

# Spreading It Around:

## Money for Researchers and Research Participants

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### Abstract

There is a consensus that inducements for participants in research studies are ethically permitted as long as they are not “undue.” The subject of inducements for investigators has not been ethically analyzed. This essay outlines the three models for compensation suggested by Dickert and Grady—market model, reimbursement model and wage-payment model—and argues that this analysis can be fruitfully applied to remuneration for investigators. Currently, investigators are compensated according to the market model, resulting in undue inducement. Investigators should be compensated according to the wage-payment model, as skilled workers, at the rate an internist earns per hour. The wage-payment model avoids undue inducement, but compensates investigators, particularly non-academic investigators who are not salaried, for their time and effort. However, additional safeguards must be erected: investigators must demonstrate research competency for the studies they are to manage; they must understand research ethics; all investigators must be routinely audited; and subjects must be informed of all remuneration that investigators receive.

**Key Words:** Inducement, ethics, clinical research, pharmaceutical research, compensation, conflict of interest, drug testing, phase I trials, healthy volunteers.

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CONTRASTING STORIES demonstrate the need to discuss distributing funding appropriately in research. The first is from Georgia, my new home state. Dr. Richard Borison, a professor at the Medical College of Georgia, opened a little drug-testing shop with his friend Bruce Diamond, a pharmacologist. They ran trials for top pharmaceutical companies such as Zeneca, Johnson and Johnson, Smith-Kline Beecham, Bristol-Myers Squibb, Lilly and Glaxo Wellcome. Both Borison and Diamond had promising academic careers, Borison having published 85 scholarly articles by the time he finished his residency and Diamond having collaborated on over 50 research projects. Borison was a full professor by 1988, and later was chair of psychiatry. With his drug-testing business booming, Borison opened a separate office in a biotech park, earning over

\$10 million. Non-medical employees treated patients, read electrocardiograms and signed medical records. Eligibility criteria were stretched; the local institutional review board (IRB) was avoided. All this proceeded unchecked until an employee moved to another research office and quickly found out that that was not the way research was conducted. The former employee's new boss alerted the medical college (1). Drs. Borison and Diamond are not alone, joining the company of the infamous Dr. Fiddes, who stored other people's urine in his refrigerator in order to have urine with the proper acidity available for the auditors (2).

Hoi Yan Wan, a 19-year-old student at the University of Rochester, volunteered for a smoking and air pollution study that involved a bronchoscopy. She was paid \$150. She reacted to the high dose of lidocaine used to anesthetize her throat for the procedure and died later that day of cardiac arrest (3). In a similar case, Bernadette Gillcrist, a 23-year-old nursing student who lied about her anorexia nervosa and two previous cardiac arrests in order to earn \$1,300 in a sleep study, also died of a cardiac arrest (4).

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## Subjects

Much attention has been paid to the ethical framework for compensating participants in research studies. What has not been analyzed is the ethical way to compensate physician-researchers for their contribution to studies. I will argue that the analysis used for participants must now be applied to researchers and that additional safeguards must be erected for both groups.

An ethical consensus has developed that research participants may be paid or otherwise compensated for their participation, as long as the inducement is not “undue.” The Belmont Report defines “undue” as “an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance” and warns that otherwise acceptable offers may be considered undue influence for some vulnerable populations (5). The National Commission for the Protection of Human Subjects states that “limiting remuneration to payment for time and inconveniences of participation and compensation for any injury resulting from participation “is the best way to keep inducement due” (6). Although the “Common Rule” is not specifically cited, the Food and Drug Administration agrees that “the IRB should review both the amount of payment and the proposed method and timing of disbursement, to assure that neither are coercive or present undue influence” (7).

Dickert and Grady offer an excellent analysis of three models of compensation, the market model, the wage model and the reimbursement model. They indicate a preference for the wage model, partly because it avoids undue inducement (8). In the market model, the market determines how much the subject is paid, with higher payments for top priority trials for which subjects are difficult to recruit, and lower or no payment for those trials with more than enough recruits. Dickert and Grady complain (and I agree) that this model has ethical drawbacks, including different payments for the same work, the possibility of undue inducement for unpopular experiments, competition among researchers for participants, and the potential to coerce vulnerable groups that have few options. Dickert and Grady also reject the reimbursement model, the one most widely used today, which merely reimburses subjects for their expenses. They judge this model to be too restrictive, potentially not attracting enough research participants, and being inequitable if partici-

pants are reimbursed for time lost at work. Since participants’ day jobs pay differently, they have to be reimbursed at different rates to match what they earn at their jobs. I judge this model to be an acceptable ethical model, if time lost at work is not reimbursed, but I agree with Dickert and Grady that the third model, the wage-payment model, is preferable.

The wage-payment model treats research participants as unskilled labor and argues that they should be paid at, or slightly above, the minimum wage. This model avoids inequitable pay for the same work and undue inducements, recognizes the contribution that research participants make, and reduces or eliminates the financial sacrifice resulting from research participation. Others recommend the wage-payment model as well (4, 9–11).

There are several important objections to the wage-payment model. Some assert that it commercializes research and eliminates altruism. In a small study of 67 research participants recruited for a vaccine trial, some of whom entered the trial and some of whom did not, Russell, Moralejo and Burgess found that most participants (57%) did not think that either patients or healthy volunteers should be paid. One person expressed the view that “people should volunteer because they want to help. Not because they will receive a fee!” (12). On the other hand, people who contribute to society’s welfare are typically recognized with pay (e.g., fire fighters, police, and sanitation workers). Further, receiving pay is compatible with altruistic motives. In a wage-payment model, wages would not be paid for all research participation, allowing altruism full play in the unpaid experiments. For trials that pay wages, potential participants who choose research work rather than other unskilled jobs could do so for altruistic reasons. Also, it is naïve to believe that research is not already commercialized for researchers, who can hold patents, biotech stock options, and lucrative consulting positions. A wage-payment model offers some, albeit a small amount, of the available money to the participants.

A second objection is that wage-payment will increase the enrollment of persons in a lower socio-economic group, thus shifting the burden of research unfairly to a vulnerable group in society. This possibility is a concern, though as Robert Levine states, “one notes without serious dismay that corporate executives are not competing for employment as office secretaries, meter readers, jurors or research subjects” (11). Several safeguards

should be erected to minimize this potential harm. Some have suggested that only studies with an increment above minimal risk should be considered for wage-payments (9, 11). The burden borne by low income groups would then not include great risk. I agree with this position, in most cases, but will make the case below that certain therapeutic studies that are above minimal risk should be included. Dickert and Grady, who include more risky studies as appropriate for the wage-payment model, suggest that payment should not escalate according to risk (8). Since greater risk would not entail more payment, a potential participant could compare studies and decide which risks are acceptable to him or her. Others argue that, rather than increasing burden, offering wages gives those in lower socio-economic groups more choices and options for improving their situation (13). Offering wages does increase options, but this response does not address the inequity in the share of research burdens. The well-off have more options and therefore are not as attracted to low-paying research. My own position is that, since lower socio-economic groups are currently underrepresented in research, payment of wages may improve the balance. Empirical studies are needed to determine if this hypothesis is correct.

A related concern is that minimum wage will be an undue inducement for certain groups. For Bernadette Gillcrisp, who lied about her cardiac history, \$100 a day appears to have been an undue inducement. Eli Lilly used homeless alcoholics as healthy volunteers for phase I research, raising concerns about faked eligibility claims and participants' inaccurate description of side effects (14). The analysis of whether wages would be an undue inducement has several components, as explained by Macklin (4). First, people differ in their view of the importance of money. Second, people of all income groups have different levels of risk tolerance and aversion. Even though it is reasonable to assume that minimum wage may be attractive to certain groups, it may not be enough to override their risk aversion and thus would not be an undue inducement. In order to determine if a certain wage rate is an undue inducement for a particular person, such variables as their view of the worth of money, their current economic situation and their level of risk tolerance and aversion, would have to be measured. It is not clear either how to measure these variables or what weight to give them. Another partial solution to this concern would be to require testing

for any condition warranting exclusion from a trial because of likely harm to the participant (13). The potential participant's word would not be sufficient if wages are to be paid. If this safeguard had been in place, Bernadette Gillcrisp would have had a cardiac test before being allowed to enter the sleep trial. Such tests would raise the cost of research, but may be necessary if wages are to be offered. Furthermore, participants should not be penalized financially if they discontinue the study due to toxic side effects, since they might be tempted to underreport such side effects and put themselves at risk (15). However, financially penalizing those who leave the study for personal reasons would be allowed. In short, although concerns about the wage-payment model are valid, safeguards can be erected to minimize the potential for harm.

A final concern with the wage-payment model takes the opposite tack. According to this criticism, limiting wages to approximately the minimum wage is paternalism. Participants should be allowed to earn whatever they can (16). Ethical codes, however, have never relied solely on patient autonomy to ensure that research is ethically acceptable (17). The Nuremberg Code (18), which opens with the requirement of voluntary consent, also stipulates that research meet certain standards before it is worthy to be offered to potential participants. Requirements 2 through 8 state that every experiment must yield useful results, avoid unnecessary suffering, demonstrate an acceptable risk-benefit ratio, and be conducted by qualified persons. In the United States, IRBs are ethically mandated to assure that all of these ethical requirements are met. The whole research design, including determining the amount of payment to participants, is well within IRB purview.

Most discussions of payment for research limit their scope to nontherapeutic research, typically research utilizing healthy volunteers. Access to innovative treatments of potential therapeutic benefit is thought to be sufficient reward for participating in therapeutic research. Although phase I research with healthy volunteers is the most likely candidate for wage-payment, some therapeutic research could be included. Phase I research with potentially toxic therapies designed for life-threatening diseases, such as AIDS and cancer, where subjects are terminal patients, offers little chance of benefit (19, 20). Yet people do enter these studies hoping to personally benefit (21). Paying wages to these research participants may lower therapeutic

tic misconception, alerting the participants to the fact that these trials are research, not therapy (8, 22).

Paying healthy volunteer and patient research participants approximately the minimum wage shows respect for their contribution to society, removes some financial barriers to research, may increase participation by those in lower socio-economic groups, and may mitigate therapeutic misconception. Any potential for such wages to be undue inducement could be minimized by such safeguards as mandatory testing for exclusionary criteria if harm might result, and not increasing payment with increasing risk.

### Researchers

At present, it appears that researchers are reimbursed according to the market model. Researchers can earn more than \$5,000 a subject, sometimes as much as \$19,000 a subject, with bonuses for meeting a quota or for speed in recruiting. The average investigator grant has been estimated at \$43,000, with some investigators earning from \$500,000 to one million dollars a year (23). With such large amounts of money involved, individual cases of fraud have been uncovered (2). And there is always the danger that true informed consent may be short-circuited and eligibility criteria stretched. Dr. Robert Tenery, past chair of the Council on Ethical and Judicial Affairs for the American Medical Association, has objected to research bonuses: "Why would you get an extra \$500? How can you explain that rationale? Maybe you took a patient who really didn't need to be enrolled." And one thoughtful IRB member has wondered, "If it is coercive to pay a patient \$500, why is it not coercive to pay the clinical investigator \$5,000?" (23).

To minimize the possibility of coercion for investigators, the wage-payment model should be applied to their remuneration. I propose that investigators be paid by the hour, as skilled, not unskilled, workers, at the hourly rate that an internist usually earns. Alternatively, investigators could be paid a flat fee based on an estimate of the number of hours it takes to enter and maintain a participant on a trial. This standardization would remove the undue inducement currently found in the market model of payment.

Why pay researchers at all? Because it does take time, skill and effort to recruit and maintain participants in research trials. The National Cancer Institute (NCI) reimburses the institu-

tion, not the individual investigator, \$2,000 per participant enrolled in their trials. Academic investigators estimate that the true cost in these academic settings is \$4,000 per participant. Furthermore, academic medicine cannot meet the demand for the number of participants needed to test new agents, with the proportion of drug studies handled by academic researchers dropping from one-third in 1990 to one-quarter in 1997. Private doctors, who (unlike many academic doctors) do not receive a salary, will need to be paid for their time.

In a wage-payment system for investigators, additional safeguards for participants would need to be established. Not only must the pay be standardized at a reasonable level, but careful control of researcher qualifications must be maintained, since instances of researchers running studies outside their areas of expertise have been reported. Training in research conduct should be required, since there is no assurance that private physicians are trained in research conduct, regulations or ethics. All investigators, both academic and private, must be routinely audited. Academic researchers have succumbed to the temptation of fame and glory (24), just as private practitioners have succumbed to the allure of big money. Only a careful audit system with "teeth" can protect us from such abuses. Finally, complete disclosure to the potential participant is the minimum requirement of any remuneration system.

### Conclusions

Inducement is rampant in research. Academic researchers' careers are built on performing successful research. Private practitioners can make significant amounts of money. I suggest that payment of money to researchers be standardized at a reasonable rate, the hourly charge of an internist, and that careful controls and audits be instituted. But if we are to pay researchers for their time and effort, we should also pay participants, with safeguards for them as well. In short, I suggest that we spread the money around.

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