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Replication

The adoption of new prescription drugs is strongly associated with prior category prescribing rate

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ABSTRACT

We investigate whether doctors who adopt a new drug in its first year on the market tend to be heavier category prescribers. Early studies of pharmaceutical prescribing and packaged goods purchasing suggest that innovators are heavier category users; however, this finding has received little attention and the evidence remains sparse. We examine the adoption of 36 new drugs by doctors in the United Kingdom and find that, on average, the prior category prescribing rate of innovators is about 50% higher than that of non-innovators.

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1. Introduction

There is an established research tradition on the social aspects of innovation traceable to the landmark paper of Coleman, Katz, & Menzel, 1957. This work examined the spread of information about a new drug among doctors' professional and personal networks. The authors found that doctors with higher social integration first prescribed the new drug 3.1 to 4.3 months earlier than those with lower social integration. This finding heavily influenced subsequent work on the diffusion of innovations and helped to establish the view that social influences are a major factor in the spread of innovative behaviours (e.g. Rogers, 2010).

Coleman et al. (1957) also reported, in a footnote to the original article, that doctors with a high category prescribing rate prescribed the new drug 5.0 months earlier than those with a low category prescribing rate—a larger effect size than their more influential finding on social integration. A similar phenomenon has been observed in consumer markets: Taylor (1977) found that, for eleven new packaged goods, households purchasing the new product earlier had a higher category purchase volume than those who purchased the new product later. Taylor's finding, though potentially important, has received little attention—whereas Google Scholar shows that Coleman et al. have received an average of 21 citations per year since publication, Taylor has attracted an annual average of just over 3.

Coleman et al.'s work on the adoption of new drugs has been extended. Van den Bulte & Lilien (2001) showed that the original study conflated social contagion with marketing effects, while Manchanda, Xie, & Youn (2008); Liu and Gupta (2012); Iyengar, Van den Bulte, & Valenta (2011) and Iyengar, Van den Bulte, & Lee (2015) have all investigated aspects of social contagion and marketing for new drug launches. These studies mention category prescribing rate but only in passing; their foci remain on social contagion, opinion leadership and marketing effects.

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Taken together, these prior studies examine the launches of four new drugs, all in the United States. These include the antibiotic tetracycline (Coleman et al., 1957), an unnamed statin (Liu & Gupta, 2012) and two unnamed drugs from unnamed therapeutic areas. The association between category prescribing rate and the adoption of new drugs thus rests on a narrow empirical base. We therefore replicate and extend prior research through an extensive study of 36 named new drug launches in the United Kingdom.

2. Data and method

The data source is a unique panel of UK doctors (in this case general practitioners) that records all new and switch prescriptions over a period of 23 years. Over the life of the panel, more than 1500 doctors participated and on average they wrote 1800 new or switch prescriptions. The number of prescriptions recorded exceeds 2.7 million and covers all main therapeutic classes.

The data used in this study cover 36 drug launches in the following six pharmaceutical therapeutic classes: Angiotensin II receptor blockers, Cox II inhibitors, erectile dysfunction, anti-depressants, osteoporosis and statins. We select these therapeutic areas as they had five or more new drug launches from the second year of the panel onwards. From these therapeutic areas, we take a census of new drug launches with two exceptions; where the first drug launched created a new therapeutic area, no analysis of prior category prescribing rates is possible.

Our analysis protocol for each new drug launch is to: (i) compute the date of the first prescription; (ii) select records for all doctors who prescribed any drug in that category in both the 12 months prior to and also following that first prescription; (iii) identify doctors who prescribed the new drug in the first 12 months on the market and define these doctors as innovators; (iv) calculate category prescribing rates for the 12 months prior to the first prescription for both innovators $R(i)$ and non-innovators $R(ni)$; and (v) compute the ratio of these prescribing rates $R(i)/R(ni)$. We report results for each new drug individually and for all 36 drugs combined.

To validate our simple approach, we undertake three checks. First, for each new drug, we apply the nonparametric Mann–Whitney U test to the category prescribing rates for innovators and non-innovators to evaluate whether these groups are from different populations. We then relax the assumption of equal variances, at the cost of some statistical power, by applying the Kolmogorov–Smirnov test to the same data. As our hypothesis is directional (that innovators have higher prior category prescription rates) we report one-tailed p -values.

Second, to check whether the results are unduly influenced by the choice of a 12-month cutoff for innovators, we reapply step (iii) of our analysis protocol to define innovators for each of three additional time periods. These time periods are 3, 6 and 9 months post-launch. We report the $R(i)/R(ni)$ aggregated to category level for each time period.

Third, we apply Cox proportional hazard regression models to check the impact of prior category prescribing rates on the hazard of innovating. We right-censor the non-innovators at week 52 and test the proportionality assumption of Cox regression by examining the interaction of prior category prescription rates with time. Having tested this assumption, we drop the interaction term and re-estimate the model to examine $\text{Exp}(B)$ —the increase in the hazard ratio that arises with each successive prior category prescription. We report two-tailed p -values for tests of the Cox proportionality assumption and for the improvement in the $-2LL$ of the final model. We report one-tailed p -values for the difference between the estimated value of $\text{Exp}(B)$ and the no-change value of 1.0, reflecting the directional nature of the hypothesis that the hazard of innovating increases as prior category prescribing rate increases.

3. Results

Table 1 shows the results for all 36 cases. The first column indicates the category, the second column identifies the new drug, the third column reports the ratio of prior category prescribing for innovators $R(i)$ to non-innovators $R(ni)$. The fourth and fifth columns report descriptive statistics on the number of doctors selected by our analytical protocol and the number of these who adopted the new drug in its first year on the market. The fifth and sixth columns report p -values for the Mann–Whitney and Kolmogorov–Smirnov tests.

These results show that, on average, innovators prescribed the category about 50% (ratio: 1.46) more than non-innovators in the 12 months prior to the launch of a new drug. There is some variation in the ratio for individual drugs: the Mann–Whitney tests show that eight out of 36 cases have $p > .05$; the Kolmogorov–Smirnov tests with their lower statistical power show 13 out of 36 cases of $p > .05$. Some of these cases do have relatively low sample sizes (Table 1) or relatively low prior category prescription rates (see column 3, Table 3).

This pattern of results is familiar from meta-analyses, as these typically show a distribution of effect sizes with those in the left tail of distribution being non-significant when considered on their own. The effect sizes in the left tail are nonetheless important, as omitting these would bias the estimate of the overall effect size upwards. Observing this distribution of effect sizes highlights the risk of availability bias from the study of a single new drug launch. Individual studies may easily be drawn from the left or right tail of the distribution, giving results that are not representative.

Table 2 reports $R(i)/R(ni)$ for four different time periods for each of the six categories studied. There is remarkable stability across the time periods analysed and some (but not large) differences in the category ratios.

Table 3 reports the Cox proportional hazard regression results for each of the 36 new drugs. This table includes the combined prior category prescribing rate $R(x)$ as an additional descriptive statistic. The table then reports the value of $\text{Exp}(B)$ —the change in the hazard ratio for respondents who differ by one unit in prior category prescribing rate. Finally, Table 3 reports p -values arising from the statistical tests described earlier.

The results in Table 3 show a similar pattern to those in Table 1. On average, each prior category prescription is associated with an increase of about 4.5% (1.045) in the hazard ratio for innovating. There is again variation at the level of individual drugs, including

Table 1

Prescribing ratios.

	Brand	Ratio of $R(i)/R(ni)$	n	i	One tailed Mann–Whitney p -value	One tailed Kolmogorov–Smirnov p -value
Statins	Zocor	2.3	115	35	0.00	0.02
	Lescor	2.0	170	19	0.00	0.01
	Crestor	1.8	304	157	0.00	0.00
	Lipostat	1.7	145	35	0.01	0.07
	Lipitor	1.7	269	152	0.00	0.00
	Lipobay	1.6	269	73	0.01	0.02
Erectile dysfunction	Uprima	1.7	215	47	0.00	0.01
	Viridal	1.7	203	18	0.04	0.04
	Viagra	1.4	196	57	0.13	0.40
	Levitra	1.4	249	51	0.01	0.04
	Cialis	1.1	243	79	0.11	0.21
Depression	Cipralext	2.0	303	61	0.00	0.00
	Cymbalta	1.9	196	12	0.00	0.00
	Cipramil	1.4	322	68	0.00	0.00
	Seroxat	1.4	266	89	0.00	0.01
	Lustral	1.3	277	46	0.01	0.03
	Effexor	1.3	316	100	0.00	0.01
	Prozac	1.2	333	79	0.00	0.00
	Dutonin	1.1	315	81	0.10	0.21
Cox-2 inhibitors	Arcoxia	1.5	316	115	0.00	0.00
	Prexige	1.5	288	23	0.01	0.02
	Celebrex	1.4	360	169	0.00	0.00
	Bextra	1.4	305	66	0.01	0.03
	Vioxx	1.2	377	226	0.00	0.01
Angiotensin Receptor Blockers	Rasilez	2.2	299	21	0.07	0.08
	Micardis	1.5	268	49	0.00	0.03
	Olmotec	1.5	282	47	0.00	0.01
	Amias	1.4	180	48	0.02	0.07
	Teveten	1.2	275	18	0.07	0.21
	Diovan	1.1	105	28	0.08	0.23
	Aprovel	1.0	152	60	0.30	0.44
Osteoporosis	Bonviva	1.7	212	53	0.00	0.02
	Fosamax	1.3	45	4	0.42	0.50
	Protelos	1.3	211	43	0.03	0.16
	Evista	1.3	183	42	0.01	0.09
	Actonel	1.2	222	40	0.04	0.26
	Mean	1.46*	244	64	0.04	0.09

Note: the brand names are those used in the UK market, other brand names were occasionally used in other markets.

* Geometric Mean.

eight cases of $p > .05$ for $\text{Exp}(B)$ and 12 cases of $p > .05$ for the improvement in the likelihood of the final model over the base model. Only one of the 36 models shows an interaction that violates the proportionality assumption (for Lipobay, $p = .05$) and chance alone might result in at least one violation.

Taken together these results indicate that identifying heavier category prescribers, prior to launch, provides a simple predictor of which doctors are more likely to adopt a new drug in its first year on the market.

Table 2Variations in $R(i)/R(ni)$ by category and time period*.

	3-Months	6-months	9-months	12-months
Statins	2.00	1.91	1.92	1.84
E. Dysfunction	1.22	1.44	1.32	1.44
Depression	1.44	1.41	1.46	1.42
Cox-2 Inhibitors	1.25	1.22	1.37	1.40
Angiotensin RB	1.42	1.40	1.36	1.37
Osteoporosis	1.55	1.45	1.35	1.34
All	1.47	1.46	1.46	1.46

* Geometric means.

Table 3

Cox proportional hazard model results.

	Drug	Mean prior Rx rate	Exp(B)	One tailed <i>p</i> -value Exp(B)	Two tailed <i>p</i> -value change in -2LL	Two tailed <i>p</i> -value interaction with time
Statins	Zocor	3	1.119	0.00	0.00	0.91
	Lescol	5	1.111	0.00	0.00	0.67
	Crestor	18	1.025	0.00	0.00	0.83
	Lipostat	4	1.041	0.00	0.04	0.38
	Lipitor	8	1.030	0.00	0.00	0.74
	Lipobay	8	1.044	0.00	0.00	0.05
Erectile dysfunction	Uprima	4	1.093	0.00	0.00	0.09
	Viridal	4	1.081	0.01	0.05	0.77
	Viagra	4	1.053	0.02	0.05	0.75
	Levitra	6	1.031	0.02	0.08	0.72
	Cialis	6	1.015	0.17	0.37	0.77
Depression	Ciprallex	34	1.026	0.00	0.00	0.15
	Cymbalta	32	1.022	0.00	0.01	0.20
	Cipramil	43	1.011	0.00	0.00	0.54
	Seroxat	30	1.010	0.00	0.01	0.40
	Lustral	31	1.010	0.01	0.04	0.67
	Effexor	42	1.006	0.01	0.02	0.39
	Prozac	30	1.008	0.01	0.02	0.48
	Dutonin	42	1.004	0.10	0.22	0.94
Cox-2 inhibitors	Arcoxia	57	1.005	0.00	0.00	0.84
	Prexige	49	1.004	0.05	0.16	0.19
	Celebrex	65	1.005	0.00	0.00	0.42
	Bextra	56	1.004	0.00	0.02	0.17
	Vioxx	69	1.002	0.00	0.01	0.99
Angiotensin Receptor blockers	Rasilez	11	1.032	0.00	0.03	0.15
	Micardis	6	1.038	0.00	0.02	0.98
	Olmotec	8	1.029	0.01	0.03	0.41
	Amias	4	1.073	0.01	0.03	0.52
	Teveten	6	1.032	0.18	0.39	0.31
	Diovan	3	1.018	0.40	0.80	0.59
	Aprovel	3	1.009	0.40	0.80	0.33
Osteoporosis	Bonviva	4	1.061	0.00	0.00	0.72
	Fosamax	1	1.499	0.15	0.38	0.54
	Protelos	5	1.050	0.03	0.09	0.68
	Evista	3	1.068	0.05	0.13	0.50
	Actonel	3	1.041	0.18	0.38	0.90
	Mean	19.6	1.045*	0.05	0.12	0.55

* Geometric mean.

4. Discussion

According to [Uncles & Kwok's \(2013\)](#) classification of replication research, the present study provides a differentiated replication of the association between heavy prescribing and adoption of new drugs. Compared to prior work, we examine a broader range of time periods; in a different country with a different medical reimbursement system; with a much larger number of new drugs; or utilizing a systematic decision rule. The results show that innovators are, on average, heavier prescribers. If it is appropriate to identify potential innovators on the basis of their social integration then it also makes sense to identify innovators on the basis of their category prescribing rate. The original (but hardly discussed) finding of Coleman et al. still holds half a century later while Taylor's finding from 1977 is shown to generalize to a fundamentally different setting.

These findings rest on a firm empirical base. The present study increases the number of new drugs examined in the literature from four to 40. The 36 new drugs are all named; and there is no possibility of availability bias arising from the industry-supported study of a limited number of datasets.

We encourage further research into the basis of the association between category prescribing rates and innovation. For example, is the relationship category-specific or is it a more general behaviour that extends across multiple new drug launches? Is the effect of prior prescription rate consistently higher than the effect of social integration? How much of the innovative behaviour is explained by the detailing efforts of drug companies in the year of launch, and how much by the intrinsic characteristics of the innovators? These questions all invite further study. Our own speculation is that we are observing a form of the lead user phenomenon ([Von Hippel, 1986](#)), whereby heavy prescribers are more familiar with the limitations of existing drugs, and thus more likely to innovate to solve problems about which they hold some specialist knowledge.

We hope that this replication will encourage extensions to consumer packaged goods innovation, where we expect to see similar patterns. The results also have implications for modelling: the confirmation that category prescribing rate is a correlate of new drug

adoption suggests that this variable ought to be included in models that forecast the uptake of new drugs, with the prior expectation that doctors who are heavy prescribers will be more likely to adopt.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ijresmar.2015.12.002>.

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