

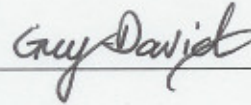
**A Proposal Submission for the 2007/2008 Russell Ackoff Doctoral Student Award
for Research on Decision Processes and Risk Management**

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Project Title: Pharmaceutical R&D Response to Shifts in Direct-to-Consumer Advertising Policy

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Proposal

Background: In 1997 the US Food and Drug Administration (FDA) relaxed the guidelines which stipulated that pharmaceutical advertising must thoroughly discuss all major risks and benefits within the context of any advertisement targeted toward consumers. This ruling effectively prompted extensive television advertising of prescription pharmaceuticals as well as more direct, clear promotion in print media. Prior to the policy shift, direct-to-consumer (DTC) advertising accounted for a modest share of overall promotional spending, but DTC has rapidly grown both in real terms and as a percentage of total promotional spending over the last decade.¹ Growth in spending increased most dramatically in television commercials.

This proposed study will examine one effect of the new DTC regulations: the effect of DTC on product development decisions. More specifically this proposed study will seek to answer whether product development for particular categories amenable to DTC marketing increased, decreased or remains unchanged relative to the counterfactual level of effort without a DTC regulatory shift.

Prior literature: Some argue that product discovery in pharmaceuticals is a random process with firms randomly testing thousands of compounds for effectiveness in a range of disease categories. In fact, firms make rational R&D investments (clinical trials and/or in-licensing compounds) on the basis of expected therapeutic market size and reimbursement shifts. (Acemoglu and Linn 2004; Finkelstein 2004) If DTC alters the ability to market products in particular therapeutic categories, then product selection equilibrium will adjust to reflect these changes. This is the basis for the primary hypothesis that I wish to test.

Theory: At the therapeutic category level (essentially the aggregation of firm decisions within the category), I expect that the relative share of product in development/clinical trials will shift toward "DTC" product categories when DTC is unrestricted. (Although alternatively, one could envision that firms, in total, may restrict the R&D if the return from investing in marketing relative to R&D increases once the DTC restriction is lifted).

Objective: This research will help detect whether the pharmaceutical and biotech industry responded to DTC policy changes by shifting more of their clinical trial effort to those therapeutic categories in which DTC is more suitable for influencing prescription decisions, ceteris paribus.

¹ Between 1991 and 2001 DTC advertising spending for prescription pharmaceuticals increased exponentially from \$56 million to \$3.7 billion.

Methods: The non-negative restriction on the outcome variable typically motivates the use of a non-linear model. The difference-in-difference specification using the logged outcome variable is quite simple, but relies on several assumptions (discussed below). Given that few ‘0’ outcomes are anticipated at the industry level, it may be sensible to adopt this approach rather than a non-linear specification.

The difference-in-difference approach compares across therapeutic categories in pre-post 1997 time-frame using an interaction term (I_{jt}) which multiplies the indicator variable for “post-1997” (1 if 1998 or later, 0 otherwise) and the indicator variable for “DTC category” (1 if the category is a “DTC category”, 0 otherwise – more on this definition later). The regression(s) also accounts for factors which influence demand in a particular category (X_{jt}) and fixed effects for time period (λ_t) and therapeutic category (ϕ_j). Coefficients are interpreted as the change in outcome variable as a result of the DTC policy (ignoring endogeneity for the moment). The coefficient for the logged outcome are interpreted as semi-elasticities in the logged outcome specification. The coefficient of interest is η .

$$Outcome_{jt} \text{ or } \ln(Outcome_{jt}) = \alpha + \lambda_t + \phi_j + \beta X_{jt} + \eta I_{jt} + \varepsilon_{jt}$$

where $Outcome_{jt} = Compounds_{jt}$ (or $Trials_{jt}$ or $Patents_{jt}$ or $Spending_{jt}$)

The dependent left-hand side variables will most like be a measure of “compounds in development” indexed by time (t) and drug category (j). The appropriate definition of a market in the pharmaceutical industry is the therapeutic category (j) and, thankfully, these can be disaggregated using the definitions applied by market research and audit data collection firms so that there is a relatively large sample size. Generally there are a sufficiently large number of potential categories as defined by the European Pharmaceutical Market Research Association (25 at the one digit category ~85 at the two digit category, several hundred at the three and four digit category). The time periods (t) are years between 1995 and 2004. Compounds can also be disaggregated into phase I, phase II and phase III trials (lower phases represent earlier stage research in human subjects).

The crucial decision involves the definition of the case (“DTC”) and control (“Non-DTC”) groups as the identifying assumptions depend on the appropriate classification. In practice, much of the DTC was concentrated in particular therapeutic categories—allergy, hypertension, high cholesterol, lifestyle (erectile dysfunction) and asthma. (Berndt 2005) I could, ex-ante, claim that these are the primarily relevant therapeutic categories. Another definition might define a DTC category as one in which any DTC within the category i during year j qualifies that category as a “DTC category”. A variant of this second approach would set a certain threshold for the percentage of sales that those products that held DTC campaigns within the category contribute to the overall level of sales in the category. Categories that exceed the threshold would be considered “DTC categories”.

The coefficient of interest, η , is interpreted as the marginal impact of DTC on clinical trial activity in “high DTC” groups relative to “no/low DTC groups”. Estimation is straightforward in both contexts—maximum likelihood estimators assuming normality in the error structure are easily derived as are Huber-White robust standard errors. As indicated earlier, the logarithmic transformation of the dependent means that the economic interpretation of the coefficients is semi-elasticity – a somewhat awkward result (% change in products in development within “DTC” categories as a result of the DTC policy shift). The alternative specification (a standard linear model) which would yield coefficient with more meaningful economic interpretation

(change in the number of compounds in development as a result of the policy in DTC vs. Non-DTC categories). Note that a significant positive (negative) coefficient could occur either if the DTC category effort increased (decreased) or the non-DTC category effort decreased (increased).

Data: The definition of clinical trial effort is defined as number of compounds in trials, however, number of trials or therapeutic specific R&D spending could also serve as measures of effort (although these may be more difficult data to obtain). Private data collections have records of pharmaceutical clinical development projects -- namely A) Pharmaprojects and B) ADIS clinical trial data. The estimated cost for the Pharmaprojects data is \$2,500 (I have emailed the firm representative to confirm this quote). I will also anticipate exploring the ADIS data quality and costs and pick the best vendor for conducting this initial analysis. In the future, I hope to acquire additional data to more thoroughly explore firm-level effects as well.

Detailed Budget:

Pharmaprojects data*	:	\$2,500
Total		\$2,500

*1995-2003, # products in development by year / therapeutic category (EphRMA code) / Firm / Phase of Development.

Department Funding Policy:

The Leonard Davis Institute (affiliated with the healthcare systems department) does supply funds for data acquisition, but typically only to faculty members. Prior projects have utilized clinical trial data -- but not at the therapeutic category level and not for the dates of interest for this analysis.

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