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THE INFLUENCE OF BRAND EQUITY ON PRESCRIBER BEHAVIOUR IN A MULTISOURCE DRUG MARKET

by

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By

WANJIKU KARIUKI, MD, MPH, PhD

2020

DEDICATION

To Deborah Wanjiku Ngaruiya

THE INFLUENCE OF BRAND EQUITY ON PRESCRIBER BEHAVIOUR IN A MULTISOURCE DRUG MARKET

by

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THE INFLUENCE OF BRAND EQUITY ON PRESCRIBER BEHAVIOUR IN A MULTISOURCE DRUG MARKET

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School of Public Health, 2020

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ABSTRACT

When a patent expires, innovator (brand-name) drugs lose their monopoly status and new generic competitors are free to enter the market. Theoretically, free market entry and exit should lead to a drop in the price of the innovator drug as per the tenets of perfect competition. Yet instead of prices decreasing, innovator drug prices are often minimally impacted by generic competition and the innovator continues to maintain both market power and market share – a phenomenon labelled the generic competitor paradox (Scherer, 1993) That the expected supply and demand dynamic is less pronounced in multisource drug markets, suggests that non-price considerations influence purchasing behaviour in multisource prescription drug markets. This dissertation focuses on the marketing theory of brand equity to rationalise the non-price competitive advantages that established prescription innovator (brand-name) drugs have over newer bioequivalent generic entrants. By analysing the prescribing habits of physicians, we find that brand equity confers a

competitive advantage to the innovator drug: Brand equity is cultivated during the period of patent granted monopoly and creates a first-mover market advantage that is reinforced by the strategic creation of brand loyalty, which serves as a barrier to entry for generic substitutes.

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BACKGROUND

STATEMENT OF THE PROBLEM

DRUG MONOPOLIES AND THE TRANSITION TO MULTISOURCE DRUG COMPETITION

Drug patents filed in the United States since 1995 last for 20 years from the date of patent application filing (Hunt, 2000). Filing a patent claims proprietorship over the invention of a chemical formula found to have some therapeutic utility. However, receiving a patent is but one step in the process that may eventually lead to the commercial marketing of a drug. The innovator[1] drug must undergo a series of laboratory and clinical trials to determine safety and efficacy and be approved by the Food Drug Administration (FDA) before it can appear on the market (Statman, 1981). Due to the length and stringency of this drug approval process, nearly half the years of patent protection are lost. By one estimate, the number of years remaining on an innovator drug patent after FDA approval - the effective patent life- ranges from 7 to 12 years (Grabowski & Vernon, 1996; Grabowski, Long, & Mortimer, 2014). Hence innovating firms must face significant sunk costs to apply for approval prior to knowing the competitive landscape of the post-patent market (Reiffen & Ward, 2005) Accordingly, the innovator firm must determine if the expected post-entry rents justify the economic and opportunity costs associated with FDA application (Reiffen & Ward, 2005).

Through the lens of public health policy, the drug patent system is intended to strike a balance between rewarding innovation and maximising social benefit (Ellison & Ellison, 2011). Patents erect a competitive barrier to market entry that permits both market exclusivity and

[1] An innovator or brand drug is the first drug created containing its specific active ingredient to receive approval for use. It is usually the product for which efficacy, safety and quality have been fully established. When a new drug is first made, drug patents usually will be acquired by the founding company.

pricing above marginal cost. This transient monopoly is beneficial to innovating firms wishing to recoup the costs of R&D and to maximise profit (Ellison & Ellison, 2011). Yet the opportunity cost of rewarding innovation through patent protections is diminished social benefit. Setting aside the influence of third-party payers, the costs associated with drug patent monopolies may limit patient choice and thus be detrimental to affordable drug access and social welfare (McAffee, Mialon, & Williams, 2004). Subsequently, the rationale posited by policy makers and generic entrants alike is that by eventually expiring patents, a vibrant and competitive generic market is created that ensures that affordable medications are widely available at prices that reflect the marginal costs of production (McAffee et al., 2004). Social benefit is maximised by the removal of the cost barrier to accessing pharmaceutical healthcare options (Boldrin & Levine, 2008; McAffee et al., 2004).

A generic drug can only be marketed once the innovator drug's patent has expired. Prior to 1984, any firm that wanted to market a post-patent expiration generic undertook a similar application process (Hellerstein, 1998). Although a generic competitor did not incur the cost of determining which drugs were technically feasible and economically viable, it still faced the hurdle of demonstrating efficacy and safety by conducting the same tests required of the innovator incumbent (Hellerstein, 1998; Reiffen & Ward, 2005). This lengthy approval process constituted a substantial barrier to entry for many generic drugs, as a result of which the generic market was relatively undeveloped (Hellerstein, 1994; Hellerstein, 1998).

The 1984 passage of the Drug Price Competition and Patent Term Restoration Act of 1984, generally referred to as the Hatch-Waxman Act, reduced the regulatory burden on generic manufacturers (Hellerstein, 1998; Reiffen & Ward, 2005). This landmark legislation stipulates that

generic entrants need only demonstrate bioequivalence[2] to the innovator drug already approved by the FDA (Reiffen & Ward, 2005). By streamlining and abbreviating the regulatory process, the cost of bringing a generic to market was diminished (Hellerstein, 1994; Hellerstein, 1998; Reiffen & Ward, 2005).

The Hatch-Waxman act was a legislative compromise that sought to balance incentives for innovation against issues of access and affordability (Berndt & Aitken, 2011). Hatch-Waxman expedited the approval process for generic prescription drugs, which spurred immediate growth in the generic drug industry as many branded innovator drugs went off patent and cost containment efforts encouraged consumers to switch to more affordable generic alternatives (Grabowski & Vernon, 1996; Hunt, 2000). The generic share of retail prescriptions in the United States has grown from 18.6% in 1984 (Berndt & Aitken, 2011) to 89% in 2017(Steven M Lieberman, Margaret Darling, & Paul B Ginsburg, 2017). Conversely, Hatch-Waxman conferred certain benefits to patented originator drugs. For example, the policy extended the effective patent life of innovator drugs by restoring the patent life "lost" during the clinical testing and FDA review period for innovator branded drugs (Hunt, 2000). Ten years after implementing the policy, the average effective patent life of new compounds was 11.8 years, 2.3 years longer than the 9.5-year period applicable to a drug without Waxman-Hatch extensions (Grabowski & Vernon, 1996; Hunt, 2000).

[2] Bioequivalence: the property wherein two drugs with identical active ingredients or two different dosage forms of the same drug possess similar bioavailability and produce the same effect at the site of physiological activity. (Miriam Webster)

STRATEGIC ENTRY DETTERENCE AND THE BEHAVIOUR OF MARKET STAKEHOLDERS

To both recoup the costs of drug development and profit from a protected monopoly, innovating firms are incentivised to extend the life of patents. A common tactic is to file several secondary patents on the same drug to extend the 20-year period and impede market entry of generic competitors (Vokinger, Kesselheim, Avorn, & Sarpatwari, 2017). Another strategy is to prolong a drug patent through research on children. Any drug proposed for use in minors is automatically granted a 6-month extension (Bhat, 2005). Known as the paediatric exclusivity extension, this loophole can only be used twice. Additionally, some innovating firms will manufacture modified versions of the originator drug – a strategy known as “evergreening” (Collier, 2013). Slight alterations may be made to the original drug formula. For example, the new drug might rework the administration or dosage of the drug resulting in an extended -release formula or a rapid release formula (Collier, 2013).Though evergreening will require another patent application and clinical trials, it effectively deters the competition from producing a generic substitute, unless the FDA determines that the original innovator drug is of the same quality as the revised version(Bhat, 2005; Collier, 2013; Vokinger et al., 2017) .

Beyond patent extension, innovating pharmaceutical firms execute a range of legal manoeuvres to both extend their monopoly and deter competitors. Reverse payment patent settlements, also known as "pay-for-delay" agreements involve the innovating pharmaceutical firm compensating one or more potential generic challengers to delay their entry into the market (Fialkoff, 2013). These settlements have been criticised as anti- competitive and counter to the public interest principally because they frustrate the purpose of the Hatch-Waxman Act - to

increase competition and promote access to affordable pharmaceuticals alternatives (Fialkoff, 2013). In 2013, the United States Supreme Court ruled that the Federal Trade Commission could sue patent holders for potential anti-trust violations for engaging in these agreements (New York Times, 2013). Though reverse-payment settlements are today less ubiquitous, they now often involve convoluted arrangements intended to conceal payment (Vokinger et al., 2017).

In addition to legal recourse, innovator drug manufacturers will engage in other means of strategic entry deterrence. One ploy involves an innovating firm implementing restricted distribution arrangements to thwart generic developers from acquiring innovator drug samples thus hindering potential rivals from completing FDA-mandated bioequivalence testing (Vokinger et al., 2017). Innovator brand drug manufacturers also file frivolous petitions with the FDA to delay generic drug approvals (Balto, 2018). Typical petitions contend that the FDA's normal bioequivalence comparison method is ineffectual, and that approval of the generic application should be deferred pending further testing (Vokinger et al., 2017). Between 2013 and 2015, the FDA received 67 such petitions but approved only three (Vokinger et al., 2017).

THE PIONEER ADVANTAGE OF PATENTS

Indubitably, the market power enjoyed by individual innovator drugs derives primarily from the intentional grant of patents to allow pricing above marginal cost (Ellison & Ellison, 2011). When a patent expires, innovator drugs lose their monopoly status and new generic competitors are free to enter the market. Accordingly, the expiration of a pharmaceutical patent, and the subsequent opening of a drug market to potential entrants, is a momentous event for both the pharmaceutical firm and its competitors. Theoretically, free market entry and exit should lead to

a drop in the price of the innovator drug as per the tenets of perfect competition. Subsequently, the conventional wisdom is that the price of a patented pharmaceutical drug will often decline significantly once the drug switches to off-patent status due to the entry of generic drugs (McAffee et al., 2004). This notion is affirmed by well-publicised scenarios such as when the medication Lipitor - the most popular brand of cholesterol-lowering drugs and once the top-selling branded drug in the world - lost its patent rights in late 2011. This led to a 50% decrease of net income for Pfizer Inc. in the fourth fiscal quarter 2011 compared to the same period in 2010 (Forbes, February 2013; (Chao, Hu, Zhang, & Wu, 2016)).

Contrary to the trend of decreasing innovator drug prices with increased competition, is the observation that innovator brand-name drug prices are either sustained or increased upon generic market entry. Furthermore, innovator pharmaceutical companies continue to maintain an unexpected degree of market power– a phenomenon labelled the generic competitor paradox (Kanavos, 2008; Regan, 2008). Most innovator brand-name medications maintain large market shares upon patent expiration despite intense competition by bioequivalent generics and policies favouring generic market entry such as the Hatch-Waxman Act of 1984 (Lundin, 2000). Regan (2008) offers an independent test of the relationship between patent expiration and prescription drug prices. They identify an average $20 differential between innovator and generic prescriptions in a multisource drug market. Overall, each generic entrant is associated with an average 1% increase in the price of a branded prescription. The price differential between innovator and generic substitute grows with entry as the innovator price rises and the generic price falls (Regan, 2008).This incongruity is compounded by empirical evidence indicating that

R&D-based drug manufacturers do not attempt to deter generic entry through their pricing strategies, which remain above generic substitutes (Kanavos, 2008).

BRAND EQUITY AND ITS CONTRIBUTION TO THE GENERIC COMPETITOR PARADOX

On this line of reasoning, the generic competitor paradox may be construed as the outcome of non-price considerations in the prescribing (and consequently purchasing) of innovator drugs. This dissertation focuses on the marketing theory of brand equity to rationalise the competitive advantage that established brand-name drugs have over newer generic entrants. Brand equity is a term used in consumer marketing theory to describe the incremental utility or value added to a product by its name (Aaker, 1992; Keller, 1993; Yoo, Donthu, & Lee, 2000). Accordingly, brand equity can be estimated by subtracting the utility of physical attributes of the product from the total utility of a brand (Yoo & Donthu, 2001). The central premise of this dissertation is that brand equity is critically important for physician prescribers to make *subjective and experiential points of differentiation* between innovator drugs and their generic alternatives. Notably, these perceived differences in quality between an innovator drug and generic substitute exist despite objective bioequivalence evidence to the contrary. We propose that in the larger marketplace, entirely subjective experiential and information differences between an innovator incumbent and generic entrant signal brand equity.

Authors like Aaker and Keller have illustrated the process by which brand equity is built (Aaker, 1991; Aaker, 1992; Aaker, 1996; Keller, 2001; Keller & Lehmann, 2006) . Both theories have been subject to rigorous psychometric testing in a variety of consumer goods categories, though conspicuously less so within the pharmaceutical industry. Nonetheless, it can be argued

that the process of building brand equity within other product categories is applicable to the marketing of pharmaceuticals. However, a marked distinction in the dispensing of pharmaceuticals is the delegation of decision-making from the patient (principal) to the physician prescriber – rendering the latter both gatekeeper and agent. Due to this principal-agent arrangement, prescriber practices - in lieu of patient purchasing decisions - are essential to investigating the influence of brand equity in the multisource drug market.

At the outset, it should be reiterated that consumer-based brand equity is a psychological construct. Owing to the principal-agent structure of healthcare decisions, the corresponding terminology as it pertains to drug selection we have dubbed "physician-based brand equity". Though subjective in nature, the inherent value of building brand equity is nonetheless objectively measurable in pricing strategies and revenue streams. If the tenets of brand equity theory are applicable to the pharmaceutical context, a well marketed brand-name drug is more easily recognised, memorable, and perceived to be of higher quality than its competitors (Keller, 1993). Consequently, strong brands represent a set of distinctive characteristics and benefits, the net impact of which is the belief on the part of prescribers that the brand or innovator drug is superior to generic alternatives (Farjam & Hongyi, 2015). In accordance with Aaker's (1991) and Keller's (1993) conceptualisation of brand equity, differences in perceived quality of the innovator brand drug versus generic alternatives should develop into a positive attitude towards the branded drug, which in turn fosters a differential response in prescription rates as attitudinal loyalty to the brand morphs into behavioural brand loyalty.

Notably, brand loyalty may itself be a conscious or unconscious driver of prescription decisions. Nevertheless, the implications of brand loyalty are such that the pharmaceutical

manufacturer can set the prices of a branded drug with substantial name recognition, over and above the prices set by less familiar bioequivalent competitors, and the equilibrium market price dictated by perfect competition. Indeed, the value of branding and extensive marketing to a pharmaceutical firm, is the ability to create *perceived* differentiation of a drug despite therapeutic equivalency and indistinguishable safety and effectiveness profiles. The ability to subjectively differentiate the branded drug from its competitors permits the pharmaceutical firm to exercise a degree of control over prices, in a manner characteristic of monopolistic competition. The result is increased revenue and increased value – equity – of the branded drug (Blackett & Robins, 2001; Pradhan & Misra, 2014). Succinctly stated, cultivating brand equity involves product differentiation, which lends itself to pricing flexibility and increased revenues. Such a degree of market power would explain the sustained high prices of branded innovator drugs despite competition from viable and cheaper generic substitutes (Farjam & Hongyi, 2015; Mack, 2007). Therefore, if brand equity theory is equally applicable to the pharmaceutical context, any perceived product differentiation resultant of branding efforts lends the innovator a competitive advantage over generic entrants (Mack, 2007) such that there is a willingness to pay price premiums (Keller 1993), for a drug that is perceived to be a more superior alternative.

Various psychometric analyses of the relationship between brand loyalty and brand equity indicate a bi-directional relationship, with either dimension augmenting the other(Aaker, 2009; Farjam & Hongyi, 2015; Tuominen, 1999). Cultivated brand equity is self-sustaining – not only is it the result of brand loyalty but itself engenders further brand loyalty (Erdem & Swait, 1998). The marketing literature in other product categories establishes that high brand equity is tantamount to trust and confidence in the brand, which consistently appear in numerous

validated second order and third order confirmatory factor analyses as influential contributors to brand loyalty (Yoo et al., 2000; Yoo & Donthu, 2001). Brand equity reduces the anticipated risk, enhances anticipated confidence in the brand selection decision, and increases satisfaction with the brand (Broyles, Schumann, & Leingpibul, 2009).

As aforementioned, market exclusivity and monopoly status guaranteed by patent protections are intended to recoup costs (Mack, 2007). Yet from the perspective of building brand equity, an additional hypothesis is that a long period of market exclusivity guarantees the innovator brand drug a head start or **first-mover advantage** with which to build brand loyalty and equity to the detriment of ensuing generic competitors (Macit, Taner, Mercanoglu, & Mercanoglu, 2016). Cultivating the brand equity of a patented drug creates a momentum in demand during the years of market exclusivity that continues upon patent expiration and consequent entry of generic competitors(Blackett & Robins, 2001).

Time plays an important role in our analysis. We hypothesise that time is important in innovator brand equity cultivation. Hypothetically, the longer an innovator drug has a monopoly on the market, the greater the competitive head start to cycle through the stages of brand equity - from initial knowledge about the drug to intransigent brand loyalty or habit persistence. **Habit persistence** is the tendency of the physician to prescribe the same version of a drug to all patients regardless of their individual patient profiles. Conversely, we hypothesise that generic drugs also incur a process of time-dependent information infusion and physician learning before achieving acceptance among physician prescribers. If such physicians learn about generic alternatives and update their preferences, this would be indicative of **switching behaviour.** The crux of our analysis is determining which factors (patient, physician, drug, and market characteristics), tilt

the balance towards the innovator drug, such as habit persistence, versus which factors encourage physician learning and switching behaviour towards generic alternatives.

To recapitulate, brand equity is both a monetary and qualitative construct. As a financial construct, brand equity is represented by the price premium patients are willing to pay for an innovator drug over and above that of the bioequivalent generic. As a qualitative construct, brand equity represents a gradation of superlative, yet subjective characteristics possessed by the innovator drug versus its generic substitutes. According to Aaker, these psychological attributes include greater awareness and knowledge of the innovator drug, positive associations with the innovator brand, and perceived quality of the innovator drug (often viewed as superior to the bioequivalent generic substitute). The result of this continuum of attitudinal change is brand loyalty to the innovator, a psychological attribute that can be quantitatively assessed by calculating the likelihood of prescribing the innovator drug over its generic successor. Given these monetary and qualitative descriptors, our analysis incorporates several indicators of brand equity: 1)brand equity is quantified by the *price premium of an innovator drug ,* which physicians are willing to tolerate; 2) brand equity is evidenced by habit persistence and brand loyalty, that is, the *likelihood of prescribing* an innovator drug in a multisource drug market; and 3) Brand equity is defined as the *perceived consensus quality differential or information differential* between an innovator drug and generic substitutes.

THE IMPACT OF AGENCY AND INSURANCE STATUS ON BRAND PREFERENCES

Due to the asymmetric information problem in healthcare, whereby the physician holds greater knowledge about diseases, diagnostics and therapies, the physician must act as the agent

for the patient in medical decision making. Yet the physician is also an agent of the financier of health care (including third party payers such as insurance companies and government) and has a professional obligation to only provide medically necessary services. In this scenario, we assume that both the (indirect) utility of the patient and the insurance expenditures enter the utility function of the physician (Crea, Galizzi, Linnosmaa, & Miraldo, 2019). As a dual agent, the physician internalises a share of the patient's utility in their own utility function, but also a share of the drug costs covered by the insurer (Crea et al., 2019). The predicament of perfect physician agency is to strike the correct balance between fulfilling the needs and desires of the patient while pursuing only those therapies or interventions deemed medically necessary (Nayak, 2013).

On this line of reasoning, the generic competitor paradox could be construed as a principal-agent problem in which physician loyalty to innovator brand drugs results in prescriber decisions that differ from the wishes of either the patient or third-party insurance payers (Kanavos, 2008; Lundin, 2000). In keeping with observational evidence, we assume that the innovator incumbent is more expensive than the generic substitute. Consequently, a distortion of the principal-agent relationship would result in the observed trend of price-inelastic demand for innovator brand drugs and residual loyalty to the brand (habit persistence) even upon the entry of cheaper bioequivalent generics (Lundin, 2000).

Conversely, it may be that the demand for innovator brand-name drugs is price elastic but this price elasticity in demand is masked by insurance coverage (Lundin, 2000) . While the physician is a perfect agent for the patient, neither the principal patient nor the physician agent is incentivised to prefer the lower-priced generic products because of insulation from the extra

cost by low insurance deductibles. If the physician places a higher weight on the patient's utility than on insurance expenditures, increased insurance coverage leads to a lower probability of generic prescribing when the physician values the utility of the patient more than the insurance expenditure (Crea et al., 2019). The physician is a perfect agent for the patient but an imperfect agent for the insurer. If patients required to pay large sums out-of-pocket are less likely to have innovator brand-name versions prescribed than patients getting most of their costs reimbursed, this would be indicative of moral hazard as defined by Pauly 1968: the existence of insurance leads patients to overconsume medical care because they do not bear the full marginal cost of provision (Lundin, 2000; Nayak, 2013).

In accordance with Pauly (1968), the use of the term "moral hazard" refers to patients who may demand (and receive) too much or too expensive care relative to the social optimum because the existence of insurance coverage, as a consequence of which the patient does not directly bear the full marginal cost of care (Pauly, 1968) . This characterisation of moral hazard in insurance contrasts with the more commonly used definition, which implies that the existence of health insurance encourages patients to engage in more risky behaviour (Hellerstein, 1994; Hellerstein, 1998) . While the latter type of moral hazard certainly may exist, Pauly (1968) emphasises that even with totally risk averse patients, the existence of insurance may lead to overconsumption of healthcare because the marginal cost of treatment is not borne by the patient (Arrow, 2004; Pauly, 1968). In the context of the multisource drug market, moral hazard in insurance means that despite price advantages neither the insured patient nor physician has the incentive to overcome switching costs from the well-established innovator drug to a newer unknown generic. As a result, the patient does not demand the socially optimal amount of

prescription drugs and instead receives either too many drugs or overly expensive drugs relative to what is socially optimal (Hellerstein, 1994). Despite the suboptimal use of prescription drugs, the physician in their prescribing role is a perfect agent for the patient but an imperfect agent to the financier of healthcare.

Insurance coverage is incorporated in our conceptual framework of prescriber brand equity as a moderating variable. We hypothesise that cultivating the brand equity of innovator drugs during the drug patent term explains residual brand loyalty or habit persistence in subsequent multisource drug markets. We expect that the consequences of brand equity - brand loyalty and habit persistence- are further bolstered by insurance coverage that cushions patients from incurring the extra cost (price premium) associated with prescribing the innovator drug over generic equivalents. Therefore, the removal of third- party payer insulation from costs, encourages patient switching behaviour from the innovator to generic drug, which is reflected in prescriber practice. Findings that support the preferential prescribing of innovator drugs to patients based on insurance coverage would be evidence of moral hazard.

CAVEATS REGARDING NOMENCLATURE

A noteworthy disclaimer regarding diction in this dissertation: The term “generic” is used rather loosely in many discussions of prescription pharmaceuticals. It can variously refer to versions of a drug sold under the actual generic name, or to drugs not marketed by the original innovator firm (Hellerstein, 1994; Hellerstein, 1998). Moreover, while most of these newer bioequivalent entrants are designated generic status, some of these newcomers may be labelled as “brand generic drugs” as they are marketed under a name other than the chemical name

(Berger, 2018). To clarify this ambiguity in terminology, first-to-market originator branded drugs are henceforth labelled “innovator” with all successive bioequivalent competitors referred to as the “generics”. Therefore, some “generics’” in our analysis include FDA reference listed drugs which are bioequivalent but approved and marketed after the originator drug. Generic designation is also assigned to drugs recorded by physician under the chemical name.

JUSTIFICATION

PUBLIC HEALTH SIGNIFICANCE

Conceptualising brand equity from the perspective of the prescribing physician provides a rationale as to why health care payers and consumers alike are failing to realise the cost savings of a competitive off-patent drug market despite proven bioequivalence of generics, policies favouring generic drugs, and pressure from payers towards generic substitution.

Notably, brand equity is but one aspect of the prescription decision. External influencers such as drug availability, the patient's preference and medical profile, payer preference, pharmacy substitution, pharmaceutical marketing efforts and generic drug policy, all impact the final prescription decision. However, the central argument put forward in this project is that, ceteris paribus, brand equity as perceived by the prescribing physician establishes brand preference, which in turn has a strong impact on prescription decisions. Indeed, the afore-mentioned external factors are but modifiers of prescription behaviours which come into play only after notions of drug brand superiority (or lack thereof) are already deeply entrenched.

SIGNIFICANCE FOR PAYERS

An appreciation of how brand equity drivers and moral hazard impact the prescription decision will enable third party payers to better align their policies and incentives to those of the physician prescriber, thus lowering formulary costs where pharmacy substitution is over-ridden on the prescription order.

SIGNIFICANCE FOR PHARMACEUTICAL FIRMS

Notwithstanding the *cost of research and development* (Ellison & Ellison, 2011), the period of market exclusivity granted by a patent remains fixed. There is therefore a need for innovators to recoup costs and maximise their return on investment far beyond patent expiration. A crucial means of achieving this end is to sustain brand loyalty beyond patent expiration and upon entry of new generic competitors. Cultivating the brand equity of a patented drug creates a momentum in demand during the years of market exclusivity that continues upon patent expiration and consequent entry of generic competitors (Blackett & Robins, 2001).

Realising brand value and extending brand equity beyond patent expiration requires a systemic and strategic approach in marketing efforts targeting physicians. Understanding the brand equity drivers of physician prescription behaviour is the first step in tailoring pharmaceutical marketing and branding efforts to achieve greatest impact on the prescribing behaviours of physicians.

HYPOTHESES AND THEORETICAL RATIONALE

The overarching assertion of this dissertation is that **brand equity is critically important for physician prescribers to make points of differentiation between innovator branded drugs and their generic alternatives.** Accordingly, physician prescribers will - ceteris paribus – preferentially prescribe drugs with highest brand equity, which for the reasons subsequently cited tend to be innovator branded drugs.

Of note, there are 3 assertions drawn from Aaker's and Keller's customer-based brand equity model that inform the ensuing hypotheses. Namely, that an innovator drug with high brand equity will: (1) command a price premium over and above that of substitute generics; (2) be perceived as qualitatively superior to empirically bioequivalent substitutes; and consequently, (3) be prescribed more frequently than these generic alternatives having cultivated its own intractable brand loyal prescriber base.

Subsequently, brand equity is characterised by both a price differential and an informational differential between the innovator branded drug and generic alternatives. Extrapolating from Aaker's and Keller's conceptualisation of brand equity (Aaker, 1991; Aaker, 1992; Aaker, 1996; Keller, 2001; Keller & Lehmann, 2006) , the assumed directionality of these associations is such that innovator drugs with higher perceived quality than their bioequivalent generic substitutes, engender a greater sense of brand loyalty from prescribers. This instilled brand loyalty to the innovator drug serves to bolster market demand as signalled by a price premium, the added value of which, constitutes brand equity.

HYPOTHESIS 1

Longer periods of innovator market exclusivity bestow a first-mover (pioneer) competitive advantage to the innovator drug in subsequent multisource markets

Our central premise is that *innovator drugs have a first-mover competitive advantage over subsequent generic market entrants.* We contend that this first mover advantage is granted in part by the monopoly protections of a drug patent and monopoly gains are paradoxically evident once patent protections expire and new generics enter the market. We hypothesise that innovator incumbents that previously held a longer tenure of market exclusivity (through patent extensions or other afore-mentioned means of strategic entry deterrence) will have price and brand loyalty advantages in post-patent multisource markets.

Accordingly, our analytic model measures the impact of monopoly in facilitating the creation of innovator brand equity that persists long after the removal of barriers to entry and the creation of a multisource drug market. Our theoretical rationale is that if brand equity is indeed an experiential outcome, then innovator drugs with longer periods of market exclusivity have a longer duration in which to cultivate this equity which is evidenced by physician loyalty to the innovator drug that persists in the subsequent multisource drug market.

Moreover, because brand equity is by definition "added value" owing to the brand name, we expect that patients will be willing to pay a price premium for an innovator drug with positive brand equity despite the entry of viable (often cheaper) substitutes. This sustained loyalty to the innovator drug can be a strategic barrier for newer generic players to overcome; they too must cycle through the process of building their own "brand equity". Extrapolating Aaker's theorem, we hypothesise that for physicians to switch to the newer generic or indeed minimise the

perceived quality differential between the innovator and the new generic, the latter must at least in part catch up with the brand equity head start that the innovator incumbent already possesses. Succinctly stated, our model tests whether generic drugs pitted against innovator incumbents with an extended period of market exclusivity face an uphill battle despite favourable pricing. Perceptibly, if this hypothesis is confirmed by our model, extending innovator monopoly protections (such as through patent term extensions) serves the purpose of strategic entry deterrence even when monopoly barriers to entry are themselves removed.

Certainly, Aaker's proposed brand equity model (Aaker, 1992; Aaker, 1996) includes a domain for proprietary assets such as patents, which give a firm a temporary monopoly and thus create circumstantial loyalty (Aaker, 1991). We hypothesise that this circumstantial loyalty to the innovator (imposed by a lack of alternatives), morphs into deeply rooted brand loyalty that persists beyond patent expiration (despite the competitive benefits of a multisource drug market). Keller provides a theoretical rationale through his pyramidal brand resonance model (Keller, 2001), which delineates a psychological process by which intransigent brand loyalty (aptly labelled "brand resonance") is achieved in a series of sequential steps. Perceptibly, the implementation of this process requires an investment in time. In context, the longer an innovator drug has a monopoly on the market, the lengthier its lead time to build up physician-based brand equity. Protracted market exclusivity - granted by either patent protections or other barriers to entry for generic substitutes - confers the vanguard innovator crucial time to cultivate brand equity and form a loyal customer base. Conversely, later generic entrants must in addition to marketing themselves to prescribers (to establish Aaker's domains of knowledge and awareness), also establish perceived quality and therapeutic equivalency to the innovator(Aaker,

1991; Aaker, 1992; Aaker, 1996). Inevitably, these ensuing generics must either chip away at the innovator drug's loyalty base and/or create their own loyal customer base, which takes time.

In contrast, innovator drugs with longer periods of market exclusivity, have a head start over generic entrants – extra time during which to cultivate brand equity, and form a loyal customer base. Upon patent expiration, built-up brand equity is manifested as product differentiation in the face of other highly substitutable alternatives (Aaker, 1996). Due to perceived product differentiation, the temporary monopoly created by the patent converts not to a perfectly competitive open market, but rather a situation of monopolistic competition in which the innovator has the competitive advantage. This hypothesised first-mover lead would be evident in both the innovator's ability to sustain a price premium, and the prescriber's willingness to continue to preferentially prescribe the innovator despite the competitive challenge imposed by cheaper bioequivalent generic substitutes

For these reasons, we expect that longer periods of innovator market exclusivity will be associated with a greater likelihood of innovator prescriptions once the market is open to competition from generics. Additionally, we predict that because of cultivated brand equity, physicians will be more likely to prescribe innovator drugs regardless of sustained price premiums in multisource drug markets

HYPOTHESIS 2

Physicians will initially overestimate the perceived relative therapeutic benefit between an innovator drug and a generic entrant. This consensus quality differential between an innovator and its bioequivalent generic will diminish over time as physicians familiarise themselves with the generic.

The estimation models related to our second hypothesis expound on prescriber learning and switching behaviour by *delineating the process of time-dependent information diffusion* and generic drug acceptance among physicians. We compare prescribing behaviour for newer generics against that of older generics to determine how physicians' attitudes towards generics differ based on market tenure. Aaker and Keller's brand equity theories lead us to hypothesise that the information differential between innovator and generic will diminish over time. The key assumption of this model is that the duration of generic market availability reflects the degree of learning and knowledge about the generic, which in turn is a good proxy for the generic's consensus perceived quality. We assert that the information differential between newer versus older versions of a drug reflects the consensus quality differential (Howard, 1997). If indeed brand equity is at play in prescription decisions, we expect that physicians will be less likely to prescribe newer generics versus the older innovator drug due to an overestimation of the quality differential of the innovator drug relative to the newer generic. Over time, physicians familiarise themselves with the generic substitute, the information differential lessens, and thus the consensus quality differential diminishes to approach that of the true quality differential.

If indeed innovator drugs have a head start on subsequent generics, it stands to reason that generics could eventually bridge this gap. Time confers generic substitutes the opportunity

to build their own “equity”, as physicians familiarise themselves with the drug. Accordingly, the likelihood of prescribing the innovator or generic version of a drug could be indicative of information diffusion and learning - the gap in prescriber knowledge and familiarity between the innovator and generic entrants. As per Aaker’s model – product awareness and perceived quality are essential contributors to brand equity(Aaker, 1991). Physicians will more readily switch to older generics but remain loyal to the innovator drug (i.e. habit persistence) in the case of newer generics. This process of time-dependent information diffusion is borne by the literature (Howard, 1997).

HYPOTHESIS 3

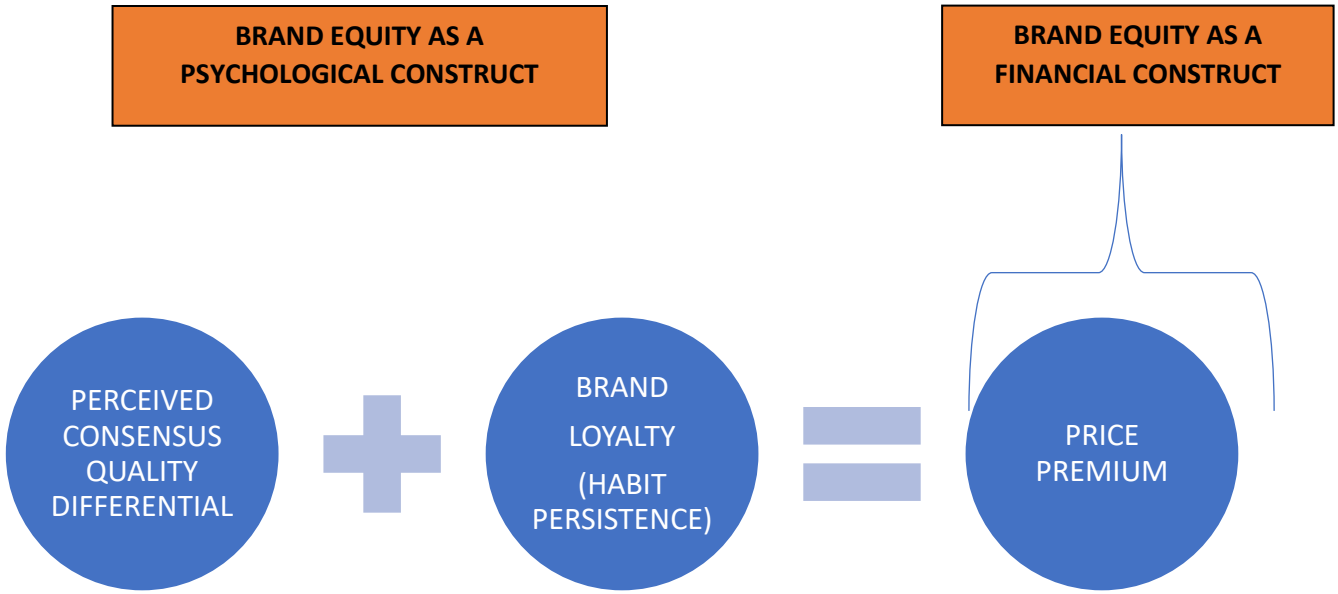
Insurance status overrides brand equity preferences

A factor that is likely to override physician preferences for innovator drugs is insurance coverage. Our third hypothesis tests the influence of external nudges exerted by third party payers. The corresponding analytical objective *examines the role of insurance coverage in qualifying physician brand loyalty***.** Our estimated model tests whether habit persistence and brand loyalty are altered by insurance coverage. Thus, it is essential to investigate whether physicians are more sensitive to costs incurred by individual patients or certain insurance types, and less responsive to costs borne by other third-party payers. If physicians in our study sample systematically vary prescription decisions based on patient insurance coverage or lack thereof, this is evidence of moral hazard - whilst a perfect agent to the patient, the physician is a less perfect agent to the financier of healthcare. As innovator drugs tend to be more expensive than ensuing generics, we hypothesise that patients in my reference category of uninsured or self-pay patients will be least likely to receive branded innovator drugs, which is evidence of moral hazard (Lundin, 2000; Nayak, 2013). Consistent with the literature, we also expect fewer innovator drug prescriptions to be dispensed to patients enrolled in public health insurance schemes such as Medicaid and Medicare (Rice, 2011), and cost containment payer systems such as Health Maintenance Organisations (HMOs) (Nayak, 2013; Thier, 2011).

In accordance with the literature, we hypothesise that the innovator drug has a competitive advantage granted in part by its first-mover market presence and monopoly patent protections. Subsequently, physicians have greater familiarity and experience with the innovator than the ensuing generics. Brand equity theory asserts that such familiarity with the innovator is

over time translated to a perception of superior quality. Thus, when faced with a patient encounter featuring third party financing, in which generic-innovator cost differences are masked, we theorise that the only criterion under consideration is quality. We hypothesise that the trade-off between cost and quality is eliminated. For the reasons given, a prescription decision process hinging on quality alone favours the innovator. Hence insurance coverage in this scenario alters the physician's prescription decision by eliminating the cost-quality trade-off. This alteration of prescription behaviour because of third-party financing typifies moral hazard. If our hypothesis of moral hazard is valid, we expect that patients with insurance will be more likely to be issued prescriptions for the innovator drug even if it is only marginally perceived to be of higher quality. Conversely, we hypothesise that uninsured (self-pay) patients, will be more acutely aware of innovator-generic price differentials and because of this price-sensitivity, will receive the more inexpensive generic at higher rates.

Figure 1: The Three Domains of Physician-Based Brand Equity



HYPOTHESIS 1

EXTENDED MONOPOLY --> FIRST-MOVER ADVANTAGE --> BRAND LOYALTY AND HABIT PERSISTENCE

HYPOTHESIS 2

LONGER DURATION OF GENERIC AVAILABILITY --> PRESCRIBER LEARNING --> ESTIMATION OF GENERIC QUALITY INCREASES --> SWITCHING BEHAVIOUR

HYPOTHESIS 3

INSURANCE STATUS OVERRIDES BRAND EQUITY PREFERENCES

SPECIFIC AIMS AND OBJECTIVES

Upon patent expiration, branded innovator drugs face competition from newer generic entrants, which should theoretically drive prices down. In this dissertation, we posit that innovator drugs with long periods of monopoly and sustained prices above those of competitors have achieved brand equity - added value endowed by the brand to the product (Farjam & Hongyi, 2015) .

The overarching goal of this dissertation is to ascertain whether brand equity influences prescriber preferences between innovator (brand) drugs and generic alternatives and if third party payers can override such preferences. This will be accomplished by the following aims:

AIM 1: To verify the presence of an innovator <u>first-mover advantage</u> and quantify its impact on physician preferences in a multisource drug market

- ➔ Are innovator drugs preferentially prescribed over generic drugs in a multisource drug market?
- ➔ Do the most frequently prescribed innovator drugs retain a significant price premium over bioequivalent generics?
- ➔ Is there an association between the length of innovator monopoly and ensuing prescriber preferences once generics are made available?

AIM 2: To delineate the process of <u>generic drug acceptance</u> (learning and switching behaviour) **among physician prescribers**

- ➔ Does increased prescriber experience with new generics counteract the first-mover advantage and brand equity of innovator drugs?

➔ How do market conditions (timing of market entry, price differentials and number of generic competitors) influence prescriber switching behaviour away from the innovator brand?

AIM 3: To examine the role of <u>insurance coverage</u> in qualifying physician brand loyalty

➔ How do prescription brand preferences vary based on patient insurance coverage?

➔ Are physicians more responsive to costs incurred by patients than costs incurred by third-party payers?

CONCEPTUALISING BRAND EQUITY

Brand equity in this dissertation is defined as the incremental monetary value accrued by the innovator drug due to its brand status in comparison to bioequivalent generic substitutes. The prescriber perspective portrayed in this dissertation is an adaptation of consumer-based brand equity: The two most influential conceptualisations of consumer-based brand equity are those of Aaker (1991) and Keller (1993).

Aaker (1991) defines brand equity as "a set of brand assets and liabilities linked to a brand, its name and symbol, that add to or subtract from the value provided by a product or service to a firm and/or to that firm's customers" (p.15). Aaker (1991) provides a comprehensive brand equity model comprised of five domains: *brand loyalty*; *brand name awareness*; *perceived brand quality*; *brand associations* in addition to perceived quality; and other *proprietary brand assets* – e.g., patents, trademarks, and channel relationships.

Keller (1993) develops the consumer-based brand equity model (CBBE), which is the most widely used model today. Keller defines CBBE by stating that the power of a brand rests on what the clients have "learned, felt, seen, and heard about it through time, that is, rests in their minds". Hence, CBBE is "the differential effect of brand knowledge on consumer response to the marketing of the brand" (Keller, 1993). Keller's (1993) definition of CBBE is used in arguing that brand equity is positioned based on what consumers feel, see, and hear about the brand through time, therefore, the meaning of brand equity rests in the consumers' minds. Keller's brand resonance model (2011) adds to Aaker's conceptualisation by introducing a stepwise sequential series of steps, from bottom to top: (1) ensuring identification of brand with customers and an

association of the brand in customers' minds with a specific class or customer need; (2) firmly establishing the totality of brand meaning in the minds of customers by strategically linking a host of tangible and intangible brand associations. (3) Eliciting the proper customer responses in terms of brand- related judgment and feelings, and (4) converting brand response to create an intense, active loyalty relationship between customers and the brand.

Our depiction of brand equity as a psychological construct draws upon Aaker's and Keller's models: Keller's stepwise brand resonance pyramid is adopted and applied to Aaker's interpretation of brand equity. The first step to building the brand equity of a drug is brand awareness or salience. Brand salience relates to how often and easily the brand is evoked in the mind of the prescriber – it includes brand-name recognition and recall. Steinman et al concluded that a characteristic as elementary as the length of the drug name in comparison to competitors, can influence prescriber decisions towards the drug with shorter appellation, as longer names are less easy to recall (Steinman, Chren, & Landefeld, 2007). Conjointly, brand salience and brand awareness establish brand identity in the mind of the physician prescriber (Aaker, 1991; Aaker, 2009; Keller, 1993; Keller & Lehmann, 2006).

The second step in building brand equity of an innovator drug is instilling positive brand associations within the mind of the prescriber (Aaker, 1991); The equivalent of brand associations in Keller' s model is brand performance and brand imagery. Brand performance relates to how the drug meets physician's functional objectives regarding treatment. Brand imagery deals with the extrinsic properties of the drug, including abstract associations(Keller, 2001). Together brand performance and brand imagery establish brand meaning within the mind of the prescriber.

The penultimate step towards establishing brand equity is to influence the physician's brand response to the brand-name by influencing attitudinal aspects of perceived quality (Aaker, 1991) . This response according to Keller's brand resonance model includes formation of brand judgements and brand feelings towards the drug brand in question. Brand judgments focus on the physician's own personal opinions and evaluations. Brand feelings are the physicians' (subconscious) emotional responses and reactions with respect to the brand.

The final step in the brand equity continuum is establishing brand loyalty (Aaker, 1991) or brand resonance (Keller, 1993; Keller, 2001). Brand resonance refers to the nature of the relationship that customers have with the brand and the extent to which customers feel that they are "in sync" with the brand. Resonance is characterised in terms of the intensity or depth of the psychological bond customers have with the brand, as well as the level of activity engendered by this loyalty (Keller, 2001; Pradhan & Misra, 2014).

At this juncture, we reiterate our contextual definition of brand equity: the value premium that an innovator drug with a recognisable name generates when compared to its bioequivalent generic. Drawing from Aaker and Keller's conceptualisation of brand equity, this added value is determined by consumer perceptions and experiences with the brand. Due to the principal-agent relationship within the healthcare context, we assert that the key decision-maker or "consumer" subject to brand equity influence is the physician agent. Referencing our conceptual model, brand equity is an experiential outcome: It develops and grows because of a physician's experiences with the innovator brand drug. The brand equity process typically involves a progression of interaction with the innovator brand drug that unfolds following a predictable model: Awareness → Recognition → Trial → Development of preferences and positive

associations → Brand Loyalty. Brand equity is attained when an innovator drug is well recognised and easily recalled by prescribers, subjectively perceived to be of superior quality to bioequivalent generics, and hence preferentially prescribed in a multisource drug market.

Figure 2: Brand Equity as a Psychological Construct

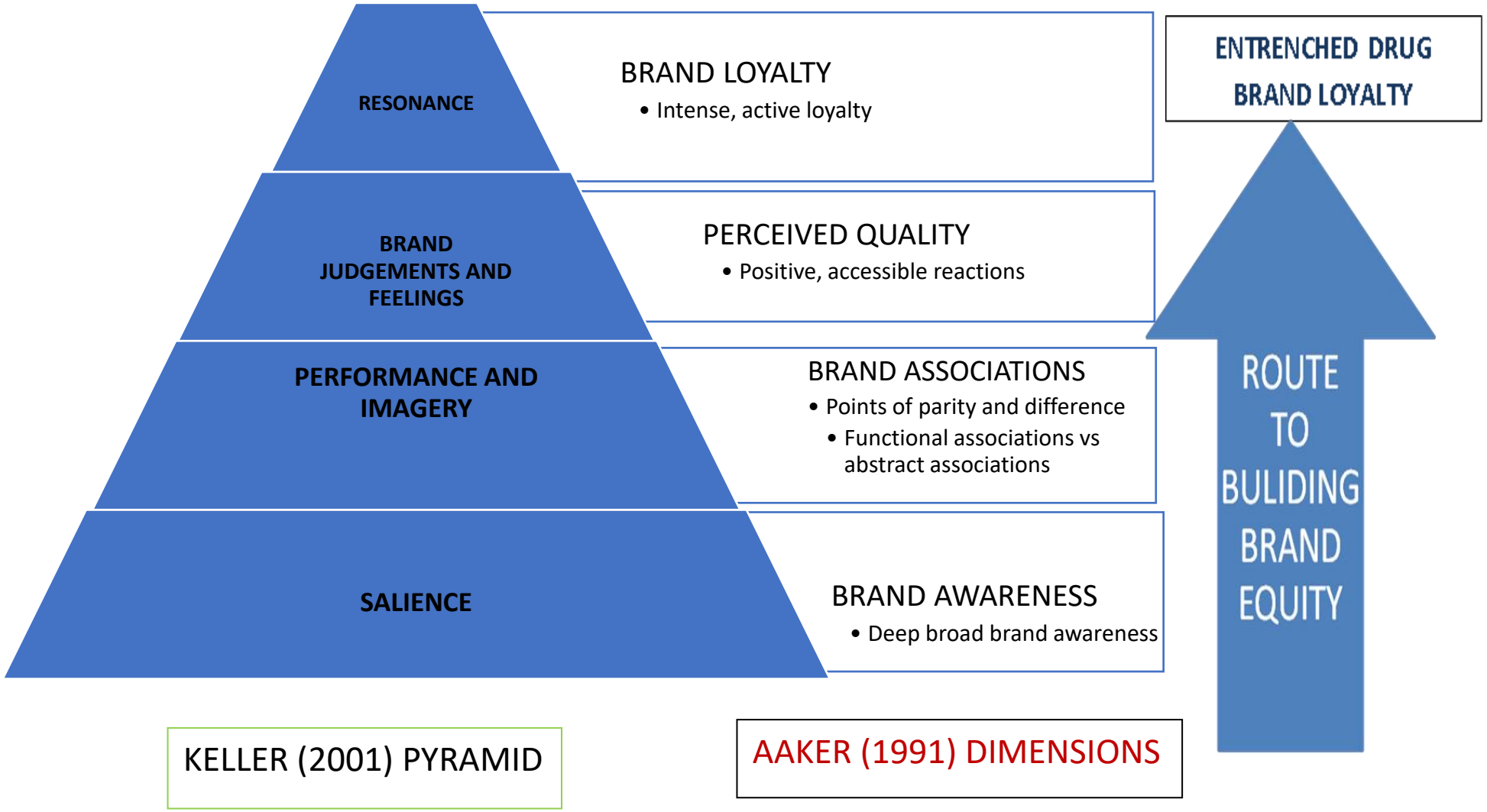
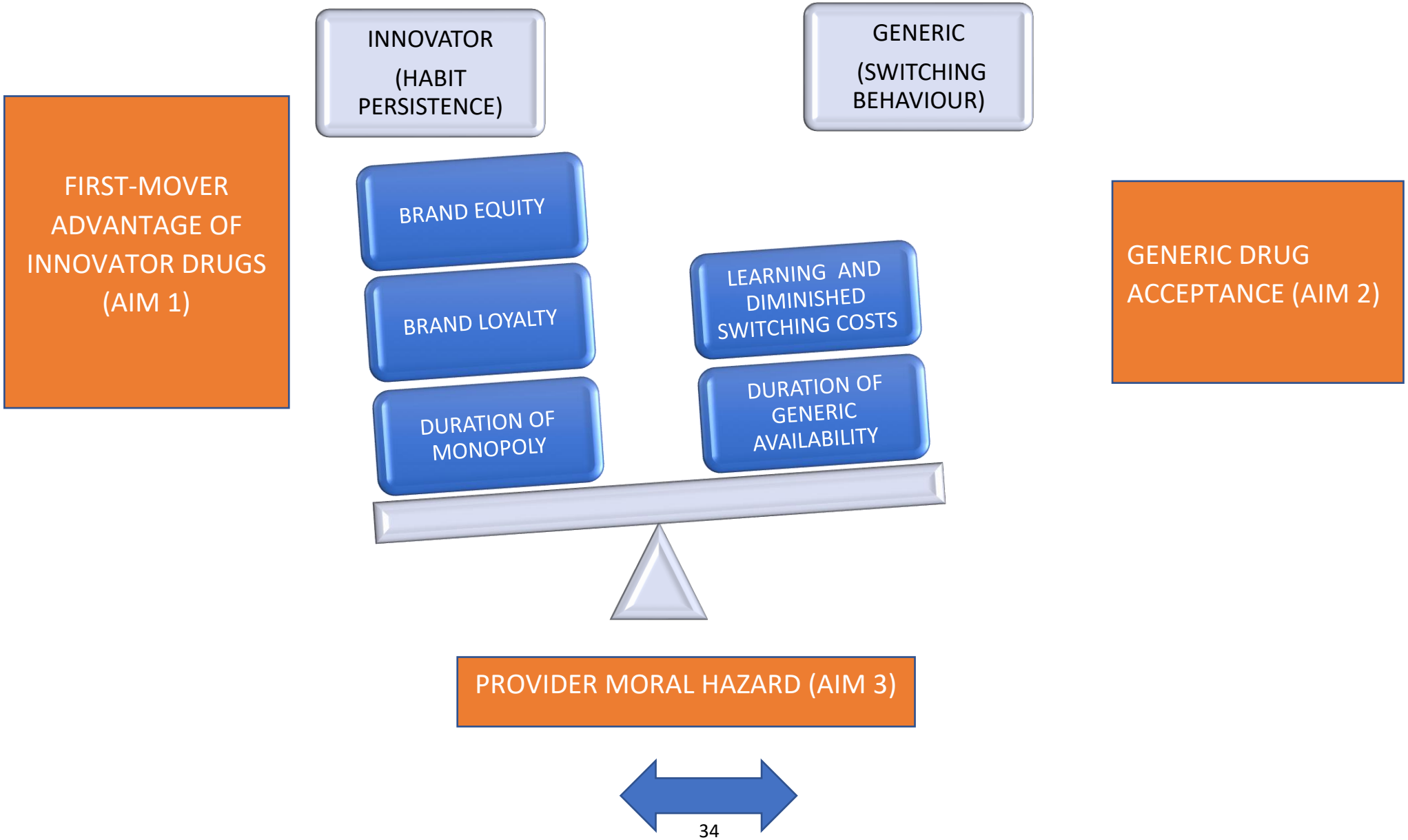


Figure 3: Conceptual Summary of Objectives and Hypotheses



METHODS

STUDY DESIGN

This dissertation relies on secondary data from the 2015 and 2016 National Ambulatory Medical Care Survey (NAMCS), which is a cross-sectional national survey of non-federally employed office-based physicians who are primarily engaged in direct patient care(National Center for Health Statistics, 2019b).

The data set is uniquely suited to assessing physician demand for innovator ("brand") drugs because one can decipher which version of the drug – innovator or generic successor – was initially prescribed by the physician hence surmise physician preferences. In contrast, drug mentions on most other secondary data sources- such as insurance claims datasets-are of drugs ultimately dispensed to the patient, which might instead reflect pharmacist substitution and/ or drug formulary restrictions imposed by the payer. As our interest is primarily in physician prescription behaviour, the focus is on the physician's choice of medication, as initially entered, regardless of the version of the drug eventually dispensed.

DESCRIPTION OF DATA SET

Sampling Strategy

The National Ambulatory Medical Care Survey (NAMCS) is a nationally representative survey of non-federally employed office-based physicians who are primarily engaged in direct patient care. The annual survey randomly selects a group of office-based physicians to record information on approximately 30 patient visits for a randomly assigned 1-week reporting period. The basic sampling unit for the NAMCS is the physician-patient encounter or visit. The survey is purposed to address the need for empirical information about the provision and use of ambulatory medical care services in the United States. Each year, physicians in ambulatory

settings are recruited to complete data forms for a representative sample of patient visits. Sampling is conducted using a multi-stage stratified probability approach and visit weights and clustering variables are available to convert survey data to nationally representative estimates (CDC/National Center for Health Statistics, 2019).

The NAMCS utilises a **multistage probability design** that involves probability samples of primary sampling units (PSUs), physician practices within PSUs, and patient visits within practices. The first-stage sample includes 112 PSUs (CDC/National Center for Health Statistics, 2019). PSUs are geographic segments composed of counties, groups of counties, county equivalents. Using these geographical groupings, a probability sample of practising physicians is selected from the master files maintained by the American Medical Association and the American Osteopathic Association. Within each sampling unit, all eligible physicians were stratified by specialty (CDC/National Center for Health Statistics, 2019) . Physicians were then assigned to 52 random subsamples of approximately equal size – corresponding to 1 of the 52 weeks of the survey year. Finally, a systematic random sample of visits is selected by the physician during the reporting week. The sampling rate varies for this final step from a 100 percent sample for very small practices, to a 20 percent sample for very large practices as determined in a presurvey interview (CDC/National Center for Health Statistics, 2019; National Center for Health Statistics, 2019)

Data Collection

Notably, prescription data collection directly from the physician, rather than from the patient, pharmacy or payer; dovetails well with the overall analytical objective - to evaluate the physician prescription decision, separate from the constraints of generic substitution policy,

payer mandates, and drug formulary restrictions, all of which may alter which version of the drug the patient receives ((Steinman et al., 2007)

The U.S Census Bureau acts as the data collection agent. Each physician is randomly assigned to a 1-week reporting period. During this week, physicians or medical office personnel are instructed to keep a daily record of all patient visits. Often, the maintenance of this log falls instead to Census field representatives. For example, more than half of the NAMCS Patient Record forms submitted in 2009 (51.5 percent) were abstracted by Census Bureau staff rather than by the physician or medical office personnel (CDC/National Center for Health Statistics, 2019). During this 1-week reporting period, data for a systematic random sample of visits are recorded using an automated Patient Record form developed for this purpose. Visits were selected from the list using a random start and a predetermined sampling interval based on the physician's estimated visits for the week and the number of days the physician was expected to see patients that week. In this way, a systematic random sample of visits was obtained. The sampling procedures were designed so that about 30 Patient Record forms were completed during the assigned reporting week. This minimised the data collection workload and maintained about equal reporting levels among sample physicians regardless of practice size (CDC/National Center for Health Statistics, 2019; National Center for Health Statistics, 2019a).

Data are obtained on patient characteristics such as age, sex, race, and ethnicity, and visit characteristics such as patient's reason for visit, physician's diagnosis, services ordered or provided, and treatments, including medication therapy(CDC/National Center for Health Statistics, 2019; National Center for Health Statistics, 2019). In addition, data about the physician

and his or her practice characteristics are collected as part of a survey induction interview. The data set also includes expected sources of payment for a visit including private insurance, public insurance and self-pay options, which allows us to assess for the influence of a third-party payer on the prescription decision and the existence of possible moral hazard among prescribers (CDC/National Center for Health Statistics, 2019; Hellerstein, 1998; Howard, 1997) .

Scope and Limitations

The basic sampling unit for the NAMCS is the physician-patient encounter or visit. Only visits to the offices of non-federally employed physicians classified by the American Medical Association or the American Osteopathic Association as "office-based, patient care" are included in the physician universe. Physicians in the specialties of anaesthesiology, pathology, and radiology are excluded. Types of contacts not included are those made by telephone, those made outside the physician's office (for example, house calls), visits made in hospital settings (unless the physician has a private office in a hospital and that office meets the NAMCS definition of "office"), visits made in institutional settings by patients for whom the institution has primary responsibility over time (e.g., nursing homes), and visits to doctors' offices that are made for administrative purposes only (e.g., to leave a specimen, pay a bill, or pick up insurance forms) (CDC/National Center for Health Statistics, 2019; National Center for Health Statistics, 2019; Nayak, 2013).

Of note, the NAMCS has practice characteristics, physician characteristics, patient characteristics, but does not have information about interactions with pharmaceutical sales representatives or other forms of industry influence which might influence the prescription decision through increased brand awareness (Nayak, 2013).

It is also important to reiterate that medications ordered are not necessarily the medications ultimately dispensed to the patient by the pharmacist. Barring physician injunction, the pharmacist has leeway to substitute an innovator for a generic or vice versa. Hence one cannot ascertain based on NAMCS disclosures which drug was ultimately dispensed to the patient (Hellerstein, 1998). Nevertheless, as our research question focuses on the physician order rather than the execution of it, any such discrepancies do not impact our conclusions.

DRUG SELECTION

This dissertation examines physician prescribing habits for the top multisource drugs reported in the NAMCS database. We narrow our focus to the top 6 most prescribed multisource drugs. Drugs in the database are assigned characteristics during data processing, based on the Lexicon Plus®, a proprietary database of all prescription drugs products available in the United States drug market (CDC/National Center for Health Statistics, 2019). Of note, NAMCS drug variables are coded twice: first "as entered" by the physician on the survey data collection form, using an NCHS-assigned 5-digit code, and second using a corresponding 6-digit generic-equivalent code based on the Multum classification (National Center for Health Statistics, 2019) . The Multum code for a given drug reflects up to 6 of its components. Therapeutic class (drug category) is also assigned using Multum; up to 4 therapeutic classes can be assigned per drug in NAMCS. Additionally, the NAMCS data set lists up to thirty drugs prescribed by the physician for each patient encounter. To increase study power, all drug mentions are included in this analysis and matched with the appropriate coded chemical entity. However, to avoid biasing the analysis to physician specialties that prescribe/record many drugs, we calculate drug frequency (to determine top multisource drugs) based only on the first drug mention(Steinman et al., 2007).

To achieve our stated objectives and avoid confounding, it is necessary to supplement the data set with drug-specific characteristics garnered from the publicly available FDA Electronic Orange book (https://www.accessdata.fda.gov/scripts/cder/ob/). This resource details drug idiosyncrasies such as narrow therapeutic indices, approved generic competitors, and drug approval dates (if after January 1, 1982). The Orange Book also discloses therapeutic equivalency concerns about generic successors, which is an important consideration impacting the likelihood of substitution.

OTHER INCLUSION/EXLUSION CRITERIA

We will impose inclusion and exclusion criteria to the NAMCS data set to meet the stated objectives regarding the physician prescription decision. At the outset, all records in which the patient was seen by a non-physician provider or physician extender such as a nurse practitioner or physician assistant, are dropped.

To reiterate, the analysis is limited to “multi-source” drugs (primary inclusion criterion). By implication all “single source” drugs, that is, innovators without a generic equivalent on the market (or vice versa) will be dropped from the analysis. Among the remaining multisource drugs, supplementary information regarding drug-specific characteristics and pricing information from the FDA Electronic Orange Book and Micromedex IBM Red Book respectively, is sought out for the identified multisource drugs.

Moreover, as there is a tendency to code biologics and supplements by the generic name of the product (e.g. “Hepatitis Vaccine,” “Vitamin B", “Iron Supplements"), without consideration of the original trade names of the product prescribed, all prescriptions for these types of products

are excluded from the analysis (Nayak, 2013). Also excluded from the analysis are drugs for which a match could not be found with Multum Lexicon (a, c, or n codes).

Physician visits for which a drug was not prescribed are also excluded from the sample as a prescription decision was not involved. Similarly, physician visits for which there is insufficient payment information are dropped from the analysis, as these records may skew our assessment of moral hazard.

MEASUREMENT AND INSTRUMENTATION

Table 1: Measurement Matrix

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
AIM1: To verify the presence of an innovator first-mover advantage and quantify its impact on physician preferences in a multisource drug market				
OUTCOME MEASURE (Y)				
Likelihood of prescribing an innovator drug	NAMCS data set	Binary outcome measure of the decision to prescribe an innovator drug or its generic alternative	Binary outcome measure 1= Innovator Prescribed 0= Generic prescribed	This variable directly measures **prescriber choice** and thus is a proxy measure for **prescriber preference** and brand loyalty. In this model, preferential prescriptions for the innovator drug imply a first-mover advantage.
PRIMARY PREDICTORS OF FIRST-MOVER ADVANTAGE				
Innovator Monopoly Period	FDA "Orange book" https://www.accessdata.fda.gov/scripts/cder/ob/	The period during which the innovator drug has no competitors i.e. has a monopoly on the market. Measures the impact of innovator market exclusivity (including patent protections) on prescriber preferences in the subsequent multi-source drug market.	Time elapsed (in years) between FDA approval of innovator drug to FDA patent approval of first generic competitor.	We hypothesise that initial **market exclusivity is the main contributor to the first-mover advantage** of innovator drugs. This variable confirms our hypotheses as to whether the length of innovator monopoly confers it a pioneering advantage by way of pricing or physician preference.

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
Innovator Price Premium	IBM Micromedex Red Book	Price differential between the innovator drug and the generic substitute. Proxy measure for brand equity (value premium of innovator drug generated by physician and patient perception of superiority).	Unit = Average Wholesale Price (AWP) Natural log of the ratio of the AWP of the innovator to the median AWP of generic substitutes. The ratio of prices is used in lieu of the arithmetic difference in price between both versions of a drug because innovator/ generic price differences vary considerably based on dosage and product-form but the ratio of generic price to innovator price is largely unaffected by these superficial characteristics. The ratio of prices is transformed into a natural logarithm so that equivalent percentage differences in the ratio will have equivalent impacts.	The price premium is a tacit measure of the strength of a brand and thus a **proxy for brand equity**, which results in a first mover advantage(Aaker, 1996) . We assume that an innovator brand with high brand equity will be priced higher than empirically substitutable generics. By expressing the price difference as a ratio, we assume that physicians are aware of the relative price differences between brand drugs and generic drugs (if not necessarily the particulars), that is, physicians are price sensitive

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
AIM 2: To delineate the process of generic drug acceptance among physicians				
OUTCOME MEASURE (Y)				
Likelihood of prescribing an innovator drug (Model 2)	NAMCS data set	Binary outcome measure of the decision to prescribe an innovator drug or its generic alternative	Binary outcome measure 1= Innovator prescribed 0= Generic prescribed	This variable directly measures **prescriber choice** and thus is a proxy measure for prescriber preference and brand loyalty. In the context of generic drug acceptance, the likelihood of prescribing the innovator drug is hypothesised to diminish as information and awareness about successive generic substitutes diffuses through the marketplace of physician agents. Prescriber choice in this model, reflects the **degree of awareness and acceptance of generic alternatives** in a multisource drug market.

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
PRIMARY PREDICTORS OF TIME-DEPENDENT INFORMATION DIFFUSION (X)				
Information Differential	FDA "Orange book"	Consensus information differential between an innovator drug and generic substitute. This is also a measure of the consensus quality differential between innovator and generic. **The ratio of the duration of generic market availability relative to duration of innovator market availability** is the proxy for the information differential. Represents the degree of information diffusion of a generic relative to the innovator incumbent.	Log of $\frac{\text{Years of generic drug availability}}{\text{Years of Innovator drug availability}}$ Units: Time elapsed (in years) between FDA approval of brand or generic drug to January 1, 2015. Generics approved prior to 1982 (i.e. prior to FDA data collection period in orange book) are assigned a ratio of 1. The generic availability ratio is measured in logarithmic terms to render equal percentage differences in the ratio equivalent for purposes of the estimation.	**The information differential measures degree of awareness and learning about a generic. The information differential also represents the perceived quality estimation of the generic relative to the innovator. As physicians know more about a generic their estimation of the generic's quality increases to approach that of the brand.** In keeping with our hypotheses and preceding literature (Howard, 1997), we expect that physicians will initially overestimate the quality differential between the innovator and the new generic substitute. As physicians have no experience with the generic, its true quality is unknown – there is a large information differential between the innovator and a new generic. As time passes, physicians become familiar with therapeutic attributes of the generic substitute. The information differential between generic and innovator diminishes. Concurrently, physicians revise their estimation of the generic's quality to approach that of the true quality differential (Howard, 1997).

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
Innovator Price Premium	The Red Book (Truven Health Analytics)	Price differential between the innovator drug and the generic substitute	Unit = Average Wholesale Price (AWP) Natural log of the ratio of the AWP of the innovator to the median AWP of generic substitutes.	The price premium is a tacit measure of the strength of a brand and thus is a **proxy for brand equity**(Aaker, 1996)**.** In context, the price premium quantifies the impact of generic drug acceptance, such that innovator predecessors of well-known and widely accepted generic drugs, are hypothesised to have a lower or non-significant price premium as the perceived information differential between both versions of the drug diminish. By reviewing the correlation between the price premium and the information differential we can ascertain whether the gap between the price of a generic drug and its innovator counterpart grows smaller as the perceived relative therapeutic benefit associated with the brand-name decreases.

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
AIM 3: To examine the role of moral hazard in qualifying physician brand loyalty				
OUTCOME MEASURES (Y)				
Likelihood of prescribing an innovator drug (Model 3)	NAMCS data set	Binary outcome measure of the decision to prescribe an innovator drug or its generic alternative	Binary outcome measure 1= Innovator Preference 0= Generic preference	Measure of brand loyalty and prescriber preference.
PRIMARY PREDICTORS OF MORAL HAZARD AND HABIT PERSISTENCE (X)				
Insurance Type	NAMCS data set	Type of Insurance coverage	5 dummy categories: HMO/other prepaid plan, Medicaid, Medicare, private /commercial insurance, and self-pay Reference category is self-pay	If physicians exhibit **moral hazard**, we expect that prescriptions of the innovator drug will vary across insurance categories (Lundin, 2000; Nayak, 2013). If one or more of the dummy insurance coefficients is significant it may be construed as evidence of moral hazard - physicians have a different likelihood of prescribing generics to the reference category of self-pay/uninsured patients than to patients holding certain types of insurance. However, if all categories of health insurance exhibit no differential prescribing (no significant coefficients) this supports the notion of habit persistence i.e. physicians prescribe the same drug to all patients regardless of insurance status.

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
Innovator Price Premium	IBM Micromedex Red Book	Ratio of average innovator drug price to average generic drug price in 2015	Unit = Average Wholesale Price Natural log of the ratio of the innovator price to the median generic price	The price differential is included as an independent variable to pre-empt omitted variable bias: The difference in price between an innovator drug and its generic successor is correlated with both the patient's or third party's willingness to pay for the drug and the physician's willingness to prescribe the drug. Significant coefficients would suggest that physicians are in part conscious of the price differential between an innovator drug and its generic substitutes.
Innovator price premium *Insurance interactive term	IBM Micromedex Red Book) NAMCS data set	Interactive variable of Price and Insurance Describes how the price difference between the innovator and its generic substitutes influences the physician prescription decision for patients with different insurance coverage	Interaction variable	Impact of innovator price premium on prescriber preference for patients with different insurance coverage. If any of these variables is significant, the implication is that physicians consider the innovator price premium when prescribing the innovator drug to patients with different insurance coverage – an indication of moral hazard.

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
Innovator Monopoly Period	FDA "Orange book" https://www.accessdata.fda.gov/scripts/cder/ob/	The period during which the innovator drug has no competitors i.e. has a monopoly on the market. Measures the impact of innovator market exclusivity (including patent protections) on prescriber preferences in the subsequent multi-source drug market.	Time elapsed (in years) between FDA approval of innovator drug to FDA patent approval of first generic competitor.	We hypothesise that initial **market exclusivity is the main contributor to the first-mover advantage** of innovator drugs. This variable confirms our hypotheses as to whether the length of innovator monopoly confers it a pioneering advantage by way of pricing or physician preference.
Years of Generic Availability	FDA "Orange book"	The duration generics have been available Duration of multisource market competition	Time elapsed (in years) between FDA approval of first generic drug to January 1, 2015	Explicitly this variable measures the **effect of generic competition on the innovator's brand equity and physician prescription preferences**. Included in this first model to avoid overstating the impact of innovator monopoly on prescriber preferences thus avoiding omitted variable bias). Implicitly, this variable also indicates **whether older generics ever catch up** to their innovator counterparts' pioneering advantage as determined by both a smaller price differential and prescribing practices in favour of the generic.

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
COVARIATES FOR AIMS 1-3				
Physician Characteristics –	NAMCS data set	Includes physician characteristics available in data set – specialty, and demographics	Vector of dummy variables	This vector controls for heterogenous physician characteristics. We expect that specialty physicians will be more likely to have similar prescription habits with high concordance within the group as to which drug classes are prescribed in the generic form and which drug classes are prescribed as brand-name only. The drug case-mix will therefore determine likelihood of generic substitution.
Practice characteristics - **Region, Practice type**	NAMCS data set	Includes: Region; Practice type; Practice Ownership; Patient record system; Electronic prescriptions; Drug formulary checks	Vector of dummy variables	This vector controls for heterogenous practice characteristics. Moreover, If the physician is a perfect agent for the patient, then physician characteristics should have no impact on the prescription decision. Health economists have proposed that physician practice follows a "**Bayesian learning process",** whereby physicians **update their behaviour by observing the behaviour of peers** and **adapts to the "local style of practice**" (Frank & Zeckhauser, 2007; Phelps & Mooney, 1993). We expect to observe similar prescribing habits among physicians in similar practice types and regions. We also expect changes in prescribing practices based on physician ownership – Rice (2011) found that prescribing habits differ for those in HMO owned practices. Moreover, the implementation of electronic health records and prescribing platforms is likely to modify behavioural switching costs and, in the case of drug formularies, encourage generic substitution

MEASURED VARIABALE	DATA SOURCE	DESCRIPTION OF VARIABLE	TRANSLATION PROCEDURES / CONSTRUCTON OF VARIABLE	RATIONALE
Patient characteristics	NAMCS data set	A vector of patient characteristics including their age and race	Vector of dummy variables	This covariate measure controls for heterogenous patient characteristics
Drug Specific Idiosyncrasies	NAMCS data set	Controls for whether drug is combination therapy; controlled substance; narrow therapeutic index; continued or new medication	Vector of dummy variables	Whether an innovator drug is considered as part of a narrow therapeutic index will increase perceived risk such that physicians are less willing to substitute with a generic (Nayak, 2013) Because of behavioural switching costs and inertia, I anticipate that those continuing an already existent prescription of a branded drug will continue receiving the branded drug (Nayak, 2013).
Drug Controls	NAMCS data set	5 individual drug dummy variables to flag prescriptions for the most frequently prescribed multisource drugs within the database	Vector of dummy variables	Included dummies for the top individual multisource drugs and top therapeutic drug classes to control for the influence of unobservable drug characteristics other than those already specified, for example case-mix effects.

Price Differentials

By explicitly incorporating price differentials as covariates in our analysis we can determine whether physicians weigh drug costs against perceived therapeutic benefit when prescribing a multisource drug. If indeed brand equity theory plays a significant role in multisource drug markets, we expect that the price premium of the brand will reflect the perceived superiority of the brand. We therefore predict that the gap between the price of a generic drug and its innovator counterpart reflects the differences in perceived relative therapeutic benefit.

Furthermore, the inclusion of price differentials in the third model facilitates an assessment of moral hazard including the possibility of subtler interactive effects between an innovator's price premium and insurance type. For example, it is conceivable that physicians are indeed creatures of habit prescribing innovator or generic versions of a drug to all patients (Hellerstein, 1998) except in cases where the price premium of the innovator alternative exceeds a certain expense threshold at which point, patients who face high out-of-pocket costs (such as those classified self-pay or uninsured) are less likely to receive a significantly more expensive innovator drug if cheaper generic substitutes are available.

Admittedly, drug prices are both opaque and constantly mutable, which impacts both the reliability and validity of pricing data. As previously stated, we utilise average wholesale prices (AWPs) culled from the Red Book to determine price differentials. According to the Red Book, published by IBM Micromedex, the pricing information is "based on data obtained from manufacturers, distributors, and other suppliers." However, despite the data source, published AWPs have widely been recognised to be grossly inflated relative to actual market prices for

prescription drugs. Nonetheless, we believe our findings about drug pricing to be valid, reliable, and generalisable because our interest lies in the relative difference in drug pricing. Presumably, physicians are themselves not privy to precise drug pricing information, and instead are more likely to be cognisant of the relative price differences between innovator and generic drugs and if price-sensitive will vary their prescribing behaviour based on this relative assessment of expense, which is captured with enough accuracy by the price premium variable.

The Information Differential

The Information differential variable introduces the concept of information diffusion into the second estimation equation. The intention of this variable is to capture how accurately a physician can gauge the quality difference between innovator and generic substitute. Our conceptualisation of this variable (The ratio of the duration of generic market availability relative to duration of innovator market availability) accounts for the notion that a physician's awareness and knowledge about a given drug increases over time. Accordingly, the physician's assessment of quality differences between an innovator and its generic substitutes increases in accuracy the longer the generic has been on the market. These arguments regarding consensus awareness, knowledge, and perceived quality over time, echo both Aaker's and Keller's models of brand equity. Yet despite theoretical grounding, the true market consensus quality differential remains a latent variable, and thus inherently introduces some degree of measurement error into the estimation.

DATA MANAGEMENT

HUMAN SUBJECTS CONSIDERATION

This project relies primarily on publicly available secondary data from the National Centre of Health Statistics, which has been anonymised to circumvent potential ethical concerns including physician privacy protection and patient confidentiality. Though unlikely, any incidental patient information disclosures are discarded in keeping with The Health Insurance Portability and Accountability Act (HIPPA) guidelines. Supplementary drug pricing information sourced from the Redbook (IBM Micromedex) is considered proprietary. Accordingly, the relevant precautions have been taken in keeping with the organisation's terms and conditions and the protocol specified by the Office of Institutional Compliance at UTHealth. The use of a password is required to access any proprietary data, which is stored and maintained in a manner consistent with UTHealth research guidelines. Only academic advisors directly related to the project, supervisory project/dissertation committee, and the study investigator have access to this portion of data. All study protocols will undergo scientific review by the relevant University of Texas project/dissertation review committees, and approval by the UTHealth Institutional Review Board.

DATA INTEGRITY – MISSING DATA

NAMCS has a defined protocol for handling missing data. As per the microdata file for the 2015 survey, some survey items such as vital signs (e.g. height and weight) are presented with calculated non-response rates. Other missing data items are imputed by randomly assigning a value from a patient record form with similar characteristics, where similar visits are generally those of the same specialty, geographic region or diagnostic group. Other data items such as race, ethnicity, and time-spent with physician are imputed using a model-based, single,

sequential regression imputation method (NAMCS microdata file, 2015 and 2016). Following a convention implemented in 2007, missing data in the 2015 and 2016 dataset have consistent negative codes indicating blank, unknown or inapplicable data. These coding conventions are accounted for in the initial data cleaning in preparation for data analysis.

DATA ANALYSIS

KEY A PRIORI ASSUMPTIONS IN THE MODEL DESIGN

In our analysis, we assume that the physician is a perfect agent for the patient. However, the role of physician agency with respect to third-party financiers of healthcare is less clear, and thus a subject for examination in our analysis.

In choosing between an innovator and its generic successor, the patient's preferences for either version of the drug is based solely on a trade-off between quality and cost. Notably, the assessment of quality is subjective and person-specific hence the designation of "perceived quality. It should also be explicitly stated that the entire rationale behind the analytical model is built on the well-established premise that, in general, innovator drugs tend to be more expensive than their generic successors. As such, the physician (as a perfect agent of the patient) will choose the costlier innovator drug over less expensive generics only if the innovator drug is perceived to have a higher quality value.

Our analysis tests if this quality and cost trade-off can be over-ridden by the presence of a third-party payer, that is if insurance status alters the decision outcome. Particularly, we test the hypothesis that insurance coverage (which presumably reduces out-of-pocket payments by the patient) masks the true cost differences between the costlier innovator and the less expensive generic successor thus altering the prescription decision (moral hazard). Notably this investigation of moral hazard assumes that the physician is cognisant of the patient's payer status and price sensitivity, and as a perfect agent reflects these preferences in their prescription decision. The analytical model also assumes that the physician is aware of the relative magnitude and direction of the innovator-generic price differential (large, small, inversely related), even if

unclear about exact price points. A qualitative judgement that an innovator drug is more, less, or comparably expensive than its generic equivalent, should suffice. If indeed insurance coverage masks the true innovator-generic cost differential, then the only criterion under consideration is quality. As neither patient nor physician perceive a cost difference between an innovator and its generic, the physician will prescribe the version of a drug considered to be of higher quality.

While physicians may be somewhat cognisant of the relative cost differences between an innovator and its generic equivalents, a priori, the physician agent is somewhat less certain about the quality of the generic relative to its innovator predecessor. This assumption underscores our second hypothesis that physicians will initially overestimate the perceived relative therapeutic benefit between an innovator drug and a generic entrant. This information differential between an innovator and its bioequivalent generic will diminish over time as physicians familiarise themselves with the generic.

The rationale here is that there is a cost to ascertain the quality of a generic - time invested in experience and research, that is, a switching cost associated with prescribing a generic. While the price of the drug is borne by the insurer and patient, the switching cost is incurred by the physician prescriber. Therefore, this switching cost must be tagged onto the retail price to assess the total cost incurred by both patient and physician i.e. Total *Cost of Generic = Price of Generic + Switching Cost.* A rational decision-maker would choose to have the generic form of a drug prescribed only if his or her assessment of quality far supersedes the total cost of the generic, which is comprised of the accounting cost of the drug and the switching cost (Nayak, 2013). Given that generics are only available once patent protections for the innovator drug have expired, this switching cost is the effort required of the physician to update their information about the new generics relative to the incumbent innovators and as such is a time dependent

(Nayak, 2013). Indeed, at the point of generic market entry, physicians are already familiar with the innovator drug's quality profile. Thus, the decision to instead prescribe a generic would involve effort, psychological and time-based switching costs whereby the physician evaluates the quality of the newer generic against the quality profile of the time-tested innovator drug.

Empirically, this means that generic substitution practices (and associated switching costs) should change as physician awareness and knowledge regarding the generic's quality profile increases. Consequently, switching costs contingent on a trade-off between novelty versus certainty should diminish over time until they are almost negligible. Succinctly stated, the total cost of the generic (i.e. *Price of Generic + Switching Cost*) diminishes but perception of quality increases as more is known about the generic, that is, as the generic builds its own brand equity. The cost-quality trade-off is altered during the lifecycle of the generic, becoming more favourable over time.

The following is succinct equational portrayal of the preceding discussion.

- A rational and perfect physician agent would choose the innovator drug where

$$Q_B - Q_G > C_B - C_G + C_s$$

- Where Q_B is the quality of the innovator drug; Q_G is the quality of the generic; C_B is the cost of the innovator drug; C_G is the cost of the generic; C_S is the switching cost

- Conversely, under perfect agency a rational physician would opt for the generic successor drug where: $Q_G – Q_B > C_B - C_G + C_s$ or $Q_B - Q_G < C_B - C_G + C_s$

MODEL ESTIMATION

A physician's prescription decision process is influenced by a complex range of person-specific, socioeconomic and pharmacological considerations unique to the agency relationship and healthcare. Appreciably, modelling these determinants would involve capturing latent, interactive, and complex measures by substituting observable characteristics to glean insight into the drivers of brand preferences.

The dynamics of the multisource drug markets including the impact of market exclusivity, perceived quality and moral hazard on physician prescription decisions have been investigated repeatedly. Concurrently, far-removed within the subject area of marketing there have been vigorous psychometric analyses of both Aaker's and Keller's domains of brand equity. What hitherto has yet to be achieved is the combination of these two distinct spheres of expertise. To this end, our analytical approach measures the competitive advantage an innovator incumbent has over subsequent bioequivalent generics owing to brand equity. Our estimation models explore the merits of brand equity for the innovator drug as it pertains to market **monopoly protections and strategic entry deterrence** (aim 1); **switching behaviour** versus **habit persistence** (aim 2); and **favourable payment structures** (aim 3).

Our regression analysis builds upon the work of 5 authors namely, Hellerstein (1994 & 1998), Howard (1997), Steinman (2007), Rice (2011), and Nayak (2013). Using NAMCS as a sample frame and similar estimation methods, each of these authors has found evidence consistent with brand equity in multisource prescription decisions including: "habit persistence, "switching costs", "brand preferences" and "economic branding". Yet to date, none of the vanguards within this niche of the literature have incorporated brand equity theory to explicate results or to inform their analytical approach. Our contribution to the literature is formalise what have previously

been consistent though unexplained findings about a provider's pharmaceutical brand preferences, by utilising brand equity theory.

To reiterate, the basic sampling unit for NAMCS is the physician-patient encounter or office visit. It is likely that prescriptions written by the same physician are correlated. This line of reasoning is further bolstered by repeated evidence of habit persistence among individual physicians. For example, Howard (1997) found that specific antimicrobial drugs e.g. sulfamethoxazole-trimethoprim, are always prescribed by physicians as either Bactrim or Septra (brand-name forms), while amoxicillin is mostly prescribed as the generic. Therefore, in keeping with the precedent set forth by Hellerstein (1994), we estimate our model using a logit specification with clustering of prescriptions written by the same physician. By controlling for the physician cluster effect, each physician cluster forms the unit of observation in lieu of using each patient encounter as the unit of observation (Rice, 2011). Notably, Rice (2011) found that standard errors based on the physician clusters minimise the effect of multiple observations per physician. In comparison to non-clustered robust standard errors, the clustered standard errors tended to be larger, reducing the statistical significance of most covariates (Rice, 2011).

To test our hypotheses, we propose a series of logistic regression models that align with study objectives. Each of the logistic regression models separately tests a different group of independent variables in relation to our outcome variable. These independent variable sets pertain to pioneer/ first-mover advantage characteristics, information diffusion characteristics, and Insurance coverage characteristics. Our primary outcome measure is a binary variable which describes the likelihood of a physician prescribing an innovator (brand-name) drug. This binary prescription decision variable is assigned as: 1- Physician prescribes the innovator version of a drug or 0 – Physician prescribes the generic version of a drug. Notably, having a first-mover

advantage and information diffusion are inherent to the process of creating brand equity (Aaker, 1992). Moral hazard is introduced to the equation as a mitigating factor through the insurance coverage variable. The same set of covariates are included in each model and are purposed to control for practice, physician, patient and drug characteristics. Though we will separately model the relationship between our regressors and our outcome prescription decision variable, the basic model for this analysis can be expressed as:

$$E(Y|\mathbf{x}) = F(\beta_0 + \beta_1 X_1 + \ldots + \beta_k X_k)$$

Where:

Y = *likelihood of Prescribing an Innovator drug (1) or a Generic Drug;*

X_1 - X_k = *observed independent variables;*

β_0 - β_k = *estimated model coefficients; and*

$F(.)$ = *the logistic function.*

Estimation Equation

The estimation equation surmises the decision on whether to prescribe the innovator version of a drug, for the *d*th drug, *i*th patient and *j*th physician.

$$Log\left(\frac{Innovator}{1-Innovator}\right) = \beta_0 + \beta_z Z + \beta_D D_d + \beta_P P_j + \beta_x X_i + \beta_I I_i + \varepsilon_{ijd}$$

Where:

Z = *A vector of brand equity characteristics including length of monopoly, length of generic drug availability, information differential, and price premium*

D_d= *A vector of drug dummies and prescription characteristics*

P= *A vector of physician and practice characteristics*

X= *A vector of patient characteristics*

I_i = *A vector of patient's insurance coverage or expected payment source*

Of note, I do not consider medical condition as part of the patient's relevant personal characteristics. Indeed, while the patient's condition affects the type of drug prescribed, it is unlikely to dominate the decision to prescribe innovator version of a drug versus the generic. Referencing Hellerstein, 1998, the condition of the patient can be construed to be an unobserved characteristic of the patient that remains in the residual.

Based on the results of the logistic regression models aligned with each of the 3 aims, a composite prescription decision model will be constructed. This final model blends all 3 groups of independent variables – brand equity, information diffusion, and moral hazard variables – adjusting the regression based on fit, collinearity, specification, significance of predictors, and parsimony. Parameter level tests of significance will use the z-statistic based on each parameter's robust standard error. Overall model significance will be assessed using a Wald test.

POWER ANALYSIS

Anticipating a small effect size, Power analysis for a logistic regression was conducted using the guidelines established in Lipsey & Wilson, (2001) and G*Power 3.1.7 (Faul, Erdfelder, Buchner, & Lang, 2013) to determine a sufficient sample size using an alpha of 0.05, a power of 0.80, a small effect size (odd ratio = 1.2) and two-tailed test. Based on the assumptions, the desired sample size is 1484(Lipsey, 1990) .

Table 2: Data Analysis Matrix

AIM	HYPOTHESES	ANALYSIS	PRIMARY OUTCOME	PRIMARY PREDICTORS	ANALYTICAL PREMISE
AIM 1: To verify the presence of an innovator **first-mover (or pioneer) advantage** and quantify its impact on physician preferences in a multisource drug market	Longer periods of innovator market exclusivity bestow a first-mover (pioneering) competitive advantage to the innovator drug upon generic entry.	Logistic regression	Likelihood of Prescribing an Innovator Drug	**MODEL 1** • **Innovator Price Premium** • **Innovator Monopoly Period** • Generic Availability Period	Monopoly protections granted by patents favour the innovator drug long after the removal of competitive barriers (a pioneering advantage). If innovator drugs have a competitive advantage, we expect: 1. Longer innovator monopoly periods associated with greater likelihood of prescribing the innovator drug 2. Longer innovator monopoly periods strongly correlated with sustained innovator price premiums in a multisource drug market 3. Generic Availability period may attenuate the effect size of Price premiums and Monopoly periods
AIM 2: To delineate the process **generic drug acceptance** among physicians	Physicians will initially overestimate the quality differential between an innovator drug and a generic entrant The quality differential between an innovator and its bioequivalent generic will diminish over time.	Logistic Regression	Likelihood of Prescribing an Innovator Drug	**MODEL 2** • **Information Differential** • Innovator Price premium	Newer generics need time to establish their therapeutic credentials (i.e. build their own brand equity) relative to those of the innovator. Therefore, physicians will *initially overestimate quality differentials* between innovator drugs and newer generics but arrive at the true (smaller) quality differential with time and experience. If there is evidence of time-dependent information diffusion for generic drugs, we expect: 1. New generics have large consensus quality differentials; older generics have small consensus quality differentials. 2. The innovator price premium will diminish over time to reflect revisions in quality differentials

AIM	HYPOTHESES	ANALYSIS	PRIMARY OUTCOME	PRIMARY PREDICTORS	ANALYTICAL PREMISE
AIM 3: To examine the role of i**nsurance coverag**e in qualifying physician brand loyalty	Moral hazard alters brand equity preferences	Logistic regression	Likelihood of Prescribing an Innovator Drug	**Model 3** • **Insurance Type** • **Innovator Price Premium** • **Innovator Price Premium * Insurance Type** interactive variable • Innovator Monopoly Period • Generic Availability Period	Moral hazard and other restrictions (e.g. formulary allowances, co-pay) associated with third party payers will change the magnitude of effect associated with brand equity. If there is evidence of moral hazard, we expect: 1. An increased likelihood of prescribing an innovator drug for patients with private insurance particularly where a significant price differential exists 2. A decreased likelihood of prescribing an innovator drug for patients without insurance coverage 3. Adding insurance variables will decrease the effect sizes associated with price premiums, market exclusivity, and consensus quality differentials on prescribing preferences
COVARIATES FOR ALL MODELS	• Physician characteristics • Practice Characteristics • Patient Characteristics • Drug Controls				

RESULTS

DESCRIPTIVE STATISTICS

Following the inclusion and exclusion criteria specified in our study design we selected the top 6 multisource drugs in the sample based on first drug mentions. The specified drug sample is depicted in Appendix A. The breakdown of innovator / generic binary decisions by physicians in our sample are depicted in *Table 3.* There are 143,081 prescriptions or drug mentions in the combined 2015 and 2016 data set. Of these, our drug sample comprises 7.4% of all prescriptions (10648 drug mentions). Notably there is a high generic substitution rate of 72%, a marked increase when compared to analysis of the generic prescription rate in previous years. For example, Hellerstein (1998) looked at the 1989 NAMCS and noticed only about a 30% generic substitution rate.

As specified in the proposed study design, the unit of analysis is the physician-patient encounter. The larger data set includes 41,497 total patient visits of which 98% are with a physician. A prescription is dispensed in 72% of these physician-patient encounters (Table 5). Overall, there are 8072 Physicians in the data set though only 12.5% write a prescription involving any of the 6 drugs in our sample (Figure 4).

Furthermore, most patients in the sample are over the age of 45 (91%), have seen the physician before (85%) and have at least one chronic condition (90%). Regarding expected source of payment, 36% of patients in the sample have private insurance coverage and 47% have Medicare. Other insurance categories are relatively uncommon (Table 4).

95% of physician prescribers included in the analysis are Doctors of Medicine, while 5% are Doctors of Osteopathy. Prescriptions of the 6 drugs of interest are roughly distributed

equally between primary, medical and surgical specialties. 74% of prescriptions are prescribed by physicians operating in individual or physician group practices. Additionally, 42% of prescriptions in the sample are prescribed by physicians operating in the Midwest (Table 5).

Table 3: Distribution of Prescription Decisions by Drug

VERSION OF DRUG PRESCRIBED	DRUG						
	AMLODIPINE	**ATORVASTATIN**	**AMOXICILLIN**	**LISINOPRIL**	**LEVOTHYROXINE**	**ALPRAZOLAM**	TOTAL
No. GENERIC PRESCRIPTIONS	1340	1338	567	2416	1590	405	7656 **(72%)**
No. OF INNOVATOR PRESCRIPTIONS	417	1040	64	87	819	565	2992 **(28%)**
TOTAL DRUG MENTIONS	1757 (16.5%)	2378 (22%)	631 (6%)	2503 (23.5%)	2409 (23%)	970 (9%)	**10,648**

Table 4: Prescription Choice by Patient Characteristics

PATIENT CHARACTERISTICS	VERSION OF DRUG PRESCRIBED	
	No. OF GENERIC PRESCRIPTIONS	No. OF INNOVATOR PRESCRIPTIONS
RACE		
→White	5978 (56%)	2488 (23%)
→Black	745 (7%)	231 (2%)
→Hispanic	651 (6%)	191 (2%)
→ Other	282 (3%)	82 (1%)
AGE		
Under 15 years	289 (3%)	52 (0.5%)
15-24 years	83 (0.8%)	38 (0.4%)
25-44 years	498 (5%)	270 (2.5%)
45-64 years	2530 (24%)	1034 (10%)
65-74 years	2140 (20%)	813 (8%)
75 + years	2116 (20%)	785 (7%)
GENDER		
Male	3650 (34%)	1211 (11%)
Female	4006 (38%)	1781 (17%)
NEW PATIENT		
Yes	1198 (11%)	449 (4%)
No (Established Patients)	6458 (61%)	2543 (24%)
CHRONIC CONDITION		
Yes	6559 (62%)	2495 (23%)
No	1040 (10%)	471 (5%)
INSURANCE		
Private	2737 (26%)	1076 (10%)
Medicare	3637 (34%)	1397 (13%)
Medicaid	660 (6%)	214 (2%)

PATIENT CHARACTERISTICS	VERSION OF DRUG PRESCRIBED	
	No. OF GENERIC PRESCRIPTIONS	No. OF INNOVATOR PRESCRIPTIONS
Workers' Compensation	23 (0.2%)	6 (0.05%)
Self	126 (1%)	61 (0.6%)
Other	73 (0.7%)	25 (0.2%)
GENERAL CHARACTERISTICS		
Total number of drug mentions		10,648
Generic prescription rate		72%
Innovator prescription rate		28%

Figure 4: Summary of Physician-Patient Encounters

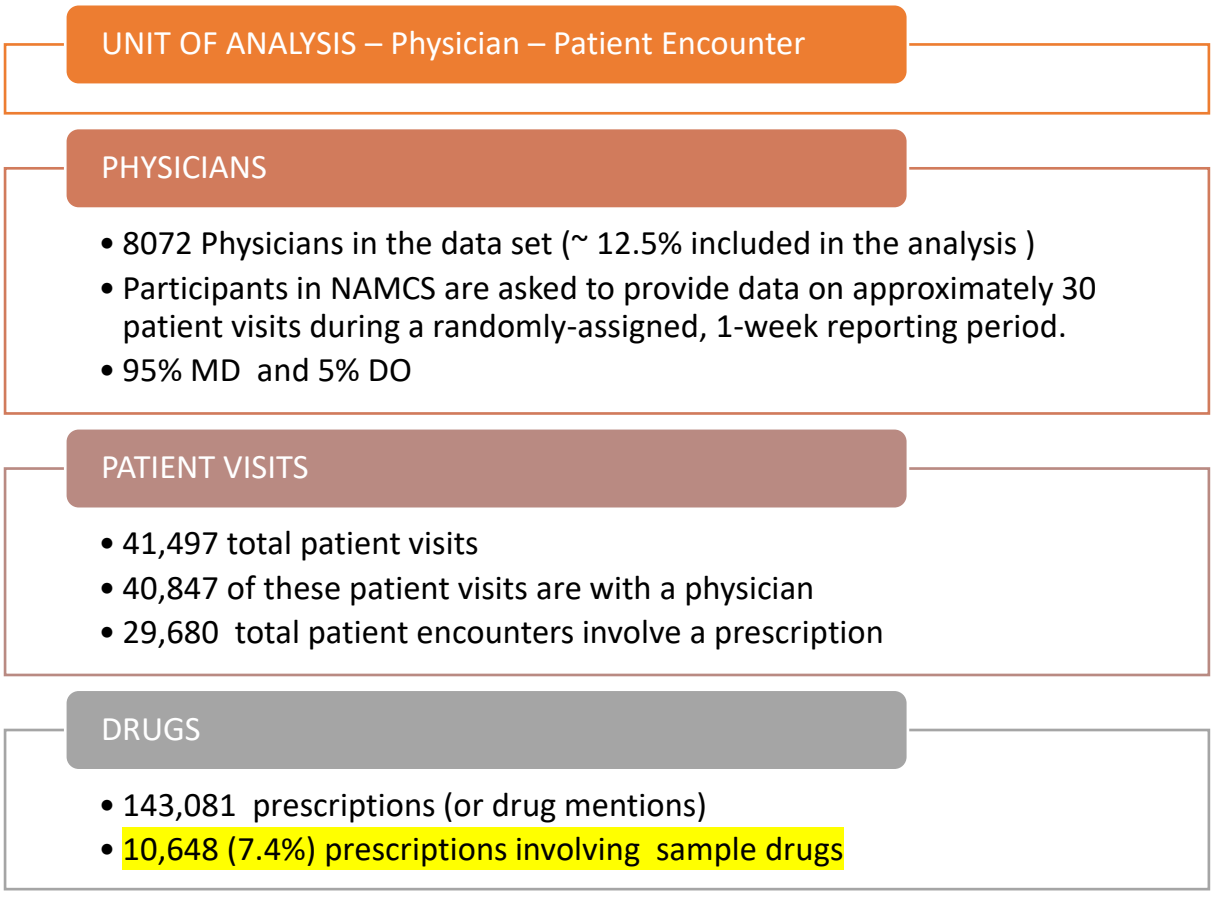


Table 5: Prescription Choice by Physician and Practice Characteristics

PHYSICIAN AND PRACTICE CHARACTERISTICS	VERSION OF DRUG PRESCRIBED	
	No. OF GENERIC PRESCRIPTIONS	No. OF INNOVATOR PRESCRIPTIONS
SPECIALTY		
Primary Care	2452 (23%)	940 (8%)
Surgical Care	2862 (27%)	1106 (10%)
Medical Care	2252 (21%)	946 (9%)
OWNER		
PHYSICIAN SOLO OR GROUP PRACTICE	5763 (54%)	2161 (20%)
MEDICAL/ ACADEMIC HEALTH CENTRE	905 (9%)	312 (3%)
HOSPITAL	775 (7%)	383 (4%)
REGION		
Northeast	1216 (11%)	542 (5%)
Midwest	2190 (21%)	1192 (11%)
South	2181 (20%)	649 (6%)
West	2069 (19%)	609 (6%)
GENERAL CHARACTERISTICS		
Total number of drug mentions	10,648	
Generic prescription rate	72%	
Innovator prescription rate	28%	

MARGINAL EFFECTS

Table 6: Average Marginal Effects of Logistic Regression

PROB (Y=INNOVATOR)	MODEL 1		MODEL 2		MODEL 3	
	MARGINAL EFFECT	SE	MARGINAL EFFECT	SE	MARGINAL EFFECT	SE
BRAND EQUITY PRIMARY PREDICTORS						
INNOVATOR MONOPOLY DURATION	0.0141 ***	0.002	_____	_____	0.0094 ***	0.001
YEARS OF GENERIC AVAILABILITY	_____	_____	_____	_____	- 0.0022 ***	0.001
GENERIC AVAILABILITY RATIO	_____	_____	- 0.1467 ***	0.014	_____	_____
PRICE PREMIUM	- 0.3480 ***	0.012	- 0.3876 ***	0.009	- 0.3222 ***	0.015
PRESCRIPTION CHARACTERISTICS						
NUMBER OF MEDICATIONS	0.0009	0.001	0.0002	0.001	- 0.0001	0.001
CONTINUED MEDICATION	0.0001	0.012	0.0233 **	0.010	- 0.0006	0.009
NO USE OF ELECTRONIC PRESCRIBING	0.0279 *	0.015	0.0275 *	0.014	0.0233 *	0.012
DRUG DUMMYS						
LISINOPRIL	- 0.0246 ***	0.008	- 0.0408 ***	0.009	- 0.0169 ***	0.008
AMLODIPINE	0.0273 ***	0.005	0.0435 ***	0.006	0.0154 ***	0.005
LEVOTHYROXINE	- 0.0500 ***	0.009	0.0329 ***	0.005	- 0.0259 ***	0.009
ALPRAZOLAM	0.0829 ***	0.011	0.1256 ***	0.013	0.0829 ***	0.011
ATORVASTATIN	- 0.0003	0.0062	- 0.0734 ***	0.011	- 0.0003 **	0.0062
PHYSICIAN VARIABLES						
SURGICAL CARE SPECIALTY	0.0022	0.008	0.0128	0.008	0.0045	0.062
MEDICAL CARE SPECIALTY	0.0019	0.008	0.0155	0.008	0.0042	0.061
D.O – DOCTOR OF OSTEOPATHY	0.0067	0.010	0.0093	0.011	0.0069	0.008
PRACTICE VARIABLES						
OWNER = MEDICAL/ACADEMIC HEALTH CENTER; HOSPITAL	0.0042	0.011	0.0064	0.011	0.0066	0.009
OWNER= INSURANCE COMPANY, HEALTH PLAN, OR HMO	0.0139 *	0.011	0.0160*	0.012	0.0199 **	0.010
SOLO PRACTICE	0.0020	0.007	0.0049	0.007	0.0037	0.006
MIDWEST	0.0116 *	0.008	0.0138*	0.009	0.0170 ***	0.007
SOUTH	0.0034	0.009	- 0.0043	0.009	0.0036	0.007
WEST	- 0.0204	0.010	- 0.0234	0.011	- 0.0118	0.008

PROB (Y=INNOVATOR)	MODEL 1		MODEL 2		MODEL 3	
	MARGINAL EFFECT	SE	MARGINAL EFFECT	SE	MARGINAL EFFECT	SE
NON-MSA	- 0.0012	0.011	0.0064	0.012	- 0.0026	0.008
PATIENT DEMOGRAPHICS						
AGE	0.0001	0.001	0.0003	0.001	-0.0001	0.001
MALE	- 0.0072	0.004	- 0.0092	0.005	- 0.0072	0.004
RACE =BLACK	- 0.0056	0.008	- 0.0034	0.008	- 0.0054	0.006
RACE = HISPANIC	0.0008	0.010	0.0081	0.010	0.0043	0.009
RACE = OTHER	- 0.0087	0.012	- 0.0087	0.013	- 0.0024	0.010
NEW PATIENT	0.0020	0.006	0.0027	0.006	0.0004	0.005
CHRONIC CONDITION	- 0.0130	0.009	- 0.0080	0.008	- 0.0050	0.006
PATIENT INSURANCE						
MEDICARE	0.0012	0.005	- 0.0034	0.005	0.0011	0.005
MEDICAID	0.0034	0.012	- 0.0012	0.012	0.0034	0.013
WORKER'S COMPENSATION	- 0.0041	0.018	0.0039	0.023	- 0.0031	0.014
SELF	0.015	0.014	0.0189	0.014	0.014	0.016
OTHER	0.015	0.018	0.0111	0.018	0.015	0.018
PSEUDO R2	0.6886		0.6696		0.6910	
LOG LIKELIHOOD	-1730.8519		-1836.6456		-1828.2494	
OBSERVATIONS	9459		9459		1012	
NUMBER OF PHYSICIAN CLUSTERS	1102		1102		1143	
PREDICTIONS CORRECTLY CLASSIFIED	97.90%		96.54%		97.85%	

Note 1: ***, ** and * are significant at the 1, 5 and 10% levels, respectively

Note 2: Standard Errors based on Physician clusters

Note 3: Reference Variables – New medications, Use of electronic prescribing, Amoxicillin, Primary Care Specialty, M.D., Physician or Physician Group, Non-Solo Practice, Northeast, MSA, Female, White, Established Patient, No Chronic Conditions, Private Insurance

SUMMARY OF RESULTS

To analyse the influence of brand equity on physician's decision to prescribe a generic or innovator drug, a logit model that considers the effect of physician clustering is estimated. By controlling for the physician clustering effect, each physician cluster is used as the unit of observation instead of treating each individual patient office visit as the unit of observation (Pepper, 2002; Wooldridge 2003; Rice, 2011). The estimated standard errors are then robust and provide unbiased statistical inferences. The estimates are presented in Table 6. Our analysis incorporates several indicators of brand equity: 1)brand equity defined as the *price premium between an innovator drug* and its generic successor; 2) brand equity is evidenced by brand loyalty and habit persistence, that is, the increased *likelihood of prescribing* an innovator drug in a multisource drug market; and 3) Brand equity is quantified as the *perceived consensus quality differential* between an innovator drug and generic substitutes.

BRAND EQUITY PREDICTORS

Innovator Monopoly duration

In the first model, the coefficient for innovator monopoly duration is positive and significant, which confirms our stated hypotheses : The longer an innovator has a monopoly in the market, the more likely it is that the innovator will be prescribed over its generic successors in subsequent multisource markets. In the first model, each year of prior innovator monopoly is associated with a 1.4% greater likelihood that physicians in the sample prescribe the innovator over other generic substitutes. Accordingly, we corroborate our first hypothesis that an innovator drug with a long period of market exclusivity has a first-mover advantage in subsequent multisource markets. The positive and significant coefficient for innovator monopoly duration, confirms that this first-mover advantage is extra time with

which to cultivate brand equity and form a loyal customer base. The result of brand loyalty is that physicians in a multisource market are more likely to opt for the established innovator over newer bioequivalent generic substitutes.

Generic Availability

Notably, the first model does not account for the length of generic availability. Indeed, when the duration of generic availability is accounted for in model 3, the average marginal effect of innovator monopoly diminishes though remains statistically significant - each year of prior innovator monopoly is associated with a 0.94% greater likelihood of prescribing the innovator version of the drug.

Indeed, a generic availability ratio with a significantly negative coefficient in model 2 conforms with expectations – the longer a generic is available on the market the more likely it is to be prescribed in generic form as the length of market availability increases. In our sample, physicians are 15% less likely to prescribe the innovator the longer the length of generic availability increases. In model 3, it is notable that a single year of generic availability is associated with a small (0.2%) but significant decrease in the likelihood of prescribing a drug in its innovator form.

The generic availability ratio pits the duration of generic availability against the duration of innovator availability (pre- and post-patent) in the market. Accordingly, this availability ratio is a proxy that can intuitively be understood as the consensus among physicians as to the quality difference between an innovator and its generic successors. We hypothesised that the medical community is risk-averse with a new and untested generic and will significantly overestimate the difference in quality between the novel generic and the established innovator incumbent. However, with experience and time, physicians' quality

perceptions are revised and the perceived difference in quality between the innovator incumbent and generic substitute diminishes. This hypothesis is confirmed by a significantly negative marginal effect for the generic availability ratio. This signifies that the longer a generic is available on the market relative to the innovator incumbent's time on the market, the more likely the generic will be prescribed over the innovator.

Price Premium

The price premium variable is measured as the natural log of the ratio of innovator price to generic price. In all three models, the coefficient of the logistic regression is negative and significant. Estimations of average marginal effect suggest that physicians in our sample are between 32 to 38 percent less likely to prescribe a drug in its innovator form as the relative price of the innovator increases.

Previous studies often exclude drug prices from the empirical analysis because of the assumption that physicians do not account for cost effectiveness in their prescription decision and are, furthermore, unaware of actual drug prices (Temin, 1980). By including the price premium ratio in our models, we assert that while physicians may be unaware of exact price points, they do acknowledge relative differences in price especially when the differences between alternatives are large. The negative and very significant regressors for the price premium variable in the three models suggests that physicians are price sensitive. As the innovator-generic price differential increases, physicians are less likely to prescribe the innovator over its less expensive generic substitutes.

While this result validates the notion of a price sensitive physician it does however reveal the limits of brand equity in our sample of physicians. One tenet of brand equity is that demand for the brand exists despite and even because of a price premium. The incremental

price difference signifies a perceived difference in quality between the brand and its substitutes. As a financial construct, brand equity is represented by the price premium patients are willing to pay for an innovator drug over and above that of the bioequivalent generic. Yet as agents to the principal patient, physicians in our sample are unwilling to accommodate the price premium associated with the innovator. Instead they opt for the cheaper generic. While physicians in our sample are loyal to an innovator drug with a long monopoly, this brand loyalty does not extend to a willingness to accommodate a price premium.

PRESCRIPTION AND DRUG CHARACTERISTICS

Prescription Characteristics

The estimated effect of a patient being prescribed more than one medication is small and insignificant. This variable is included in the model to reduce correlation across prescriptions written for the same patient. Based on this result, dropping the variable from the model would barely affect the other estimates and it is doubtful that an estimator that accounts for clustering of prescription by patients is needed.

A significant finding in all three models is the impact of electronic prescribing. It is notable that physicians who do *not* use electronic prescribing are more likely to prescribe the innovator version of a drug than those who do use electronic prescribing and that this difference is significant. Moreover, the variable for electronic prescribing is highly correlated to a separate variable determining the use of computerised systems to perform drug formulary checks. However, preliminary regression including both variables resulted in one of these variables being dropped from the model due to near perfect multicollinearity. This suggests that in our sample of physicians, those who do use electronic prescribing also have

a tendency or at least the capability to perform drug formulary checks, which may explain their inclination to consider more cost-effective generic options.

Drug Dummies

The coefficients estimated for drug dummies in all 3 logistic regressions are remarkably large and highly statistically significant. There is considerable variation in innovator prescribing across individual drugs. Perceptibly, individual drug dummies account for a considerable share of the models' explanatory power and when these regressors are dropped from the model, the probability of specification error is increased. Drug characteristics strongly influence the decision to prescribe either the innovator incumbent or generic substitute. Observed drug characteristics are the same for all physicians in the sample, so any degree of variation in innovator prescribing rates across drugs is an indication that physicians perceive drug attribute differently.

The significant explanatory power of drug dummy variables in all three models supports the notion that physician behaviour is largely explained by habit persistence as argued in previous literature including Hellerstein (1998), Howard (1997) and Nayak (2013). Physicians in our sample tend to prescribe the same form (generic or innovator) of a drug to every patient regardless of patient characteristics.

PHYSICIAN AND PRACTICE VARIABLES

In all three models, while specialty and training bear no influence on the binary prescription decision, certain practice characteristics do influence which version of a drug is prescribed. Physicians practicing in the Mid-West are at a 10% level of statistical significance between 12% -17% more likely to choose an innovator drug than the reference group of

physicians practicing in the North East. Physicians in the West are consistently less likely to prescribe innovator drugs than the reference group of physicians practicing in the North East, though the difference is not statistically significant. Contrary to stated expectations, physicians working at practices owned by an insurance company, health plan, or HMO are between 14% and 19% more likely to prescribe the innovator version of a drug than physicians working in individual or physician group practices.

As is the case with the generic availability ratio, these findings further bolster our second hypothesis of their being a process of information diffusion and consensus building among physicians about a drug's quality. The implication is that physicians with characteristics in common share information about the efficacy of individual drugs and that a consensus is formed within groups of associating physicians (be it by region or practice) regarding the efficacy of innovator incumbent versus its generic successors.

PATIENT DEMOGRAPHICS

In all models, the coefficients of patient demographic variables are small and not statistically significant. Though not statistically significant, the direction of regressors suggests that patients with chronic conditions may be less likely to receive the innovator compared to patients with no chronic conditions. Also, new patients may be more likely to receive innovator drugs than established patients. Previous literature (Nayak, 2013) have found these two variables to be statistically significant. Notwithstanding, patient demographics and traits do not appear to influence the prescription decision.

Nonetheless, small non-significant patient demographic regressors in conjunction with the highly statistically significant drug dummy variables hints again at habit persistence. My results imply that physicians do not consider patient profiles when making prescription

decisions. Instead, physicians in our sample are making the choice between an innovator or generic substitute based on ingrained pharmacological judgements rather than varying prescriptions according to patient characteristics. Thus, every patient in the physician's cluster is prescribed the same form (generic or innovator) of a drug regardless of individual differences.

PATIENT INSURANCE

Using ordinary least squares, the regressor for no charge/ charity patients is negative, large, and significant. This implies that patients in this no charge category are significantly less likely than patients with private insurance to receive an innovator drug. However, as the no/charity parameter perfectly predicts failure (that is, all patients in this category receive a generic drug), it is dropped from the estimation of the logistic regression.

The remaining regressors for insurance variables are not statistically significant and are small relative to their standard errors. We conducted a Wald test to evaluate the difference between nested models to determine if insurance parameters were simultaneously equal to zero. The squared value generated by the Wald test was 1.39 with five degrees of freedom. Based on the p-value of 0.9253 we fail to reject the null hypothesis, indicating that insurance coefficients are simultaneously equal to zero. Including insurance variables does not improve the fit of the model. Thus, in the interests of parsimony we would be justified in dropping insurance coefficients all together. However, in the literature there is compelling evidence that patient insurance status significantly impacts prescription decisions. This is in part supported by the excluded variable of no charge/charity patients, which perfectly predicts the failure condition in our model, that is, the prescribing of a generic.

Therefore, as this is a hypothesis driven model, we have chosen to keep insurance variables in our final model.

DISCUSSION

THE CONCEPTUAL THEORY

In this dissertation, we propose that the most salient factor influencing physician behaviour is brand equity, which is both a monetary and qualitative construct. As a financial construct, brand equity is represented by the price premium patients are willing to pay for an innovator drug over and above that of the bioequivalent generic. As a qualitative construct, brand equity represents a gradation of superlative, yet subjective characteristics possessed by the innovator drug versus its generic substitutes. Consistent with the marketing literature (Aaker, 1996; Keller, 1993; Keller 2001), these psychological attributes include greater awareness and knowledge of the innovator drug, positive associations with the innovator brand, and perceived quality of the innovator drug (often viewed as superior to the bioequivalent generic substitute). The result of this continuum of attitudinal change is entrenched brand loyalty to the innovator and habit persistence, a psychological attribute that can be quantitatively assessed by calculating the likelihood of prescribing the innovator drug over its generic successor.

Given these monetary and qualitative descriptors, our analysis incorporated several indicators of brand equity: 1)brand equity defined as the *price premium between an innovator drug* and its generic successor; 2) brand equity quantified by the increased *likelihood of prescribing* an innovator drug in a multisource drug market; and 3) Brand equity quantified as the *perceived consensus quality differential* between an innovator drug and generic substitute.

THE STUDY OBJECTIVES

The overarching goal of this dissertation was to ascertain whether brand equity influences prescriber preferences between innovator (brand) drugs and generic alternatives and if third party payers can override such preferences. As such, our first aim was to establish whether innovator drugs have a first-mover advantage over generic successors in multisource markets. Conversely, our second aim was to determine whether upon the removal of barriers to entry, generics can catch up with the pioneering advantages of the innovator. By so doing, our objective was to delineate the process of generic drug acceptance (including learning and switching behaviour) among physician prescribers. The final aim was to examine the role of insurance status in qualifying physician brand loyalty.

EXPECTED FINDINGS VS MODEL RESULTS

In keeping with the first aim, we hypothesised that longer periods of innovator market exclusivity bestow a first-mover competitive advantage to the innovator drug in subsequent multisource markets. We expected that longer periods of innovator market exclusivity are associated with a greater likelihood of innovator prescriptions once the market is open to competition from generics. Additionally, we predicted that the first mover advantage results in a greater likelihood of prescription despite their being a sustained price difference between the innovator and its generic substitutes. The results of the analysis partially corroborate the first hypothesis. Indeed, an innovator drug with a long period of market exclusivity has the first-mover advantage of brand loyalty in subsequent multisource markets. A long period of market exclusivity is associated with a greater likelihood of prescribing a drug in its innovator form. However, while physicians are price sensitive, they are *less likely* rather than more likely to prescribe an innovator drug with a substantial price premium.

The second hypothesis states that physicians will initially overestimate the perceived relative therapeutic benefit between an innovator drug and a generic entrant. This consensus quality differential between an innovator and its bioequivalent generic we expected to diminish over time as physicians familiarised themselves with the generic. The results fully support this second hypothesis. The longer a generic is available on the market relative to the innovator incumbent's time on the market, the more likely the generic will be prescribed over the innovator. Accordingly, the results delineate a process of time-dependent information diffusion and generic drug acceptance. The length of generic availability facilitates prescriber learning and switching behaviour from innovator to generic. Our results also intimate a process of consensus building among associating physicians within the same region or practice type.

Finally, the third hypothesis asserts that insurance status will override the brand equity preferences of physicians. As innovator drugs tend to be more expensive than ensuing generics, we hypothesised that patients in my reference category of uninsured or self-pay patients will be least likely to receive branded innovator drugs, which is evidence of moral hazard (Lundin, 2000; Nayak, 2013). Consistent with the literature, we also expected fewer innovator drug prescriptions to be dispensed to patients enrolled in public health insurance schemes such as Medicaid and Medicare (Rice, 2011), and cost containment payer systems such as Health Maintenance Organisations (HMOs) (Nayak, 2013; Thier, 2011). However, our analysis does not affirm this hypothesis. On the contrary, insurance variables individually and jointly have no impact on the prescription decision between generic and innovator alternatives. While physicians are price sensitive, there is no evidence that physicians are more responsive to the costs borne by patients than costs incurred by third-party payers.

IMPLICATIONS

Substantiating the existence of prescriber-based brand equity explains why health care payers and consumers alike are failing to realise the cost savings of a competitive off-patent drug market despite bioequivalency data, favourable generic substitution policies, and pressure from payers to minimise cost. Various elements of our proposed analysis intimate possible remedies. Given that extended innovator monopoly is found to significantly favour prescribing of the innovator over ensuing generics, it behoves policy makers to reconsider brand patent extensions as a means of strategic entry deterrence with far-reaching consequence. That extended innovator market exclusivity becomes a first-mover advantage evident in prescriber loyalty in subsequent multisource drug markets infers that innovating firms are incentivised to protect and capitalise on this head start.

Conversely, it is evident that new generic competitors face the prospect of overcoming physicians' knowledge gap and developing trust as physicians trial the new generic alternatives. By building their own equity, new generic entrants bridge prescribers' perceived quality differentiation between the innovator incumbent and novel generic options. If indeed innovator drugs have a head start on subsequent generics, it stands to reason that generics could eventually bridge this gap. Time confers generic substitutes the opportunity to build their own "equity", as physicians familiarise themselves with the drug. As per Aaker's model – product awareness and perceived quality are essential contributors to brand equity(Aaker, 1991). Accordingly, physicians will more readily switch to older generics but remain loyal to the innovator drug (i.e. habit persistence) in the case of newer generics. This process of time-dependent information diffusion is borne by the literature (Howard, 1997).

Other notable findings include the tendency of physicians to prescribe the same version of a drug to all patients regardless of their demographics or medical profile. Hellerstein (1998), labels this inclination among prescribers as “habit persistence”. Yet the implementation of certain nudges may discourage habitual prescribing and instead encourage switching behaviour towards more cost-effective generic alternatives. One strategy implied by the results is the universal implementation of electronic prescribing using default options to increase generic medication prescribing rates. The efficacy of this behavioural nudge is borne out by the literature : In a pilot study (Patel et al, 2014) of internal medicine practices at Penn Medicine, researchers found that changes to medical display defaults in the electronic health record resulted in higher rates of generic prescribing. After reviewing these findings, default settings were further refined and then launched throughout all practices among all specialties at Penn Medicine. Before the intervention, the generic prescribing rate at Penn Medicine was steadily hovering around 75%. Immediately after the change in defaults, the generic prescribing rate increased to 98.4% (Patel et al, 2014).

CONCLUSION

SUMMARY

The goal of this dissertation is to understand the influence of brand equity on the physician prescriber decision-making process. We determine that brand equity is critically important for physician prescribers to make points of differentiation between innovator branded drugs and their generic alternatives**.** We establish that time is a critical factor in cultivating brand equity thereby influencing prescriber choice. For innovator drugs, we find that extended periods of market exclusivity result in an increased likelihood of prescribing the innovator once the market is open to competition from generics. Conversely, we also determine the likelihood of switching to the generic in multisource drug markets. In weighing physician loyalty to the innovator (habit persistence) against the physician's propensity to switch to the generic (switching behaviour), we examine how consensus perceived quality estimations between innovator and generic are revised over time and how such differentiation is reflected in prescriber habits. Finally, we determine that while the physician is price sensitive, they do not vary their prescription decision based on insurance status.

LIMITATIONS

Of note, our sample frame – The National Ambulatory Medical Care Survey (NAMCS) – is limited to non-federally employed office-based physicians who are primarily engaged in direct patient care. Accordingly, results of our analysis have limited generalisability to inpatient care settings. Furthermore, the pooled cross-sectional design of the NAMCS survey hinders the possibility of examining individual preferences over time. To fully portray the impact of brand equity and moral hazard on prescriber practice, one would ideally like to observe a physician repeatedly prescribe the same drug over an extended period. Analysing

longitudinal data would better render a more accurate estimation of switching behaviour and habit persistence.

Moreover, the analysis hinges on drug mentions. It is important to reiterate that medications ordered by the physician are not necessarily the medications ultimately dispensed to the patient by the pharmacist. Barring physician injunction, the pharmacist has leeway to substitute an innovator for a generic or vice versa. Generally, because of pricing considerations and formulary restrictions, dispensing rates of generic drugs are higher than prescribing rates (Nayak, 2013). The effect of such discretionary changeover is to de-link the physician's prescription decision from what is dispensed. Without a data set that links the prescribing habits of physicians to pharmacist substitutions, it is difficult to extrapolate and quantify the influence that prescription habits exert on healthcare costs (Nayak, 2013).

Nevertheless, as our research question focuses on the physician prescription order rather than the execution of it, discrepancies between prescriber choice and end-user practice do not impact the validity or accuracy of our conclusions. Relevance is still maintained because despite generic substitution policy, innovator dominance in the marketplace -both in pricing and volume- remains a current and intractable issue for policy makers and insurers alike. Hence an empirical analysis of prescriber habits and brand preferences would better elucidate the origins of this paradox.

Finally, our analysis includes no controls for advertising and marketing efforts, which could potentially influence prescriber choice. Therefore, we cannot assess how the promotion of the innovator brand or generic alternative bridges the physician knowledge gap or impacts perceived therapeutic equivalence. Appreciably, a well strategised marketing campaign eases the path towards strong brand identity or, in the case of the generic, counters

any potential first mover advantage of the incumbent. As an accurate measure of effort is difficult to construe, we have instead chosen to substitute effort with time. We include time variables such as the innovator monopoly period and the generic availability ratio asserting that, ceteris paribus, brand equity is a function of market presence.

AVENUES FOR FUTURE RESEARCH

Many authors have studied the binary prescription decision between an innovator drug and a generic substitute. They separately examined the impact of monopoly, price, and insurance status on prescriber behaviour. Indeed, some such as Hellerstein (1998) noted elements of habit persistence and brand loyalty among physician prescribers. Yet these observations, though repeated in the literature, were curious but incidental findings in the larger exploration of pharmaceutical demand.

My contribution to the literature is to streamline these overlooked behavioural eccentricities by appropriating the concept of brand equity from marketing theory and applying it to the novel context of prescriber choice. Future research could delve into other aspects of brand equity, such as the influence of brand salience (name recognition and recall) and marketing, on prescriber choice. To better conceptualise prescriber learning and switching behaviours, prospective research could investigate the synergy between generic options. This could include an assessment of how switching behaviour alters based on generic order of entry and the number of generic competitors. Additionally, by varying and expanding the array of drug choices and therapeutic classes, one could better understand the extent to which a drug's idiosyncrasies (such as narrow therapeutic index) promote either brand loyalty or switching behaviour. Moreover, in expanding the scope of drugs and number of physicians in the study, one could re-examine the effect of insurance status on prescribers' brand loyalty.

Finally, there is an exciting avenue of behavioural economic research, including the role of behavioural nudges (such as default generic prescriptions), Bayesian updating, and heuristics, in determining prescriber brand preferences.

APPENDIX

Appendix 1: Drug Sample

CHEMICAL NAME OF DRUG	VERSIONS	BROAD THERAPEUTIC CLASS	MARKETING DATE (ordered)
Amlodipine	Norvasc*	Cardiovascular agent	31 July 1992
	Amlodipine		3 October 2005
Atorvastatin	Lipitor*	Metabolic agent	17 Dec 1996
	Atorvastatin		30 November 2011
Amoxicillin	Amoxil*	Anti-infective	1 January 1982
	Trimox		1 January 1982
	Amoxicillin		1 January 1982
Lisinopril	Prinivil*	Cardiovascular agent	29 December 1987
	Zestril		19 May 1988
	Lisinopril		1 July 2002
Alprazolam	Xanax *	CNS Agent	1 January 1982
	Alprazolam		19 October 2003
	Xanax XR*		17 January 2003
	Niravam		19 January 2005
LEVOTHYROXINE SODIUM	Synthroid	Hormones	1 January 1982
	Unithroid		21 August 2000
	Levoxyl		25 May 2001
	Levothyroxine Sodium		5 June 2002
	Levothroid (thyro-tabs)		24 October 2002
	Tirosint		13 October 2006
*Innovator designation			

Of note, the innovator designation is given to the first version of the drug to be marketed and generic designation to all bioequivalent successors be they branded or otherwise. Per this classification, the innovator drug is usually but not always the Reference Listed Drug (RLD)[3]. Additionally, marketing dates for drugs approved prior to 1982 are top coded at 1 January 1982 as per the FDA orange book convention.

[3] A Reference Listed Drug (RLD) is an approved drug product to which new generic versions are compared to show that they are bioequivalent. A drug company seeking approval to market a generic equivalent must refer to the Reference Listed Drug in its Abbreviated New Drug Application (ANDA).

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