

# What Makes Inducements Undue?

**Jon F. Merz**

University of Pennsylvania  
Department of Medical Ethics



# Overview

- Focus on monetary inducements
  - Set aside other inducements (access to Tx/drugs)
- The ethical concerns
- Some thoughts and data about money for Subjects
- Summary and suggestions

# The Ethical Concerns

- First, let's set aside the issue of *Coercion*
  - “Coercion occurs when an overt threat of harm is intentionally presented by one person to another to obtain compliance.”

(Belmont Rep. 1979, p. 7)
  - Coercion threatens to leave a person worse off if they do not comply  
(Cf. Wertheimer & Miller, J Med Ethics 2008; 34:389, 390)
- Second, let's situate monetary incentives as a form of manipulation of subjects' decisions that risks undermining voluntariness
  - “Undue influence. . . occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.”

(Belmont Rep. 1979, p. 7)



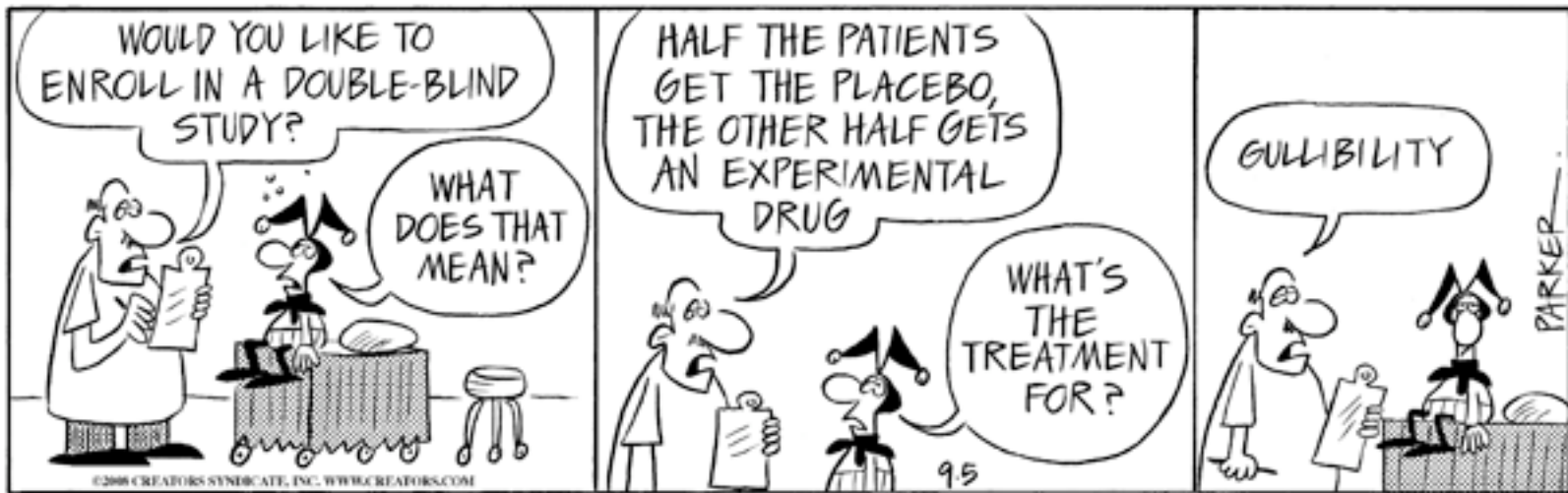
# What is Vulnerability?

- “Some research populations are vulnerable and need special protection. The particular needs of the **economically and medically disadvantaged** must be recognized. Special attention is also required for
  - **those who cannot give or refuse consent** for themselves, for
  - **those who may be subject to giving consent under duress**, for
  - **those who will not benefit personally** from the research and for
  - **those for whom the research is combined with care.**

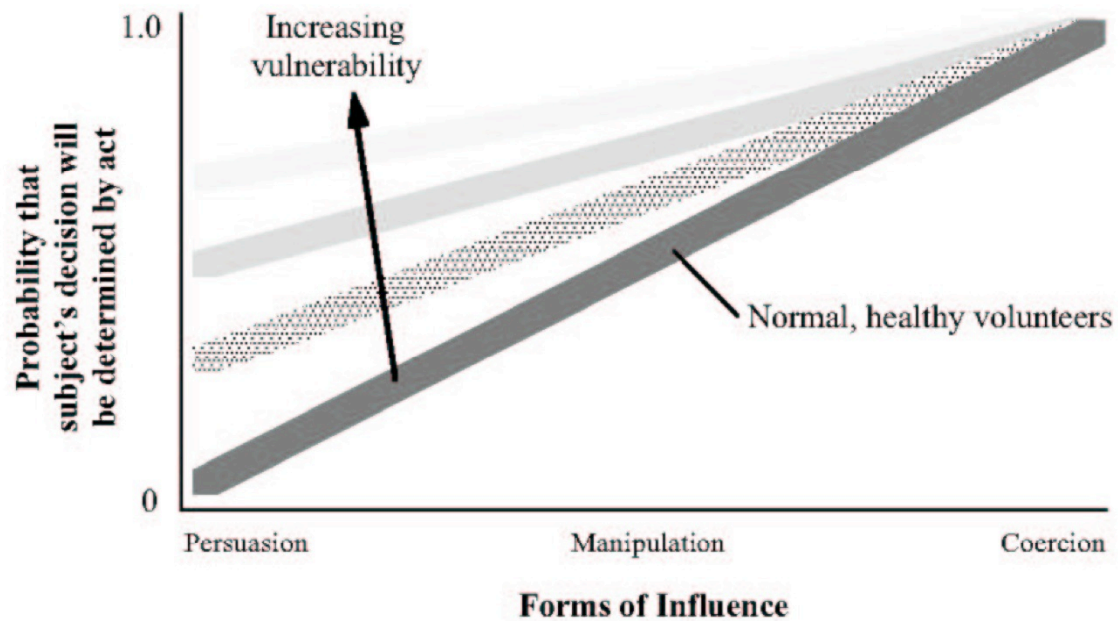
(Declaration of Helsinki, ¶8 (2000))

- “Vulnerable persons are those who are **relatively (or absolutely) incapable of protecting their own interests**. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.

(CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, Guideline 13 (2002).)



Copyright © 2008 Creators Syndicate, Inc.



Vulnerable individuals are particularly susceptible to acts having the purpose or effect of having potential subjects behave in a desired way.

Nelson & Merz, *Med Care* 2002; 40 (9 Suppl.): V69-80



# The Ethical Concerns

- Inducements may undermine voluntariness of consent
  - an offer one cannot reasonably refuse
  - leads one to make an irrational decision
  - leads one to do something she wouldn't otherwise do
  - leads to decisions against one's better judgment
  - assume substantial risks that compromise welfare
  - clouds people's judgment

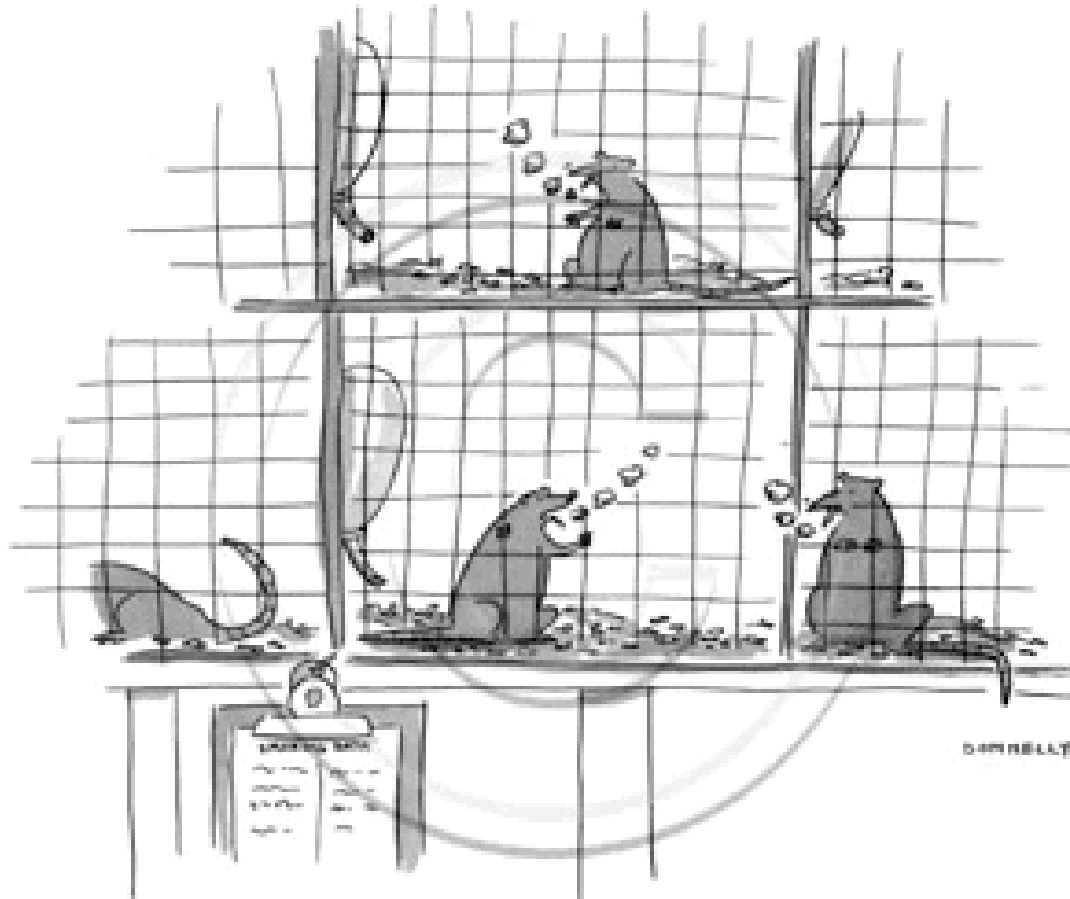
(numerous authors; email me for reference list)

- An early analysis suggested some paradigmatic problems:
  - Moral hazard: excess incentive could lead to lying in order to qualify for a study, exposing the subject to excess risk
  - Justice concerns: a given sum is likely to be a greater inducement to the poor than to the rich
  - An incentive could lead subjects to agree to things that violate moral values and intuitions

(Macklin, IRB 1981; 3(5):1-6)







*“I’m down to two hundred and sixty-three packs a day.”*

# The Ethical Concerns (continued)

- There is no standard to differentiate “due” from “undue”
  - an “undue” inducement is one that is judged unreasonably excessive given the
    - Subjects’ time, effort, discomfort, inconvenience and risk faced in the research activities, and the
    - PI’s need for *timely enrollment* of *enough* subjects,
    - as measured by an IRB’s collective experience and values

(Merz, <http://www.irbforum.org/> Jan. 11, 2004)

- IRBs vary widely in their approaches
  - Very few have written guidelines, and the guidelines that do exist range from total bans to liberal policies

(Weise et al. Pediatrics 2002; 110:577; Dickert et al. Annals Intern Med 2002; 136:368; Fry et al. Med Ethics 2005; 31:542)

e.g., some ban lottery payments,  
others permit progress and completion payments

# What Has Been Proposed?

- Dickert & Grady examined 3 models:
  - Market (price set by negotiation)
  - Reimbursement (cover S's specific expenses, time)
  - Wage-Payment (set pay for unskilled labor w/time, risk, etc.)  
(Dickert & Grady, New Engl J Med 1999; 341:98)
- Saunders & Sugar added a 4th:
  - Fair share (payment a percentage of the sponsor's per-pt costs or reimbursement)  
(Saunders & Sugar, New Engl J Med 1999; 341:1550)
- Grady added a 5th:
  - Appreciation (reward to thank and acknowledge contribution)  
(Grady, J Clin Invest 2005; 115:1681)

# What Else Has Been Proposed?

- Grant & Sugarman suggested that payments are only problematic in particular cases and need to be carefully examined:
  - Where subject is dependent upon the researcher
  - Where risks are particularly high
  - Where the research is potentially degrading
  - Where a large incentive is needed to overcome strong aversion
  - And where that aversion is principled

(Grant & Sugarman, *J Med Philos* 2004; 29:717)

- Sofaer and colleagues suggest rewarding all solicited potential subjects regardless of participation
  - But this evokes powerful duties of reciprocity that are unsolicited and extremely difficult to avoid!

(Chialdini, *Influence: The Psychology of Persuasion*. 1993)

# And, lastly (but not leastly...)

- Zeke Emanuel expresses the idea that this is much ado about nothing
  - “We need to stop talking about undue inducement in clinical research.”
  - Conceives the problem as one of inducing subjects to take unreasonable risks of serious harm, which exposures are necessarily limited by IRBs
  - Isolates other ethical concerns he believes are subsumed in the concept of undue inducement, each of which can be addressed independently of the monetary payment:
    - IRBs are not particularly good at regulating risks of trials
    - Informed consent is quite difficult and untrustworthy
    - Exploitation of the poor and disenfranchised; unfair subject selection

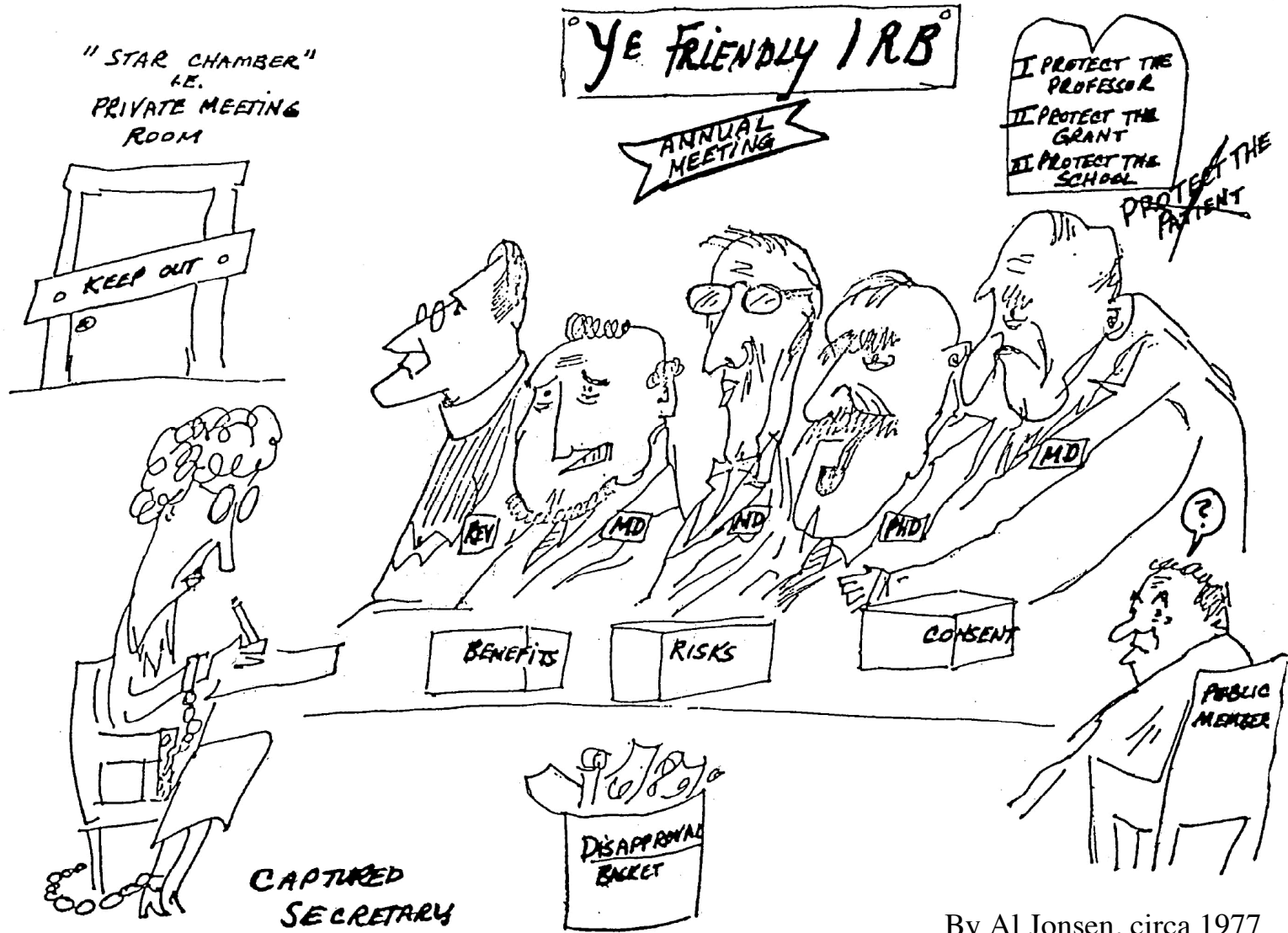
(Emanuel, J Law Med Ethics 2004; 32:100;  
Emanuel, Am J Bioethics 2005; 5(5):9)



**You'd think the FDA would  
notice this kind of thing.**

PAUL MALDEN '08

# IRBs Protect Rights, not Welfare



By Al Jonsen, circa 1977



*C. Bazzotti*

*“There. Now it’s all on paper. Feel better?”*



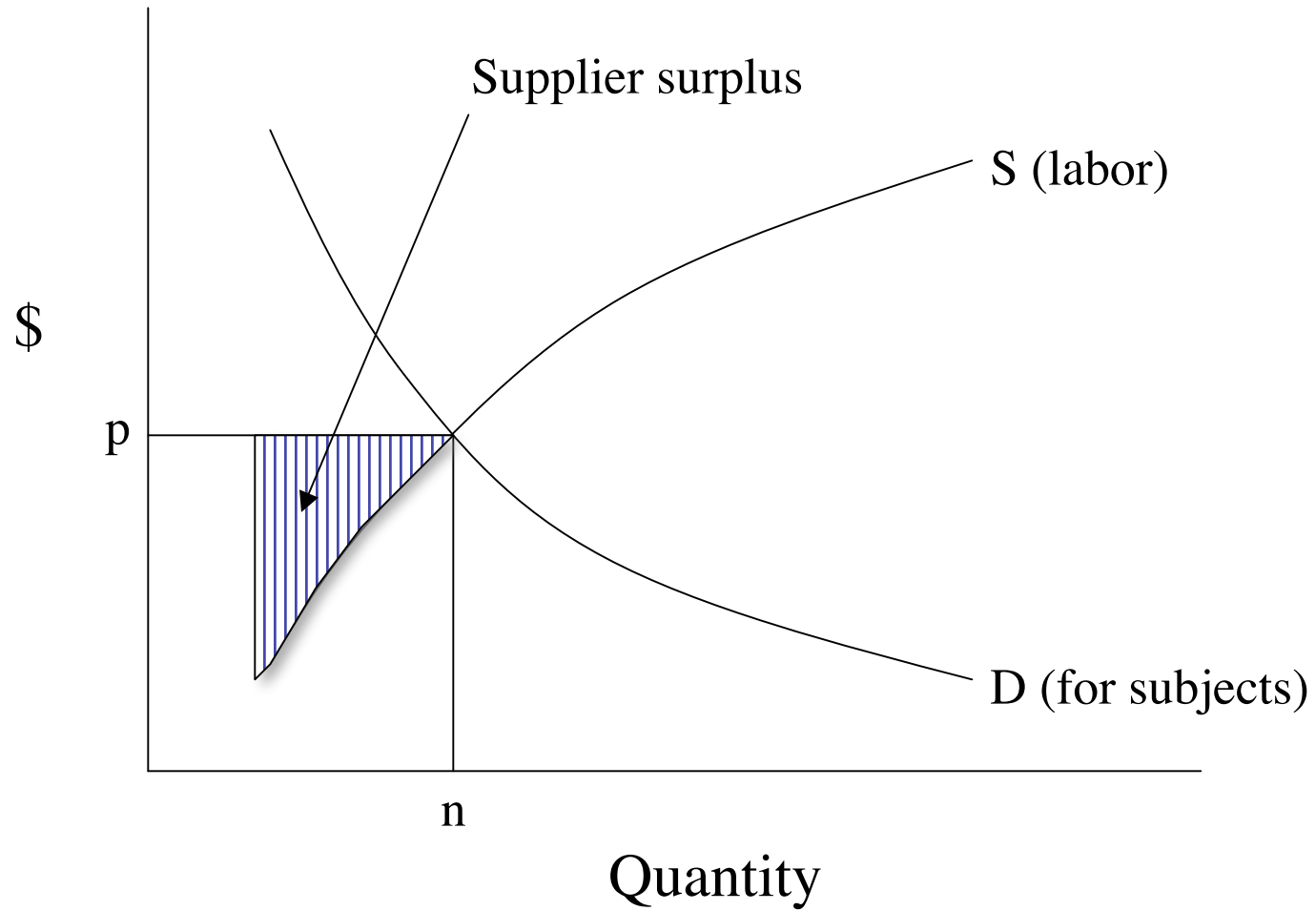
# Some Thoughts and Data

- Dunn & Gordon suggested that it will be helpful to think of the issue in economic terms

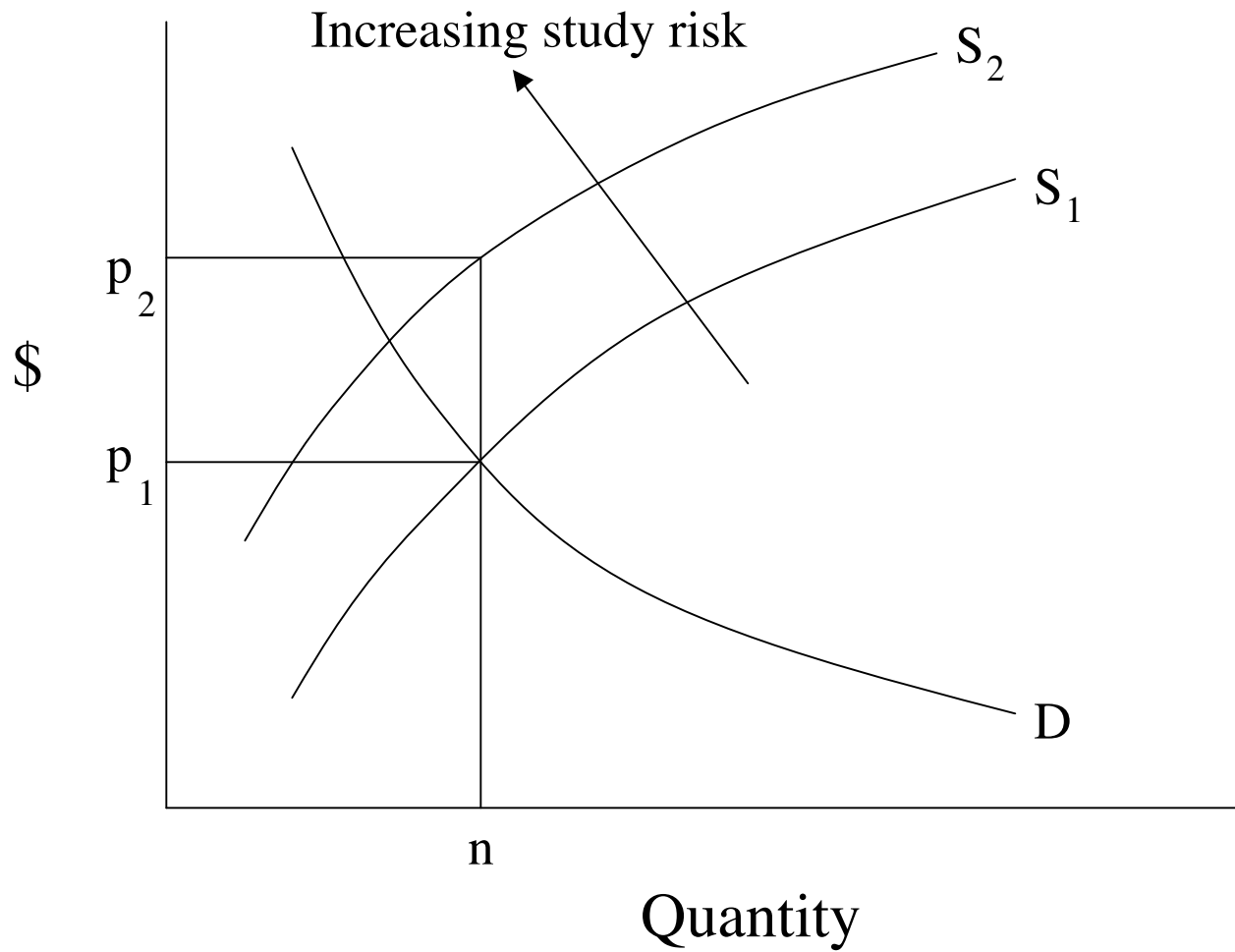
(Dunn & Gordon, JAMA 2005; 293:609)

- Economics is the foundation of this issue
  - Everyone agrees that paying subjects is necessary because it is the only way various types of research will get done
  - Many IRB policies and extant recommendations suggest that payments should compensate for actual expenses, time, effort, inconvenience, distasteful or uncomfortable procedures, risks, and sometimes an incentive or reward

# Supply & Demand



# Supply & Demand



# Why Do Ss Participate?

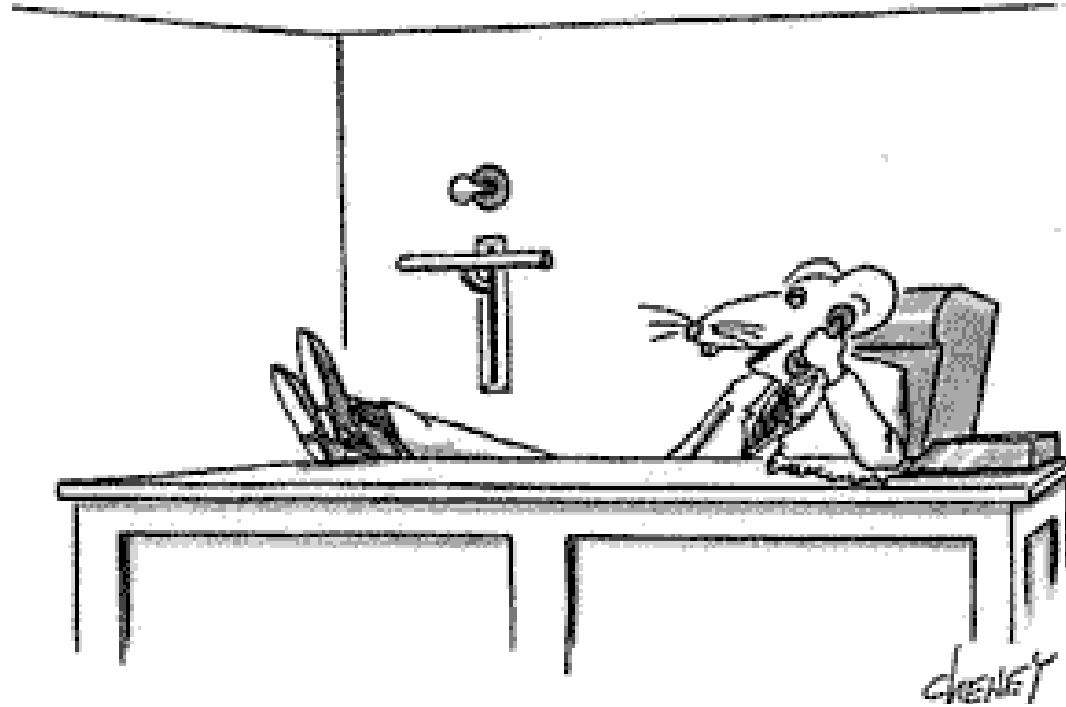
- We know something about why subjects participate in research
  - Reasons Subjects participate commonly include:
    - Altruism
    - A sense of duty to others
    - The chance for personal medical benefit



# Why Do Ss Participate?

- We know something about why subjects participate in research
  - Reasons Subjects participate commonly include:
    - Altruism
    - A sense of duty to others
    - The chance for personal medical benefit
    - Trust in the provider, the institution, the sponsor
  - Money
    - Especially healthy volunteers  
(See the review of Tishler & Bartholomae, J Clin Pharmacol 2002; 42:365)
    - Many studies show willingness to participate and actual response rates to surveys increase with increased payments  
(e.g, Asch et al., Med Care. 1998; 36:95; Halpern et al. Med Care. 2002; 40:834; etc.)

ALL RIGHTS RESERVED  
<http://www.cartoonbank.com>



*“Oh, not bad. The light comes on, I press the bar, they write me a check.  
How about you?”*

# Why Do Ss Participate?

- We know something about why subjects participate in research
  - Reasons Subjects participate commonly include:
    - Altruism
    - A sense of duty to others
    - The chance for personal medical benefit
    - Trust in the provider, the institution, the sponsor
    - Money
  - Intellectual curiosity



© Cartoonbank.com



*“I don’t usually volunteer for experiments,  
But I’m kind of a puzzle freak.”*

# Why Do Potential Ss Refuse?

- We also know something about why potential subjects do not participate in research
  - Distrust, distrust, distrust
  - Do not want to be “guinea pigs”
  - Belief that standard care is adequate
  - Unwilling to accept the risks and discomforts of research
  - Do not want to be randomized or risk getting a placebo

(Nelson & Merz, Med Care 2002; 40(9 Suppl.):V69  
and references cited there)

# Actual Payments Appear Reasonable

- We have a little data that suggests actual inducements paid appear reasonable and loosely related to what is asked of Subjects
  - Analysis of 109 published US-based studies in medicine and psychology showed that Ss were paid an average of \$9.50/contact hour plus about \$12 for each separable task involved; no risk premium was evident  
(Latterman & Merz, Am J Bioethics 2001; 1(2):45)
  - Analysis of protocols and consent forms for 467 studies at 11 US sites, found higher payments for studies offering therapeutic benefit, at least 1 invasive procedure, and more clinic visits; no relationship of payment to time spent nor type of study  
(Grady et al. Cont Clin Trials 2005; 26:365)
  - Survey of authors of 81 published pediatric studies, found that cash and other payments were made in 42 of the studies, where investigators considered time, discomfort, and age of subjects in setting payments  
(Iltis et al. Pediatrics 2006;118:1546)

# No Evidence that \$ Effects Risk Perception

- 3 studies have examined risk taking and incentives for willingness to participate (WTP) in research:
  - Hypothetical study with 126 hypertension pts found that WTP increased with payment and with decreasing study risk, with no interaction (meaning high payments did not alter risk tolerance)  
(Halpern et al. Arch Intern Med 2004; 164:801)
  - Hypo study in 270 pharmacy students manipulated payments and risk levels, finding money influenced WTP but not risk ratings; Ss stated a slightly greater propensity to conceal information in order to get into a study (esp. a low risk study)  
(Bentley & Thacker, J Med Ethics 2004; 30:293)
  - Hypo study in 46 schizophrenia pts found that WTP increased with increasing personal chance of benefit, payment, and decreasing risk, and no evidence that high payments influenced risk tolerance  
(Dunn et al. Schizophr Bull 2008; Feb. 14:1)

# Lotteries too. . .

- Some concern that lottery chances will over-entice Ss because of cognitive limits on decision-making skills (that is, people are not economically rational)

(Brown et al. IRB 2006; 28(1):12)

- No evidence that this is so...

- Mail survey of ER docs found significantly higher response rate for \$2 cash over lottery chance to win \$250

(Tamayo-Sarver & Baker, Acad Emerg Med 2004; 11:888)

- Mail and internet survey of med students and PGY2s suggested no effect of \$100 lottery offer on response rates (compared to prior years)

(Grava-Gubins & Scott, Can Fam Physician 2008; 54:1424)

- Mail survey of AU citizens showed small N.S. increase in response rate (75 vs. 68%) for instant lottery ticket over no incentive

(Kalantar & Talley, J Clin Epidemiol 1999; 52:1117)

# Some summary thoughts. . .

- Individuals vary extremely widely in their risk perception and risk tolerance, their valuation of money, and how they weight these and other factors in making decisions
- Research budgets are not unlimited, and PIs have to responsibly marshal their resources to ensure completion
- If risk and other activities required of Ss are high or burdensome, then compensation should be high
- There is a market of paid, professional healthy subjects (see <http://www.guineapigzero.com/>) but in general subjects are not organized, have no bargaining power, and are on the losing side of an information disequilibrium
  - The most notable exception may be *astronauts*

# And finally my opinion. . .

- The human subjects research enterprise should internalize the costs of human participation: all subjects should be compensated
- PIs should clearly state and justify in protocols and consent forms what payments are for and amounts, including as applicable:
  - Expenses
  - Time spent traveling, waiting, and participating
  - Inconvenience
  - Discomfort and pain
  - Risk of injury or other harms
  - Incentive to ensure adequate enrollment or reward to acknowledge contribution
  - *IRBs should flag unreasonable mismatches*