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Incentive Use in Research: Protecting Vulnerable Populations from Exploitation

Bilimsel Araştırmada Teşvik Kullanımı: Savunmasız Toplulukların İstismardan Korunması

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ABSTRACT

Global investment in Medical Research and Development has markedly increased in the last few decades. However, due to the decreasing public altruism, researchers have come under increased pressures from the funding bodies to produce results. Out of desperation, some researchers have resorted to using incentives as a means of sourcing for volunteers. Consequently, the research burden has disproportionately been shared among the most vulnerable populations in the society. Incentives especially monetary ones present an ethical dilemma because of the uncertainties' surrounding the morality, amount and type of payment, vulnerability of volunteers and possible threats to voluntary participation. Several studies done on the use of incentives in medical research have noted that financial motivation was the number one reason for subjects to volunteer in Medical research. Mutual benefit and freedom of choice by participants were given as reasons to support their use. However, scientists who are against the use of incentives believe that they are coercive or undue inducements, and may influence a subjects' ability to give an informed consent. Guidelines exist that protect vulnerable groups from exploitation, although none sheds light into the use of incentives. Nonetheless, in the face of the waning public altruism, the benefits of using incentives far outweigh the dangers, although researchers should avoid situations where their use may become problematic. As a mode of payment to research subjects, researchers should adopt a combination of the Dickerts' Wage and re-imbursement models as guides in quantifying the incentive.

Key words: Research ethics, incentives, informed consent.

ÖZET

Dünya genelinde geçen son 20-30 yılda tıbbi araştırma ve geliştirmeye yönelik yapılan yatırımlar önemli derecede artış göstermektedir. Ancak, eşitlik anlayışındaki yıpranmadan dolayı fon organları araştırmacılara sonuç üretmeleri için baskı uygulamaktadır. Çaresizlikten ötürü, bazı araştırmacılar gönüllüler için kaynak olarak teşviklerin kullanımına başvurmuşlardır. Sonuç olarak; araştırma yükü orantısız olarak toplumun en savunmasız bireyleri arasında paylaşılmıştır. Özellikle parasal olan teşvikler, ödemenin miktarı ve cinsi, gönüllülerin güvenlik açığı ve gönüllü katılımına yönelik olası tehditler etik bir çelişkiye yol açmaktadır. Tıbbi araştırmalarda teşvik kullanımına ilişkin çalışmalar göstermektedir ki finansal motivasyon deneklerin tıbbi araştırmalarda gönüllü olmasının en temel sebebidir. Karşılıklı fayda ve seçim özgürlüğü katılımcıların bu çalışmalarda kullanılmalarının bir dayanağı olarak gösterilmiştir. Ancak; teşviklerin kullanılmalarına karşı olan bilim adamları katılımcıların kandırıldığına ve mecbur tutulduğuna dolayısıyla bilgilendirilmiş onam temininde katılımcılarının yeterli ve doğru düşünemediklerini vurguluyorlar. Teşviklerin kullanımına dair herhangi bir vurgu yapmamasına rağmen, savunmasız grupları istismardan korumaya yönelik öğeleri içeren yönergeler bulunmaktadır. Araştırmacılar problem oluşabilecek vakaları kullanımından kaçınmasına rağmen toplumda azalan eşitlik anlayışı eşliğinde teşvikleri kullanımının faydalarının risklerinden daha ağır bastığını göstermektedir. Araştırma vakalarına yapılacak ödemelerde, araştırmacılar teşvik miktarının tespitinde Dickerts' Ücret ve geri-ödeme modellerinin birleşimini kendilerine rehber olarak almalıdır.

Anahtar kelimeler: Araştırma etiği, teşvik, aydınlatılmış onam.

Introduction

Research has been a backbone for medical advancement for centuries. In the last century alone, increased resources towards research have led to accelerated advances in medicine leading to a better quality of life amongst people worldwide.

Although the majority of the community that participate as subjects in medical research do it for altruistic reasons, the last few decades have seen that number dwindle over time despite the inverse increase in research demands[1,2]. The ensuing outcome has made it difficult for researchers who are under pressure from funding organizations to meet stringent project deadlines. This desperation has consequently led to some resorting to using incentives[3], sometimes viewed as undue inducements to entice study subjects to enroll in research studies. An incentive may be defined as any factor (financial or non-financial) that enables or motivates a particular course of action, or counts as a reason for preferring one choice to the

alternatives. It is an expectation that encourages people to behave in a certain way[4]. Incentives can be tangible goods, such as cash payments, gifts or intangible rewards, such as altruistic feelings.

Because of expectation of payment, the lions' share of the research burden has disproportionately been shared amongst some most vulnerable groups in the society who in most cases have everything to lose in case they don't participate. Vulnerable research groups may include: the poor, people suffering from a life limiting illness, homeless people, elderly, the disabled, drug addicts, the illiterate, people experiencing mental health problems, children, those with learning difficulties, ethnic minorities, asylum seekers and refugees, and prisoners[5].

The lack of a general consensus on the use of incentives in research amongst ethicists has further compounded this problem. As a result, most national and institutional Ethical Review Committees have no clear cut written guidelines on the use of incentives in enrolling study subjects, with majority of the Institutional Ethical Review Boards (IRBs) leaving it to a researcher to decide when and how much of the incentive can be given.

Incentives especially monetary ones present an ethical dilemma because of the uncertainties surrounding the morality of payment, the amount of payment that is reasonable to offer, the type of payment, the payment schedule, the research risks subjects are exposed to, threats to voluntary participation and informed consent, and the vulnerability of volunteers[6-9].

The above facts raise a number of ethical issues for discussion in this article. The most prominent concerns the role of incentives in the uneven distribution of clinical research burden and whether incentives should be fronted as a tool to attract potential subjects in medical research.

Distribution of Research Burden

Information regarding the distribution of research burden amongst different socioeconomic classes in societies of developed countries is scanty. However on an international scale, there is sufficient evidence that points to the fact that pharmaceutical, biotechnology and device manufacturers have dramatically increased outsourcing of drug and product research to the developing world, especially in countries of Sub-Saharan Africa, South East Asia, Latin America, and Eastern Europe[10]. These developments arouse concern because research

participants and populations in developing countries may be particularly vulnerable to exploitation due to poverty, illiteracy, limited resources, education and health care[11]. In further support of the exploitation claim, it is stated that some research sponsors conduct studies in the developing world that would be declared unethical in industrialized nations, thus establishing double standards[12,13].

An example of a case of unfair distribution of research burden pertains to HIV/AIDS related international clinical research. United States Government trial sponsors such as the National Institutes of Health, Center for Disease Control (CDC) and some private pharmaceutical companies prefer resource poor settings for their studies because they offer cheaper trial costs, a larger pool of potential research subjects and the opportunity to speed up the time it takes to get the drug to the market[13,14]. However, some people may argue that the exploitation claimed is mutually advantageous; i.e. the potential research subjects get access to life prolonging Anti-retroviral therapy (ART) whereas researchers (possibly with altruistic motives) achieve their intended aims. A win-win on both sides! Nevertheless, although the above scenario may seem mutually beneficial, there still remains an issue of uneven distribution of risks; i.e. The research participants are gambling for their health and lives (access to free treatment vs. drug side effects, drug resistance, social stigmatization), whereas trial sponsors are only undertaking a financial gamble (expenses/losses vs. profits from licensed drug)[14].

Empirical Findings

Among the scientific community, divergent views and opinions are held both for and against payment of human subjects for research participation[15] and no consensus has been reached on when and what ways it is ethical to pay subjects[16,17], a factor that has partially contributed to an equivocal stand by many regulatory bodies. Although regulations and guidelines call to attention some of the moral issues that payment raises, they offer little substantive guidance for clinical investigators, institutional review boards, or contract research organizations on how to pay subjects ethically[18].

Those who are pro-payment argue that the payment of subjects is never an ethical problem and that the practice has long been an integral part of the recruitment of research participants for decades[18], the outcome being beneficial to both the researcher and subject[3]. Evidence to support this argument comes from a systematic review done by Tishler [7] on recruitment of

normal healthy volunteers. In this paper, it was established that financial motivation was as important a motivator in the decision to participate in clinical trials as the altruistic motives. In a particular study by van Gelderen et al[19], 93% of the 144 volunteers chose financial compensation as the most important reason for volunteering and thought the money earned from participation was "a pleasant part of the experiment". A similar study by Vrhovac et al [20] found that 79% of volunteers had participated in Phase III or IV clinical trials for the financial reward, and only the 21% had participated for humanitarian reasons.

Although paying subjects might appear as a fair way to compensate subjects for their participation, some ethicists have argued against the payments, denoting the payments as coercive or undue inducements[7,21]. Undue inducements may occur when an excessive offer or unwarranted or inappropriate reward is given to a subject in order to obtain their compliance[7]. Such offers are likely to undermine voluntary decision-making and consent especially in circumstances when the subject is from a vulnerable group[9,22]. Predominantly, incentive use has been deemed problematic when[23]: the subject is in a dependency relationship with the researcher, when the study risks are very high, when the research carried out is degrading to the subject, when the participant will only consent if the incentive is relatively large because of their strong and principled aversion to the study. An example is using large sums of money to entice subjects who are Jehovah's witnesses to enroll in to a study aimed at determining acute blood transfusion reactions.

Autonomy, the ability of self-determination that is free from control or influence by others[24], and the avoidance of conditions in which the individual may be "coerced or unduly influenced" are what must be maintained and/or protected when recruiting research subjects. If a subject is economically vulnerable, he or she could have diminished autonomy when given a lucrative incentive[7,9]. In a cross sectional study done to determine the effects of incentives on a subject's decision[25], 350 American jurors were asked questions on whether a payment of USD $500 would impair someone's ability to carefully think about the risks and benefits before enrolling in to a clinical trial, 261 (74.6%) believed it would. Therefore, undue inducements decrease voluntariness, which is an essential component of a valid consent[22,26].

In addition, payment for research participation especially in research that has more than minimum risk was viewed by some as commodification of an individuals' health [27] because even when a perfect informed consent has been provided, potential participants must weigh a

guaranteed offer of payment against the possibility of risk to their health. In some extreme instances, participants even fail/refuse to report untoward effects of a study/trial for fear that they may be withdrawn from the study and lose on the benefits/incentives.

Proposed Guidelines on the Use of Incentives

According to Ari Vanderwalde et al [16], there is still a lack of consensus on the use of incentives in Medical research. Because of that, there have been disparities in the judgment of the appropriateness/suitability and the range in which incentives can be used in medical research by several IRB's. Nonetheless, several payment schemes regarding incentive use have been proposed. The most prominent of the payment schemes was that proposed by Dickert and Grady in 1999[28]. Three payment models were proposed under this scheme and they include: (1) The market model where the principle of supply and demand determines whether and how much subjects should be paid for participating in a given study at a specific site; i.e. when a research is risky and offers little or no prospect of direct benefit to subjects, there is little apparent reason for a person to participate. This model allows money to be the reason. For example money may be an incentive in a study of natural patterns of sleep or in phase 1 pharmacokinetic study of a treatment for a disease the person does not have. (2) The wage payment model which operates on the notion that participation in research requires little skill but does require time, effort and the endurance of undesirable or uncomfortable procedures. This model adopts a position that subjects performing similar functions should be paid similarly. The wage-payment model thus involves the payment of subjects on a scale commensurate with that of other unskilled but essential jobs. The payment of completion bonuses is also consistent with this model. (3) The reimbursement model where payment is provided simply to cover subjects' expenses for example reimbursing subjects only for expenditures such as travel, meals and parking. However, of all the above models, Dickert and Grady concluded that the wage-payment model represented the best and more ethical approach to paying research subjects.

In evaluating Dickerts' models of payment and taking into consideration the concerns scientists have on the use of incentives, it is more appropriate to adopt a mixture of the wage payment and re-imbursement model. An illustration used to support this argument considers a scenario where a research subject has to drive 100 miles from home to come to the study facility and spends 4 hours going through the study routines. The wage payment model

applied in this case will ensure that incentives are given to a participant as a wage of an unskilled worker depending on the time and effort dedicated to the study protocols for that day. However, the participant is not guaranteed re-imbursement of the costs incurred for example on transport to and from the facility. Therefore, a mixture of payment as a wage and re-imbursement for travel costs will be more encompassing.

Money vs. Gifts

The nature of incentive given has been found to influence the recruitment and retention rate of subjects in medical research. Incentives can be given in form of cash, a cheque, gifts, a service e.g., free consultation, free treatment, free surgery or a refreshment e.g. a diet coke, free lunch or a cup of tea. Nevertheless, cash incentives are still the most commonly used of all incentives. In a systematic review done by Cara, et al. it was found that cash incentives were associated with a higher retention rate of study participants than gift based incentives and that the higher the amount given the better the retention[17]. However, despite the clear advantage, a few scientists still feel that offering cash to participants as opposed to gift nullifies the researchers' appreciation of the subjects' voluntariness[29].

Although guidelines from regulatory bodies are non-committal on issues regarding use of incentives in research, most strongly favor and support protection of vulnerable populations in research.

Conclusion

It can be agreed that using incentives may sometimes influence the judgment of a potential research subject. However, in the face of the slowly waning community altruism and voluntariness, it is apparent that incentives have a positive effect on study recruitment and retention despite the research subjects' vulnerability or social class. To reduce the probability of incentives being viewed by some as undue inducements, researchers should avoid situations where incentive use may become problematic. For example: a situation when a potential research subject is in a dependency relationship with the researcher, when the study risks are very high, when the research carried out is degrading to the subject, or when the participant will only consent if the incentive is relatively large because they have a strong or principled aversion to the study or study procedures. In simple terms, the cautious use of incentives should be strongly supported.

In consideration of the quantity of the incentive, depending on the wages and expenses incurred by the study subject, a mixture of Dickerts' wage payment and re-imbursement models should be adopted as guides in computing the estimates of the incentive to be awarded. Payments to research subjects should preferably be in cash because it can easily be standardized to all regions.

All the above recommendations should be incorporated into the existing guidelines by the Institutional Ethics review boards clearly indicating when and how much of the incentive should be given to the different subject categories. Without this guidance, protecting vulnerable populations from inappropriate incentive use amidst an increased number of research proposals submitted to the IRBs for review will continue to be a "wild goose chase".

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