the TAC might provide an opportunity for the healthcare system to extend their budget and invest in clinical research infrastructure (e.g. organization that promotes, supports, and coordinates clinical research in the institution), in core facilities (i.e. new instruments), and in human resources (i.e. partially support salaries of staff) that can increase the quality of clinical research. It is thus an opportunity for the trial site and/or academic medical institution to become more attractive for pharmaceutical companies and, therefore, for the possibility to conduct clinical research.

Lastly, in our opinion, this type of evaluation should be performed in all clinical research areas in order to inform the healthcare institution about the impact of conducting clinical trials.

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