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SPECIAL ISSUE PAPER



The impact of drug quality ratings from health technology assessments on the adoption of new drugs by physicians in Germany

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Abstract

Payers are increasingly calling for the value of new drugs to be measured explicitly. We analyze how the availability of drug quality ratings by health technology assessment (HTA) agencies affects the adoption of new drugs by physicians in Germany. We combine data from drug quality ratings, promotional spending, and a physician panel. In a latent utility model, time to adoption is specified as a function of quality rating, promotional spending by manufacturers, and physician-specific variables. As expected, drugs with a positive rating were adopted faster (p < 0.001) than those without. However, our results suggest that it was the publication of the quality rating itself that affected adoption. Indeed, before a quality rating was published, drugs that went on to receive a positive quality rating were not adopted significantly faster than drugs that went on to receive a negative quality rating. In contrast, after the publication of the HTA quality rating, drugs with a positive rating were adopted significantly faster than those without (p < 0.05). The per physician value of a positive quality rating was EUR 393.50. Our results suggest that there are returns from HTAs beyond their use in price negotiations.

KEYWORDS

duration analysis, government policy, information and knowledge, public health, regulation

JEL CLASSIFICATION 118; C41; M38; D80

1 | INTRODUCTION

In most industrialized countries in 2020, health expenditure continues to rise and public budgets remain tight. At the same time, awareness is growing that rational approaches to resource allocation are preferable to ones that rely purely on market forces. It is no surprise, therefore, that public and private payers of health care are increasingly calling for the value of new drugs to be measured in an explicit manner (Neumann & Cohen, 2015). This has spawned a flurry of comparative effectiveness research and paved the way for the use of health technology

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assessments (HTAs) to evaluate the relative advantage of new drugs or other health technologies over existing treatments.

To determine the value of a new drug, HTA agencies typically ask two questions: 'Does it work?' and 'Is it worth it?' (Luce et al., 2010). Whereas the former involves measuring the clinical effectiveness of a drug, the latter examines a drug's economic value and includes cost considerations. Although the Affordable Care Act in the United States does not allow cost per quality-adjusted life year to be used to establish which type of health care is cost-effective or recommended, state-level programs like Medicaid in New York have nonetheless begun to consider the effectiveness of drugs, the availability of alternative treatments, and the severity and prevalence of disease to negotiate rebates with manufacturers (Hwang, Kesselheim, & Sarpatwari, 2017; Text - H.R.3590-111th Congress (2009–2010), 2010).

Meanwhile, at the micro level, it is physicians who ultimately decide which drugs they will prescribe to their patients. Research on physician learning and the adoption of health technologies among physicians suggests that prescribing behavior is influenced by a range of information sources, including the promotional activities of manufacturers (Berndt, Gibbons, Kolotilin, & Taub, 2015; Berndt, Pindyck, & Azoulay, 2000; Kremer, Bijmolt, Leeflang, & Wieringa, 2008), physicians' own previous experience (Coscelli, 2003; Coscelli & Shum, 2004), and signals from market authorization documents (Kalra, Li, & Zhang, 2011; Serra-Sastre & McGuire, 2013).

An additional source of information for physicians about drugs is the documents generated by HTA agencies. As part of their assessment and appraisal activities, these agencies develop explicit statements about a drug's quality compared with an existing medical technology and publish these shortly after a drug enters the market. The evidence generated by HTA agencies is typically used by regulators to set the price of drugs and to reduce uncertainty about their clinical and cost-effectiveness. Because such statements are generally published after a drug has received market authorization, HTAs have come to be known as the 'fourth hurdle' after the classical three hurdles of market access for biotechnologies (which comprise quality, efficacy, and safety assessments) (Taylor, 2004).

Although market authorization decisions like those of the US Food and Drug Administration (FDA) already provide some information about the quality of a drug, such decisions typically do not reflect the relative advantage of a new drug compared with an existing one because the new drug is often tested only against a placebo. Understanding the relationship between the information on quality provided by HTAs and the length of time it takes for physicians to adopt a drug can help payers, regulators, and the industry to better understand the market diffusion of new drugs and the product life cycle. This, in turn, has a variety of implications for measuring health gains for society, health care costs, and the resources available to manufacturers to fund research and development (Sorescu, Chandy, & Prabhu, 2003). However, although both comparative effectiveness research and HTAs have generated a large body of literature over the past decade, research on the information signals provided by HTAs and how these affect the adoption of new drugs at the micro level has been scant. In our study, we attempt to fill this gap in the research by (a) exploring how the drug quality rating in an HTA appraisal document affects the speed with which physicians adopt a new drug and (b) calculating the financial value of a positive quality rating in terms of manufacturers' spending on promotional activities. Our study contributes to the literature by offering a novel approach to quantifying the impact of quality ratings on the speed of drug adoption and the economic value of these information signals.

2 | BACKGROUND

2.1 | HTA organizations as change agencies

The organizations responsible for conducting HTAs may be thought of as change agencies. These are defined in the literature as organizations whose formal role entails influencing clients' decisions about the adoption of a new product in a direction deemed desirable by the organization (Rogers, 2003)—for example, by giving guidance and encouragement or helping clients change their behavior (Thompson, Estabrooks, & Degner, 2006). This influence is not restricted to encouraging physicians to adopt a new drug, but can also be used to slow down diffusion or even prevent the adoption of undesirable products. Although change agencies do not necessarily have better information than others in the market, they should have the capacity and expert knowledge to assess and endorse the quality of a product in a comprehensive manner (Rogers, 2003).

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2.2 | Impact of HTA on adoption

The adoption of health technologies by physicians has been examined in relation to their previous experience with these technologies (Berndt et al., 2015). Models of learning behavior have been developed in which physicians incorporate information from previous patients when updating their beliefs about the quality of a drug (Ching, 2010; Coscelli & Shum, 2004; Kalra et al., 2011). For example, the approach by Kalra et al. (2011) separates the quality of a drug into its effectiveness and safety and examines the responses of physicians to contradictory information from drug warnings released after the drug has been on the market for some time.

Many studies have analyzed the relationship between market authorization or the timing of market entry and phenomena such as competition, pharmaceutical detailing (i.e., face-to-face sales promotion to physicians), and price setting (Danzon & Chao, 2000; de Frutos, Ornaghi, & Siotis, 2013). The relationship between various pharmaceutical market regulations and price setting and demand has also been studied, predominantly in the off-patent market (Brekke, Canta, & Straume, 2016; Granlund, 2010).

The potential effects of HTAs on physicians' decision to adopt a new technology, however, and how these effects interact with marketing efforts (especially promotional activities) by the industry, are largely unknown. The only study to have touched upon this topic is that by De Frutos et al. (2013), who provide evidence that, depending on brand loyalty of consumers, better quality products (as measured by the FDA's priority review status) are the ones that are advertised most frequently through the practice of detailing and that brand loyalty is endogenously determined by promotional activities.

However, a growing body of literature is using proxies for quality (Miller, 2016), such as the FDA's 'standard' versus 'priority' review classification. That is, drugs are assigned priority review if they are expected to represent major improvements in safety or effectiveness compared with existing treatments. Other studies have used negative information from safety warnings released by market authorization agencies or information about clinical effectiveness (Azoulay, 2002; Bradford & Kleit, 2015; Serra-Sastre & McGuire, 2013). Azoulay (2002) found evidence that if a drug has greater clinical effectiveness, uncertainty is reduced, leading to increased sales. Venkataraman and Stremersch (2007) use data from the appraisals published by the UK National Institute of Health and Care Excellence (NICE) as a proxy for product quality, that is, a meta-analytic z score for product effectiveness, but not the actual guidance for the product's use in the National Health Service (NHS). Serra-Sastre and McGuire (2013) use a matrix of variables that represent the flow of information about product quality but do not consider information signals provided by HTA agencies.

Information provided by an HTA agency is different from information on clinical effectiveness. This is because, in practice, physicians have little time to search for, identify, and evaluate clinical evidence on new products (Gallan, 2004; Stros & Lee, 2015). HTAs are made publicly available at no charge. Moreover, they are communicated through press releases and other channels such as physician associations. In fact, in a survey, 90% of physicians in Germany considered HTA results to be relevant to their prescribing behavior (Greiner & Witte, 2017). Lastly, the decisions reached by HTA agencies ideally already reflect the current context of clinical care, whereas articles in scientific journals generally report efficacy results generated under the ideal clinical care conditions of randomized controlled trials.

Another reason why we use HTA agency decisions as a proxy for the quality of a drug in our analysis is that the alternative of using drug warnings relies on data that stem from an action that takes place after the drug has been adopted and not at the beginning of the product life cycle. Furthermore, previous studies have typically measured the effects of negative information signals only (Bradford & Kleit, 2015; Dorsey, Rabbani, Gallagher, Conti, & Alexander, 2010; Lasser et al., 2002; Libby et al., 2007; Venkataraman & Stremersch, 2007; Wagner et al., 2006; Weatherby, Nordstrom, Fife, & Walker, 2002), whereas information from HTAs can be positive or negative.

| METHODS 3

3.1 | Data

For our empirical analyses, we combined data from five different sources, as detailed in the following subsections.

3.1.1 | HTA agency appraisal in Germany

Although the off-patent market was highly regulated in Germany from the mid-1990s until 2010, brand name drugs could freely enter the German pharmaceutical market and their cost was covered by statutory health insurance at the price listed by the manufacturer at market entry. This free-pricing policy ended when the Pharmaceutical Market Restructuring Act (Arzneimittelmarktneuordnungsgesetz) was passed. Since January 2011, manufacturers may set a price for a new drug at market entry, but this remains valid only for 12 months. During this time, manufacturers must demonstrate to the Federal Joint Committee (FJC, German: Gemeinsamer Bundesausschuss) that the drug has an added health benefit over an appropriate comparator treatment (Fischer & Stargardt, 2014). This information is used for subsequent price negotiations between the manufacturer and the umbrella organization of the statutory health insurers (German: Spitzenverband Bund der Krankenkassen) (Lauenroth & Stargardt, 2017; Schlette & Hess, 2013).

Statutory health insurance covers approximately 90% of the population in Germany and co-payments for drugs for people with this form of insurance generally range from EUR 5 to 10 per package. The amount of co-payment is independent of a drug's marketing status (brand name or generic) and tier in the treatment episode. Private health insurers in Germany, who cover most of the remaining 10% of the population with fully substitutive insurance, participate in the assessment and appraisal process, but do not have any voting rights or negotiating power. Co-payments among people with private insurance vary by insurance contract and are typically only covered after a deductible is met.

The FJC is a non-governmental, self-governing body and is responsible for making coverage decisions for the statutory health insurers. The FJC's appraisal committee includes payer, provider, and patient representatives. The FJC's rating is based on a comprehensive evidence assessment of the documents submitted by the manufacturer. This assessment is typically performed by the Institute of Quality and Efficiency in Health Care. In addition, the FJC considers written comments submitted by stakeholders, comments that come up during the hearing session that is part of the process, and its own interpretations of the evidence (Fischer & Stargardt, 2014). The final decision is always published in an appraisal document 6 months after the market launch of a drug.

The FJC's decision in this regard is based on its assessment of multiple dimensions of quality, which typically include mortality, morbidity, quality of life, and safety. The document states whether a drug has an added benefit over an appropriate comparator treatment or no added benefit. For our analysis, we defined the former as a positive quality rating and the latter as a negative quality rating. A positive quality rating can be further broken down into four levels of added health benefit: major, considerable, minor, and not quantifiable.

We reviewed all final appraisal documents published by the FJC between January 2011 and March 2014 (Federal Joint Committee, 2015). Our unit of analysis was the chemical substance, that is, Level 5 of the Anatomical Therapeutic Chemical (ATC) Classification System. These contained quality ratings for 65 drugs. We extracted data on these ratings if a drug (a) was newly licensed and had not been on the market before 2011, (b) was not an orphan drug, (c) was administered predominantly in ambulatory care, and (d) had been prescribed more than 100 times by our panel of physicians.

Although separate appraisals are also undertaken by the FJC for subgroups of patients, we extracted data on the quality rating published in the final appraisal documents at the substance level (Blankart & Stargardt, 2017). We also recorded when the final appraisal document for each of the drugs considered in our analysis had been published. Drugs rated as having no added benefit are still reimbursed through statutory insurance in Germany, albeit at the reference price, unless the manufacturer decides to opt out of the market altogether (a rare exception) (A. D. Stern, Pietrulla, Herr, Kesselheim, & Sarpatwari, 2019). Importantly, the mechanism to determine co-payments for people with statutory health insurance does not vary across drugs within the same reference price group. If no reference price group is assigned, co-payments are determined by ex-factory list prices before any additional discounts and rebates are granted regardless of the marketing status of the drug.

3.1.2 | Data on prescriptions and promotional spending

For data on physicians' decisions to adopt certain drugs, we relied on the CEGEDIM MEDIMED prescriber panel. The database contains the complete prescribing data of 3,026 office-based physicians from January 2011 to June 2014. It also includes data on physician characteristics and selected patient attributes. The panel comprises a representative sample of physicians balanced across regions, specialties, and prescription volumes in the German health system. For each drug

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in our sample, we included physicians if their specialization group had written more than 5% of all prescriptions for that drug during our observation period.

We obtained data on promotional activities by manufacturers from the CEGEDIM PROMO database. This includes the monthly spending of pharmaceutical companies in Germany at the level of individual drugs for detailing, sampling, and multimedia advertisements during the same period as that covered by the prescriber panel. Direct-to-consumer advertising for drugs was not a relevant category because it is banned in Germany.

3.1.3 | Other

Given that scientific journals represent another avenue for physicians to learn about a drug's properties, we additionally collected data on the number of articles on each drug from two databases of the scientific literature. From the first, the Web of Knowledge database,¹ we extracted the number of publications on each drug in scientific journals in any language, and from the second, the EMBASE database,² we extracted the number of publications on each drug in scientific journals in scientific journals in German only. We calculated a score by weighting the number of publications by the number of citations as of 20 October 2016. We obtained annual data on adverse events from the national database of adverse events provided by the German Federal Institute for Drugs and Medical Devices (2015).

3.1.4 | Descriptive statistics

Of the 65 drugs for which the FJC had provided a quality rating between January 2011 and March 2014, we excluded six because they had been launched before the observation period, 36 because these had been prescribed fewer than 100 times by our physician panel, and two for which no data on manufacturers' promotional activities were available. The 36 drugs prescribed fewer than 100 times by our panel were mostly drugs with orphan drug status or cancer treatments for diseases with a very low prevalence or whose treatment generally takes place in the hospital.

In total, we included 134,525 prescriptions for our 21 drugs, corresponding to 7,679 adoption decisions (i.e., the first prescription of a drug) made by 2,293 physicians (Table S1 provides an overview of the 21 drugs we ultimately included in our analysis). This corresponds to gross sales of about EUR 70 million for all drugs in the sample. The FJC published a positive quality rating for 11 of the 21 drugs and a negative quality rating for the remainder. In total, 59% of the drugs were for chronic conditions.

Among all of the drugs adopted, the mean time to adoption was 13 months (SD 10). By Month 6 after market entry, an average of 9.35% (Month 12: 13.69%) of the physicians in our sample whom we had classified as potential adopters of each of the included drugs had adopted those drugs. In concordance with previous studies that have captured product life cycles (Lee, Smith, & Grimm, 2003), we found that a high percentage of physicians had not adopted the included drugs by the end of the study period (79.34% on average across drugs).

3.2 | Empirical strategy

3.2.1 | Regression specification

Our regression specification is based on the model of new drug adoption proposed by Liu and Gupta (2012), which captures micro-level diffusion to analyze individual physicians' adoption of drugs that have newly entered the market. The goal is to model the adoption probability as a function of a set of factors such as marketing activity. The model allows a situation to be considered in which a physician makes the decision to adopt a drug—that is, use it for the first time because the expected utility gained from its use exceeds its cost (Liu & Gupta, 2012). The cost may be expressed as the opportunity cost of using another (potentially inferior) drug and the cost of obtaining information about the new drug. As a reduced form specification, we modeled the probability P that physician i will adopt a new drug j in month t, as follows:

¹www.webofknowledge.com/, last access January 28, 2019

²http://www.elsevier.com/solutions/embase, last access January 28, 2019

$$P_{ijt} = P\left(y_{ijt} = 1 | U_{ijt1}; U_{ijt0}\right) = P\left(U_{ijt1} > U_{ijt0}\right) = P\left(\tilde{U}_{ijt} > 0\right) \tilde{U}_{ijt} = V_{ijt} + \varepsilon_{ijt}, \varepsilon_{ijt}\tilde{N}(0, 1), i = 1, ..., I; t = 1, ..., T.$$
(1)

 \tilde{U}_{ijt} is the difference between the latent utility of adopting a drug U_{ijt1} versus not adopting it U_{ijt0} . We assumed the outside option U_{ijt0} to be zero. V_{ijt} reflects the deterministic or observable component of the latent difference in utility \tilde{U}_{ijt} . This deterministic component relates to physician *i*'s intrinsic adoption propensity, manufacturers' marketing activities, patient–physician interactions, and contagion. ϵ_{ijt} is the error term, which reflects random variation in perceived relative advantage across physicians. In addition to the factors identified by Liu and Gupta (2012), we hypothesized that the information about a drug's quality that is published by the FJC in its final appraisal document influences the deterministic part V_{ijt} , helping reduce information asymmetry and uncertainty about the true quality of the drug.

In addition, we considered the timing of a physician's decision to adopt a drug in relation to when the quality rating was published by the FJC. Typically, physicians face uncertainty about the latent utility of a drug once it has entered the market. Because health care services such as prescription drugs are experience goods, physicians in the market typically suffer substantial information asymmetries and uncertainty (Dranove, 2012).

Finally, we allowed the deterministic part of the utility function V_{ijt} to include information that stems from the marketing of a drug and can influence a physician's perception of relative advantage and which is complementary to the quality rating in the final appraisal document published by the FJC. We considered this information to be price, promotional activities, and the body of scientific evidence.

We transformed the latent utility model into a hazard model as suggested by Liu and Gupta (2012). The dependent variable measures the time until physician *i* adopts drug *j*. Accordingly, the general accelerated failure time model is defined as

$$h_{ij}(t) = \exp(\beta' x_{ijj}) h_0(t),$$

where x_i is the vector of variables that describe the deterministic component V_{ijt} of physician *i*'s decision to adopt drug *j*. This vector includes our variable of interest and the control variables. $h_0(t) = \gamma t^{\gamma - 1}$ represents the baseline hazard function for Weibull regression with γ being the shape parameter. To identify the accelerated failure time model specification with the best fit, we estimated a generalized gamma model and tested the exponential, Weibull, and lognormal specifications. We found that the Weibull distribution fits the model best.

To measure the effect of information about the quality of a drug and of promotional activities on adoption decisions, we specified three models. Model I analyzed the effect of positive quality ratings versus negative quality ratings on the time it took for physicians to use a drug for the first time (variable: *quality*). Model II analyzed, in addition, whether the speed of adoption for each of these two ratings differed before and after the publication of the final appraisal document. We therefore included an interaction effect between quality rating (positive/negative) and the date of the publication of the final appraisal document (before adoption/after adoption) (variables: *quality*decision*). In Model III, we distinguished between the quality ratings by taking the highest level of added health benefit assigned by the FJC (major/considerable/minor/not quantifiable) for each drug to analyze whether the speed of adoption differed according to these. Again, we included an interaction effect between levels of added health benefit and the date the final appraisal document was published.

3.2.2 | Measures of product quality, prices, promotion, and available scientific evidence

We defined the quality of a drug (variable: *quality*) as positive if it was appraised at any point during the observation period by the FJC as having an added health benefit and negative if it was not. We also captured the cumulative number of reported adverse events normalized to prescription volume by the variable *adverseevents* (Bradford & Kleit, 2015).

To control for the impact of manufacturers' marketing activities (Agarwal & Bayus, 2002), we measured the following variables at the drug level *j*: *Price* captures the price per prescription of the dosage formulation most frequently prescribed in the panel. *Promostk* measures promotional spending, such as detailing and sampling, as the cumulative stock of promotional spending per physician at Month 6 after launch, that is, the month the FJC publishes its final appraisal document (Kalra et al., 2011). We did so to rule out strategic behavior of the manufacturer based on the outcome of the quality rating. The stock of promotional spending on drug *j* in month *t* is calculated as

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 $PROMOSTK_{jt} = PROMOTION_{jt} + \alpha \cdot PROMOSTK_{jt-1}, 0 < \alpha < 1$ assuming the carryover parameter α to be 0.95 (Azoulay, 2002; Berndt et al., 2000).

To approximate the amount of scientific evidence available (Azoulay, 2002), we introduced two variables: (1) *Evidint* captures the cumulative number of international scientific publications up to date *t*, which we weighted by the number of citations, and (2) *Evidnational* measures the cumulative number of scientific publications in German.

3.2.3 | Accounting for heterogeneity of physicians and drugs

At the level of physician *i*, we accounted for several other physician characteristics (Tamblyn, Mcleod, Hanley, Girard, & Hurley, 2003). *Experience* captures a physician's experience by counting the range of drug classes prescribed as defined by the EPHMRA Anatomical Classification of pharmaceutical products (Berndt et al., 2015; European Pharmaceutical Market Research Association, 2016). *Contagion* captures the percentage of physicians who have already adopted drug *j* by time t - 1 in physician *i*'s social network, which was defined by the regional physician association of which the physician is a member. *Specialist* is a dummy variable capturing whether the physician is a specialist or general practitioner. *Group practice* is a dummy variable taking the value 1 if the physician works in a group practice and 0 for a solo practice. *Age* measures the physician's age. *Gender* is a variable taking the value of 1 for a male physician and 0 otherwise.

We also included information about the case mix of a physician's practice: *shareSHI* measures the share of patients covered by statutory health insurance compared with private health insurance. *Sharechronic* captures the share of prescriptions for chronic conditions of all prescriptions compared with acute conditions using the pharmacy-based metrics (Huber, Szucs, Rapold, & Reich, 2013). *Shareabove65* measures the share of patients 65 years of age or older. *Region* represents one of 17 possible geographic areas in which a physician can be located. This is because the regional associations of physicians in Germany may stipulate slightly different recommendations and policies on efficient prescribing.

We also controlled for whether the product was for a chronic condition (*Chronic*) because we assumed that, for chronic conditions, physicians need longer time to switch patients from their previous treatment compared with patients with acute diseases. Table 1 reports the descriptive statistics of the specified variables.

Finally, because we observed repeated events by drug, we adjusted for unobservable variables that are constant over time by clustering standard errors at drug level. We allowed for cases in which physicians had not decided to adopt a product by the end of our observation period and treated these as right censored.

3.2.4 | Comparing adoption rates pre- and post-HTA agency appraisal process implementation and robustness checks

We identified 26 drugs that were launched in the 2 years (i.e., 2009 and 2010) before the HTA agency appraisal process was introduced in 2011 (see Table S2). First, we compared the adoption rates of these drugs with those that underwent the HTA agency appraisal process. Second, we randomly assigned a signal of product quality (positive or negative) to the 26 drugs. We did so 50 times and then estimated 50 accelerated failure time models to test for a difference between our two randomly assigned categories of product quality.

4 | RESULTS

4.1 | Impact of quality ratings on the adoption of new drugs

As seen in the first three columns of Table 2, in which we report effect estimates and odds ratios (ORs), our analysis reveals a significant association between a drug's quality rating and the length of time until a drug was adopted (Model I). When we included only the rating of drug quality as a predictor of time to adoption (Model Ia), drugs with a positive rating were adopted faster, but the effect was not significant. Once we controlled for measures such as prices, promotion, and available scientific evidence (Model Ib) or estimated the full model (Model Ic), drugs with a positive rating were adopted significantly faster compared with drugs with a negative rating (OR: 0.223, p < 0.001, Model Ic). That is, the chance that the physician has adopted the product increases by 348.83% compared with a drug with a negative

TABLE 1Descriptive statistics

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				N (physician-drug
Variable	Definition	Mean	SD	combinations)
Drug quality				
quality	1 if positive quality rating, 0 otherwise	0.42	0.49	31,006
adverseevents	Cumulative adverse events registered until month 6	0.61	0.98	31,006
Prices, promotion	, and available scientific evidence			
price	Price per package	1,278.41	1,972.77	31,006
promostk	Stock of promotional spending (in EUR until Month 6 per physician)	120.74	132.10	31,006
evidint	Cumulative number of international publications, weighted by number of citations until Month 6	8,646.72	11,856.39	31,006
evidnational	Cumulative number of publications in German language until Month 6	22.99	17.70	31,006
Physician charact	eristics and characteristics of the prescribed drug			
experience	Range of prescribed Anatomical Therapeutic Chemical classes ^a	272.63	49.38	31,006
contagion	percent of physicians in social network having adopted	0.15	0.2072	31,006
	previously			
specialist	1 if specialist, 0 otherwise	0.25	0.4347	31,006
group	1 if physician works in group practice, 0 otherwise	1.78	0.4128	30,991
shareSHI	Share SHI Patients	0.92	0.08	31,006
sharechronic	Share chronic patients	0.52	0.11	31,001
shareabove65	Share patients > 65 years of age	0.51	0.13	31,006
age	Physician age	58.18	6.84	31,006
gender	1 if physician gender is female, 0 otherwise	0.69	0.0026	31,006
chronic	1 if drug treats chronic condition, 0 otherwise	0.58	0.4929	31,006

Abbreviation: SHI, statutory health insurance.

^aAccording to European Pharmaceutical Market Research Association (EphMRA) classification Level 4.

rating. The number of registered adverse events, as an alternative measure of quality in the model, was not significantly associated with time to adoption.

When we accounted for the date on which the FJC published each final appraisal document (second set of regression results of Table 2, Model IIc), our analysis again revealed a significant association between the length of time it took for a physician to adopt a drug before versus after this date when we accounted for adverse events, prices, promotion, and the body of scientific evidence. Before a given final appraisal document was published, a drug that went on to receive a positive quality rating was not adopted significantly faster (OR: 0.919) than drugs that went on to receive a negative quality rating. This changed, however, after the publication of the final appraisal document: drugs that received a positive quality rating were adopted significantly faster (OR: 0.3553, p < 0.05) than drugs that received a negative quality rating.

In both models, we identified a number of additional variables that influenced the length of time until a drug was adopted. We focus on the results of Model IIc. The length of time until a drug was adopted was shortened when manufacturers had undertaken a larger amount of marketing activities, as measured by the cumulative stock of promotional spending for a drug (OR: 0.998, p < 0.001). Moreover, the length of time until a drug was adopted was lengthened by higher product price (OR: 1.0008, p < 0.001). The effect sizes here were, however, comparatively small. Some of the physician characteristics and the characteristics of their office-based practices generally also affected the length of time until a drug was adopted. Drugs were adopted later by a physician if a higher percentage of physicians in his or her physician association had previously adopted the drug (OR: 3.705, p < 0.001). There was an association between a drug being adopted sooner and the prescribing physician being a medical specialist (OR: 0.895, p < 0.05) and having a larger share of patients with statutory health insurance (OR: 0.615, p < 0.001). The following factors did not have an impact in this regard: whether a physician was working in a group practice setting (OR: 1.044, p > 0.05); the share of chronic patients seen by an office-based practice (OR: 2.019, p > 0.05); the share of patients older than 65 years of age seen by an office-based practice (OR: 0.76; p > 0.05); physician age (OR: 1.004, p > 0.05); physician gender (OR: 0.969; p > 0.05); or whether the drug in question was for a chronic condition (OR: 0.975, p > 0.05).

		Model Ia		Model Ib		Model Ic		Model IIa	
		Estimate	Odds ratio	Estimate	Odds ratio	Estimate	Odds ratio	Estimate	Odds ratio
Constant		s4.7160 ^{***} (0.6108)	111.7172^{***} (68.2421)	4.3057*** (0.3961)	74.1239^{***} (29.3635)	5.0634*** (1.0772)	158.1244^{***} (170.3294)	1.3364 ^{***} (0.1361)	3.8051*** (0.5177)
Drug quality and date quality	of publication of final appraisal Positive	-0.3189	0.7270	-1.1680**** /////////////////////////////////	0.3110***	-1.5015***	0.2228***		, ,
quality*decision	Negative Positive, after decision	(0.6933) Reference cat	(U.SU4U) egory	(8062.0)	(1601.0)	(0.7/16)	(<000.0)	-0.4816	0.6178
quality*decision	Positive: considerable, after decision Positive: minor, after decision Positive: not quantifiable, after decision Negative, after decision							(0.5812) 3.0203*** (0.0000	(0.3591) 20.4983*** 20.4083
	Positive: considerable, before decision Positive: minor, before decision Positive: not quantifiable, before decision							(0.3260)	(0.0833)
adverseevents	Negative, before decision Cumulative adverse events registered mutil Month 6			0.8977* (0.3018)	2.4541 [*] (0 9615)	1.1346 (0 5966)	3.1099 (1 8555)	Reference cat	gory
Prices, promotion, and	l available scientific evidence			(01(00)					
price	Price (in EUR)			0.0008 [°] (0.0003)	1.0008 (0.0003)	0.0013 (0.0004)	1.0013 (0.0004)		
promostk	Stock of promotional spending (in EUR until Month 6 per physician)			-0.0035^{**} (0.0011)	0.9965^{**} (0.0011)	-0.0053^{**} (0.0019)	0.9948^{**} (0.0019)		
evidint	Cumulative number of international publications, weighted by number of citations until Month 6			-0.00000586 (0.00001855)	0.99999414 (0.00001855)	-0.00003065 (0.00002621)	0.99996935 (0.00002621)		
evidnational	Cumulative number of publications in German language until Month 6			0.0155 [*] (0.0078)	1.0156 [*] (0.0079)	0.0198^{*}	1.0200^{*} (0.0081)		
Physician characterist experience	ics and characteristics of the prescribed drug Range of prescribed ATC classes			×	×	-0.0027 0.0010)	0.9973		
contagion	Percent of physicians in social network having adopted previously					(0.0019) 2.7085*** (0.6163)	(0.0019) 15.0067*** (9.2488)		
specialist	1 if specialist, 0 otherwise					-0.1557	0.8558		
group	1 if physician works in group practice, 0 otherwise					(0.0582 0.0582 (0.0541)	(2010-0) 1.0600 (0.0573)		
shareSHI	Share SHI patients					-0.7783*	0.4592*		
sharechronic	Share chronic patients in physician's practice					0.6264 0.6264 0.6264	(1261.0) 1.8710 (2004 1)		
shareabove65	Share patients > 65 years of age					(006/10)	(760 1 .1)		(Continues)

TABLE 2 Models of new product adoption

$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
$\begin{array}{ccccc} 0.2403 & 1.2717 \\ 0.2403 & 1.2717 \\ (0.5600) & (0.7121) \\ \text{Included} \\ 1.2309 & 0.5488^{*} & 1.7312^{*} & 0.5687^{***} & 1.7659^{***} \\ 0.1804) & (0.2347) & (0.4063) & (0.1252) & (0.2212) \\ -14.870 & -14.870 & -15.685 \\ 30,986 & 31,006 \end{array}$
$\begin{array}{cccccccccccccccccccccccccccccccccccc$
-14,870 -15,685 30,986 31,006

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$(.2366$ 4.8869 2.11° (0.2448) (1.1963) (0.5441) $publication of final appraisal 0.2445^{\circ} -1.0 0.3130) 0.4455^{\circ} -1.0 0.3130) 0.4455^{\circ} -1.0 0.3130) 0.4455^{\circ} -1.0 0.3130) (0.1394) (0.4175) (0.2140) (0.1394) (0.4175) (0.2740) (0.1394) (0.4175) (0.2740) (2.9982) (0.4399) (0.2740) (2.9982) (0.4399) (0.2740) (2.9982) (0.4399) (0.2740) (2.9982) (0.4399) (0.2740) (2.9982) (0.4399) (0.2740) (2.9982) (0.4399) (0.2740) (2.9982) (0.4399) (0.2241) (0.3697) (0.2314) (0.2241) (0.3697) (0.2003) (0.0005^{\circ}) (0.0002) (0.0003) (0.0005) (0.0002) (0.0003) $	(4.5077) (4.5077)	Estimate	Odds ratio	Estimate	Odds ratio	Estimate	Odds ratio
eference category 0.8086 ^{**} 0.4455 ^{***} -1.0 (0.3130) (0.1394) (0.4175) (0.3130) (0.1394) (0.4175) (0.2740) (2.9982) (0.4399) (0.2740) (2.9982) (0.4399) (0.2741) (2.9982) (0.4399) eference category 2005 ^{**} 1.6496 ^{**} 0.5 (0.2241) (0.3697) (0.2514) 0.025 1.0005 ^{**} 0.000 (0.0000) (0.00002) (0.0003) 0.0016 ^{***} 0.984 ^{****} -0.0007 0.00006 (0.0006) (0.0007)		1.3612*** (0.1412)	3.9008*** (0.5507)	1.6733*** (0.1844)	5.3299*** (0.9826)	2.4805*** (0.5472)	11.9469*** (6.5372)
2.3926 ^{***} 10.9421 ^{***} 1.92 (0.2740) (2.9982) (0.4399) (0.2741) (2.9982) (0.4399) (0.2714) (2.9982) (0.4399) (0.2114) (2.9982) (0.2514) (0.2211) (0.3697) (0.2514) (0.2211) (0.3697) (0.2514) (0.002) (0.0005) (0.0003) (0.0006) (0.0006) (0.0007) (0.0006) (0.0006) (0.0007)	0349* 0.3533*) (0.1483)	-1.2377^{***} (0.3448) -0.0695	0.2901*** (0.1000) 0.9329	-0.9282*** (0.2515) -0.3615	0.3952*** (0.0994) 0.6967	-1.2741*** (0.3445) -0.4272	0.2797*** (0.0964) 0.6523
		(0.4648) 2.0880 ^{***} (0.3280)	(0.4336) (0.4336) 8.0688*** (2.6465)	(0.2542) 2.2492 ^{***} (0.2524)	(0.1771) 9.4804*** (2.3928)	(0.2799) 2.4324 ^{***} (0.3902)	(0.1826) 11.3861 ^{***} (4.4426)
Reference category .5005* 0.5 1.5005* 1.6496* 0.5 (0.2241) (0.3697) (0.2514) ailable scientific evidence 0.00 0.0002* 1.0005* 0.00 0.0002) (0.0002) (0.0003) 0.0006) (0.0006) 0.00070	6.8882 *** (3.0303) (3.0303)	2.7871 (0.2833) 0.6675 (0.1465) -0.1840 (0.1931) -0.2530 (0.1852)	16.2333 (4.5987) 1.9494 (0.2857) 0.8320 (0.1607) 0.7764 (0.1438)	2.3100 (0.2523) 0.6595 (0.2496) -0.2650 (0.1292) -1.5413 (0.4471)	10.0748 (2.5418) 1.9338 (0.4827) 0.7672 (0.091) 0.2141 (0.0957)	1.8457*** (0.3472) 0.7385* (0.2993) -0.4602** (0.1757) -2.0921*** (0.4522)	(5.3327 (5.1988) (2.1988) (0.6263) (0.6263) (0.6311 (0.1109) (0.1109) (0.1234 (0.0558)
$ \begin{array}{ccccc} (0.2241) & (0.3697) & (0.2514) \\ allable scientific evidence & 0.00 \\ 0.0005^* & 1.0005^* & 0.00 \\ 0.0002) & (0.0002) & (0.0003) \\ -0.0016^{**} & 0.9884^{**} & -0.00 \\ (0.0006) & (0.0006) & (0.0007) \\ 0.00000 & 0.00006 & -0.0007 \\ \end{array} $	5807* 1.7872*	Reference cate	:gory	0.6887^*	1.9912^{*}	0.7181	2.0505
0.0005* 1.0005* 0.00 (0.0002) (0.0002) (0.0003) -0.0016** 0.9984** -0.00 (0.0006) (0.0006) (0.0007) (0.0005) (0.0005) (0.0007)	(0.4492)			(0.3224)	(0.6420)	(0.3870)	(0.7936)
-0.0016 0.9984 - 0.00 (0.0006) (0.0006) (0.0007) -0.0000457 0.0009543 -0.0000	008** 1.0008**) (0.0003)			0.0002^{*} (0.0001)	1.0002^{*} (0.0001)	0.0004^{*} (0.0002)	1.0004^{*} (0.0002)
	(0.022 0.978) (0.0007) (0.0007)			-0.0017 (0.0004)	0.9983 (0.0004) 1.002 - 00*	-0.0014 (0.0007)	0.9986 (0.0007) 1.002 - 000
(0.00001233) (0.00001233) (0.00001 0.0004 0.0001233) (0.00001 0.0094 0.00	1546 0.00001544 1544) (0.00001544) 0137 1.0138			0.00002184 (0.00000916) 0.0003	1.006 ± 00 (0.00000916) 1.0003	c2c200000 (0.00000931) -0.0006	1.00 $ + 00$ (0.00000931) 0.9994
(0.0067) (0.0067) (0.0082) and characteristics of the prescribed drug	(0.0083)			(0.0039)	(0.0039)	(0.0050)	(0.0050)
-0. (0.0007) 1.3(0.4377) -0.1 (0.0448) (0.0448)	.0005 0.9995 097** 3.7052** 097** 3.7052** 105* 0.216) 1105* 0.8954* 0133 1.0443					-0.0011 (0.0008) 1.3511*** (0.3947) -0.0534 (0.0404) 0.0110	0.9989 (0.0008) 3.8617*** (1.5243) 0.9480 (0.0383) 1.0111

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	Model IIb		Model IIc		Model IIIa		Model IIIb		Model IIIc	
	Estimate	Odds ratio	Estimate	Odds ratio	Estimate	Odds ratio	Estimate	Odds ratio	Estimate	Odds ratio
shareSHI			-0.4870^{**}	0.6145^{**}					-0.3811^{*}	
			(0.1796)	(0.1104)					(0.1656)	0.6831^{*}
										(0.1131)
sharechronic			0.7030	2.0198					0.4337	1.5430
			(0.4320)	(0.8726)					(0.3840)	(0.5925)
shareabove65			-0.2742	0.7601					-0.1953	0.8226
			(0.1736)	(0.1320)					(0.1475)	(0.1213)
age			0.0004	1.0004					0.0003	1.0003
			(0.0007)	(0.0007)					(0.0006)	(0.0006)
gender			-0.0312	0.9693					-0.0320	0.9685
			(0.0190)	(0.0184)					(0.0177)	(0.0171)
chronic			-0.0253	0.9750					-0.4095	0.6640
			(0.2578)	(0.2513)					(0.2708)	(0.1798)
region			Included						Included	
Shape parameter	0.7214^{***}	2.0573***	0.8737^{***}	2.3958***	0.6604^{***}	1.9356^{***}	0.7799****	2.1812	0.9862^{***}	2.6811^{***}
	(0.0903)	(0.1857)	(0.1812)	(0.4340)	(0.1147)	(0.2221)	(0.0975)	(0.2127)	(0.1654)	(0.4435)
Log-likelihood	-11,806		-10,920		-13,324		-10,942		-9,620	
N (physician–drug	31,006		30,986		31,006	31,006	31,006	31,006	30,986	30,986
combinations)										

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Note. Standard errors in parentheses. Abbreviations: ATC, Anatomical Therapeutic Chemical; SHI, statutory health insurance. p < 0.05. p < 0.01.

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We found that the contribution of HTA to the deterministic component of the utility function V_{it} was rather large in relative terms. For example, the effect of an increase of one SD in promotional spending is about one third of the effect of the drug with a positive product quality rating (i.e., 0.291 vs. 1.035).

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The results of Model III suggest that the effect of a positive quality rating is not uniform across the four levels of added health benefit. Indeed, the results of Model IIIc suggest that having a 'considerable added health benefit' leads to a drug being adopted faster after the publication of the final appraisal document (OR: 0.280, p < 0.01) than before publication of this document. In contrast, drugs rated as having a 'minor added health benefit' appear to have the same pattern of adoption regardless. Drugs rated as having a 'not quantifiable added health benefit' (OR: 11.386, p < 0.001) or 'no added health benefit' (OR 6.333, p < 0.001) both take longer to be adopted after the publication of the final appraisal document than they do before this date.

Figure 1 illustrates how the publication of the FJC's final appraisal documents affected the length of time until a drug was adopted. The difference in the length of time until adoption between products that ultimately received a positive quality rating and those that ultimately received a negative quality rating increased over time. For example, the difference in the predicted adoption rate was 2.65% at Month 10 and increased to 13.54% at Month 20 (Model IIc) (Figure 2).

4.2 | Interaction effects between HTA and manufacturers' marketing activities

The FJC's quality rating may interact with the marketing activities of the pharmaceutical manufacturers, for example, price, promotional activity, and with the scientific evidence base (Table 3). Although we found that investment in promotional activities compensated for a negative quality rating (OR: 0.996; p < 0.001), marketing did not seem to affect the time to adoption in the case of a positive quality rating (OR: 0.999; p > 0.05). For prices and the body of scientific evidence, we did not find such effects.

4.3 | Value of HTA quality rating for the pharmaceutical industry

To valuate the quality rating, we calculated the ratio between the coefficients for the rating and for manufacturers' promotional spending, which we obtained from Models Ic–IIc. Table 4 relates these to average spending on promotional activities by the manufacturer in Month 6 after market entry.



Note: FJC announces product quality at month six after market entry.



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FIGURE 2 Drugs rated by HTA agency (2011–2014) versus drugs launched before HTA agency process implemented (2009–2010). HTA, health technology assessment

TABLE 3	Interaction effects of drug quality and date of publication of final appraisal: prices, promotion, and available scientific
evidence	

Drug quality and date of publication of	Baseline (Model II)		Interaction effects (Model II)
final appraisal	Estimate	Odds ratio	Estimate	Odds ratio
Positive after decision	$-1.0349^{*}(0.4175)$	$0.3553^{*}(0.1483)$	1.5087 (1.3101)	4.5211 (5.9233)
Negative, after decision	$1.9298^{***} \left(0.4399\right)$	6.8882*** (3.0303)	2.6091**** (0.3322)	13.5864*** (4.5136)
Positive, before decision	-0.0846 (0.4415)	0.9189 (0.4057)	-1.2935 (1.4991)	0.2743 (0.4112)
Postitive, after decision [*] price			0.0008 (0.0009)	1.0008 (0.0009)
Negative, after decision [*] price			0.0005 (0.0012)	1.0005 (0.0012)
Positive, before decision [*] price			-0.0004 (0.0009)	0.9996 (0.0009)
Postitive, after decision [*] promostk			-0.0008 (0.0015)	0.9992 (0.0015)
Negative, after decision [*] promostk			-0.0039^{***} (0.0010)	$0.9961^{***} (0.0010)$
Positive, before decision [*] promostk			0.0002 (0.0038)	1.0002 (0.0038)
Postitive, after decision [*] evidint			-0.0001(0.0001)	0.9999 (0.0001)
Negative, after decision [*] evidint			0.0000(0.0000)	1.0000 (0.0000)
Positive, before decision [*] evidint			0.0002 (0.0001)	1.0002 (0.0001)
Shape parameter	2.3958		2.8121	
Log-likelihood	-1.09e + 04		-8.45e + 03	
N (physician–drug combinations)	30,986		30,986	

Note. Standard errors in parentheses. Stock of promotional spending in Month 6 after market approval (in EUR per physician). Cumulated evidence weighted by number of citations in Month 6 after market approval.

 $^{***}p < .001.$

We found that, ceteris paribus, ultimately receiving a positive quality rating (Model Ic) had a value equivalent to 283.30 EUR in promotional spending per physician more than the value per physician of ultimately receiving a negative quality rating. Aggregated to the market of 54,000 general practitioners in Germany who are the primary target for 16 of our 21 drugs, the average value of a positive quality rating amounted to an equivalent of EUR 15.3 million in promotional spending during the first 6 months after market entry per drug (see Table 4).

^{*}p < .05.

^{**}*p* < .01.

TABLE 4 Value of product quality rating by health technology assessment agency

		Value/loss per physician in promotional spending	Stock of promotional spending per physician at Month 6
Model I	$\frac{\beta_{positive quality} - \beta_{negative quality}}{\beta_{detstk} per physician in month 6}$	EUR 283.30	Mean: EUR 261.41
Model	$\frac{\beta_{\text{positive quality, before decision} - \beta_{\text{negative quality, before decision}}}{\beta_{\text{negative quality, before decision}} \beta_{\text{detsik}} per physician in month 6}$	EUR 38.45	Median: EUR 225.23
11	a Betstk per physician in month 6	EUR 1,347.59	95% CI [20.05, 396.13]
Model	$\frac{P_{\text{considerable benefit,after decision}}{P_{\text{negative quality,after decision}}}$	EUR 2,228.42	EUR 203.47 [114.66, 292.27]
III	P detsik per physician in month p , drugs with considerable benefit P minor benefit, after decision P negative quality, after decision R	EUR 1,623.50	EUR 249.01 [3.93, 963.62]
	β'_{detsik} per physician in month 6, drugszwith minor benefit $\beta'_{not quantifiable quality,after decision - P negative quality,after decision \beta_{detsik} per physician in month 6, drugs with not quantifiable benefit$	EUR -419.07	EUR 25.73 [15.74, 34.22]

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Note. All values expressed in promotional spending in EUR by Month 6 after market entry.

When we took into account whether the quality rating of the FJC had been published yet (Model IIc), the faster adoption of a drug with a published positive rating compared with a drug with a published negative one was equivalent to an increase in promotional spending per physician of EUR 393.50 or EUR 21.3 million aggregated to the market for general practitioners in Germany. Here, we considered that the speed of adoption for drugs (whether they went on to receive a positive quality rating or not) was roughly the same before the actual publication of the quality rating (EUR 38.45 in promotional spending per physician). When we distinguished between positive quality ratings in terms of the added health benefit a drug was assigned by the HTA agency (Model IIIc), a rating of 'considerable added health benefit' or 'minor added health benefit' appears to be equivalent to an increase in promotional spending per physician of EUR 2,228 and EUR 1,623, respectively, compared with a drug with a published negative quality rating. This may be regarded as the value of the FJC's publication of product quality.

4.4 | Comparing adoption rates before and after the introduction of the HTA agency appraisal process in Germany and robustness checks

When comparing adoption rates of the drugs launched in the 2 years before the HTA agency appraisal process was introduced in Germany with drugs that underwent the process (Figure 2), we found that drugs with a published positive quality rating were adopted significantly faster compared with drugs that had not undergone the appraisal process (OR: 0.429, p < 0.001, see Table S3). The adoption of drugs with a published negative quality rating did not significantly differ from that of drugs that had not undergone the appraisal process.

The placebo regressions were in line with expectations and supported our results. Across the 50 regression estimates, the difference between a randomly assigned positive and negative rating of drug quality became significant only twice (see Table S4).

5 | DISCUSSION

This study shows that the speed with which physicians adopted new drugs was affected by information on the quality of these drugs that was published by the German HTA agency, known as the FJC. First, we found evidence that the FJC's published rating of a drug's quality may play an important role in its adoption by physicians. Drugs that had been rated by the FJC as having an added health benefit were adopted sooner than drugs that had not. Although the FJC may not necessarily provide its audiences with higher quality or more trustworthy information, it has the capacity to synthesize the evidence on the quality of a drug compared with the current standard of care.

Second, the publication of the FJC's quality rating itself would appear to be very important. Six months after a manufacturer has submitted its evidence dossier, the FJC publishes the rating of drug quality and all documents related to the appraisal process, including the results of the appraisal hearing and the comments of the various stakeholders. Before the publication of these documents, drugs that ultimately received a positive quality rating were not adopted more quickly than drugs that ultimately received a negative quality rating. Once the final appraisal document was published, however, uncertainty about the quality of the drugs was reduced and those with a positive rating were adopted faster than those with a negative one. Therefore, we show that the publication of the quality rating itself matters.

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Third, we were able to calculate the per physician value of a positive drug quality rating from the FJC. We demonstrated that effect sizes in manufacturers' promotional spending were substantial (EUR 283.30 per physician in Model Ic; EUR 393.50 per physician in Model IIc; and between 1,623.50 and 2,228.42 in Model IIIc).

In cases where the cost-(effectiveness) of a new technology is uncertain, small changes in how the productivity of a technology is perceived may have a large impact on utilization and expenditure (Chandra & Skinner, 2012). For drugs that have not demonstrated an added benefit compared with the standard therapy, the predicted adoption rate of about 2% by Month 20 suggests that these technologies are still considered by physicians but at a much lower rate than products with an added benefit. Given that prices for products that are found to have no added benefit over standard therapy are negotiated to reflect the price of the standard therapy, the decisions to adopt these products should not lead to considerable changes in pharmaceutical expenditure if they are replacing the current standard of care. As in our sample, about half of the new drugs entering the German market are not rated as having an added benefit (Wieseler, McGauran, & Kaiser, 2019).

Our findings shed light on physicians' adoption of new drugs in the dynamic context of the diffusion of new technology and based on evidence other than physician's own experience. In the majority of studies that have analyzed the adoption of new technologies by physicians, the pharmaceutical industry has been the only type of change agency considered (Gallan, 2004). The information provided by HTA agencies, an additional type of change agency, not only affects total pharmaceutical spending when being used to negotiate prices and/or rebates, but also influences the degree of a product's diffusion because physicians consider this information when deciding whether to adopt a new drug.

Our main results are supported by a comparison of drug adoption times before and after the HTA appraisal process was introduced, as well as placebo regressions as a robustness check. Nevertheless, it would be a mistake to regard the relationships we have identified as causal—not least because identifying the effect of the publication of the quality rating is very difficult from a methodological perspective. Although the drug appraisal process was introduced at a single point in time for all newly launched drugs, the 'population' of drugs before and after this policy change did not remain stable. That is, the 26 drugs that were launched in the 2 years before the appraisal process was introduced differ substantially from the 21 drugs that were launched in the 3 years afterwards (different areas of disease, different market environment, etc.). Moreover, the relatively small sample size of drugs that we observe within our sample of 3,026 physicians does not allow for a meaningful matching (Austin & Stuart, 2015) or balancing approach (Hainmueller, 2012) or a valid identification using difference-in-difference estimates (Abadie & Cattaneo, 2018). Lastly, even if there was a comparable sample of drugs available before the implementation of the HTA process, we would not be able to disentangle (a) the effect of drug quality (because it was not evaluated before the implementation of the HTA process) and (b) the effect of the publication of the drug quality rating. Thus, the most viable option is to concentrate on the difference between drugs with a positive rating and those with a negative rating during the same time period in order to identify the role played by the publication of the drug quality rating.

Our findings are equally important to regulators and the pharmaceutical industry. From the perspective of the latter, a positive HTA quality rating is also equivalent to a substantial amount of investment in marketing. Producing a high-quality dossier for submission to the HTA agency should therefore be seen not only as a compulsory exercise for entering into price negotiations at a later date but also as a way to reach physicians and support a product. Pricing, on the other hand, appears to play only a minor role in physicians' decisions to adopt a new drug in the German market. This is not surprising given that (a) drugs in Germany are fully reimbursed with only a small co-charge for patients and (b) physician drug budgets have little influence on product choice (Fischer, Koch, Kostev, & Stargardt, 2018).

From the regulator's point of view, beyond the impact of HTA decisions on price negotiations, an additional return on investment in HTAs in the form of their impact on a technology's diffusion would be highly welcomed. Such a return makes it easier to justify the high process costs associated with HTA, such as funding an assessment agency, external reviewers, and product-specific experts, as well as the costs imposed on the industry, including those of generating the product dossier and participating in the HTA process (Rogowski, 2013). HTAs have been criticized for having a negative impact on innovation by creating an additional hurdle (Ciani & Jommi, 2014). Our results suggest that the resources needed to conduct HTAs might be partly compensated by products with a positive health benefit being adopted more quickly (Sorenson & Chalkidou, 2012). However, the fact that negative quality ratings may be overcome through greater investment in promotional spending by the industry is a concern from the perspective of policymakers.

Because HTA information is generated in nearly every European country and, in the United States, public and private sector initiatives are emerging to provide comparable information (Hwang et al., 2017; Neumann & Cohen, 2015), our results are highly relevant beyond Germany. We expect physicians elsewhere to react in similar ways because we assume that the factors known to influence the latent utility function of physicians are independent of the health

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What may vary, however, is the type of information assessed in the HTA decision-making process and thus the content of the drug quality rating. Because proof of an added health benefit is presumably the most important information that might change a physician's clinical practice, we would expect similar adoption patterns in countries that publish information only on differences in effectiveness, such as France. In countries that use cost-effectiveness as a criterion, for example, the United Kingdom, economic information often comes with a high degree of uncertainty (Sculpher & Claxton, 2005). At the aggregate level, it has been shown that drug utilization responds strongly to positive HTA recommendations and that effects vary by the administrative level at which HTAs are implemented, that is, centralized processes like those in the United Kingdom versus regionally organized recommendations like those in Spain (Corbacho et al., 2020).

Our results also have important implications for health policy. HTA is an important means of influencing the diffusion of new technologies beyond the promotional activity of manufacturers. Thus, in addition to using the information produced by HTAs for price negotiations, it is important to consider how and when product quality signals are communicated to physicians given the evidence from our study that the publication of a drug's quality rating may alter physician behavior. Thus, regulators may want to consider making the information produced by HTAs more accessible to physicians, which would tend to increase the diffusion of more effective drugs and decrease the diffusion of less effective ones. For example, (extended) abstracts or policy briefs based on the documentation produced by the appraisal process and directed at physicians could provide useful and more easily digestible information. In addition, information could be provided through prescription information technology (IT) systems, which has been under discussion in Germany.

Our study has several important limitations. First, we focus on the first time a product is used by a physician rather than its use over time because the time horizon of our study is limited to a maximum of 3.5 years. Second, one could argue that our analyses do not account for information signals about drug quality originating from the market approval process, particularly aspects related to dosing and route of administration. However, if we control for priority status assigned by the US FDA, this variable turns out not to be significant in our model. Future research could also explore diffusion by analyzing not only the overall adoption decision (intensive margin) but also the level of adoption (extensive margins).

6 | CONCLUSION

The findings of our study suggest that information signals related to product quality that are published by HTA agencies have consequences for the adoption of drugs by physicians beyond their direct effect on negotiations/pricing. As expected, products that received a positive quality are adopted faster. However, it is also the publication of the quality rating by the HTA agency itself that affects adoption behavior. For regulators and payers, this means increased returns beyond the use of HTA information in price negotiations. For manufacturers, producing a high-quality dossier to submit to an HTA agency should therefore be seen not only as a compulsory exercise to achieve higher prices but also as a way to support the diffusion of their products by providing physicians with information about the products' quality. HTA agencies could extend their communication policies to target physicians more directly to increase the speed with which more effective drugs are adopted.

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CONFLICT OF INTEREST

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