MERGERS AND INNOVATION IN THE PHARMACEUTICAL INDUSTRY

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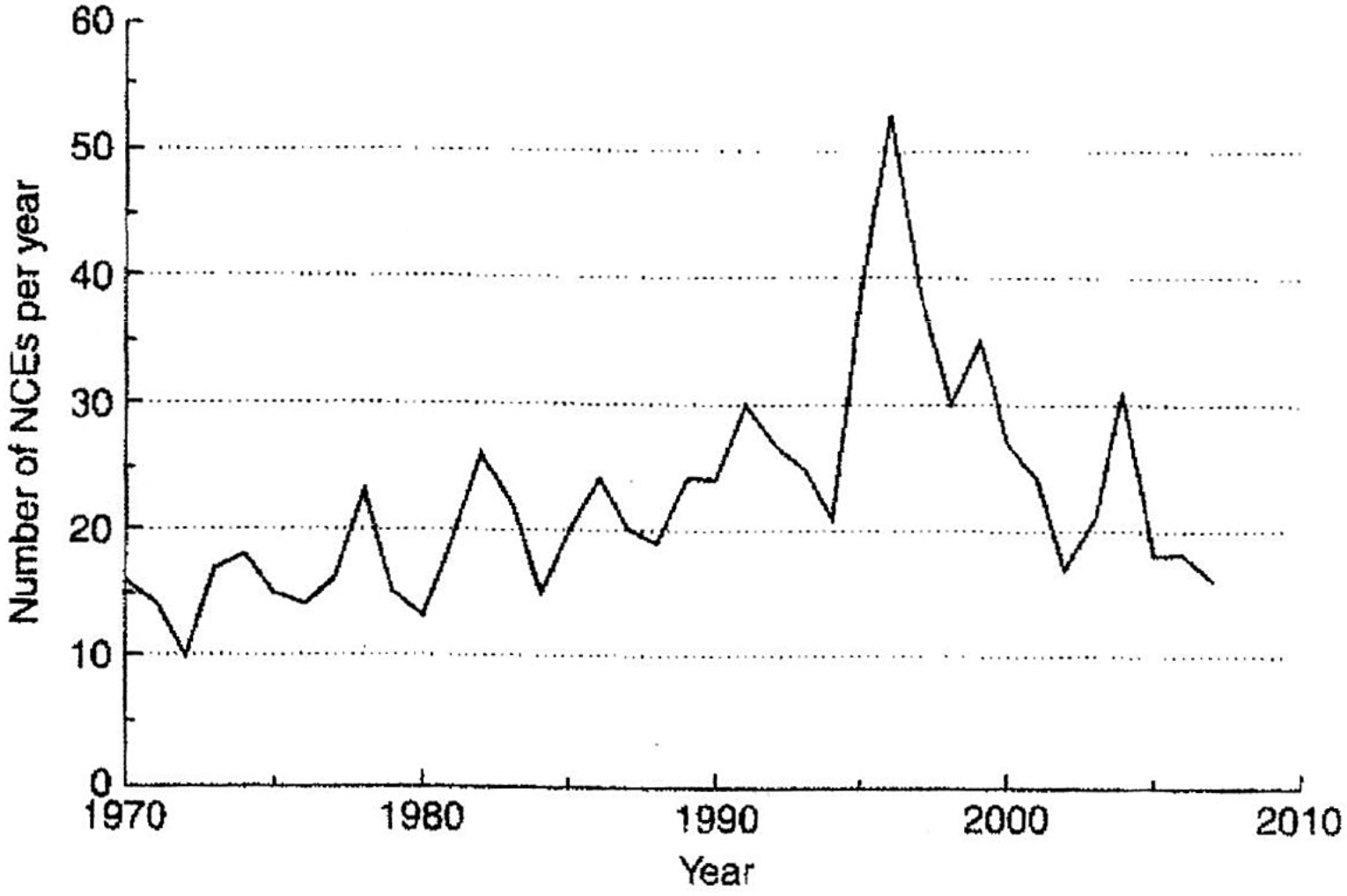
Introduction (1)

- Research productivity in the pharmaceutical industry has declined in recent years.
  - expenditures on R&D has more than doubled in the ten years between 1998 and 2008.
  - number of new chemical entities introduced into U.S. markets has remained relatively stable at between 20 and 30 per year.
  - see Figure 1.

Figure 1

New Chemical Entities Approved for Marketing
in the United States, 1970-2007



Introduction (2)

- Cohort of large companies who engage in substantial R&D efforts has become increasingly concentrated.
  - in 1998, leading 8 companies controlled 36% of industry shipments.
  - by 2002, this share had risen to 53%.
  - resulted largely by recent merger wave.
- Explore the likely impact of this merger wave on the rate of pharmaceutical innovation.

The Theory of Parallel Paths (1)

- Uncertainty is dominant reality of pharmaceutical R&D
  - for every successful agent, hundreds (or even thousands) are discarded along the way.
- Critical element of any research policy is how to confront this uncertainty.
- A long recognized means of coping with this problem is to support parallel paths intended to achieve a specific objective.
- This approach contrasts with a more sequential approach to development planning, which leads to forgone payoffs during the period of delay.

The Theory of Parallel Paths (2)

- Supporting more parallel paths leads to higher immediate costs but quicker payoffs.

- A more sequential strategy involves leaving more to chance; possibly lower costs.

- Parallel paths represents a hedge against the consequences of failure.

A Dartboard Experiment

- Choice of R&D projects is represented as throwing darts randomly at a dartboard.
- Cells of dartboard represent varying payoffs contingent upon research and marketing success.
- Assume that the returns from new pharmaceuticals are highly skew and can be represented by a log normal distribution.
  - top 10% of distribution captures roughly 80% of total payoffs.
- The cost of each “throw” is the cost of the R&D project, which varies across experiments.

Simulation Analysis

- Goal was to find the net value-maximizing number of throws.

- As expected, more throws were optimal with lower R&D costs per throw.
  - ranged from 25 throws to more than 100 at R&D costs of $2,000.

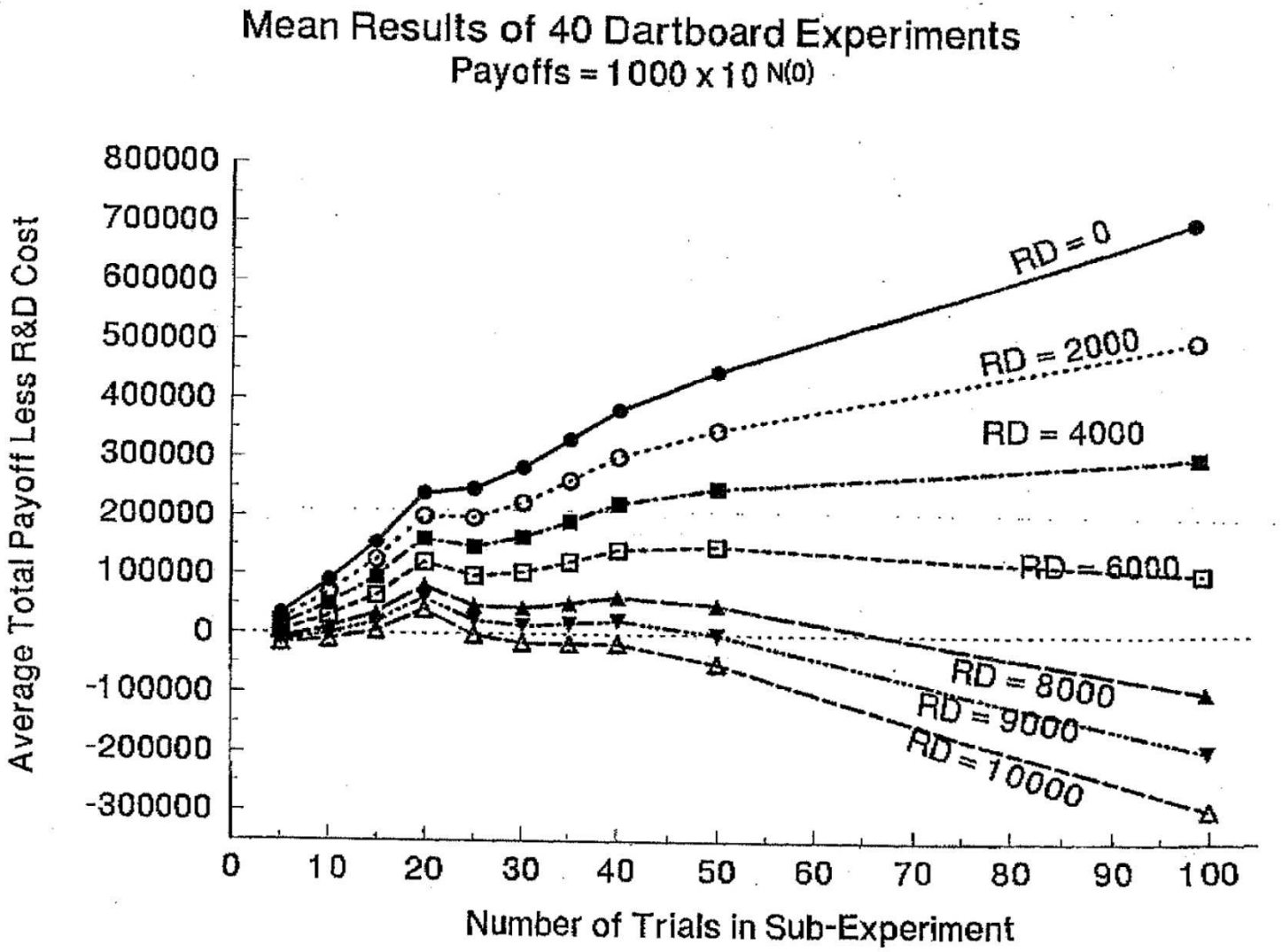
- Each hit location was statistically independent of other trials; required for R&D programs to be independent.

Simulation Results (1)

- See Figure 2 for the results from 40 experiments; with the number of trials per experiment ranging from 5 to 100.

- Values graphed are total payoffs less total R&D costs, averaged across all 40 experiments.
  - each payoff value is based on an assumed level of R&D costs and a particular number of trials.
  - payoffs are derived from the simulations.

Figure 2


Mean Results of 40 Dartboard Experiments
Payoffs = 1000 x 10 N(0)
Average Total Payoff Less R&D Cost
800000
700000
600000
500000
400000
300000
200000
100000
0
-100000
-200000
-300000
0
10
20
30
40
50
60
70
80
90
100
Number of Trials in Sub-Experiment
RD = 0
RD = 2000
RD = 4000
RD = 6000
RD = 8000
RD = 9000
RD = 10000

Simulation Results (2)

- With low R&D costs, net payoffs are maximized by extending the number of trials beyond 100.
- With high R&D costs, net payoffs eventually turn negative as the number of trials increases.
- At moderate R&D costs, $6,000 in this example, there are two local maxima: at 20 trials and at 50 trials.
- Critical result is the number of trials that maximizes net payoffs at break-even values.
  - reached when the number of trials lies between 15 and 40.
- These values represent the optimal number of parallel research paths at which net payoffs are maximized.

Critical Assumptions
Which Underlie This Result

- Log normal distribution of payoffs.
- Pharmaceutical research is a rent-seeking activity in which R&D programs are pursued so long as expected payoffs exceed R&D costs.
  - driven by competition among companies.
- Both assumptions are consistent with the current structure of pharmaceutical R&D.

Current Structure of Pharmaceutical R&D (1)

- Increasing vertical disintegration where much work at the “discovery” stage is carried out in small biotech firms.
- Major companies often provide financial support through contracts, alliances, or acquisitions. Has major impact on the work that is done.
- As the number of large companies available to support independent R&D declines, so might the number of independent paths that are supported.
- Some “discovery” research is carried out within the major companies.
- There is some prospect for parallel research paths to be pursued within the largest companies.

Current Structure of Pharmaceutical R&D (2)

- Approximately two-thirds of R&D dollars are used for drug "development" which leads to the creation of marketable products.
- Also quite risky with less than one in five compounds that start clinical testing leading to drugs which reach the marketplace.
- Since individual projects cost an average of about $200 million each, even the large companies generally have limited their efforts to a single one in a particular therapeutic area.
- Therefore, the number of research paths pursued at the development stage can be equated with the number of large companies engaged in pharmaceutical R&D.

Evidence from Phase III Clinical Trials

- Disease areas for 5 largest US companies in 2009 and 2010

  Merck engaged in 25 trials, of which 2 were for the same condition; 92% were not duplicated.

  Johnson & Johnson engaged in 21 trials, of which 2 were for the same condition; 90% were not duplicated.

  Pfizer engaged in 12 trials, of which 2 were for the same condition; 83% were not duplicated.

  Lilly engaged in 13 trials, of which 7 were for the same condition; 46% were not duplicated.

  Bristol-Myers Squibb engaged in 8 trials, of which 2 were for the same condition; 75% were not duplicated.

- The five companies together engaged in 79 trials, of which 15 represented parallel efforts. Thus, 81% were not duplicated in terms of their therapeutic goals.

Rates of Return to Pharmaceutical R&D

- Not only do drugs survive the clinical testing process, but also the returns to new drugs that are introduced are highly skew.
- The top decile of new drugs typically garners more than half of aggregate returns. These observations are consistent with our use of the log normal distribution of payoffs from R&D.
- Also, for drugs introduced in the 1990s, their aggregate rate of return is estimated at 11.5% as compared to estimated cost of capital of 11.0%.
- This finding is consistent with our earlier assumption that R&D costs approach expected payoffs.

Social and Private Rates of Return

- The simulation analysis modeled private returns to pharmaceutical R&D.
- However, the greater the gap between social and private benefits from this research, the larger is the optimal number of parallel paths.
- The returns to society from pharmaceutical R&D are estimated at 68% per annum, which is nearly six times larger than the estimated private returns.
- The number of optimal research paths might therefore exceed the profit maximizing values of 15 to 40 parallel paths found in the simulation analysis.

Effects of Two Recent Mergers on R&D

- Pfizer acquired Wyeth and Merck acquired Schering-Plough in 2009.
- Combined Pfizer/Wyeth invested $11.3 billion on R&D: 22% of world-wide spending.
- Combined Merck/Schering-Plough invested $8.3 billion on R&D: 17% of world-wide spending.
- Post-merger Pfizer reduced R&D spending to $9.3 billion in 2010 and expects further reductions to $6.5 - $7.0 billion by 2012.
- Post-merger Merck announced it would close 3 research facilities but did not specify the amount of reduced spending.

Policy Conclusions (1)

- There is a major public interest in promoting pharmaceutical innovation and achieving maximum productivity of pharmaceutical R&D.

- Although the number of parallel research paths is not limited to the number of major companies, these companies play a critical role in the innovation process.
  - at Discovery stage, they provide both funding and technical support in the regulatory process.
  - at Development stage, where clinical trials can cost $200 million each, large companies generally support only one trial per therapeutic area at a time.

Policy Conclusions (2)

- Even if pre-merger research paths approached optimal levels, that number has declined as a result of recent mergers.

- In 2008, the largest 12 drug companies accounted for about two-thirds of global pharmaceutical R&D. And, the largest 20 companies represented 83% of world-wide R&D. These percentages have increased with recent mergers as the leading firms have became more dominant.

- Past mergers may have contributed to the observed decline in the rate of pharmaceutical innovation.