Indication-based pricing for multi-indication drugs

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Many pharmaceutical drugs have multiple indications, for which they offer a varying degree of benefit for patients. Yet, in the current US pricing system, the price of the drug is the same regardless of the indication for which it is prescribed. This uniform pricing policy can deter the payer from providing coverage for low-value indications, if the price is high relative to the potential benefit for patients, which can reduce patients' access to the drug. It can also deter the drug manufacturer from investing in obtaining FDA approval for new indications, as the lack of flexibility in pricing can result in too low demand (and thus profits) to recoup fixed investment costs. Indication-based pricing has been proposed as a new pricing mechanism for multi-indication drugs allowing the price to differ according to the indication, to better align the price of the drug to its value. In this paper, we analyze the effect of indication-based pricing in comparison to uniform pricing on the drug manufacturer's profit and investment incentives, the patient demand and utility, the payer's coverage incentives, and the payer's objective. Under uniform pricing, we consider both the cases when the price can *vs.* cannot be adjusted upon introduction of a new indication. We find that the drug manufacturer earns higher profits under indication-based pricing than under uniform pricing. Moreover, indication-based pricing improves incentives for the manufacturer to invest in a new indication and for the payer to cover the drug. If the fixed investment cost is high, indication-based pricing also benefits patients and the payer's objective. Otherwise, the patient demand, patient utility and payer's objective may be lower under indication-based pricing. Hence, payers who value the patient utility should carefully consider the trade-offs involved in implementing this pricing system and where the bottlenecks are under uniform pricing.

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1. Introduction

US prescription drug spending has increased dramatically over the past two decades and is expected to continue growing at a rapid pace. Conti et al. (2021) estimate that the total drug spending will grow from about $500 billion in 2018 to $863 billion in 2028, representing about 13.9% of national health expenditures. A main factor contributing to this spending growth is the high price of certain drugs. High drug prices not only strain payers' budgets, they also reduce access to medication for many consumers (Congressional Budget Office 2022). Indeed, three in ten adults report not taking

their medicines as prescribed because of the cost (Kirzinger et al. 2019).

To try and address the high prices of pharmaceutical drugs, health policy makers have been proposing to move towards "value-based pricing", that is, a better match between the price of medications and the value they provide to patients. Prescription drugs are priced in the US primarily on the basis of what the market will bear (Kesselheim et al. 2016), while European countries often consider the *value* of the drug in their price negotiations with drug manufacturers (Vokinger and Kesselheim 2022). For example, in the UK, cost-effectiveness analysis is used to determine an appropriate price for a drug according to the Quality-Adjusted Life-Years (QALYs) gained from treatment. In Germany and Switzerland, the added benefit of the drug, compared to other drugs, influences the price (Vokinger and Kesselheim 2022). Value-based pricing may also help manage the uncertainty in the value that a treatment provides to a patient, through the use of outcomes-based contracts, which link the price to the actual treatment outcome (Mytelka et al. 2020).

Among proposals of value-based pricing for drugs, indication-based pricing has been discussed to specifically address drugs with multiple indications (Sachs et al. 2017; Pearson et al. 2018). Indeed, a pharmaceutical drug may have more than one indication, and the same drug usually does not provide patients the same benefit across indications. Multi-indication drugs have become increasingly common, particularly in oncology (Vokinger and Kesselheim 2022). IQVIA (2018) reports that "of all targeted treatments in oncology, 75% are used in multiple indications". Yet, in the current US drug pricing system, the price of a drug is the same regardless of the indication for which it is prescribed (Bach 2014). Bach (2014) gives the example of nab-paclitaxel (Abraxane) which "improves median survival in metastatic breast cancer by 0.18 years, but the improvement in survival for metastatic non–small lung cancer (NSCLC) is less than half that (0.08 years). The treatment costs are similar for each indication, both per month and over the average duration of treatment." Chandra and Garthwaite (2017) detail another example for the drug cetuximab (Erbitux): "When used as first line treatment for recurrent or metastatic squamous-cell carcinoma of the head and neck, cetuximab is associated with a median survival gain of 0.23 years, and it costs $10,000 per month. (...) When cetuximab is used to treat locally advanced squamous cell carcinoma, by contrast, it offers a median survival gain of 1.64 years. Under uniform pricing, patients (...) also pay $10,000 per month." The key idea behind indication-based pricing is to allow the price of a drug to vary according to the indication for which it is prescribed, to better align the drug price to the expected benefit that the drug provides for patients. Namely, the manufacturer would be paid more when the drug is used for a "high-value indication" than when it is used for a "low-value indication". Indication-based pricing is reportedly being tested by ExpressScripts and CVS Caremark (Loftus 2015; Staton 2015; Kaltenboeck et al. 2020).

Supporters of indication-based pricing for multi-indication drugs appreciate the improved transparency of this pricing system, which would help "rationalize drug pricing" because prices would be better linked to the value that the drug provides for patients (Bach 2014). Because prices would be better aligned with value, payers may be more likely to cover the drug for a variety of indications. Improved coverage may make the drugs more affordable for patients. Indication-based pricing may also reduce prices for low-value indications, which would then further facilitate patient access. Thanks to improved patient access, societal welfare could increase (Preckler and Espín 2022). In addition, indication-based pricing may improve incentives for manufacturers to invest in research and development (R&D) and to launch new indications for an existing drug, regardless of how their value compares to the value of the existing indication (Preckler and Espín 2022). However, critics warn that indication-based pricing may also have some drawbacks. Discriminating price according to value could help the manufacturer extract more profit, leaving no surplus for patients. The price of high-value indications may increase, which could hurt coverage and access for the patients who stand to benefit the most from the drug (Chandra and Garthwaite 2017), and thus could lower social welfare. Therefore, it remains unclear what the overall effect of indication-based pricing would be. In this paper, we aim to use an analytical model to answer this question.

Consider the decision that a patient with a prescription for a multi-indication drug must make. While the drug is medically indicated for the patient's condition, the price may be quite high—oncology drugs are often very expensive. Even if the drug is covered by the patient's insurance plan, the patient usually bears a significant fraction of the cost as co-insurance, which can make the drug difficult to afford. For example, Caremark lists both nab-paclitaxel (Abraxane) and cetuximab (Erbitux) on Tier 4 or 5 of its formulary, as specialty drugs, for which the co-insurance is 30% (Caremark 2022, pp. 5, 21). If the drug is not covered, the patient can still choose to buy it and pay the entire price out-of-pocket. The patient must thus balance her cost share with the anticipated benefit she stands to receive from the treatment, to decide whether or not to obtain the drug. While this decision is complex and includes consideration of many factors unique to each patient, one can reasonably expect that the demand for the drug decreases with the price. We introduce a utility-maximization model for heterogeneous patients that yields a demand function for the drug.

Now, consider the decisions faced by the payer. The payer's mission is to maintain the health of its beneficiaries, but it must also contain costs. For each indication of a drug, the payer must decide whether to offer coverage.[1] Covering an indication would improve access and thus benefit patients' health status. It may also indirectly benefit the payer due to avoiding future healthcare

[1] Through the use of coverage restrictions and pre-approval, a payer can designate which indications are covered for a given drug; see for example the Aetna criteria for approval of Abraxane, listing the covered indications `https://www.aetna.com/cpb/medical/data/800_899/0834m.html`.

costs, if negative health outcomes can be prevented by the use of the drug. However, coverage is costly; it also increases demand for the drug, and thus the total expenses. The payer's coverage decision, for each indication, must resolve this trade-off. We model the payer as deciding coverage so as to maximize a combination of its own payoff and the patients' utility.

Finally, consider the decisions faced by the drug manufacturer who has a drug with both an indication approved by the Food and Drug Administration (FDA), and another indication that has not yet been FDA-approved, but has been identified for example from off-label use (American Cancer Society 2015). On the one hand, the manufacturer must decide whether or not to invest in going through the FDA approval process for the second indication, a lengthy and costly process. The investment would open a new market for the drug but incurs a large fixed cost. The drug manufacturer makes the investment only if it anticipates that the additional profits earned after introduction of the new indication exceed the investment cost. On the other hand, the manufacturer must decide the price of the drug. A higher price brings in more revenue for each filled prescription (variable production costs are usually very low for pharmaceutical drugs) but could reduce demand, especially if the high price causes the payer to deny coverage for the drug.

Under indication-based pricing, the price of the drug for each indication can be set independently—i.e., a high-value indication is priced higher than a low-value indication. In contrast, under uniform pricing, the drug must be priced at the same level for all available indications. The sequencing of indication approvals may play a role. In certain contexts, it may be practically difficult for the manufacturer to increase the price of a drug upon introducing a new indication because increased volumes may lead to an expectation of price decreases (Lawlor et al. 2021). Mestre-Ferrandiz et al. (2015) report that in some European countries "given that prices can seldom increase, the launch price sets the maximum price for additional indications. Indeed, this price will then usually decrease as new indications are available". In such cases (e.g., in European countries with strong regulations), the new indication must thus be priced at the price of the currently available indication. However, in other contexts (e.g., in the US), the manufacturer can have more pricing flexibility and would thus be able to adjust the uniform price should a new indication be approved—price hikes of existing drugs are not uncommon in the US. For example, Bennette et al. (2016) empirically examine post-launch prices of orally administered anticancer drugs recently approved by the FDA; they find that prices rose an additional 10 percent with each supplemental indication approved by the FDA. Chandra and Garthwaite (2017) highlight that under uniform pricing the manufacturer would select the profit-maximizing price. In either case, the price that the manufacturer anticipates setting, and the ensuing profits, play a role in the initial decision of whether or not to invest in the new indication approval.

Our goal is to analyze the effect of indication-based pricing for multi-indication drugs on patients, payer and drug manufacturer. We propose to answer the following research questions: are the patient, the drug manufacturer and the payer better or worse off under indication-based pricing compared to uniform pricing? How does indication-based pricing affect the manufacturer's incentives to launch new indications and the payer's incentives to offer coverage? The answers to these questions could impact both health policy makers and pharmaceutical executives in determining whether or not to work toward implementing indication-based pricing. For health policy makers, it is crucial to understand if patients and payer necessarily benefit from implementing this new pricing system. For pharmaceutical firms, it is important to measure how such a pricing scheme could impact future profits and the benefit of new indications' R&D investment.

To achieve this goal, we take a model-based approach. We introduce an analytical model that incorporates heterogeneous utility-maximizing patients deciding whether to obtain a drug, a welfare-maximizing payer deciding whether to cover each indication, and a profit-maximizing drug manufacturer deciding whether to invest in getting a new indication approved and how to price the drug. We consider both indication-based pricing, where the manufacturer can set the price of each indication independently, and uniform pricing, where both indications are priced at the same level. For uniform pricing, we analyze the case where the price can be adjusted upon introduction of the new indication, as well as the case where it cannot. We investigate how the pricing mechanism affects the manufacturer's profit and incentives to invest in a new indication, the payer's incentives to offer coverage, the patients' utility and access to drugs, and the payer's objective.

We find that the drug manufacturer obtains a higher profit under indication-based pricing than under both types of uniform pricing. Moreover, indication-based pricing improves the manufacturer's investment incentives and the payer's coverage incentives. When the investment fixed cost is high enough so that the manufacturer would invest in the new indication only under indication-based pricing, this new pricing scheme improves both the patient utility and the payer's objective. However, when the investment fixed cost is less high, so the new indication would receive investment even under uniform pricing, indication-based pricing may hurt the patient utility, the patient access to drugs, and the payer's objective. When the uniform price *cannot* be adjusted, indication-based pricing worsens patient access, patient utility and payer's objective if the new indication offers a higher value than the currently available indication. When the uniform price *can* be adjusted, indication-based pricing worsens patient access, patient utility and payer's objective if the gap in value between the two indications is not too large and/or the low-value indication has a large enough market size. Hence, the payer should carefully consider where the uniform pricing bottlenecks are and the consequences for beneficiaries of implementing indication-based pricing for multi-indication drugs.

2. Literature

The health policy and health economics literatures discuss indication-based pricing from a qualitative perspective, analyzing implementation issues in different countries and possible solutions; see, e.g., Pearson et al. (2017); Cole et al. (2018); Towse et al. (2018); Campillo-Artero et al. (2020); Preckler and Espín (2022) for reviews of this literature. These papers, and references therein, tend to view indication-based pricing in a positive light, emphasizing the potential improved access to drugs for patients and the benefit of aligning the price of a drug indication to its value. They recognize that practical implementation is not straightforward, and they review how indication-based pricing could fit in the system in place in different countries. Bach (2014) assesses that indication-based pricing could help lower prices for low-value indications, and thus could be an effective step to pay rational prices for expensive drugs for which efficacy varies across conditions. Mestre-Ferrandiz et al. (2018) opine that indication-based pricing should be beneficial, but recognize that the effectiveness of the pricing mechanism hinges upon how prices are set. Cole et al. (2020) survey a range of stakeholders among industry, regulators, payers, and academics, and find that a large majority (78%) believe that indication-based pricing would be a good thing, while more than half of respondents (57%) think that all stakeholders stand to gain from indication-based pricing. One of the only papers casting some doubt on the benefits of indication-based pricing is Chandra and Garthwaite (2017). Chandra and Garthwaite are concerned that the positive assessment of indication-based pricing in prior literature relies on the misguided expectation that low-value indications would see their prices drop but high-value indications would remain at the same price level. Instead, Chandra and Garthwaite believe that indication-based pricing would result in "higher prices for patients who benefit the most, higher utilization by patients who benefit least, higher overall spending, and higher manufacturer profits." As a price discrimination tool, indication-based pricing would thus help extract all surplus from patients. In an effort to explain the contrast of opinions in Chandra and Garthwaite (2017) and in Bach (2014), Cole et al. (2018) and Campillo-Artero et al. (2020) recognize that the price starting point is crucial, i.e., whether the uniform price is set initially according to the high- or low-value indication. Campillo-Artero et al. (2020) also state that more economic theory-based assessments of the pros and cons of indication-based pricing are needed to capture their intricacies and specificities, given the lack of publicly available data on any practical application of indication-based pricing. Our paper aims to fill this gap.

A few health economics papers have taken a modeling approach for understanding the effect of a pricing system for a medical treatment when different patients do not benefit from the treatment equally. Levaggi and Pertile (2020) consider a two-stage process. In the first stage, a firm decides the level of investment; in the second stage, it selects the fraction of patients (equivalently, the set of indications) who receive the treatment. The regulator sets the price either equal to the benefit

of the treatment for the marginal patient, or in a way that varies across subgroups of patients to reflect effectiveness. The authors find that the pricing scheme that is equivalent to indication-based pricing leads to first-best outcomes but increases expenditures and lowers consumer surplus. Levaggi and Levaggi (2021) consider uncertainty in the treatment outcome and assume that the firm first selects the price, and a regulator then selects the patients (i.e., the indications) who can receive the drug, so as to maximize consumer surplus. They find that the number of patients getting the drug is only half that at the first best. Hlávka et al. (2021) consider a setting where the payer and the manufacturer use a Nash bargaining process to determine both the price of the drug and which indications are covered. The authors find that uniform pricing can lead to the first-best outcome in efficient markets, but indication-based pricing can be helpful in the presence of market failures. In contrast to these papers, and aligned to the US market for pharmaceuticals, we consider simultaneously a decision-making role for (i) heterogeneous patients who decide whether or not to obtain the drug (with or without coverage) to maximize their utility, (ii) a payer who decides whether or not to cover the drug to maximize the combination of patient and payer utility, and (iii) a manufacturer who makes investment decisions and is able to set the price to maximize profits.

This paper is most closely related to a growing body of literature in healthcare operations management that studies the role of new pricing mechanisms for pharmaceuticals. In this body of literature, several papers focus on outcomes-based pricing. Adida (2021) studies the impact of outcomes-based pricing and finds that for high-risk drugs, a pricing mechanism that does not require any payment when the treatment does not yield expected results would only benefit the drug manufacturer due to the higher price. Xu et al. (2022) analyze the effect of outcomes-based pricing on formulary placement and find that it can increase payer spending. Olsder et al. (2022) consider outcomes-based pricing as a mechanism to improve access to orphan drugs when government allocates subsidies. Regarding other drug pricing mechanisms, Li and Wu (2022) empirically study the price effect of price ceiling policies for pharmaceuticals. King et al. (2019) analyze how copay coupons affect patients, insurance companies, and drug manufacturers. We contribute to this stream of literature by focusing on indication-based pricing for multi-indication drugs.

3. Model

Our model builds upon that in Adida (2021) but is tailored to address the specific context of indication-based pricing for multi-indication drugs. We consider the interaction between a drug manufacturer, a payer, and a population of patients insured by the payer. The manufacturer has developed a drug for which one indication, indication A, has received FDA approval. There are n_A patients in the considered population who are prescribed the drug for indication A. We model these patients as heterogeneous, with a benefit to be gained from treatment that is uniformly distributed

in $[0, v_A]$. The drug manufacturer is aware of another possible indication for the drug: indication B, which has not received FDA approval yet. Going through this process (FDA application, clinical trials, etc.) would incur a fixed investment cost $I > 0$. There are n_B patients in the population who are eligible to be prescribed the drug for indication B; these patients do not overlap with the indication A patients. We model the benefit to be gained from treatment for indication B as uniformly distributed in $[0, v_B]$. Variable production costs tend to be small compared to fixed drug development and approval costs, and pricing decisions in the pharmaceutical industry are typically not driven by variable costs, so for ease of exposition we assume that the variable production cost is zero. This is a common assumption in the literature (e.g., Hlávka et al. 2021).

We consider two possible pricing systems: indication-based pricing and uniform pricing. Under indication-based pricing, each approved indication of the drug may be priced at a different level. Under uniform pricing, there must be a unique price of the drug regardless of the indication for which it is prescribed. We consider two subcategories within uniform pricing: adjustable and non-adjustable price (which setting applies depends in large part on the country and the strength of drug pricing regulation). Under uniform pricing with adjustable price, after indication B is approved, the manufacturer is free to adjust the (common) price of the drug for both indications. As a result, the price that applied to indication A when it was the only approved indication could increase, decrease, or stay the same once indication B is approved. Under uniform pricing with non-adjustable price, the drug manufacturer cannot adjust the price that had been in place for indication A, and thus indication B must be sold at that same pre-existing price.

Consistent with the US environment, we model the drug manufacturer as having pricing power, and able to set the drug price to optimize its profit (albeit possibly under the no-adjustment constraint in the case of uniform pricing with non-adjustable price). First, the manufacturer decides whether or not to invest in indication B. Second, the manufacturer sets the price for any FDA-approved indication, according to the pricing system described above. Next, the payer decides whether or not to cover each approved indication. Finally, each patient suffering from an approved indication decides whether or not to fill her prescription for the drug, according to a utility-maximization principle. If the indication corresponding to the patient's condition is covered by the payer, the patient pays a fraction $\beta < 1/2$ of the drug price as co-insurance. If the indication is not covered, the patient can still choose to purchase the drug and pay the entire price out of pocket.

The payer makes the coverage decision in order to maximize the payer's objective, which is composed of the cumulative patient utility and the total payer utility. A given patient's utility is normalized at zero if the patient does not purchase the drug; otherwise it consists of the value this patient gains from treatment after deducting the out-of-pocket cost. For every patient who obtains the drug, the payer earns a utility that may be composed of up to two elements. First, the payer

may share the cost of the drug, by paying the fraction $1-\beta$ of the drug price if the indication is covered. Second, the payer also receives an indirect benefit, e.g. through reduced future healthcare costs. We model this benefit as a multiple $k>0$ of the value gained by the patient. That is, if the patient anticipates gaining utility v from treatment, the payer anticipates gaining utility kv. The total payer utility is the sum of the utilities associated with each patient purchasing the drug.

We use the following tie-breaking rules. When the patient is indifferent between getting the drug or not, she does not get the drug. When the payer is indifferent between covering the drug or not, it does not offer coverage. When the drug manufacturer is indifferent between investing in indication B or not, it does not invest. When the drug manufacturer is indifferent between several optimal prices, it selects the lowest possible optimal price.

3.1. Discussion of Modeling Assumptions

Our model makes a number of modeling assumptions aiming at (i) considering a setting comparable to what other papers in the literature have considered so we can compare findings, and (ii) maintaining analytical tractability while still capturing the main trade-offs. We model the patient's cost share as a co-insurance with rate β. In practice, some patients are subject to a fixed co-payment (fixed amount independent of the drug price) instead of a co-insurance. However, for specialty drugs, the use of co-insurance is common, (e.g., Caremark 2022). In addition, we do not model the co-insurance rate as a decision variable of the payer. Indeed, the payer usually sets co-insurance rates in advance based on tiers in a formulary, and specialty drugs, when covered, tend to be located on the highest tier of the formulary, where the co-insurance rate is set and does not vary for different drugs on the tier. Both assumptions have been used in the literature (e.g., Adida 2021).

Similar to Adida (2021), we model the value gained from treatment as heterogenous across patients (uniformly distributed random variable). The patient's decision-making process on whether to obtain the treatment is complex and includes many individual factors, such as sensitivity to side-effects, illness severity, interactions with other drugs, presence of co-morbidities, etc. We summarize these factors together with the expected benefit of the drug into a single quantity represented by the patient's value gained from treatment. Because a patient, with the help of her physician, is able to observe idiosyncratic factors, she can anticipate this value before making the purchase decision. Hence, we assume that the patient observes the value she stands to gain from treatment before making the decision to purchase the drug. The value gained in case of no treatment is normalized at zero without any loss of generality. King et al. (2019) take a similar approach. Like Adida (2021), we use the uniform distribution for analytical tractability, as it gives rise to a demand function that is linear in the price, but still captures the key property that a higher price will restrict access to the drug. For each indication, the maximum gain from treatment (i.e., v_A and

v_B) can be estimated by noting that the average gain from treatment equals respectively $v_A/2$ and $v_B/2$. Cost effectiveness studies quantify the average benefit of a drug as the average QALY gained from treatment. QALYs can then be converted into dollars using a common valuation of \$100,000–150,000 per QALY (Institute for Clinical and Economic Review 2020).

We assume that the maximum value gained from treatment for indication B, denoted v_B, is deterministic. In practice, v_B can be known before the FDA approval process because of limited off-label use of the drug.[2] Indeed, effectiveness studies on the off-label use of a drug are common (e.g., Saiyed et al. 2017). According to Wittich et al. (2012), "Medical journals and their readers may have a keen interest in original observations related to this [off-label] form of drug use. (...) A journal may publish OLDU [off-label drug use] articles on drugs' effects and adverse effects related to indications for which FDA approval may never be sought." Clinical trials and the official drug approval process are necessary for a new indication to widen the market size even if the potential value to patients of the drug under this indication is known. Indeed, many drugs are used off-label not for clinical reasons or due to uncertainty on the drug potential, but simply for financial reasons: "To add additional indications for an already approved medication requires the proprietor to file a supplemental drug application, and, even if eventually approved, revenues for the new indication may not offset the expense and effort of obtaining approval. (...) For these financial reasons, drug proprietors may never seek FDA approval for a new drug indication" (Wittich et al. 2012).

Contrary to papers studying outcomes-based pricing for pharmaceuticals, such as Adida (2021); Xu et al. (2022); Olsder et al. (2022), we do not model the outcome of treatment as stochastic (failure or success). With outcomes-based pricing, the patient and/or payer pay less for the drug when the drug treatment "fails", and so it is necessary to consider the possibility of treatment failure. Similarly, these papers also model the patient as risk-averse/seeking and/or loss-averse because the primary goal of outcomes-based pricing is to reduce the patients' exposure to the risk of paying for a treatment that fails. These considerations are no longer relevant when payment is not contingent on treatment outcome. Similarly to our paper, King et al. (2019) model a patient's decision of selecting among two possible drug treatments by maximizing a linear utility, without modeling the possibility of treatment failure, and assuming patients are risk neutral.[3]

We model the payer as gaining a benefit from treatment that is proportional to the patient's, with multiplier k. Adida (2021) considers a similar model as an extension to the main model

[2] Appendix C considers explicitly off-label use of the drug under indication B. While off-label use reduces the incentives to invest in the new indication, qualitatively our results continue to hold in this setting as long as off-label use is not too extensive; see Appendix C for details.

[3] Note that in our model, the patient's decision of obtaining the drug or not would be the same if we considered risk aversion, as the condition for purchase, $v - \beta p > 0$, is equivalent to $U(v - \beta p) > U(0) = 0$ for an increasing concave patient utility function $U(\cdot)$.

presented in her online Appendix F (the main model assumes a constant payer's benefit). The intuition behind including this term is that when the patient gains a higher benefit from treatment, she will likely incur less healthcare costs in the future (e.g., via fewer Emergency Department visits, hospital stays, or other healthcare procedures to relieve symptoms) which lowers the payer's future healthcare expenses. The value of k can be affected (i.e., lowered) by the potential need for future healthcare expenses associated with the drug treatment itself (e.g., to relieve side effects). Adida (2021) also justifies this benefit as "indirect cost savings for society due to avoiding a loss of productivity, and a mission-driven benefit to the payer from a beneficiary's good health status." We use a proportional benefit rather than a fixed one to link the patient's gain to the payer's. We recognize that the specific value of parameter k is difficult to estimate in practice. This said, several of our main results do not depend on k. Other results depend not necessarily on the specific value of k, but rather on whether k is low, intermediate or high, and we provide analytical results for all possible ranges to understand the effect of this parameter value.

Similar to Adida (2021), we model the payer as selecting its coverage decision so as to maximize the combination of payer utility and patient utility. The payer thus balances the total cost of the drug charged by the drug manufacturer with the benefits gained by both the patients (through the value gained from treatment) and the payer (through the proportional benefit mentioned above). To resolve this trade-off, the payer takes into account the effect of coverage on the total number of patients obtaining the drug. Even a private insurer can be modeled as internalizing the patient's out-of-pocket because otherwise, the extent of coverage would be drastically reduced (limited to cases when the payer saves money by providing coverage) and in the long-term, this would hurt the payer's market share as patients would be likely to switch to other insurers.

Our model does not consider competition with other drugs for either indication. This assumption is aligned with other papers on indication-based pricing, such as Bach (2014); Chandra and Garthwaite (2017); Levaggi and Pertile (2020); Levaggi and Levaggi (2021); Hlávka et al. (2021), which allows us to place our findings into relevant context. Like ours, these papers ignore competitive effects to better isolate the role of the pricing system. In addition, many oncology drugs benefit from very little competitive pressure on prices (Bennette et al. 2016). Understanding how a competitive environment affects the benefit of indication-based pricing in detail is beyond the scope of this manuscript and is left as a direction of future research.

Finally, our main model does not incorporate any stochasticity in the FDA approval process, i.e., we do not consider the possibility that FDA approval could be denied for the new indication. An extension analyzed in Appendix B shows that all our results continue to hold when FDA approval is denied with a known probability.

4. Analysis

In this section, we derive the optimal decisions made by each agent. Using backwards induction, we start with the patient's drug purchase decision. Then, we investigate the payer's coverage decision. Next, we analyze the drug manufacturer's pricing decision, and finally, the drug manufacturer's investment decision on indication B's approval, under indication-based pricing, uniform pricing with adjustable price, and uniform pricing with non-adjustable price.

4.1. Patients

We first analyze each patient's drug purchase decision, for a given price and coverage by the payer. As described in Section 3, the patient seeks to maximize her utility, and thus purchases the drug if doing so yields a positive utility, as she gains a utility normalized to zero without purchase. Hence, a patient who would gain benefit v from treatment purchases the drug iff $v - \bar{\beta}p > 0$, where $\bar{\beta} = \beta$ if the indication is covered and $\bar{\beta} = 1$ if the indication is not covered. The following result uses this observation to derive the demand function as well as the cumulative patient utility.

LEMMA 1. *Consider a drug indication with market size n_i, price p and value to patients uniformly distributed on $[0, v_i]$. The demand is $(n_i/v_i)(v_i - \bar{\beta}p)^+$, where $\bar{\beta} = \beta$ if the indication is covered and $\bar{\beta} = 1$ if the indication is not covered. Moreover, the cumulative patient utility is*

$$\Pi_{patient} = \begin{cases} 0 & \text{if } v_i \leq \bar{\beta}p \\ \frac{n_i}{2v_i}(v_i - \bar{\beta}p)^2 & \text{else.} \end{cases} \tag{1}$$

The above result shows that for any given indication, the demand function is linear and decreasing in the price, and the slope is steeper without coverage than with coverage.

4.2. Payer

We now consider the payer's coverage decision for an indication, for a given price set by the manufacturer. For each patient who obtains the drug and receives value v from treatment, the payer receives utility $kv - (1 - \bar{\beta})p$. We denote Π_{payer} the cumulative payer utility. For a drug indication with market size n_i, price p and value to patients uniformly distributed on $[0, v_i]$, the cumulative payer utility is 0 if $v_i \leq \bar{\beta}p$ (as there is no demand), and otherwise it is equal to

$$\Pi_{\text{payer}} = n_i \int_{\bar{\beta}p}^{v_i} (kv - (1 - \bar{\beta})p) \frac{1}{v_i} dv = \frac{n_i}{v_i}(v_i - \bar{\beta}p)^+ \left[\frac{k}{2}(v_i + \bar{\beta}p) - (1 - \bar{\beta})p \right].$$

The payer decides whether or not to cover the drug to maximize its objective, composed of the payer benefit and patients' utility. The payer's objective is given by $W = \Pi_{\text{patient}} + \Pi_{\text{payer}}$, i.e.,

$$W = \frac{n_i}{v_i}(v_i - \bar{\beta}p)^+ \left[\frac{k}{2}(v_i + \bar{\beta}p) - (1 - \bar{\beta})p + \frac{1}{2}(v_i - \bar{\beta}p) \right] = \frac{n_i}{v_i}(v_i - \bar{\beta}p)^+ \left[\frac{k+1}{2}(v_i + \bar{\beta}p) - p \right].$$

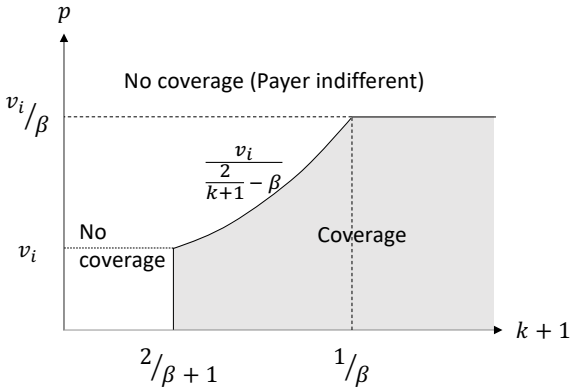
LEMMA 2. *Consider a drug indication with price $p > 0$ and value to patients uniformly distributed on $[0, v_i]$. The payer's coverage decision is as follows:*

(i) If $k+1 \le 2/(\beta+1)$ the payer does not cover the indication.

(ii) If $2/(\beta+1) < k+1 \le 1/\beta$, the payer covers the indication iff $p < v_i/(2/(k+1)-\beta)$.

(iii) If $k+1 > 1/\beta$, the payer covers the indication iff $p < v_i/\beta$.[4]

Figure 1 **Payer's optimal coverage decision.**



Lemma 2 is illustrated in Figure 1, and can be interpreted as follows. When deciding coverage, the payer must balance the total cost of the drug, which increases as the demand rises, with the benefit brought to the payer (via parameter k) and to the patients for every filled prescription. When k is small (i.e., $k+1 \le 2/(\beta+1)$), the payer's benefit from treatment is small, and thus the payer chooses not to cover the drug to limit demand and thus keep costs down. When k is intermediate (i.e., $2/(\beta+1) < k+1 \le 1/\beta$), the indication is covered as long as its price is not too high. When k is large (i.e., $k+1 > 1/\beta$), the payer's benefit from treatment is large enough that the payer offers coverage for any price (with non zero demand). In the conditions defining the three cases, parameter k is connected to β because $k+1$ is a measure of how valuable the drug is to the payer, and $1-\beta$ is a measure of how costly covering the drug is. When deciding coverage, the payer must resolve a (nonlinear) trade-off between the cost (i.e., $1-\beta$) and the benefit (i.e., $k+1$). For example, as β becomes larger, the payer's cost share of the drug shrinks, and so the payer can demand a more moderate value of the benefit $k+1$ to broadly offer coverage (i.e., the range of "large" k expands). Conversely, when β is small, the payer bears a larger fraction of the drug price, and thus is less inclined to offer broad coverage. Hence, k would need to be very large for the payer to offer coverage at any price. In this case, reasonable values of parameter k are more likely to match the case of "small" k, where no coverage is offered.

[4] Regardless of k, when $p \ge v_i/\beta$, the payer is indifferent as demand is zero, but, by the tie-breaking rule, elects not to cover the indication.

4.3. Drug Manufacturer: Case of Indication-Based Pricing

The drug manufacturer's decisions depend on the pricing mechanism. In this section, we first analyze the optimal pricing decision, then the investment decision, under indication-based pricing. Under indication-based pricing, the drug manufacturer can set the price for each indication independently. The price p for indication i is selected so as to maximize profit from this indication, given by $\Pi^i_{\text{manufacturer}} = p \cdot (n_i/v_i)(v_i - \bar{\beta}_i p)^+$ (using Lemma 1), where $\bar{\beta}_i = \beta$ if the indication is covered and $\bar{\beta}_i = 1$ if the indication is not covered (for ease of exposition, we omit to state explicitly the dependency of $\bar{\beta}_i$ on price). The next result establishes the pricing decision for a single indication.

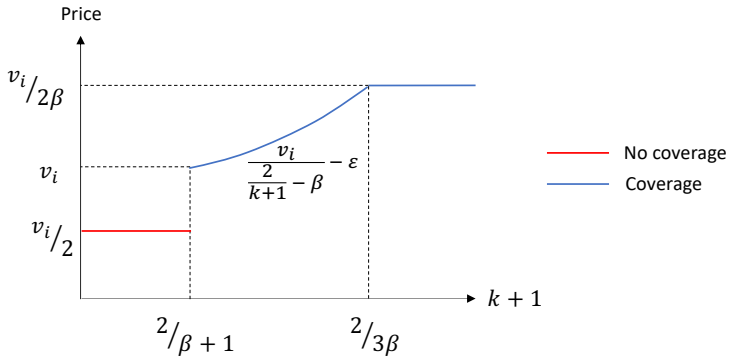
LEMMA 3. *For a single indication with value to patients uniformly distributed on* $[0, v_i]$*, the drug manufacturer's optimal pricing decision (and the ensuing payer's coverage decision) is as follows:*

(i) If $k+1 \leq 2/(\beta+1)$*, then* $p = v_i/2$*, and the payer does not cover the indication.*

(ii) If $2/(\beta+1) < k+1 \leq 2/(3\beta)$*, then* $p = v_i/(2/(k+1) - \beta) - \epsilon$ *(where* ϵ *is an infinitesimal quantity), and the payer covers the indication.*

(iii) If $k+1 > 2/(3\beta)$*, then* $p = v_i/(2\beta)$*, and the payer covers the indication.*

Figure 2 **Drug manufacturer's optimal price decision and ensuing payer coverage decision for a single indication.**



Lemma 3 is illustrated in Figure 2 and can be interpreted as follows. When k is low (i.e., $k+1 \leq 2/(\beta+1)$), from Lemma 2 there is no coverage so the drug manufacturer selects the price that maximizes profits from patients who pay the entire price out of pocket. When k is intermediate (i.e., $2/(\beta+1) < k+1 \leq 2/(3\beta)$), the payer offers coverage (benefiting demand) if the price is not too high. The drug manufacturer earns a higher profit with coverage. Therefore, it sets the price as high as possible while ensuring coverage. When k is sufficiently high (i.e., $k+1 > 2/(3\beta)$), the payer offers coverage at any price with a positive demand. The drug manufacturer thus sets the price at the level that maximizes profits knowing that patients enjoy drug coverage.

We observe that under indication-based pricing, both indications are covered as long as $k+1 > 2/(\beta+1)$. Moreover, both indications receive a positive demand in all scenarios of parameter k.

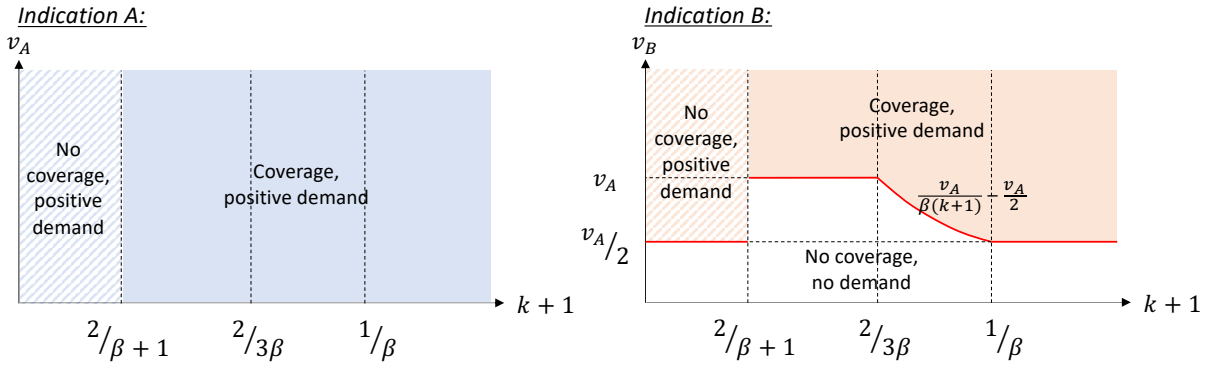
Now, consider the drug manufacturer's decision of whether to invest in getting indication B approved. Lemma A4 in Appendix E proves that as long as the investment fixed cost I is not too high (i.e., $I < \bar{I}$), the drug manufacturer chooses to invest in indication B's approval (that is, the threshold $\bar{I}$ is positive, and is provided in closed-form in Appendix E).

4.4. Drug Manufacturer: Uniform Pricing with Non-Adjustable Price

We next turn to the drug manufacturer's decisions under uniform pricing, where the drug manufacturer must charge the same price for all available indications. In this section, we focus on the case of uniform pricing *with non-adjustable price*, i.e., the manufacturer *cannot* adjust the price of the drug (for indication A) upon introducing a new indication B. Hence, if indication B is launched, the price of the drug for indication B must match the price currently charged for indication A. The current price of indication A is set as described in Lemma 3 (where v_i equals v_A).

Let us analyze the coverage decision and demand size for both indications, assuming that the manufacturer has invested in indication B. Combining results from Lemmas 1 to 3, we obtain that the coverage and presence of a positive demand for both indications are as illustrated in Figure 3.

Figure 3 **Coverage and demand for both indications under uniform pricing with non-adjustable price.**



In particular, we observe that even if a new indication B is introduced, it is possible that it does not receive coverage from the payer, and that patients do not have access to it (demand is zero), if its maximum value from treatment v_B is not high enough. Because the price is pre-imposed at the level commensurate with the value of indication A, the payer could refuse to cover a new indication that provides little value for the current price. Without coverage, patients choose not to pay out of pocket for a drug that delivers little value for their indication.

In particular, the new indication is more likely to be covered under indication-based pricing than under uniform pricing with non-adjustable price. Indeed, Lemma 3 shows that both indications are

covered under indication-based pricing as long as $k+1 > 2/(\beta+1)$, whereas under uniform pricing with non-adjustable price, indication B may not be covered in this range of $k+1$.

Now, consider the drug manufacturer's decision of whether to invest in indication B. Lemma A5 in Appendix E proves that, even if the investment fixed cost I is zero, the drug manufacturer may still choose not to invest in indication B if the maximum value v_B is too low compared to v_A. Because the price must remain at its current level, a drug manufacturer does not choose to invest in a new low-value indication as the payer would not offer coverage, and thus the lack of demand would not allow the drug manufacturer make a profit. If v_B is not too low, the closed-form expression for the maximum fixed investment cost, $\tilde{I}$, is provided in Appendix E.

4.5. Drug Manufacturer: Uniform Pricing with Adjustable Price

In this section, we focus on the case of uniform pricing *with adjustable price*, i.e., the drug manufacturer *can* adjust the price of the drug (for indication A) upon introducing a new indication B. Hence, if indication B is launched, the drug manufacturer selects a new price that applies to both indications, so as to maximize the total profit from both indications, given by (using Lemma 1)

$$\Pi_{\text{manufacturer}} = p \cdot (n_A/v_A)(v_A - \bar{\beta}_A p)^+ + p \cdot (n_B/v_B)(v_B - \bar{\beta}_B p)^+.$$

In making this decision, the manufacturer anticipates that the payer decides coverage for each indication at this common price (i.e., the payer selects separately $\bar{\beta}_A \in \{\beta, 1\}$ and $\bar{\beta}_B \in \{\beta, 1\}$ according to Lemma 2 after observing the new price). The following result derives the optimal pricing decision should indication B be launched.

Lemma 4. *Under uniform pricing with adjustable price, if indication B is introduced, the drug manufacturer selects the joint drug price (and the insurer consequently decides coverage) as follows. Let $i, j \in \{A, B\}$ such that $v_i \le v_j$, and $X \equiv 2/(k+1) - \beta$.*

(a) If $k+1 \le 2/(\beta+1)$, then

$$p = \begin{cases} \frac{n_A+n_B}{2\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)} & \text{if } \frac{n_i}{n_j} \ge \frac{v_j}{v_i} - 2 \qquad \text{[a1]} \\ \frac{v_j}{2} & \text{else.} \qquad \text{[a2]} \end{cases}$$

(b) If $2/(\beta+1) < k+1 \le 2/(3\beta)$, then

$$p = \begin{cases} \frac{v_i}{X} - \epsilon & \text{if } \frac{n_i}{n_j} \ge \frac{v_j}{v_i} - \frac{X - \beta\frac{v_i}{v_j}}{X-\beta}, \qquad \text{[b1]} \\ \frac{v_j}{X} - \epsilon & \text{else.} \qquad \text{[b2]} \end{cases}$$

(c) If $2/(3\beta) < k+1 \le 1/\beta$, then,

$$p = \begin{cases} \frac{n_A+n_B}{2\beta\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)} & \text{if } (2\beta - X)\frac{n_i}{n_j} > X - 2\beta\frac{v_i}{v_j} \text{ and } \frac{n_i}{n_j} > \frac{v_j}{v_i} - 2, \qquad \text{[c1]} \\ \frac{v_i}{X} - \epsilon & \text{if } (2\beta - X)\frac{n_i}{n_j} \le X - 2\beta\frac{v_i}{v_j} \text{ and } \frac{n_i}{n_j}\left(1 - \frac{\beta}{X}\right) + 1 - \frac{\beta}{X}\frac{v_i}{v_j} \ge \frac{X}{4\beta}\frac{v_j}{v_i}, \qquad \text{[c2]} \\ \frac{v_j}{2\beta} & \text{else.} \qquad \text{[c3]} \end{cases}$$

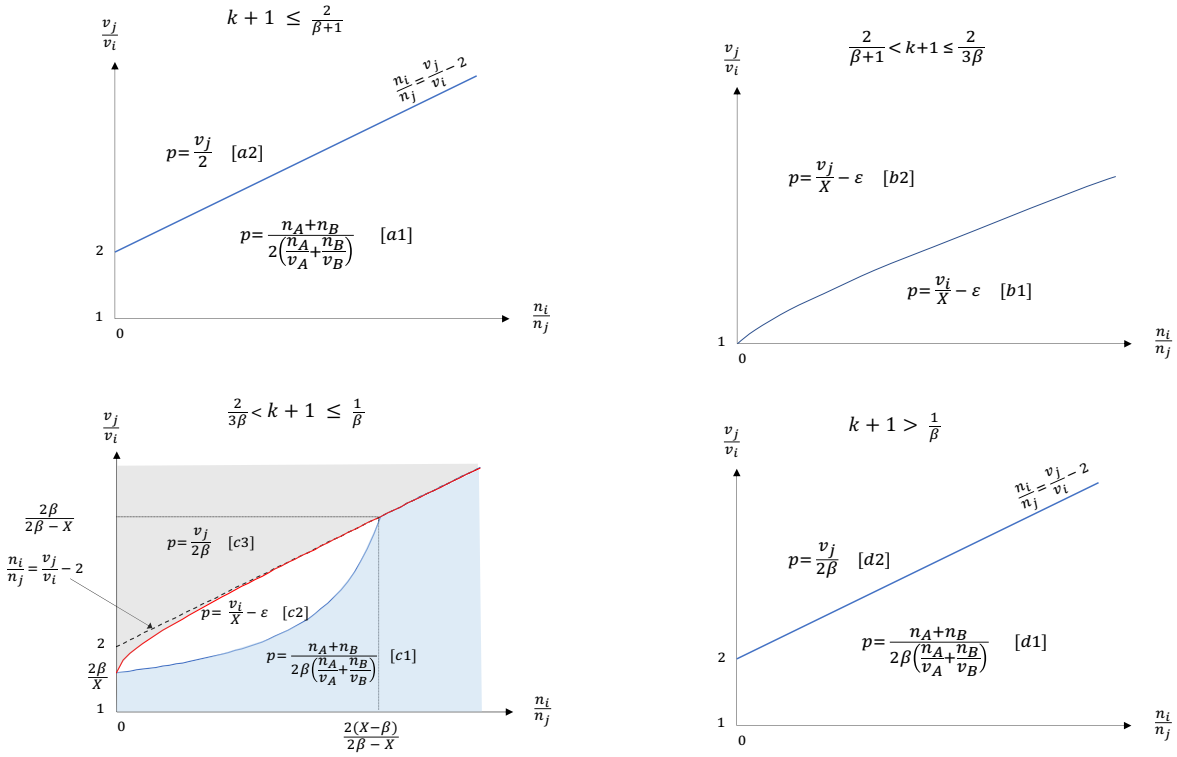
(d) If $k+1>1/\beta$, then

$$p=\begin{cases}\frac{n_A+n_B}{2\beta\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)} & \text{if } \frac{n_i}{n_j}\geq\frac{v_j}{v_i}-2 \qquad [d1]\\ \frac{v_j}{2\beta} & \text{else.} \qquad [d2]\end{cases}$$

Moreover, no indication is covered in scenarios (a1) and (a2); only indication j is covered in scenarios (b2) and (c3); both indications are covered in scenarios (b1), (c1), (c2), (d1) and (d2).

In particular, we observe that the price is not necessarily monotonically increasing in k nor in v_B. The possible scenarios and corresponding prices are illustrated in Figure 4.

Figure 4 **Drug manufacturer's optimal price decision under uniform pricing with adjustable price.**



When k is low (i.e., $k+1\leq 2/(\beta+1)$), there is no coverage so the drug manufacturer selects the price that maximizes profits from out-of-pocket patients. Case (a1), where both indications receive a positive demand, occurs when either $v_j/v_i<2$, i.e., the gap in the two indication values is not too large, or there is a large enough market size n_i for the low-value indication (i.e., $n_i/n_j\geq v_j/v_i-2$). Otherwise, in case (a2), the drug manufacturer sacrifices the low-value indication and prices (higher) to only serve the high-value indication patients paying out-of-pocket.

When k is low-intermediate (i.e., $2/(\beta+1)<k+1\leq 2/(3\beta)$), the payer may provide coverage if the price is low enough. If the low-value indication has a large enough market size (case (b1)), the

drug manufacturer prices just low enough to ensure that even the low-value indication is covered, so that it sells in both markets. Otherwise (case (b2)), the drug manufacturer gives up on the low-value indication and sets the price to ensure that the high-value indication (only) is covered, which causes the low-value indication to generate no demand.

When k is high-intermediate (i.e., $2/(3\beta) < k+1 \leq 1/\beta$), the drug manufacturer has more flexibility on pricing as the payer offers coverage for a wider range of prices. If the low-value indication has a high enough value or a large enough market size (case (c1)), the drug manufacturer maximizes its profits from both indications and the payer offers coverage to both. If the low-value indication has an intermediate value and market size (case (c2)), the drug manufacturer prices low enough to ensure coverage even for the low-value indication. Otherwise (case (c3)), when the low-value indication has too small a value and market size, the drug manufacturer abandons this indication and prices to maximize its profits from the high-value indication only.

When k is high (i.e., $k+1 > 1/\beta$), the drug manufacturer offers coverage for any price at which there is a non-zero demand. If the gap in the two indication values is not too large (i.e., $v_j/v_i < 2$), or there is a large enough market size n_i for the low-value indication (i.e., $n_i/n_j \geq v_j/v_i - 2$, case (d1)), the drug manufacturer prices to sell both indications. Otherwise (case (d2)), it prices to only optimize profits from the high-value indication, giving up on selling the low-value indication.

We observe that if $v_A < v_B$, in case of scenarios (b2) or (c3) (valid for n_A/n_B low enough), the payer would stop covering indication A upon introduction of indication B, to only cover indication B. However, such scenarios are unlikely to occur often in practice. When a new drug is showing promise in pre-clinical studies, drug manufacturers carefully consider indication sequencing options to decide which indication to prioritize (Kloeber et al. 2014). Hence, the manufacturer is likely to pursue FDA approval first either for the most valuable indication (i.e., $v_A > v_B$), or for the indication with the biggest market size (i.e., n_A/n_B large).

Note that scenarios (a1), (b1), (c1), (c2) and (d1) enable sales of the drug under both indications, while under scenarios (a2), (b2), (c3) and (d2), only the high-value indication has a positive demand. The latter scenarios occur when the gap in indication values is large (v_i/v_j small) and/or the low-value indication has a small market size (n_i/n_j small). The low-value indication i is thus less likely to be covered (and hence, to generate demand) than the high-value indication j. When the low-value indication's potential to earn profit is too weak, the drug manufacturer prefers to focus on the high-value indication only, which can be priced high, rather than price at an intermediate level that would ensure coverage and sales for both indications. It also follows that a given indication is more likely to be covered under indication-based pricing than under uniform pricing with adjustable price. Indeed, Lemma 3 shows that both indications are covered under indication-based pricing as long as $k+1 > 1/(\beta+1)$, whereas under uniform pricing with adjustable price, indication i may not be covered in this range of $k+1$.

We finally investigate the drug manufacturer's decision of whether to invest in indication B. Lemma A6 in Appendix E proves that even if the investment fixed cost I is zero, the drug manufacturer may still choose not to invest in indication B if the maximum value v_B is too low compared to v_A. To make a profit from indication B, the drug manufacturer needs this indication to receive a positive demand at the optimal price. Thus indication B needs to have a value not too low and/or a market size not too small to ensure that it generates sales (and profits). Otherwise, the closed-form expression for the maximum fixed investment cost, $\hat{I}$, is provided in Appendix E.

5. Discussion

In this section, we interpret the implications of the findings in Section 4 to derive managerial insights on what could be the consequences of moving from uniform pricing to indication-based pricing. We analyze the effect of indication-based pricing on the investment incentives, coverage for the drug, patient access to the drug, and the benefit for patients, the drug manufacturer, and the payer. The results of Sections 5.1 to 5.6 are summarized in Table 1.

5.1. Investment in a New Indication

In this section, we compare the incentives to invest in getting the new indication FDA-approved.

PROPOSITION 1. *(i) The maximum investment cost under indication-based pricing is larger than that under uniform pricing with non-adjustable price, i.e., $\bar{I} \geq \tilde{I}$.*

(ii) The maximum investment cost under indication-based pricing is larger than that under uniform pricing with adjustable price, i.e., $\bar{I} \geq \hat{I}$.

Figure 6 in Appendix D illustrates the maximum investment cost under each pricing system in a numerical example when v_B varies.

Proposition 1 shows that indication-based pricing provides better incentives to invest in getting a new indication approved, since the manufacturer is willing to invest for a larger amplitude of fixed investment cost, compared to uniform pricing (both with and without adjustable price). The maximum investment cost represents the profit improvement due to introducing the new indication. If the uniform price adjusts, to sell the drug for both indications the drug manufacturer selects a price at an intermediate level and thus forgoes earning potential from the high-value indication. In contrast, with indication-based pricing the low-value indication can be priced lower, without hurting profits from the high-value indication. If the uniform price does not adjust, the profit for the new indication is likely to under-perform under uniform pricing as the price would not match the drug value. Overall, because indication-based pricing allows the drug manufacturer to better align each indication's price to its value, both indications offer the highest possible earning potential and the manufacturer thus has more incentives to invest in the new indication. This finding is

consistent with the expectation expressed in the health policy literature (e.g., Mestre-Ferrandiz et al. 2015; Preckler and Espín 2022) that indication-based pricing may help give rise to more new indications for existing drugs thanks to better research and development incentives.

5.2. Drug Manufacturer Profit

This section focuses on how indication-based pricing affects the drug manufacturer's profit. The next result follows from Proposition 1.

COROLLARY 1. *The drug manufacturer earns higher profit under indication-based pricing than under uniform pricing with either adjustable or non-adjustable price.*

Figure 7 in Appendix D (left-hand side panels) depicts the drug manufacturer profits (not including the fixed investment cost) in a numerical example when v_B varies.

Corollary 1 confirms the intuition expressed by Chandra and Garthwaite (2017) who state that indication-based pricing could help the drug manufacturer capture higher profits because it acts as a price discrimination tool that enables the manufacturer to extract more surplus from patients. Yet, this effect of indication-based pricing may not be fully grasped by stakeholders: in the survey of practitioners conducted by Cole et al. (2020), only 31% responded that industry (as opposed to payers or patients or all stakeholders) is most likely to benefit from indication-based pricing.

It remains to assess whether patients and payer could also gain from implementing indication-based pricing. In principle, even if patients (and payer) may pay more for an indication, having better access to it and therefore enjoying the health benefit of treatment could still outweigh the price paid and thus could in theory make indication-based pricing preferable also for patients.

5.3. Coverage

As discussed in Sections 4.4 and 4.5, indication-based pricing improves incentives for the payer to provide coverage for the drug: We found that under indication-based pricing, both indications are covered iff $k+1 > 2/(\beta+1)$. Under uniform pricing, however, when $k+1 > 2/(\beta+1)$ there may be no coverage for indication B under uniform pricing with non-adjustable price, and for the low-value indication i under uniform pricing with adjustable price. Intuitively, the payer is reluctant to cover an indication when the price charged for it is too high relative to the benefits gained from treatment. Because indication-based pricing allows the price to be linked to the value of the drug for patients, the payer is willing to cover both indications (unless the benefit earned by the payer, measured by parameter k, is too low). Meanwhile, uniform pricing imposes the same price for both indications, which implies that the price can be misaligned with the value provided by the drug. When the misalignment is excessive, the payer denies coverage.

5.4. Patient Access

Section 5.3 shows that the drug coverage is improved under indication-based pricing, which might help make the drug more affordable. However, if a covered drug is priced too high, it may still remain inaccessible to patients due to the high co-insurance. In this section, we determine the effect of indication-based pricing on patients' access to the drug, as measured by patient demand.

Proposition 1 implies that it is possible that the manufacturer invests in the new indication under indication-based pricing, but not under uniform pricing, if the fixed investment cost is too high. In this case the new indication would not be accessible to patients under uniform pricing. Demand for indication A would then be the same under both pricing systems, but demand for indication B would be larger under indication-based pricing. Therefore, patient access would then be improved under indication-based pricing. The next result focuses on the situation where the fixed cost is not this high, so that the drug manufacturer invests in indication B under both pricing systems. Thus, while patients in principle can have access to both indications under both pricing schemes, we compare patient demand to understand how indication-based pricing would affect the volume of patients actually purchasing the drug, as a measure of true access.

PROPOSITION 2. *Suppose that indication B is introduced under all pricing systems.*

(i) Under indication-based pricing, indication A receives the same demand as under uniform pricing with non-adjustable price, and indication B receives a lower demand iff $v_B > v_A$. The total demand is lower under indication-based pricing than under uniform pricing with non-adjustable price iff $v_B > v_A$.

(ii) Let $i, j \in \{A, B\}$ such that $v_i \leq v_j$. Under indication-based pricing, the demand for indication i (respectively, j) is higher (respectively, lower) than or equal to that under uniform pricing with adjustable price. The total demand under indication-based pricing is either higher (case (a2), (b2), (c3), (d2)), the same (case (a1), (c1), (d1)) or lower (case (b1), (c2)) than under uniform pricing with adjustable price.

Figure 9 (right-hand side panels) in Appendix D depicts the total demand in a numerical example when v_B varies.

Proposition 2(i) shows that with indication-based pricing, patients have worse access to the drug than under uniform pricing with non-adjustable price when the new indication has a higher value than the current indication. However, patient access is improved due to indication-based pricing when the new indication has a lower value than the current indication. Essentially, under uniform pricing without price adjustment, a new high-value indication would be under-priced, leading to high demand, while a new low-value indication would be overpriced, leading to worse coverage and demand, compared to indication-based pricing.

Focusing on uniform pricing with adjustable price, Proposition 2(ii) shows that for the low-value indication, indication-based pricing expands demand or leaves it unchanged. Indication-based pricing leads to a low-value indication price commensurate with the indication value, while uniform pricing imposes a higher price, hurting demand. Conversely, for the high-value indication, indication-based pricing reduces demand or leaves it unchanged. By a similar reasoning, indication-based pricing can lead to a relatively higher price for the high-value indication, aligned with the indication's value, which lowers the demand. The cumulative effect on the total demand depends on the specific scenario of relative market sizes. Indication-based pricing reduces the total demand when the drug manufacturer sets the price just low enough so the payer offers coverage to the low-value indication under uniform pricing (cases (b1) and (c2)); but indication-based pricing would increase the total demand when the low-value indication gets zero demand under uniform pricing (cases (a2), (b2), (c3), (d2)), i.e., when v_i/v_j is low and/or n_i/n_j is low.

For both types of uniform pricing, the result implies that indication-based pricing leads to less demand for the high-value indication, and more demand for the low-value indication. This confirms the opinion stated by Chandra and Garthwaite (2017), who anticipate that indication-based pricing would result in "higher utilization by patients who benefit the least."

In summary, Proposition 2 proves that, depending on where the bottlenecks lie, indication-based pricing could worsen patient access to the drug, contrary to what is intuitively anticipated by practitioners—Cole et al. (2020) report that 83% of survey respondents believe patient access is either expanded or unchanged—and by the literature—e.g., Preckler and Espín (2022) list "improvement and acceleration of patients' access to treatment" as one of the main identified benefits from their review of the literature. Even if indication-based pricing improves the total demand, it lowers utilization by patients who would benefit the most from treatment (high-value indication patients). This said, if the fixed investment cost is so high that the manufacturer invests in the new indication under indication-based pricing but not under uniform pricing, then indication-based pricing does improve access to the drug.

5.5. Patient Utility

Section 5.4 analyzes how indication-based pricing affects patients' access to the drug. To fully assess the effect of the pricing system on patients, measuring access is not sufficient as it fails to incorporate the heterogeneity of the health benefit across patients and the patients' expenditures. Hence, in this section we measure the effect of indication-based pricing on patient utility.

PROPOSITION 3. *(i) If $I \geq \bar{I}$, patients are indifferent between indication-based pricing and uniform pricing with non-adjustable price. If $\tilde{I} \leq I < \bar{I}$, patients are better off under indication-based pricing. If $I < \tilde{I}$, so that indication B receives investment under both pricing systems,*

the total patient utility is lower under indication-based pricing than uniform pricing with non-adjustable price iff $v_B > v_A$.

(ii) Let $i, j \in \{A, B\}$ *such that* $v_i \leq v_j$. *If* $I \geq \bar{I}$, *patients are indifferent between indication-based pricing and uniform pricing with adjustable price. If* $\hat{I} \leq I < \bar{I}$, *patients are better off under indication-based pricing. If* $I < \hat{I}$, *so that indication* B *receives investment under both pricing systems, the total patient utility is lower under indication-based pricing than uniform pricing with adjustable price iff case (a1), (b1), (c1), (c2) or (d1) holds, i.e.,* n_i *and/or* v_i *are not too small so that there is a non-zero uniform pricing demand for indication* i.

Figure 7 (center panels) in Appendix D depicts the patient utility in a numerical example when v_B varies.

Proposition 3 proves that if the fixed investment cost is so high that investment in indication B would be profitable only under indication-based pricing, then the patient utility is improved under indication-based pricing thanks to access to a drug indication that would not otherwise be available. However, if the investment cost is such that the manufacturer would invest in indication B under both pricing systems, then the patient utility may be worse under indication-based pricing. In the case of uniform pricing with non-adjustable price, Proposition 3(i) shows that the patient utility is worse under indication-based pricing when the new indication is higher-value. Indeed, as we showed in Proposition 2, the total demand is then lower. In addition, the price of indication B is high, commensurate with the indication value, contributing to a worse patient expense and thus, utility. In the case of uniform pricing with adjustable price, Proposition 3(ii) shows that the patient utility is worse under indication-based pricing when there is a non-zero demand for the low-value indication under uniform pricing. In other words, patient access is the main driver behind the result: as long as indication-based pricing worsens patient access (or leaves unchanged), it also worsens the patient utility. Broadly speaking, Proposition 3 states that unless indication-based pricing enables investment in the new indication, it could worsen patient utility. This finding is aligned with Chandra and Garthwaite (2017) who are concerned that indication-based pricing would help the manufacturer extract all patient surplus.

This result demonstrates that it is crucial to understand the bottlenecks to access under uniform pricing. If the bottleneck is a high fixed investment cost hindering investment, then indication-based pricing can be beneficial to patients. If the bottleneck is the too low value of the new indication (with non-adjustable price), or a too small market size for the low-value indication (with adjustable price) hindering coverage, then again indication-based pricing can be beneficial to patients. But if the bottleneck is high prices, then indication-based pricing will not help patients.

5.6. Payer's objective

When considering a new pricing system, a payer must consider the trade-offs not only for patients, but also for the payer itself. Health policy must balance the benefits of an intervention with its costs, to be financially sustainable. In this section we analyze the effect of indication-based pricing on the combination of patient and payer utility, defined as the payer's objective.

PROPOSITION 4. *(i) If $I \geq \bar{I}$, the payer's objective is indifferent between indication-based pricing and uniform pricing with non-adjustable price. If $\tilde{I} \leq I < \bar{I}$, the payer's objective is equal or higher under indication-based pricing. If $I < \tilde{I}$, so that indication B receives investment under both pricing systems, the payer's objective is lower under indication-based pricing than uniform pricing with non-adjustable price iff $v_B > v_A$.*

(ii) Let $i, j \in \{A, B\}$ such that $v_i \leq v_j$. If $I \geq \bar{I}$, the payer's objective is indifferent between indication-based pricing and uniform pricing with adjustable price. If $\hat{I} \leq I < \bar{I}$, the payer's objective is equal or higher under indication-based pricing. If $I < \hat{I}$, so that indication B receives investment under both pricing systems, the payer's objective is lower under indication-based pricing than uniform pricing with non-adjustable price iff case (a1), (b1), (c1), (c2) or (d1) holds, i.e., n_i and/or v_i are not too small so that there is a non-zero uniform pricing demand for indication i.

Figure 7 (right-hand side panels) in Appendix D depicts the payer's objective in a numerical example when v_B varies.

The results of Proposition 4 on the payer's objective (and their interpretation) are aligned with those of Proposition 3 on the patient utility. Namely, indication-based pricing worsens the payer's objective whenever it worsens the patient utility. It follows from this result that, while in some cases indication-based pricing improves the payer's objective, this is not necessarily the case. Thus, as intuited by Chandra and Garthwaite (2017), payers who wish to maximize a combination of payer's benefit and patients' utility should carefully consider the trade-offs involved in implementing this pricing system. This is all the more crucial given that many practitioners appear unaware of the possible unintended consequences of indication-based pricing: Cole et al. (2020) report that 57% of respondents believe that all stakeholders would gain from implementing indication-based pricing.

5.7. A Numerical Example

In this section, we calibrate the parameters for the example of the chemotherapy drug Abraxane (nab-Paclitaxel). Abraxane was first FDA-approved in 2005 as treatment for metastatic breast cancer (indication A) (Drugs·com 2022). In 2012, it was approved as treatment of advanced non-small cell lung cancer (NSCLC) (indication B). Bach (2014) estimates the median survival gains (in years) as $v_A = 0.18$ and $v_B = 0.08$. There are approximately $n_A = 168,000$ women living with

Table 1 Summary of results on the effect of indication-based pricing relative to uniform pricing.

	Metric	Vs. uniform pricing with non-adjustable price $v_A > v_B$	Vs. uniform pricing with non-adjustable price $v_A < v_B$	Vs. uniform pricing with adjustable price $v_i < v_j$
	Maximum investment cost	+	+	+
	Drug manufacturer profit	+	+	+
	Demand	+	+	+
High I	Patient utility	+	+	+
	Payer's objective	+	+	+
	Coverage for indication i	+ if k intermediate (else, =)	=	+ if k intermediate and n_i/n_j low (else, =)
	Coverage for indication j	=	=	=
Low I	Demand	+	−	− or = if n_i/n_j high (else, +)
	Patient utility	+	−	− if n_i/n_j high (else, +)
	Payer's objective	+	−	− if n_i/n_j high (else, +)

Note: '+', '=' and '−' indicate that indication-based pricing respectively increases, leaves unchanged, and decreases the metric relative to uniform pricing. "High I" is the case when indication B is developed under indication-based pricing but not under uniform pricing; "Low I" is the case when indication B is developed under both pricing mechanisms; the precise thresholds can be obtained from Lemmas A4 to A6. Indication i and j are defined such that $v_i < v_j$. The specific thresholds on k and n_i/n_j can be found in the results of Sections 5.1 to 5.6. The threshold defining n_i/n_j as "high"/"low" becomes lower as k increases; hence, the lower k is, the more likely n_i/n_j is to be considered "low".

metastatic breast cancer in the US (El-Ashry 2021).[5] The US prevalence rate of NSCLC is 198.3 per 100,000 (Ganti et al. 2021). With a population of 332 million, we estimate $n_B = 658,000$. Hence, the indication B offers far less value to patients, but the market size is much larger than indication A. We estimate the co-insurance rate at $\beta = 0.30$ (e.g., Caremark lists Abraxane on tier 5 of its formulary, for which the co-insurance rate is 30%, see Caremark 2022). Estimating parameter k is challenging. To allow the possibility of coverage, it is reasonable to assume $k+1 > 2/(\beta+1)$, i.e., $k > 7/13 \simeq 0.54$. To capture the three possible scenarios associated with different ranges of parameter k (described, e.g., in Lemma 4), we consider three cases: $k = 0.9,\ 1.8$, or 2.8.

Across all scenarios of k, we find that $\hat{I} > 0$. We assume that I is low enough (i.e., $I < \hat{I} (< \bar{I})$), which is consistent with the manufacturer applying for FDA approval for indication B under uniform pricing with adjustable price. We find that under uniform pricing with adjustable price, the cases that arise for each scenario of k are respectively (b2), (c1) and (d1). Therefore, if the payer values highly the benefits from treatment, i.e., if k is large enough ($k = 1.8$ leading to (c1), or $k = 2.8$ leading to (d1)), the market size for indication B is sufficiently large to ensure that the manufacturer prices at a level low enough to serve patients under both indications. In these cases, indication-based pricing would not change the total demand, but it would reduce both the patient utility and the payer's objective compared to uniform pricing with adjustable price. Indeed, indication-based pricing would essentially replace high-value indication patients with low-value indication patients, which hurts the cumulative patient utility. If the payer values less the benefits

[5] We use the current number of patients suffering from the indication as a proxy for the market size; since the relevant quantity is solely the *ratio* of the two market sizes, this provides a sufficient approximation.

from treatment, i.e., if k is small ($k = 0.9$), scenario (b2) occurs, implying that indication B is not covered and only indication A has a positive demand under uniform pricing with adjustable price. In this case, by enabling coverage and a positive demand for indication B, indication-based pricing would improve the total demand, patient utility and payer's objective compared to uniform pricing with adjustable price.

Moreover, we obtain $\tilde{I} = -\infty$ in all scenarios of k, indicating that indication B would not have received investment under uniform pricing with non-adjustable price. Then, indication-based pricing, by providing incentives for an investment that would not have occurred under uniform pricing with non-adjustable price, would improve the demand, patient utility and payer's objective.

This example illustrates that if the superior profit incentives associated with indication-based pricing would enable investment in an indication that would not have occurred under uniform pricing, then indication-based pricing is beneficial. Indication-based pricing can also be beneficial if k is small, so the payer is little incentivized to offer coverage for the low-value indication under uniform pricing. In this case, indication-based pricing, thanks to the price alignment to value, makes coverage possible and thus is beneficial to patients. On the other hand, if investment and coverage would occur under uniform pricing, indication-based pricing could reduce the patient welfare.

Hence, to determine how promising indication-based pricing is as payment model, the payer needs to understand what the most common bottlenecks to patient access in the current uniform pricing system are. Are fixed investment cost too high, causing manufacturers to forgo investments? Are investment taking place but coverage is lacking because of the too limited value to patients (under non-adjustable pricing) or the too limited market size (under adjustable pricing) of a new low-value indication? Or is the high price of drugs the main obstacle to patient access? In the two former cases, indication-based pricing can help; in the latter case, it may not.

5.8. A Modified Pricing Scheme: Conditional Indication-Based Pricing

In the scenario where indication B receives investment across pricing schemes, we observe from our prior results that indication-based pricing may not be advantageous to the patient and payer, notably when v_B is larger than v_A. This observation motivated us to consider a hybrid pricing scheme, which we name *conditional indication-based pricing*. This modified pricing scheme consists in allowing indication-based pricing when the new indication offers a lower potential value (i.e., $v_B < v_A$). If the new indication offers a higher potential value (i.e., $v_B \geq v_A$), the uniform pricing mechanism applies. This would prevent the manufacturer from introducing a new indication at a price higher than the existing drug indication. We next analyze the performance of this hybrid pricing mechanism. It is straightforward to obtain that conditional indication-based pricing matches indication-based pricing when $v_B < v_A$, and uniform pricing when $v_B \geq v_A$. As a result, we obtain the following performance metrics comparisons from results in previous sections of the paper:

Investment incentives: The maximum investment cost under conditional indication-based pricing is larger than or equal to that under uniform pricing. Hence, conditional indication-based pricing improves incentives to invest in a new indication compared to uniform pricing.

The next results refer to the case where indication B receives investment under all pricing mechanisms. (If indication B receives investment only under conditional indication-based pricing, then this pricing scheme outperforms both types of uniform pricing across all performance metrics.)

Manufacturer profit: The drug manufacturer profit under conditional indication-based pricing is larger than or equal to that under uniform pricing. As a result, the drug manufacturer has an incentive (albeit not as strong as with indication-based pricing) to engage in conditional indication-based pricing, as profits would improve if $v_B < v_A$.

Coverage: Coverage for the drug under conditional indication-based pricing is the same or better than under uniform pricing.

Patient access: Conditional indication-based pricing can increase the total demand compared to uniform pricing with non-adjustable price. Compared to uniform pricing with adjustable price, if $v_B < v_A$, the demand under conditional indication-based pricing may be higher, the same, or lower.

Patient utility: The patient utility under conditional indication-based pricing is larger than or equal to that under uniform pricing with non-adjustable price. If $v_B < v_A$, the patient utility under conditional indication-based pricing is lower than that under uniform pricing with adjustable price in case (a1), (b1), (c1), (c2) or (d1) (i.e., n_B/n_A relatively high).

Payer's objective: The payer's objective under conditional indication-based pricing is larger than or equal to that under uniform pricing with non-adjustable price. If $v_B < v_A$, the payer's objective under conditional indication-based pricing is lower than that under uniform pricing with adjustable price in case (a1), (b1), (c1), (c2) or (d1) (i.e., n_B/n_A relatively high).

In summary, in an environment where the status quo is uniform pricing with non-adjustable price, adopting conditional indication-based pricing is a good way to maintain the main advantages of indication-based pricing (improved drug manufacturer profit, improved investment incentives, improved coverage) while eliminating its main drawbacks (risk of hurting the patient utility and payer's objective). In an environment where the status quo is uniform pricing with adjustable price, adopting conditional indication-based pricing also maintains some advantages of indication-based pricing, but it does not fully eliminate the drawbacks of indication-based pricing in *all* cases, in particular in the region where v_B is below v_A (but not so low that indication B does not receive investment under uniform pricing) and n_B/n_A is relatively high.

6. Concluding Remarks and Limitations

This paper analyzes the effect of indication-based pricing in comparison with uniform pricing. By allowing the price to align to the drug value for each indication, indication-based pricing improves

the manufacturer's profit, and thus the incentives to invest in getting a new indication approved. Hence, a major advantage of the pricing mechanism is that it might give rise to FDA-approved indications that would not have existed under uniform pricing. Yet, when the indication would have been developed under uniform pricing, the patient and payer may in some cases be worse off under indication-based pricing, as the drug manufacturer captures more surplus. Many stakeholders appear unaware of this potential drawback of indication-based pricing. Indeed, practitioners cite practical implementation issues of indication-based pricing (e.g., data infrastructure, regulations) as main impediments to adoption of this pricing mechanism. Yet, the perhaps larger concern of potential harm to patients and even payers has received scant attention. This paper is an attempt at highlighting this somewhat overlooked issue.

Our work has several limitations. We assume a full information setting where patient, payer and drug manufacturer know the maximum patient benefit from treatment. The effect of information asymmetry could represent an interesting direction of future research. Some of our assumptions are key to our findings. For example, we do not consider explicitly revenue from off-label use of the drug under indication B. The analysis conducted in Appendix C shows that in the case of extensive off-label use, it is possible that our results no longer hold (although they do for moderate off-label use). It would also be interesting to analyze in follow-up research to what extent the drug manufacturer's pricing power drives our results. The Inflation Reduction Act of 2022 recently adopted in the US allows Medicare to negotiate with manufacturers the price of certain drugs. An interesting question would be to analyze the effect of indication-based pricing when prices are set by a bargaining process between payer and manufacturer (see, e.g., Yapar et al. (2022)).

Our model considers a monopoly setting. However, there could exist a competing drug available for indication B. Sarpatwari et al. (2019) demonstrate that increased competition among brand-name drugs in the US pharmaceutical market does not generally result in lower prices. This study states that "for example, FDA approval and subsequent widespread availability of dasatinib (Sprycel) and nilotinib (Tasigna) for the treatment of chronic myeloid leukemia (CML) had no effect on the list price of imatinib (Gleevec), an older CML treatment; instead, list prices for all 3 drugs increased steadily between 2007 and 2014." Similarly, Wineinger et al. (2019) find "competition among brand-name competitors appeared to do little to stymie rising costs." Hence, empirical observations of competitive forces in the US pharmaceutical market for brand-name drugs are *not* consistent with manufacturers strategically adjusting each other's prices based on their competitor's price. As explained by Rosenthal (2018), due to "sticky pricing", a new entrant in a pharmaceutical drug market is not subject to pricing pressure from an existing competitor. Even with little to no effect on pricing, competition could still play a role via the market size, which affects the demand function. In the presence of a competing drug, the market potential would be

reduced to the subset of patients who stand to gain better value from the new drug than from the existing competitor and thus have a reason to switch. The presence of a competing drug would thus lower the demand. Intuitively, a higher degree of competition would reduce the incentives to invest in getting indication B approved, as the profit potential would be more limited. It is not clear whether the presence of competition would make indication-based pricing more or less beneficial than uniform pricing to patients and payer. The study of how competition may affect the comparison of indication-based pricing vs. uniform pricing for the different agents of the system is left as a future research direction.

Indication-based pricing can be practically implemented through one of three possible routes. (i) Different indications can be authorized and marketed under different brand names and prices. This approach could work for very distinct indications. For example, sildenafil was approved for male erectile dysfunction under the brand name Viagra in 1998, and was approved for pulmonary arterial hypertension under the name Revatio in 2005 (Pearson et al. 2017). (ii) Different discounts can be applied to the drug according to the indication for which it is prescribed. This approach has been implemented in Italy but requires extensive data systems. (iii) A weighted-average price can be calculated using estimates of the population size for the different indications. A retrospective review can help make adjustments based upon actual use across indications. This approach is simpler but requires robust data capabilities (Pearson et al. 2017).

Implementing indication-based pricing presents a number of challenges, especially given the complex pharmaceutical supply chain in the US. In the current system, the prescribing clinician is not required to specify the indication for the medication, and pharmacies do not know or record the indication for which the drug is prescribed. Medications are often purchased in bulk without information on the indication for which they will be used. Data collection and data infrastructure would have to be improved so that the indication for which a drug is prescribed is tracked, and to prevent arbitrage opportunities (e.g., for drugs delivered by a provider, to prevent a provider from purchasing the drug at the low-indication price but using it for the high-value indication). The increased level of data collection and tracking would incur non-negligible administrative costs. In the complex US healthcare system, the presence of intermediaries such as pharmacy-benefits managers further complicates implementation. There may also be regulatory barriers in the US, due to the Medicaid "best price" rule which states that Medicaid must be charged the lowest possible drug price, across all indications. Pearson et al. (2017) and Kaltenboeck et al. (2020) propose ways to overcome these implementation challenges.

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Appendices

A: Notations

n_A	market size for indication A
n_B	market size for indication B
v_A	maximum value gained from treatment for indication A
v_B	maximum value gained from treatment for indication B
I	fixed cost for FDA approval of indication B
β	co-insurance rate when the indication is covered
$\bar{\beta}_i$	co-insurance for indication i under payer's optimal coverage strategy ($\in \{\beta, 1\}$)
k	multiple of the treatment value gained by the patient that the payer gains
X	$= 2/(k+1) - \beta$
p	price
Π_{patient}	cumulative patient utility
Π_{payer}	payer utility
$\Pi_{\text{manufacturer}}$	drug manufacturer profit
W	payer's objective
IBP	indication-based pricing
UN	uniform pricing with non-adjustable price
UA	uniform pricing with adjustable price

Table A1 Notations

B: Extension: Stochastic FDA Approval

Our main model assumes that the FDA deterministically grants approval if the drug manufacturer decides to invest in indication B. In reality, even if the drug is already approved for indication A, there is a chance that the FDA may deny approval for indication B, in which case the investment fixed cost is lost. In this section we show that all our results continue to hold true when there is a probability q that the indication is approved, and a probability $1-q$ it is not approved.

Consider the drug manufacturer's investment decision. Without investing, or if the manufacturer invests but the FDA denies approval, the manufacturer earns profit from indication A only, denoted $\Pi^A_{\text{manufacturer}}$, which does not depend on the pricing system. If the manufacturer invests in indication B and approval is granted, denote $\Pi^{IBP}_{\text{manufacturer}}$, $\Pi^{UA}_{\text{manufacturer}}$, $\Pi^{UN}_{\text{manufacturer}}$ the total manufacturer profit from both indications (not including fixed investment cost).

Under pricing system $S \in \{IBP,\ UA,\ UN\}$, the manufacturer invests iff the expected value of net profits is improved with investment, i.e., iff

$$\begin{aligned} &-I + q\Pi^S_{\text{manufacturer}} + (1-q)\Pi^A_{\text{manufacturer}} > \Pi^A_{\text{manufacturer}} \\ \Leftrightarrow &-\frac{I}{q} + \Pi^S_{\text{manufacturer}} > \Pi^A_{\text{manufacturer}}. \end{aligned}$$

Therefore, the problem is equivalent to the case with a deterministic approval after multiplying the fixed cost thresholds by q (in Lemmas A4 to A6). In particular, the comparison of thresholds across pricing systems is the same as in the deterministic case (Proposition 1).

Similarly, consider our results comparing performance measures (manufacturer profit, demand, patient utility, payer's objective) between indication-based pricing and uniform pricing. Quantity Π_k (e.g., Agent k's utility or demand) is improved under indication-based pricing compared to pricing system $S \in \{UA,\ UN\}$ iff

$$\begin{aligned} & q\Pi_k^{IBP} + (1-q)\Pi_k^A > q\Pi_k^S + (1-q)\Pi_k^A \\ \Leftrightarrow \quad & \Pi_k^{IBP} > \Pi_k^S. \end{aligned}$$

Therefore, these comparisons are equivalent to the deterministic case (Corollary 1 and Propositions 2 to 4).

C: Extension: Off-label use of the drug

In this section, we consider explicitly the off-label use of the drug under indication B in the case when only indication A is FDA-approved. Overall, since the drug can be used for indication B (in a limited fashion) even without approval, there are less incentives to invest in getting indication B approved (i.e., the fixed investment cost might have to be lower to ensure investment is beneficial), which may reduce the comparative benefit of indication-based pricing as the pricing system giving the best investment incentives.

Specifically, we assume that the price and coverage for indication A have been decided in a prior stage (not anticipating the presence and/or extent of off-label use). A fraction $\gamma \in [0,1]$ of the volume n_B of patients suffering from indication B receive a prescription for off-label use of the drug. If indication A is covered, a fraction $\alpha \in [0,1]$ of those with a prescription for off-label use manage to obtain coverage for the drug off-label (in some cases, a payer may accept to pay for a drug when used off-label "if the treatment has been tested in careful research studies and written up in well-respected drug reference books or medical journals", see https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/off-label-drug-use.html). Other patients have to pay for it out of pocket.

When only indication A is FDA-approved, the off-label demand for the drug under indication B equals

$$\begin{cases} \frac{\gamma n_B}{v_B}(v_B - p_A)^+ & \text{if indication } A \text{ is not covered;} \\ \frac{\alpha\gamma n_B}{v_B}(v_B - \beta p_A)^+ + \frac{(1-\alpha)\gamma n_B}{v_B}(v_B - p_A)^+ & \text{if indication } A \text{ is covered,} \end{cases}$$

where p_A is as detailed in Lemma 3. As a result, the manufacturer may earn a profit from off-label use of the drug under indication B even though the indication is not FDA-approved. This extra revenue affects the maximum fixed investment cost that the manufacturer is willing to spend to gain approval of indication B. Specifically, the off-label revenue lowers the maximum fixed investment cost by the amount equal to the off-label demand multiplied by the price of indication A, i.e., using Lemma 3, by the amount

$$\begin{cases} \frac{\gamma n_B v_A}{2v_B}\left(v_B - \frac{v_A}{2}\right)^+ & \text{if } k+1 \le \frac{2}{\beta+1} \\ \frac{\alpha\gamma n_B v_A}{Xv_B}(v_B - \beta\frac{v_A}{X})^+ + \frac{(1-\alpha)\gamma n_B v_A}{Xv_B}(v_B - \frac{v_A}{X})^+ & \text{if } \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ \frac{\alpha\gamma n_B v_A}{2\beta v_B}(v_B - \frac{v_A}{2})^+ + \frac{(1-\alpha)\gamma n_B v_A}{2\beta v_B}(v_B - \frac{v_A}{2\beta})^+ & \text{if } k+1 > \frac{2}{3\beta}. \end{cases}$$

We next investigate how robust the results in the main body of the paper are to the presence of off-label use, and how it affects our main insights.

In Section 4, our results continue to hold except Lemma A4, Lemma A5 and Lemma A6 which provide the maximum fixed investment cost such that the manufacturer finds it profitable to invest in indication B. As detailed above, these three results are modified as follows (the proofs are straightforward using the observation above and the proof of the original result; they are omitted for brevity).

LEMMA A1. *Under indication-based pricing, the drug manufacturer invests in indication B iff $I < \bar{I}$, where $\bar{I}$ is given by*

$$\bar{I} = \begin{cases} \frac{n_B v_B}{4} - \gamma \frac{n_B v_A}{2 v_B} \left(v_B - \frac{v_A}{2}\right)^+ & \text{if } k+1 \le \frac{2}{\beta+1} \\ n_B v_B \cdot \frac{2\left(\frac{1}{k+1} - \beta\right)}{X^2} - \alpha\gamma \frac{n_B v_A}{X v_B} \left(v_B - \beta \frac{v_A}{X}\right)^+ - (1-\alpha)\gamma \frac{n_B v_A}{X v_B} \left(v_B - \frac{v_A}{X}\right)^+ & \text{if } \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ \frac{n_B v_B}{4\beta} - \alpha\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2}\right)^+ - (1-\alpha)\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2\beta}\right)^+ & \text{else.} \end{cases}$$

LEMMA A2. *Under uniform pricing with non-adjustable price, the drug manufacturer invests in indication B iff $I < \tilde{I}$, where*

$$\tilde{I} = \begin{cases} (1-\gamma) \frac{n_B v_A}{2 v_B} \cdot \left(v_B - \frac{v_A}{2}\right) & \text{if } k+1 \le \frac{2}{\beta+1} \text{ and } v_B > \frac{v_A}{2} \\ (1-\gamma\alpha) \frac{n_B v_A}{X v_B} \left(v_B - \frac{\beta v_A}{X}\right) - (1-\alpha)\gamma \frac{n_B v_A}{X v_B} \left(v_B - \frac{v_A}{X}\right) & \text{if } \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \text{ and } v_B > v_A \\ (1-\gamma\alpha) \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2}\right) - (1-\alpha)\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2\beta}\right)^+ & \text{if } \left\{ \frac{2}{3\beta} < k+1 \le \frac{1}{\beta} \text{ and } v_B > \frac{v_A}{\beta(k+1)} - \frac{v_A}{2} \right\} \\ & \text{or if } \left\{ k+1 > \frac{1}{\beta} \text{ and } v_B > \frac{v_A}{2} \right\} \\ -\infty & \text{else,} \end{cases}$$

where $\tilde{I} = -\infty$ indicates that the drug manufacturer does not find it profitable to invest in indication B regardless of investment cost $I \ge 0$.

LEMMA A3. *Under uniform pricing with adjustable price, the drug manufacturer invests in indication B iff $I < \hat{I}$, where*

$$\hat{I} = \begin{cases} \frac{n_A n_B}{4\left(\frac{n_A}{v_A} + \frac{n_B}{v_B}\right)} \left(\frac{n_B}{n_A} - \frac{v_A}{v_B} + 2\right) - \gamma \frac{n_B v_A}{2 v_B} \left(v_B - \frac{v_A}{2}\right)^+ & \text{in case (a1)} \\ \frac{n_B v_B - n_A v_A}{4} - \gamma \frac{n_B v_A}{2 v_B} \left(v_B - \frac{v_A}{2}\right) & \text{in case (a2) with } v_A < v_B \\ \frac{n_B v_A}{X} \left(1 - \frac{\beta}{X} \frac{v_A}{v_B}\right) - \alpha\gamma \frac{n_B v_A}{X v_B} \left(v_B - \beta \frac{v_A}{X}\right) - (1-\alpha)\gamma \frac{n_B v_A}{X v_B} \left(v_B - \frac{v_A}{X}\right)^+ & \text{in case (b1) with } v_A < v_B \\ \frac{n_B v_A}{X} \left(1 - \frac{\beta}{X} \frac{v_A}{v_B}\right) - \alpha\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2}\right)^+ - (1-\alpha)\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2\beta}\right)^+ & \text{in case (c2) with } v_A < v_B \\ 2(n_B v_B - n_A v_A) \frac{\frac{1}{k+1} - \beta}{X^2} + \frac{n_A v_B}{X} \left(1 - \frac{\beta}{X} \frac{v_B}{v_A}\right) - \alpha\gamma \frac{n_B v_A}{X v_B} \left(v_B - \beta \frac{v_A}{X}\right)^+ & \text{in case (b1) with } v_B < v_A \\ 2(n_B v_B - n_A v_A) \frac{\frac{1}{k+1} - \beta}{X^2} + \frac{n_A v_B}{X} \left(1 - \frac{\beta}{X} \frac{v_B}{v_A}\right) - \alpha\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2}\right)^+ & \text{in case (c2) with } v_B < v_A \\ 2(n_B v_B - n_A v_A) \frac{\frac{1}{k+1} - \beta}{X^2} - \alpha\gamma \frac{n_B v_A}{X v_B} \left(v_B - \beta \frac{v_A}{X}\right)^+ - (1-\alpha)\gamma \frac{n_B v_A}{X v_B} \left(v_B - \frac{v_A}{X}\right)^+ & \text{in case (b2) with } v_A < v_B \\ \frac{n_A n_B}{4\beta\left(\frac{n_A}{v_A} + \frac{n_B}{v_B}\right)} \left(\frac{n_B}{n_A} - \frac{v_A}{v_B} + 2\right) - \alpha\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2}\right)^+ - (1-\alpha)\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2\beta}\right)^+ & \text{in case (c1) or (d1)} \\ \frac{n_B v_B - n_A v_A}{4\beta} - \alpha\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2}\right)^+ - (1-\alpha)\gamma \frac{n_B v_A}{2\beta v_B} \left(v_B - \frac{v_A}{2\beta}\right)^+ & \text{in case (c3) or (d2) and } v_A < v_B \\ -\infty & \text{else,} \end{cases}$$

where $\hat{I} = -\infty$ indicates that the drug manufacturer does not find it profitable to invest in indication B regardless of investment cost $I \ge 0$.

Since each of these thresholds is reduced by the same amount, for a given range of $k+1$, the comparison of thresholds in Proposition 1 is unchanged. Hence, our main finding stating that indication-based pricing provides better investment incentives than uniform pricing remains valid.

We next analyze how the presence of off-label use affects the comparison of patient demand, manufacturer profit, patient utility, and payer's objective between indication-based pricing and non-adjustable (resp. adjustable) uniform pricing. Clearly, if indication B is not approved under both pricing schemes, the two pricing schemes are equivalent even with off-label use. Likewise, if indication B is approved under both pricing schemes, off-label use has no impact. Therefore, in the remainder of this section, we focus on the case

when $\tilde{I} \leq I < \bar{I}$ (resp. $\hat{I} \leq I < \bar{I}$) only, that is, indication B is approved under indication-based pricing, but not under uniform pricing. Since indication A is unaffected by the pricing scheme in this scenario, it suffices to focus our analysis exclusively on the contribution of indication B (which is FDA-approved and available on-label under indication-based pricing, but not FDA-approved and only available off-label under uniform pricing) to these quantities.

Corollary 1 continue to hold true, that is, if $\tilde{I} \leq I < \bar{I}$ (resp. $\hat{I} \leq I < \bar{I}$), the drug manufacturer continues to be better off under indication-based pricing that under uniform pricing.

Proposition 2 does not apply to the considered scenario as it focuses on the patient demand in the case where indication B is approved. To better investigate the scenario considered in this extension, we compare the patient demand under indication-based pricing and uniform pricing in the scenario described above.

PROPOSITION A1. *If $\tilde{I} \leq I < \bar{I}$ (resp. $\hat{I} \leq I < \bar{I}$), the (off-label) patient demand for indication B is higher under indication-based pricing than uniform pricing with non-adjustable price (resp., adjustable price) iff*

$$\begin{array}{ll}
v_B < \frac{v_A}{2} \text{ or } \frac{1}{2} > \frac{\gamma}{v_B}\left(v_B - \frac{v_A}{2}\right) & \text{in the case } k+1 \leq \frac{2}{\beta+1} \\
v_B < \beta\frac{v_A}{X} \text{ or } 1 - \frac{\beta}{X} > \frac{\alpha\gamma}{v_B}\left(v_B - \beta\frac{v_A}{X}\right) + \frac{(1-\alpha)\gamma}{v_B}\left(v_B - \frac{v_A}{X}\right)^+ & \text{in the case } \frac{2}{\beta+1} < k+1 \leq \frac{2}{3\beta} \\
v_B < \frac{v_A}{2} \text{ or } \frac{1}{2} > \frac{\alpha\gamma}{v_B}\left(v_B - \frac{v_A}{2}\right) + \frac{(1-\alpha)\gamma}{v_B}\left(v_B - \frac{v_A}{2\beta}\right)^+ & \text{in the case } k+1 > \frac{2}{3\beta}.
\end{array}$$

Recall that, without considering off-label use, there would be no demand for indication B under uniform pricing. Hence, if either indication B offers low value or the extent of off-label usage is relatively small, it remains true that the (on-label) demand for indication B under indication-based pricing exceeds (off-label) demand under uniform pricing.

We note that in the case $k+1 \leq 2/(\beta+1)$, the condition can be rewritten as $\gamma v_A/v_B > 2\gamma - 1$, which automatically holds true as long as $\gamma \leq 1/2$. For this range of k, to have indication-based pricing demand be lower than under uniform pricing would require (i) $\gamma > 1/2$ and (ii) $v_B/v_A > \gamma/(2\gamma-1)(>1)$. Namely, off-label use would have to be extremely widespread, and indication B would have to be more valuable than indication A.

Proposition 3, which focuses on the patient utility, needs to be modified: part (i) for the case $\tilde{I} \leq I < \bar{I}$, and part (ii) for the case $\hat{I} \leq I < \bar{I}$. Without considering off-label use, indication B patients derive no utility from the drug under uniform pricing in this scenario. With off-label use, patients can now gain some utility even without FDA approval, and thus it is not necessarily the case that patients are better off under indication-based pricing.

PROPOSITION A2. *If $\tilde{I} \leq I < \bar{I}$ (resp. $\hat{I} \leq I < \bar{I}$), patients are better off under indication-based pricing than uniform pricing with non-adjustable price (resp., adjustable price) iff*

$$\begin{array}{ll}
v_B < \frac{v_A}{2} \text{ or } \frac{v_B}{8} > \frac{\gamma}{2v_B}\left(v_B - \frac{v_A}{2}\right)^2 & \text{in the case } k+1 \leq \frac{2}{\beta+1} \\
v_B < \beta\frac{v_A}{X} \text{ or } \frac{v_B}{2}\left(1 - \frac{\beta}{X}\right)^2 > \frac{\alpha\gamma}{2v_B}\left(v_B - \beta\frac{v_A}{X}\right)^2 + \frac{(1-\alpha)\gamma}{2v_B}\left((v_B - \frac{v_A}{X})^+\right)^2 & \text{in the case } \frac{2}{\beta+1} < k+1 \leq \frac{2}{3\beta} \\
v_B < \frac{v_A}{2} \text{ or } \frac{v_B}{8} > \frac{\alpha\gamma}{2v_B}\left(v_B - \frac{v_A}{2}\right)^2 + \frac{(1-\alpha)\gamma}{2v_B}\left((v_B - \frac{v_A}{2\beta})^+\right)^2 & \text{in the case } k+1 > \frac{2}{3\beta}.
\end{array}$$

Essentially, with off-label demand, patients continue to be better off in the case with investment (i.e., under indication-based pricing) if either indication B offers low value or the extent of off-label usage is relatively

small. Otherwise, patients could be better off from off-label usage of the drug under uniform pricing even when indication B is not approved.

Finally, Proposition 4, which focuses on the payer's objective, also needs to be modified: part (i) for the case $\tilde{I} \le I < \bar{I}$, and part (ii) for the case $\hat{I} \le I < \bar{I}$. Without off-label use, indication B does not add a contribution to the payer's objective. With off-label use, the payer's objective is no longer necessarily higher under indication-based pricing.

PROPOSITION A3. *If $\tilde{I} \le I < \bar{I}$ (resp. $\hat{I} \le I < \bar{I}$), the payer's objective is higher under indication-based pricing than uniform pricing with non-adjustable price (resp., adjustable price) iff*

$$\begin{array}{ll} v_B < \frac{v_A}{2} \text{ or } \frac{v_B(3k+1)}{8} > \frac{\gamma}{v_B}\left(v_B - \frac{v_A}{2}\right)\left[\frac{k+1}{2}\left(v_B + \frac{v_A}{2}\right) - \frac{v_A}{2}\right] & \text{in the case } k+1 \le \frac{2}{\beta+1} \\ v_B < \frac{v_A}{2} \text{ or } v_B\left(\frac{3(k+1)}{8} - \frac{1}{4\beta}\right) > \frac{\alpha\gamma}{v_B}\left(v_B - \frac{v_A}{2}\right)\left[\frac{k+1}{2}\left(v_B + \frac{v_A}{2}\right) - \frac{v_A}{2\beta}\right] + \frac{(1-\alpha)\gamma}{v_B}\left(v_B - \frac{v_A}{2\beta}\right)^+\left[\frac{k+1}{2}\left(v_B + \frac{v_A}{2\beta}\right) - \frac{v_A}{2\beta}\right] & \text{in the case } k+1 > \frac{2}{3\beta}. \end{array}$$

In the case $\frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta}$, the payer's objective is zero under indication-based pricing, but can be positive (if $v_B > \beta v_A/X$), thus higher, under uniform pricing.

Intuitively, consistent with the patient utility result, for low or high k, if investment takes place under indication-based pricing but not uniform pricing, the payer benefits or is indifferent under indication-based pricing if either indication B offers low value or the extent of off-label usage is relatively small. For intermediate k, in the contrary, the payer's objective could be improved under uniform pricing. This is because for this range of k, the manufacturer prices as high as possible to ensure coverage, leaving the payer with no surplus when off-label demand is ignored. Thus, the extra benefit due to the patient benefit from off-label usage gives uniform pricing an edge from the payer's perspective.

EXAMPLE 1. Consider an example where $v_B = 0.8v_A$ (i.e., $v_A/v_B = 1.25$), $\beta = 35\%$, and $k \in \{0.3; 0.7; 1.2\}$. Suppose $\tilde{I} \le I < \bar{I}$ (resp. $\hat{I} \le I < \bar{I}$), that is, indication B is developed under indication-based pricing, but not under uniform pricing. We find that, under indication-based pricing, the demand is higher, patients are better off, and the payer's objective is improved (unless k is intermediate) regardless of γ and α. Hence, despite the presence of off-label use, our findings obtained without considering off-label demand remain valid (except for the payer's objective with intermediate k).

EXAMPLE 2. Consider now the same example as above except that $v_B = 1.25v_A$ (i.e., $v_A/v_B = 0.8$). We find that the demand can be lower, patients can be worse off, and the payer's objective can be lower under indication-based pricing if γ is high enough. Specifically, demand is lower when $\gamma > 0.83$ (approximately, after rounding) for low k, $\alpha\gamma > 0.87$ for intermediate k, $\alpha\gamma > 0.83$ for high k. Likewise, patients are worse off when $\gamma > 0.69$ for low k, $\gamma\alpha > 0.76$ for intermediate k, $\gamma\alpha > 0.69$ for high k. The payer's objective is worse when $\gamma > 0.78$ for low k (but cannot be worse regardless of γ and α for high k). One might expect that α and γ take in reality values far lower than these thresholds, as the use of the drug off-label is not rare, but not generalized to most patients, and it not routine for patients to obtain insurance coverage for an off-label drug. Therefore, for realistic values of these parameters, even if the new indication is higher-valued than the existing indication, our findings would remain qualitatively unchanged (except for the payer's objective with intermediate k).

D: Supplemental Figures

Figure 5 illustrates the high, intermediate-high, low-intermediate, and low regions for k as a function of β.

Figure 6 illustrates the maximum investment cost under each pricing system in a numerical example when v_B varies from 0 to $4v_A$ in four scenarios of parameter k, illustrating that the maximum investment cost is the highest under indication-based pricing, as shown in Proposition 1.

Figure 7 depicts the drug manufacturer profits (not including the fixed investment cost), patient utility, and payer's objective in a numerical example when v_B varies from 0 to $4v_A$ in four scenarios of parameter

Figure 5 Regions of k as β varies.

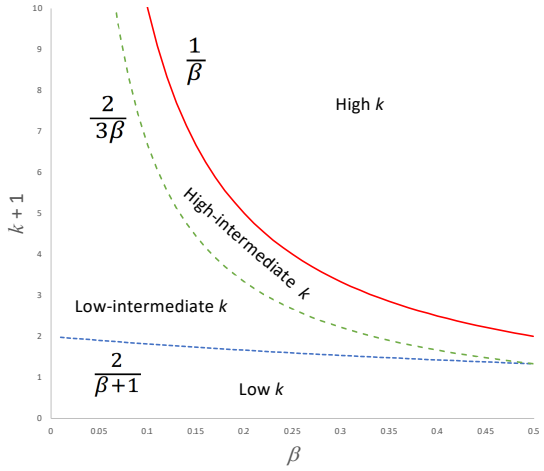
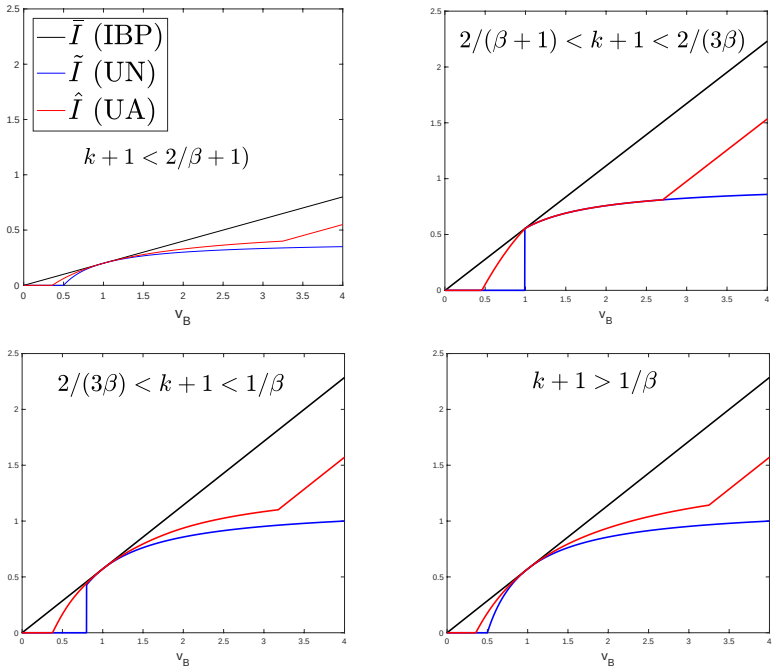


Figure 6 Maximum fixed investment cost when $\beta = 0.35,\ v_A = 1,\ n_A = 1,\ n_B = 0.8$, and $k \in \{0.3; 0.7; 1.2; 2\}$.

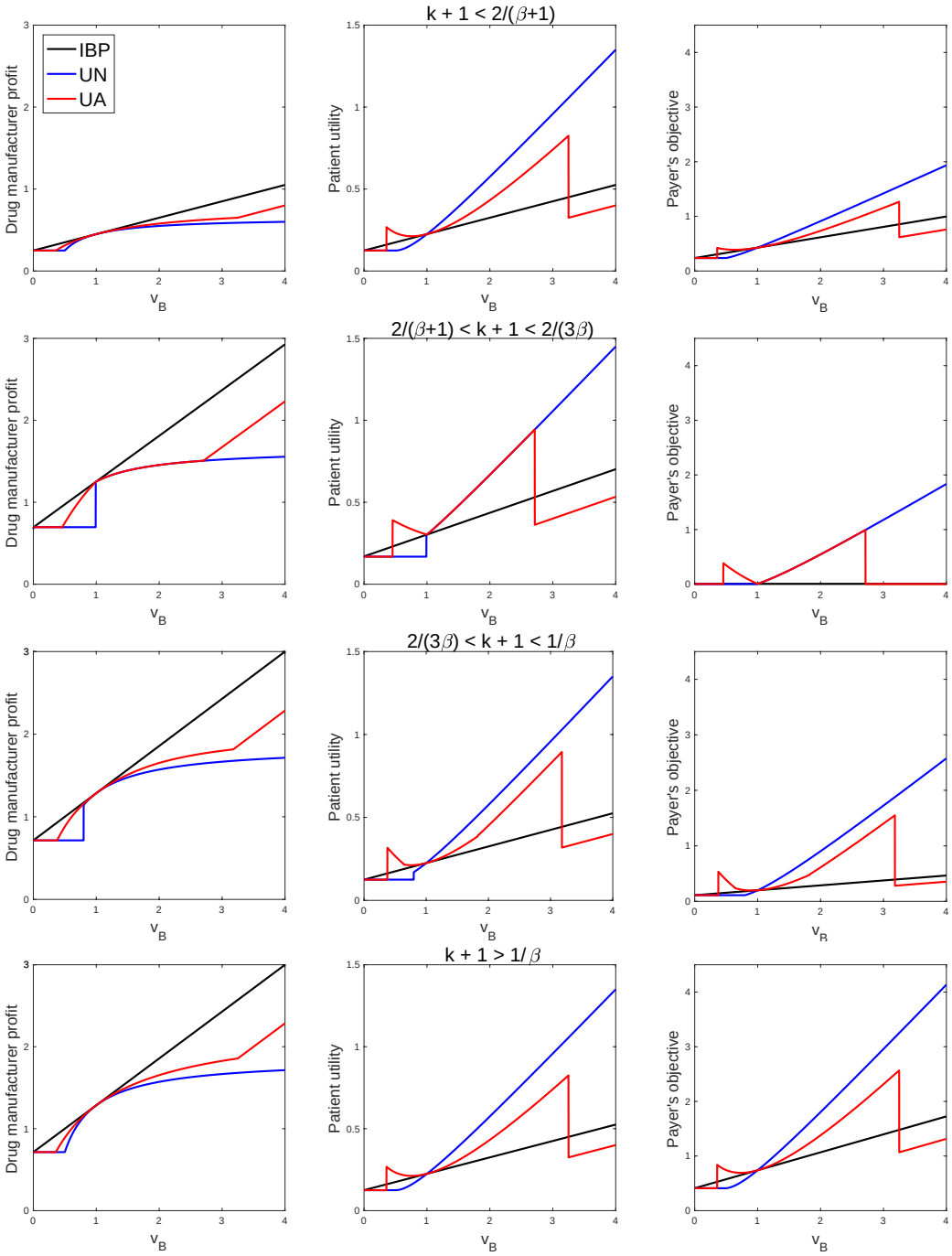


Note. 'IBP': indication-based pricing; 'UN': uniform pricing with non-adjustable price; 'UA': uniform pricing with adjustable price

k. This figure represents the case when $I = 0$ so that investment in indication B can occur for all values of v_B (unless $\tilde{I} = -\infty$ or $\hat{I} = -\infty$). If $I > 0$, then investment in indication B occurs only if I is lower than a threshold, or equivalently, if v_B is above a threshold. For v_B below this threshold, the profits and utilities are those derived from indication A only. An example of graphs for the case $I > 0$ is provided in Figure 8.

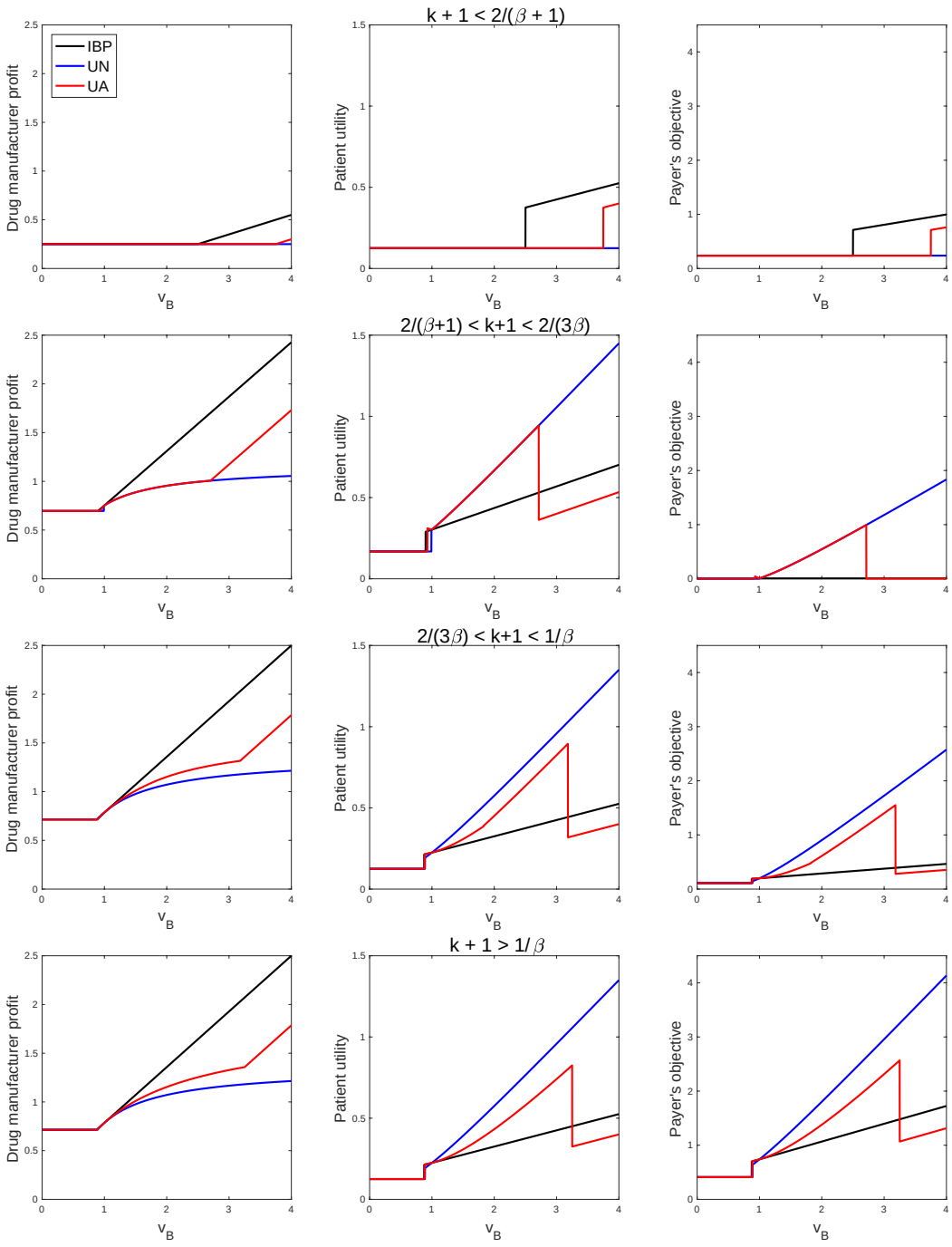
Figure Figure 9 depicts the total demand and the price when v_B varies from 0 to $4v_A$ in four scenarios of parameter k. This figure represents the case when $I = 0$ so that investment in indication B can occur for all values of v_B (unless $\tilde{I} = -\infty$ or $\hat{I} = -\infty$). If $I > 0$, then investment in indication B occurs only if I is lower than a threshold, or equivalently, if v_B is above a threshold. For v_B below this threshold, the total demand is derived from indication A only. An example of graphs for the case $I > 0$ is provided in Figure 10.

Figure 7 **Drug manufacturer profit, patient utility, and payer's objective when** $I = 0,\ \beta = 0.35,\ v_A = 1,\ n_A = 1,\ n_B = 0.8$**, and** $k \in \{0.3; 0.7; 1.2; 2\}$**.**



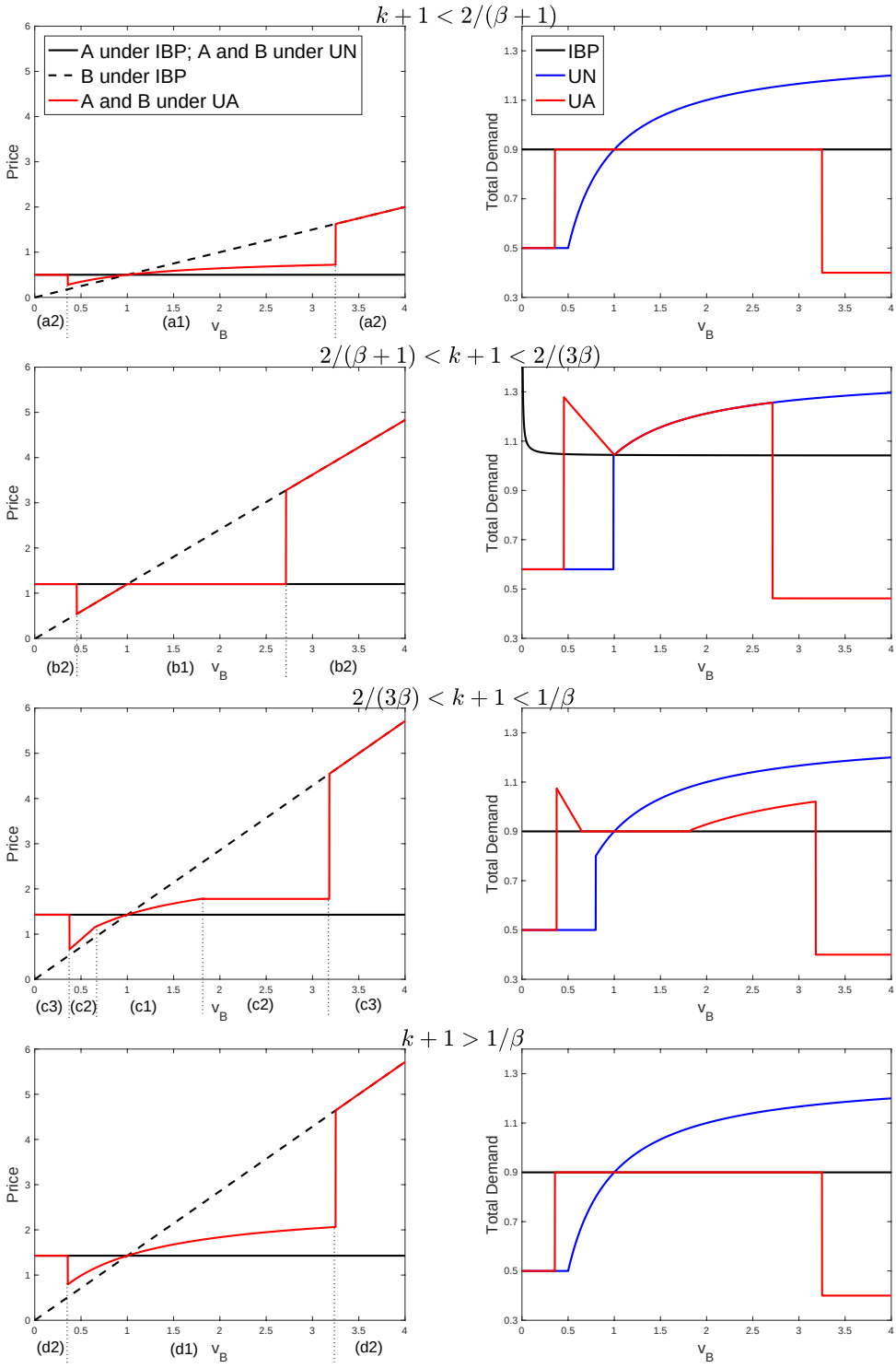
Note. 'IBP': indication-based pricing; 'UN': uniform pricing with non-adjustable price; 'UA': uniform pricing with adjustable price

Figure 8 **Drug manufacturer profit (net of investment cost), patient utility, and payer's objective when** $I = 0.5,\ \beta = 0.35,\ v_A = 1,\ n_A = 1,\ n_B = 0.8$**, and** $k \in \{0.3; 0.7; 1.2; 2\}$.



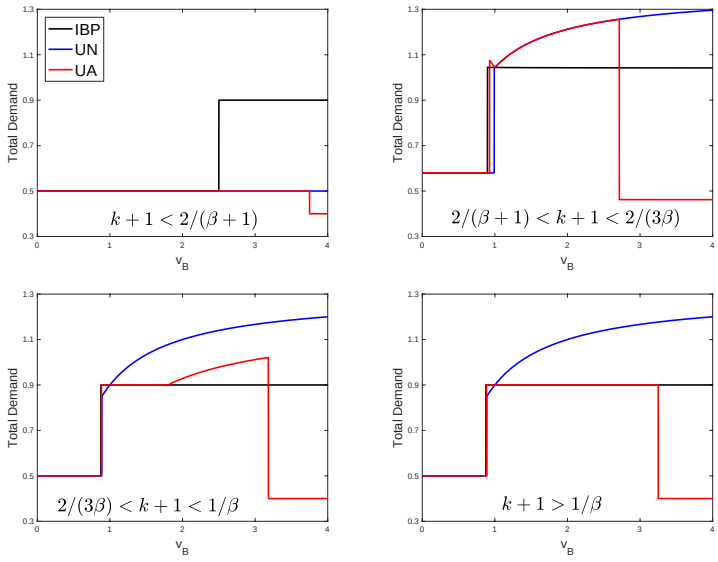
Note. 'IBP': indication-based pricing; 'UN': uniform pricing with non-adjustable price; 'UA': uniform pricing with adjustable price

Figure 9 **Price and total demand when** $I=0,\ \beta=0.35,\ v_A=1,\ n_A=1,\ n_B=0.8$**, and** $k\in\{0.3;0.7;1.2;2\}$**.**



Note. 'IBP': indication-based pricing; 'UN': uniform pricing with non-adjustable price; 'UA': uniform pricing with adjustable price

Figure 10 **Total demand when** $I = 0.5,\ \beta = 0.35,\ v_A = 1,\ n_A = 1,\ n_B = 0.8$**, and** $k \in \{0.3; 0.7; 1.2; 2\}$.



E: Proofs

Proof of Lemma 1. The patient obtains the drug iff $v - \bar{\beta}p > 0$, where v is uniformly distributed on $[0, v_i]$ and there are n_i eligible patients in total. It follows that demand equals $(n_i/v_i)(v_i - \bar{\beta}p)^+$. Moreover, the cumulative patient utility is 0 when $v_i \le \bar{\beta}p$ (as demand is zero), and otherwise it is equal to

$$\Pi_{\text{patient}} = n_i \int_{\bar{\beta}p}^{v_i} (v - \bar{\beta}p)\frac{1}{v_i}dv = \frac{n_i}{2v_i}(v_i - \bar{\beta}p)^2.$$

Q.E.D.

Proof of Lemma 2. The payer offers coverage iff $W(\bar{\beta} = \beta) > W(\bar{\beta} = 1)$, where

$$W = \Pi_{\text{patient}} + \Pi_{\text{payer}} = \frac{n_i}{v_i}(v_i - \bar{\beta}p)^+ \left[\frac{k+1}{2}(v_i + \bar{\beta}p) - p\right].$$

If $p \ge v_i/\beta$, then $W = 0$ with and without coverage, thus the payer is indifferent and, given the tie-breaking rule, does not offer coverage.

If $v_i \le p < v_i/\beta$, then $W(\bar{\beta} = 1) = 0$, thus the payer offers coverage iff $W(\bar{\beta} = \beta) > 0$, i.e., iff

$$\frac{k+1}{2}(v_i + \beta p) - p > 0.$$

This inequality is automatically satisfied when $(k+1)\beta/2 - 1 \ge 0$, i.e., when $k + 1 \ge 2/\beta$. Else, there is coverage when $p < v_i/(2/(k+1) - \beta)$. We observe that $v_i/(2/(k+1) - \beta) > v_i$ iff $k + 1 > 2/(\beta + 1)$ and $v_i/(2/(k+1) - \beta) < v_i/\beta$ iff $k + 1 < 1/\beta$. Therefore, when $v_i \le p < v_i/\beta$,

- if $k + 1 > 1/\beta$, the payer offers coverage
- if $2/(\beta + 1) < k + 1 \le 1/\beta$, the payer offers coverage iff $p < v_i/(2/(k+1) - \beta)$
- if $k + 1 \le 2/(\beta + 1)$, the payer does not offer coverage.

Finally, if $p < v_i$, the payer offers coverage iff

$$\frac{n_i}{v_i}(v_i - \beta p)\left[\frac{k+1}{2}(v_i + \beta p) - p\right] > \frac{n_i}{v_i}(v_i - p)\left[\frac{k+1}{2}(v_i + p) - p\right] \Leftrightarrow \quad \frac{k+1}{2}(1+\beta) > 1 \Leftrightarrow \quad k + 1 > \frac{2}{\beta+1}.$$

Q.E.D.

Proof of Lemma 3. If $k + 1 \le 2/(\beta + 1)$, according to Lemma 2 there is no coverage regardless of the price. Hence, the drug manufacturer selects a price $p \in [0, v_i]$ to maximize $p \cdot (v_i - p)$, which yields $p^* = v_i/2$.

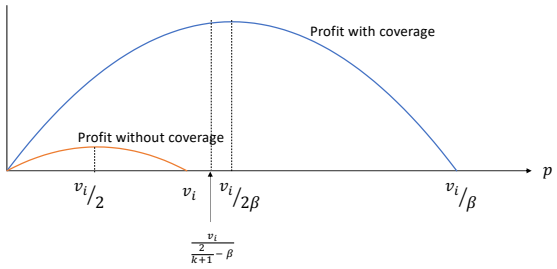
If $k + 1 > 1/\beta$, according to Lemma 2 there is coverage regardless of the price (below v_i/β, above which no patient would purchase the drug). Hence, the drug manufacturer selects a price $p \in [0, v_i/\beta]$ to maximize $p \cdot (v_i - \beta p)$, which yields $p^* = v_i/(2\beta)$.

If $2/(\beta + 1) < k + 1 \le 1/\beta$, according to Lemma 2 there is coverage iff $p < v_i/(2/(k+1) - \beta)$. When the optimal price with coverage is below the threshold, it is the optimal solution. Note that $2/(\beta+1) < k+1 \le 1/\beta$ implies $1 < 1/(2/(k+1) - \beta) \le 1/\beta$. We have

$$\frac{v_i}{2\beta} < \frac{v_i}{\frac{2}{k+1} - \beta} \quad \Leftrightarrow \quad k + 1 > \frac{2}{3\beta}.$$

Hence, when $k + 1 > 2/(3\beta)$, we have $p^* = v_i/(2\beta)$. When $k + 1 \le 2/(3\beta)$, the drug manufacturer must select either to price at $v_i/2$, which is the price that maximizes the profit without coverage, or a price within

Figure 11 **Drug manufacturer profit with and without coverage.**



$[0, v_i/(2/(k+1)-\beta)]$ to maximize profits with coverage. Since the profit function is increasing over that interval when $k+1 \le 2/(3\beta)$ (as $v_i/(2/(k+1)-\beta) \le v_i/(2\beta)$), and since the profit with coverage is strictly greater than the profit without coverage over the increasing part (see Figure 11), it follows that the optimal price is $p^* = v_i/(2/(k+1)-\beta) - \epsilon$. *Q.E.D.*

Proof of Lemma 4.

(a) If $k+1 \le 2/(\beta+1)$, the payer will not cover either one of the indications, regardless of the price. Hence, the drug manufacturer selects the price to maximize its profit $\Pi_{\text{manufacturer}} = p \cdot (n_A/v_A)(v_A - p)^+ + p \cdot (n_B/v_B)(v_B - p)^+$, which is continuous. (The investment fixed cost is sunk at this point.)

On the domain $p \in [0, v_i]$, the first order condition yields a price

$$\bar{p} \equiv \frac{n_A + n_B}{2\left(\frac{n_A}{v_A} + \frac{n_B}{v_B}\right)},$$

which is optimal as long as this price lies within $[0, v_i]$, and the profit function at this point equals $(n_A + n_B)^2/4(n_A/v_A + n_B/v_B)$. If this price is larger than v_i, the optimal price on this domain would be v_i. On the domain $p \in [v_i, v_j]$ the profit function is $p \cdot (n_j/v_j)(v_j - p)$ which is maximized at $v_j/2$ if $v_j/2 > v_i$ (taking the value $v_j n_j/4$), and otherwise at v_i. On the domain $p \in (v_j, \infty)$, the profit function is zero and the drug manufacturer is thus indifferent to the price decision.

We find that

$$\bar{p} = \frac{n_A + n_B}{2\left(\frac{n_A}{v_A} + \frac{n_B}{v_B}\right)} \le v_i \quad \Leftrightarrow \quad 1 - \frac{n_i}{n_j} \le 2\frac{v_i}{v_j}.$$

We thus have 3 cases to consider.

(i) When $\bar{p}, v_j/2 \le v_i$, the profit function reaches a maximum at $\bar{p}$ on $[0, v_i]$ and is decreasing on $[v_i, v_j]$, thus the global optimizer is $\bar{p}$.

(ii) When $\bar{p}, v_j/2 > v_i$, the profit function is increasing on $[0, v_i]$ and reaches a maximum on $[v_i, v_j]$ at $v_j/2$, thus the global optimizer is $v_j/2$.

(iii) When $\bar{p} < v_i < v_j/2$, there is a local maximum on each domain, and we must compare the value of the profit function at each of them.

Note that these are the only possible cases as it is impossible to have $v_j/2 < v_i < \bar{p}$ because $v_i < \bar{p}$ implies $2v_i/v_j < 1 - n_i/n_j < 1$.

We have (after simplifications)

$$\frac{v_j n_j}{4} > \frac{(n_A+n_B)^2}{4\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)} \quad \Leftrightarrow \quad \frac{n_i}{n_j} < \frac{v_j}{v_i} - 2.$$

We obtain after simplifications that

$$\frac{v_j}{v_i} - 2 > 1 - 2\frac{v_i}{v_j} \quad \Leftrightarrow \quad v_j/2 > v_i.$$

Therefore, the optimal price is $\bar{p}$ iff either $v_j/2 \le v_i$ or ($v_j/2 > v_i$ and $n_i/n_j \ge v_j/v_i - 2$). Finally, we note that $v_j/2 \le v_i$ implies $n_i/n_j > 0 \ge v_j/v_i - 2$. Hence, $\bar{p}$ is the optimal price iff $n_i/n_j \ge v_j/v_i - 2$.

(d) If $k+1 > 1/\beta$, the payer will cover any indication for which the price is below v/β. Hence, the drug manufacturer's profit is given by

$$\Pi_{\text{manufacturer}} = p\cdot\left(\frac{n_A}{v_A}\right)(v_A-p)^+ + p\cdot\left(\frac{n_B}{v_B}\right)(v_B-p)^+ = 0 \quad \text{if} \quad p \ge \frac{v_j}{\beta} \quad \left(> v_j, \frac{v_i}{\beta}, v_i\right)$$

$$\Pi_{\text{manufacturer}} = p\cdot\left(\frac{n_i}{v_i}\right)(v_i-p)^+ + p\cdot\left(\frac{n_j}{v_j}\right)(v_j-\beta p)^+ = p\cdot\left(\frac{n_j}{v_j}\right)(v_j-\beta p)^+ \quad \text{if} \quad \frac{v_i}{\beta} \le p < \frac{v_j}{\beta}$$

$$\Pi_{\text{manufacturer}} = p\cdot\left(\frac{n_A}{v_A}\right)(v_A-\beta p)^+ + p\cdot\left(\frac{n_B}{v_B}\right)(v_B-\beta p)^+ \quad \text{else, i.e., if} \quad p < \frac{v_i}{\beta}.$$

As a result, the problem is identical to the case $k+1 \le 2/(\beta+1)$ after replacing p with βp.

(b) and (c) If $2/(\beta+1) < k+1 \le 1/\beta$, the payer will cover any indication for which the price is below v/X. Note that for this range of $k+1$, we have $\beta \le X < 1$. Hence, the drug manufacturer's profit is given by

$$\Pi_{\text{manufacturer}} = p\cdot\left(\frac{n_A}{v_A}\right)(v_A-p)^+ + p\cdot\left(\frac{n_B}{v_B}\right)(v_B-p)^+ = 0 \quad \text{if} \quad p \ge \frac{v_j}{X} \quad \left(> v_j, \frac{v_i}{X}, v_i\right)$$

$$\Pi_{\text{manufacturer}} = p\cdot\left(\frac{n_i}{v_i}\right)(v_i-p)^+ + p\cdot\left(\frac{n_j}{v_j}\right)(v_j-\beta p)^+ = p\cdot\left(\frac{n_j}{v_j}\right)(v_j-\beta p) \quad \text{if} \quad (v_i <)\ \frac{v_i}{X} \le p < \frac{v_j}{X} \quad \left(\le \frac{v_j}{\beta}\right)$$

$$\Pi_{\text{manufacturer}} = p\cdot\left(\frac{n_A}{v_A}\right)(v_A-\beta p) + p\cdot\left(\frac{n_B}{v_B}\right)(v_B-\beta p) \quad \text{else, i.e., if} \quad p < \frac{v_i}{X} \quad \left(\le \frac{v_i}{\beta} \le \frac{v_j}{\beta}\right).$$

Note that there are two discontinuity points in the profit function (i.e., v_i/X and v_j/X), where the profit is lower to the right than to the left.

On the domain $p \in [v_i/X, v_j/X)$ (right domain), the optimal price is

$$\frac{v_i}{X} \quad \text{if} \quad \frac{v_j}{2\beta} < \frac{v_i}{X} \quad \text{i.e., if } \frac{v_i}{v_j} > \frac{X}{2\beta} \text{ (and profit function is decreasing)}$$

$$\frac{v_j}{2\beta} \quad \text{if} \quad \frac{v_i}{X} \le \frac{v_j}{2\beta} < \frac{v_j}{X} \quad \text{i.e., if} \quad k+1 > \frac{2}{3\beta} \quad \text{and} \quad \frac{v_i}{v_j} \le \frac{X}{2\beta} \text{ (and profit function is unimodal)}$$

$$\frac{v_j}{X} - \epsilon \quad \text{if} \quad \frac{v_j}{2\beta} \ge \frac{v_j}{X} \quad \text{i.e., if } k+1 \le \frac{2}{3\beta} \text{ (and profit function is increasing).}$$

On the domain $p \in [0, v_i/X)$ (left domain), the profit function is unimodal reaching a maximum at $\bar{p}/\beta$ if $\bar{p}/\beta < v_i/X$; otherwise the profit function is increasing on the domain. After simplifications, we find that

$$\frac{\bar{p}}{\beta} < \frac{v_i}{X} \quad \Leftrightarrow \quad \left(\frac{2}{k+1} - 3\beta\right) n_i < \left[\left(2\frac{v_i}{v_j}+1\right)\beta - \frac{2}{k+1}\right] n_j \quad \Leftrightarrow \quad (X-2\beta)\frac{n_i}{n_j} < 2\beta\frac{v_i}{v_j} - X. \tag{A1}$$

The above inequality cannot be satisfied when $v_i/v_j < X/(2\beta)$.

(b) When $2/(\beta+1) < k+1 \le 2/(3\beta)$, then $(X-2\beta)(n_i/n_j) \ge 0$ while, since $v_i \le v_j$, we have $2\beta\frac{v_i}{v_j} - X \le 2\beta - X \le 0$. Therefore, (A1) does not hold, and the profit function is increasing on both the domains $p \in [0, v_i/X)$ and $p \in [v_i/X, v_j/X)$. Due to the discontinuity, we have to compare the profit to the left of v_i/X with that to the left of v_j/X. The optimal price is $v_j/X - \epsilon$ when

$$\frac{n_i}{X}\left(v_i - \beta\frac{v_i}{X}\right) + \frac{v_i}{X}\frac{n_j}{v_j}\left(v_j - \beta\frac{v_i}{X}\right) < \frac{n_j}{X}\left(v_j - \beta\frac{v_j}{X}\right),$$

i.e.,

$$\frac{n_i}{n_j} < \frac{v_j}{v_i} - \frac{X - \beta\frac{v_i}{v_j}}{X-\beta} = \frac{v_j}{v_i} - \frac{\frac{2}{k+1} - \beta\left(1+\frac{v_i}{v_j}\right)}{\frac{2}{k+1} - 2\beta}. \tag{A2}$$

Otherwise, the optimal price is $v_i/X - \epsilon$. With some algebra (involving finding the roots of a degree-2 polynomial; details are omitted here due to space constraints), we find that (A2) is equivalent to

$$\frac{v_j}{v_i} > \frac{1}{2}\left(\frac{n_i}{n_j} + \frac{\frac{2}{k+1}-\beta}{\frac{2}{k+1}-2\beta} + \sqrt{\left(\frac{n_i}{n_j}\right)^2 + 2\frac{n_i}{n_j}\frac{\frac{2}{k+1}-\beta}{\frac{2}{k+1}-2\beta} + \left(\frac{\frac{2}{k+1}-3\beta}{\frac{2}{k+1}-2\beta}\right)^2}\right),$$

where the right-hand-side equals 1 when $n_i = 0$, and is increasing in n_i.

(c) In the remainder of the proof, we assume $2/(3\beta) < k+1 \le 1/\beta$ (implying $\beta \le X < 2\beta$). We have 3 cases to consider.

When $\bar{p}/\beta, v_j/(2\beta) < v_i/X$, the profit function reaches a maximum at $\bar{p}/\beta$ on the left domain and is decreasing on right domain (after a drop at the discontinuity point), thus the global optimizer is $\bar{p}/\beta$.

When $v_i/X \le v_j/(2\beta)$, $\bar{p}/\beta$, the profit function is increasing on the left domain and, after a drop at the discontinuity point, reaches a maximum on the right domain at $v_j/(2\beta)$. Thus, the global optimizer is either $v_j/(2\beta)$ or $v_i/X - \epsilon$, depending on which of these two points yields a higher profit function. Namely, the optimal price is $v_j/(2\beta)$ when

$$\frac{n_i v_i}{X}\left(1 - \frac{\beta}{X}\right) + \frac{v_i n_j}{X}\left(1 - \frac{\beta}{X}\frac{v_i}{v_j}\right) < \frac{n_j v_j}{4\beta} \quad \Leftrightarrow \quad \frac{n_i}{n_j} < \frac{\frac{X}{4\beta}\frac{v_j}{v_i} + \frac{\beta}{X}\frac{v_i}{v_j} - 1}{1 - \frac{\beta}{X}},$$

and $v_i/X - \epsilon$ otherwise.

When $\bar{p}/\beta < v_i/X \le v_j/(2\beta)$ $(< v_j/X)$, there is a local maximum on each domain, and we must compare the value of the profit function at each of them.

Note that these are the only possible cases as it is impossible to have $v_j/(2\beta) < v_i/X \le \bar{p}/\beta$ because the first inequality implies $v_i/v_j > X/(2\beta)$, so the right-hand side of (A1) is positive, so (A1) holds true (since $X < 2\beta$ implies that the left-hand side is negative), which contradicts $v_i/X \le \bar{p}/\beta$.

We now compare the profit function at the two possible maximizers, $\bar{p}/\beta$ and $v_j/(2\beta)$. Similar to what we obtained in the case of $k+1 \le 2/(\beta+1)$, we have

$$\frac{v_j n_j}{4\beta} \ge \frac{(n_A+n_B)^2}{4\beta\left(\frac{n_A}{v_A} + \frac{n_B}{v_B}\right)} \quad \Leftrightarrow \quad \frac{n_i}{n_j} \le \frac{v_j}{v_i} - 2.$$

Therefore, the optimal solution is $\bar{p}/\beta$ iff either $v_j/v_i < 2\beta/X$ or $(v_j/v_i \ge 2\beta/X$ and $(2\beta - X)(n_i/n_j) > X - 2\beta v_i/v_j$ and $n_i/n_j > v_j/v_i - 2)$. Note that, since $\beta \le X < 2\beta$, when $v_j/v_i < 2\beta/X$ (≤ 2) we have

$(2\beta - X)(n_i/n_j) \geq 0 > X - 2\beta v_i/v_j$ and $n_i/n_j > 0 > v_j/v_i - 2$. Hence, the optimal solution is $\bar{p}/\beta$ iff $(2\beta - X)(n_i/n_j) > X - 2\beta v_i/v_j$ and $n_i/n_j > v_j/v_i - 2$. Equivalently, the optimal solution is $\bar{p}/\beta$ iff either (i) $v_j/v_i \leq 2\beta/X$, or (ii) $v_j/v_i > 2\beta/X$ and $n_i/n_j > X/(2\beta - X)$, or (iii) $n_i/n_j < X/(2\beta - x)$ and $2\beta/X < v_j/v_i < 2\beta/(X - (2\beta - X)(n_i/n_j))$.

Likewise, the optimal solution is $v_i/X - \epsilon$ iff (i) $(2\beta - X)(n_i/n_j) \leq X - 2\beta v_i/v_j$ and (ii) $(n_i/n_j)(1 - \beta/X) \geq (X/4\beta)(v_j/v_i) + (\beta/X)(v_i/v_j) - 1$. The first inequality (i) is equivalent to $n_i/n_j < X/(2\beta - X)$ and $v_j/v_i \geq 2\beta/(X - (2\beta - X)(n_i/n_j))$. With some algebra (involving finding the roots of a degree-2 polynomial; details are omitted here due to space constraints), we find that the second inequality (ii) is equivalent to

$$\frac{v_j}{v_i} \leq \frac{2\beta}{X}\left[1 + \frac{n_i}{n_j}\left(1 - \frac{\beta}{X}\right) + \sqrt{\frac{n_i}{n_j}\left(1 - \frac{\beta}{X}\right)\left(2 + \frac{n_i}{n_j}\left(1 - \frac{\beta}{X}\right)\right)}\right].$$

Moreover, with some algebra, it is straightforward to show that

$$\frac{X}{4\beta}\frac{v_j}{v_i} + \frac{\beta}{X}\frac{v_i}{v_j} - 1 - \left(\frac{v_j}{v_i} - 2\right)\left(1 - \frac{\beta}{X}\right) = \frac{\left(\frac{v_j}{v_i}(2\beta - X) - 2\beta\right)^2}{4\beta X} \geq 0.$$

Therefore, the second inequality (ii) implies $n_i/n_j > v_j/v_i - 2$. Moreover, the two curves touch when $v_j/v_i = 2\beta/(2\beta - X)$ and $n_i/n_j = (2X - 2\beta)/(2\beta - X)$, which is also where the curve defining the region for case (c1) intersects the line.

Otherwise, the solution is v_j/X.

Q.E.D.

Proof of Proposition 1. We first establish three preliminary results.

Lemma A4. *Under indication-based pricing, the drug manufacturer invests in indication B iff $I < \bar{I}$, where $\bar{I}$ is given by*

$$\bar{I} = \begin{cases} \frac{n_B v_B}{4} & \text{if } k+1 \leq \frac{2}{\beta+1} \\ n_B v_B \cdot \frac{2\left(\frac{1}{k+1} - \beta\right)}{\left(\frac{2}{k+1} - \beta\right)^2} & \text{if } \frac{2}{\beta+1} < k+1 \leq \frac{2}{3\beta} \\ \frac{n_B v_B}{4\beta} & \text{else.} \end{cases}$$

Proof of Lemma A4. If the drug manufacturer does not invest in indication B, it earns profit solely from indication A equal to $n_A p_A^*(v_A - \bar{\beta} p_A^*)/v_A$. Using Lemma 3, the drug manufacturer profit then equals (neglecting terms that are proportional to ϵ)

$$\begin{cases} \frac{n_A v_A}{4} & \text{if } k+1 \leq \frac{2}{\beta+1} \\ \frac{n_A}{\frac{2}{k+1} - \beta}\left(v_A - \beta \frac{v_A}{\frac{2}{k+1} - \beta}\right) = 2 n_A v_A \frac{\frac{1}{k+1} - \beta}{\left(\frac{2}{k+1} - \beta\right)^2} & \text{if } \frac{2}{\beta+1} < k+1 \leq \frac{2}{3\beta} \\ \frac{n_A v_A}{4\beta} & \text{else.} \end{cases}$$

Similarly, if the drug manufacturer invests in indication B, it sets the price for each indication independently, and it earns revenue from both indications $n_A p_A^*(v_A - \bar{\beta} p_A^*)/v_A + n_B p_B^*(v_B - \bar{\beta} p_B^*)/v_B$, and also incurs cost I. Using Lemma 3, the drug manufacturer profit then equals

$$\begin{cases} \frac{n_A v_A + n_B v_B}{4} - I & \text{if } k+1 \leq \frac{2}{\beta+1} \\ 2(n_A v_A + n_B v_B) \frac{\frac{1}{k+1} - \beta}{\left(\frac{2}{k+1} - \beta\right)^2} - I & \text{if } \frac{2}{\beta+1} < k+1 \leq \frac{2}{3\beta} \\ \frac{n_A v_A + n_B v_B}{4\beta} - I & \text{else.} \end{cases}$$

Therefore, the drug manufacturer invests in indication B iff

$$\begin{cases} \frac{n_B v_B}{4} > I & \text{if } k+1 \le \frac{2}{\beta+1} \\ 2n_B v_B \frac{\frac{1}{k+1}-\beta}{\left(\frac{2}{k+1}-\beta\right)^2} > I & \text{if } \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ \frac{n_B v_B}{4\beta} > I & \text{else.} \end{cases}$$

Q.E.D.

LEMMA A5. *Under uniform pricing with non-adjustable price, the drug manufacturer invests in indication B iff $I < \tilde{I}$, where*

$$\tilde{I} = \begin{cases} \frac{n_B v_A}{2v_B} \cdot \left(v_B - \frac{v_A}{2}\right) & \text{if } k+1 \le \frac{2}{\beta+1} \text{ and } v_B > \frac{v_A}{2} \\ \frac{n_B v_A}{2v_B} \cdot \frac{2}{\frac{2}{k+1}-\beta} \left(v_B - \frac{\beta v_A}{\frac{2}{k+1}-\beta}\right) & \text{if } \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \text{ and } v_B > v_A \\ \frac{n_B v_A}{2v_B} \cdot \frac{1}{\beta} \left(v_B - \frac{v_A}{2}\right) & \text{if } \left\{\frac{2}{3\beta} < k+1 \le \frac{1}{\beta} \text{ and } v_B > \frac{v_A}{\beta(k+1)} - \frac{v_A}{2}\right\} \text{ or if } \left\{k+1 > \frac{1}{\beta} \text{ and } v_B > \frac{v_A}{2}\right\} \\ -\infty & \text{else,} \end{cases}$$

where $\tilde{I} = -\infty$ indicates that the drug manufacturer does not find it profitable to invest in indication B regardless of investment cost $I \ge 0$.

PROOF OF LEMMA A5. Using Lemma 3, the price charged for the drug under indication A is

$$p_A^* = \begin{cases} \frac{v_A}{2} & \text{if } k+1 \le \frac{2}{\beta+1} \\ \frac{v_i}{\frac{2}{k+1}-\beta} - \epsilon & \text{if } \frac{2}{\beta+1} < k+1 < \frac{2}{3\beta} \\ \frac{v_A}{2\beta} & \text{else.} \end{cases}$$

The drug manufacturer chooses to invest in indication B iff the profit earned from indication B at price p_A^*, which is $n_B p_A^* (v_B - \bar{\beta}_B p_A^*)^+ / v_B$ exceeds the investment cost I, where $\bar{\beta}_B$ represents the coverage decision (derived in Lemma 2) of indication B when the price is p_A^*.

If $k+1 \le 2/(\beta+1)$, using Lemma 2, the payer does not cover indication B. Therefore, the drug manufacturer invests in indication B iff $v_B > v_A/2$ and $n_B v_A (v_B - v_A/2)/(2v_B) > I$.

If $k+1 > 1/\beta$ and $v_A/(2\beta) \ge v_B/\beta$ (i.e., $v_A \ge 2v_B$) the payer does not cover indication B. Therefore, the drug manufacturer investing in indication B requires $v_B > v_A/(2\beta)$, which contradicts $v_A \ge 2v_B$.

If $k+1 > 1/\beta$ and $v_A/(2\beta) < v_B/\beta$ (i.e., $v_A < 2v_B$) the payer covers indication B. Therefore, the drug manufacturer invests in indication B iff $v_B > v_A/2$ and $n_B v_A (v_B - v_A/2)/(2\beta v_B) > I$.

If $2/(\beta+1) < k+1 \le 2/(3\beta)$ and $v_A/(2/(k+1)-\beta) \ge v_B/(2/(k+1)-\beta)$ (i.e., $v_A \ge v_B$) the payer does not cover indication B. Therefore, the drug manufacturer investing in indication B requires

$$v_B > \frac{v_A}{\frac{2}{k+1}-\beta}$$

which implies, for this range of $k+1$, $v_B > v_A$, which is a contradiction.

If $2/(\beta+1) < k+1 \le 2/(3\beta)$ and $v_A/(2/(k+1)-\beta) < v_B/(2/(k+1)-\beta)$ (i.e., $v_A < v_B$) the payer covers indication B. Therefore, the drug manufacturer invests in indication B iff

$$v_B > \frac{\beta v_A}{\frac{2}{k+1}-\beta} \text{ and } \frac{n_B}{v_B} \frac{v_A}{\frac{2}{k+1}-\beta} \left(v_B - \frac{\beta v_A}{\frac{2}{k+1}-\beta}\right) > I,$$

where the first inequality is implied by $v_A < v_B$.

If $2/(3\beta) < k+1 \le 1/\beta$ and $v_A/(2\beta) \ge v_B/(2/(k+1)-\beta)$ the payer does not cover indication B. Therefore, the drug manufacturer investing in indication B requires $v_B > v_A/(2\beta)$, which implies $v_A < v_B$, while for this range of $k+1$, $v_A/(2\beta) \ge v_B/(2/(k+1)-\beta)$ implies $v_A \ge v_B$, which is a contradiction.

If $2/(3\beta) < k+1 \le 1/\beta$ and $v_A/(2\beta) < v_B/(2/(k+1)-\beta)$ the payer covers indication B. Therefore, the drug manufacturer invests in indication B iff $v_B > v_A/2$ and $n_B v_A(v_B - v_A/2)/(2\beta v_B) > I$, where the first inequality is implied by $v_A/(2\beta) < v_B/(2/(k+1)-\beta)$. *Q.E.D.*

LEMMA A6. *Under uniform pricing with adjustable price, the drug manufacturer invests in indication B iff $I < \hat{I}$, where*

$$\hat{I} = \begin{cases} \frac{n_A n_B}{4\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}\left(\frac{n_B}{n_A}-\frac{v_A}{v_B}+2\right) & \text{in case (a1)} \\ \frac{n_B v_B - n_A v_A}{4} & \text{in case (a2) with } v_A < v_B \\ \frac{n_B v_A}{X}\left(1-\frac{\beta}{X}\frac{v_A}{v_B}\right) & \text{in case (b1) or (c2) with } v_A < v_B \\ 2(n_B v_B - n_A v_A)\frac{\frac{1}{k+1}-\beta}{X^2} + \frac{n_A v_B}{X}\left(1-\frac{\beta}{X}\frac{v_B}{v_A}\right) & \text{in case (b1) or (c2) with } v_B < v_A \\ 2(n_B v_B - n_A v_A)\frac{\frac{1}{k+1}-\beta}{X^2} & \text{in case (b2) with } v_A < v_B \\ \frac{n_A n_B}{4\beta\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}\left(\frac{n_B}{n_A}-\frac{v_A}{v_B}+2\right) & \text{in case (c1) or (d1)} \\ \frac{n_B v_B - n_A v_A}{4\beta} & \text{in case (c3) or (d2) with } v_A < v_B \\ -\infty & \text{else,} \end{cases}$$

where $\hat{I} = -\infty$ indicates that the drug manufacturer does not find it profitable to invest in indication B regardless of investment cost $I \ge 0$.

PROOF OF LEMMA A6. The drug manufacturer chooses to invest in indication B iff the total profit (net of investment cost I) earned when both indications are marketed, and are offered at the price obtained in Lemma 4, exceeds the profit when only indication A is marketed.

When only indication A is marketed, using Lemma 3, the drug manufacturer profit is

$$\Pi^A_{\text{manufacturer}} = \begin{cases} \frac{n_A v_A}{4} & \text{if } k+1 \le \frac{2}{\beta+1} \\ 2n_A v_A \frac{\frac{1}{k+1}-\beta}{X^2} & \text{if } \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ \frac{n_A v_A}{4\beta} & \text{else.} \end{cases}$$

If indication B receives investment, the total profit net of investment cost is $-I + p\cdot(n_A/v_A)(v_A - \bar{\beta}_A p)^+ + p\cdot(n_B/v_B)(v_B - \bar{\beta}_B p)^+$ where the price and coverage are set as detailed in Lemma 4. Hence, $\hat{I} = p\cdot(n_A/v_A)(v_A - \bar{\beta}_A p)^+ + p\cdot(n_B/v_B)(v_B - \bar{\beta}_B p)^+ - \Pi^A_{\text{manufacturer}}$, whenever that quantity is positive. We next go through all the cases stated in Lemma 4.

Suppose $k+1 < 2/(\beta+1)$. If $n_i/n_j \ge v_j/v_i - 2$, then

$$\hat{I} = \frac{(n_A+n_B)^2}{4\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)} - \frac{n_A v_A}{4} = \frac{n_A n_B}{4\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}\left(\frac{n_B}{n_A}-\frac{v_A}{v_B}+2\right).$$

If $n_i/n_j < v_j/v_i - 2$ and $j = A$, the drug manufacturer does not find it profitable to invest in indication B. If $n_i/n_j < v_j/v_i - 2$ and $j = B$, then

$$\hat{I} = \frac{n_B v_B - n_A v_A}{4}.$$

Suppose $2/(\beta+1) < k+1 \le 2/(3\beta)$. In case [b1] with $j=B$, then

$$\hat{I} = \frac{n_B v_A}{X}\left(1 - \frac{\beta}{X}\frac{v_A}{v_B}\right).$$

In case [b1] with $j=A$, then

$$\hat{I} = 2(n_B v_B - n_A v_A)\frac{\frac{1}{k+1}-\beta}{X^2} + \frac{n_A v_B}{X}\left(1 - \frac{\beta}{X}\frac{v_B}{v_A}\right).$$

In case [b2] with $j=A$, the drug manufacturer does not find it profitable to invest in indication B. In case [b2] with $j=B$, then

$$\hat{I} = 2(n_B v_B - n_A v_A)\frac{\frac{1}{k+1}-\beta}{X^2}.$$

Suppose $2/(3\beta) < k+1$. In case [c1] or [d1], then

$$\hat{I} = \frac{n_A n_B}{4\beta\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}\left(\frac{n_B}{n_A} - \frac{v_A}{v_B} + 2\right).$$

In case [c2] with $j=B$, then

$$\hat{I} = \frac{n_B v_A}{X}\left(1 - \frac{\beta}{X}\frac{v_A}{v_B}\right).$$

In case [c2] with $j=A$, then

$$\hat{I} = 2(n_B v_B - n_A v_A)\frac{\frac{1}{k+1}-\beta}{X^2} + \frac{n_A v_B}{X}\left(1 - \frac{\beta}{X}\frac{v_B}{v_A}\right).$$

In case [c3] or [d2] with $j=A$, the drug manufacturer does not find it profitable to invest in indication B. In case [c3] or [d2] with $j=B$, then

$$\hat{I} = \frac{n_B v_B - n_A v_A}{4\beta}.$$

Q.E.D.

We now proceed with the proof of Proposition 1.

(i) The result is trivial in cases when $\tilde{I} = -\infty$ so we focus on other cases in this proof. When $k+1 \le 2/(\beta+1)$ and $v_A < 2v_B$, then $\tilde{I} - \bar{I}$ is equal to

$$\frac{n_B v_A}{2} - \frac{n_B v_A^2}{4v_B} - \frac{n_B v_B}{4} = n_B\frac{2v_A v_B - v_A^2 - v_B^2}{4v_B} = -\frac{n_B(v_A - v_B)^2}{4v_B} < 0.$$

When $2/(\beta+1) < k+1 \le 2/(3\beta)$, for $v_A < v_B$, then $\tilde{I} - \bar{I}$ is equal to

$$\begin{aligned}
&\frac{n_B v_A}{2v_B}\cdot\frac{2}{X}\left(v_B - \frac{\beta v_A}{X}\right) - n_B v_B\cdot\frac{2\left(\frac{1}{k+1}-\beta\right)}{X^2} = \frac{n_B}{v_B}\cdot\frac{v_A v_B X - \beta v_A^2 - 2v_B^2\left(\frac{1}{k+1}-\beta\right)}{X^2} \\
=&\frac{n_B}{v_B}\cdot\frac{\beta(-v_A v_B - v_A^2 + 2v_B^2) + \frac{2}{k+1}(v_A v_B - v_B^2)}{X^2} = \frac{n_B}{v_B}\cdot(v_B - v_A)\cdot\frac{\beta(2v_B + v_A) - \frac{2}{k+1}v_B}{X^2} \\
\le&\frac{n_B}{v_B}\cdot(v_B - v_A)\cdot\frac{\beta(2v_B + v_A) - 3\beta v_B}{X^2} = -\frac{n_B}{v_B}\cdot\frac{\beta(v_B - v_A)^2}{X^2} \le 0
\end{aligned}$$

where the first inequality is due to $k+1 \le 2/(3\beta)$.

When $k+1 > 2/(3\beta)$, and v_A, v_B are such that $\tilde{I}$ is finite, then $\tilde{I} - \bar{I}$ is equal to

$$\frac{n_B v_A}{2\beta v_B}\left(v_B - \frac{v_A}{2}\right) - \frac{n_B v_B}{4\beta} = \frac{n_B}{4\beta v_B}(2v_A v_B - v_A^2 - v_B^2) = -\frac{n_B}{4\beta v_B}(v_B - v_A)^2 \le 0.$$

(ii) The result is trivial in cases when $\hat{I}=-\infty$ so we focus on other cases in this proof. When $k+1\leq 2/(\beta+1)$, then $\hat{I}-\bar{I}$ is either equal to (case [a1])

$$\frac{n_An_B}{4\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}\left(\frac{n_B}{n_A}-\frac{v_A}{v_B}+2\right)-\frac{n_Bv_B}{4}=\frac{n_B}{4}\cdot\frac{n_A(n_Bv_B-n_Av_A+2n_Av_B)-n_Av_B^2\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}{\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)n_Av_B}$$
$$=\frac{n_B}{4}\cdot\frac{n_A^2}{v_A}\cdot\frac{-v_A^2-v_B^2+2v_Av_B}{\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)n_Av_B}=-\frac{n_B}{4v_B}\cdot\frac{n_A}{v_A}\cdot\frac{(v_A-v_B)^2}{\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}<0,$$

or (case [a2] with $v_A<v_B$)

$$\frac{n_Bv_B-n_Av_A}{4}-\frac{n_Bv_B}{4}=\frac{-n_Av_A}{4}<0.$$

When $2/(\beta+1)<k+1\leq 2/(3\beta)$, then $\hat{I}-\bar{I}$ is either equal to (case [b2])

$$2(n_Bv_B-n_Av_A)\frac{\frac{1}{k+1}-\beta}{X^2}-2n_Bv_B\frac{\frac{1}{k+1}-\beta}{X^2}=-2n_Av_A\frac{\frac{1}{k+1}-\beta}{X^2}<0$$

or (case [b1] with $v_A<v_B$),

$$\frac{n_Bv_A}{X}\left(1-\frac{\beta}{X}\frac{v_A}{v_B}\right)-2n_Bv_B\frac{\frac{1}{k+1}-\beta}{X^2}=\frac{n_B(v_A-v_B)}{X^2}\left(\frac{2}{k+1}-\beta\frac{v_A+2v_B}{v_B}\right)<0$$

where the last inequality is due to $(v_A+2v_B)/v_B>2$ and $2/(k+1)-2\beta>0$ in this range of $k+1$, or (case [b1] with $v_B<v_A$)

$$2(n_Bv_B-n_Av_A)\frac{\frac{1}{k+1}-\beta}{X^2}+\frac{n_Av_B}{X}\left(1-\frac{\beta}{X}\frac{v_B}{v_A}\right)-2n_Bv_B\frac{\frac{1}{k+1}-\beta}{X^2}$$
$$=-2n_Av_A\frac{\frac{1}{k+1}-\beta}{X^2}+\frac{n_Av_B}{X}\left(1-\frac{\beta}{X}\frac{v_B}{v_A}\right)=-\frac{n_A(v_A-v_B)}{X^2}\left(\frac{2}{k+1}-\beta\frac{v_B+2v_A}{v_A}\right)<0.$$

When $k+1>2/(3\beta)$, then $\hat{I}-\bar{I}$ is either equal to one of the above values or (case [c1] and [d1])

$$\frac{n_An_B}{4\beta\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}\left(\frac{n_B}{n_A}-\frac{v_A}{v_B}+2\right)-\frac{n_Bv_B}{4\beta}=-\frac{1}{\beta}\cdot\frac{n_B}{4v_B}\cdot\frac{n_A}{v_A}\cdot\frac{(v_A-v_B)^2}{\left(\frac{n_A}{v_A}+\frac{n_B}{v_B}\right)}<0,$$

or (case [c3] or [d2])

$$\frac{n_Bv_B-n_Av_A}{4\beta}-\frac{n_Bv_B}{4\beta}=\frac{-n_Av_A}{4\beta}<0.$$

Q.E.D.

Proof of Corollary 1. If only indication A is marketed, denote $\Pi^A_{\text{manufacturer}}$ the drug manufacturer profit (which is the same under all pricing systems). Denote $\Pi^{IBP}_{\text{manufacturer}},\Pi^{UA}_{\text{manufacturer}},\Pi^{UN}_{\text{manufacturer}}$ the drug manufacturer profit when both indications are introduced (not including investment cost) under respectively indication-based pricing, uniform pricing with adjustable price, and uniform pricing with non-adjustable price. We defined $\bar{I}=\Pi^{IBP}_{\text{manufacturer}}-\Pi^{A}_{\text{manufacturer}}$, $\tilde{I}=\Pi^{UN}_{\text{manufacturer}}-\Pi^{A}_{\text{manufacturer}}$ and $\hat{I}=\Pi^{UA}_{\text{manufacturer}}-\Pi^{A}_{\text{manufacturer}}$. Proposition 1 establishes that $\bar{I}>\tilde{I},\hat{I}$. It follows that $\Pi^{IBP}_{\text{manufacturer}}>\Pi^{UN}_{\text{manufacturer}},\Pi^{UA}_{\text{manufacturer}}$.

If $I>\bar{I}$, indication B does not receive investment under any pricing system, so the drug manufacturer is indifferent. If $I<\tilde{I}$ (resp. $I<\hat{I}$), indication B receives investment under both pricing system, and since $\Pi^{IBP}_{\text{manufacturer}}-I>\Pi^{UN}_{\text{manufacturer}}-I$ (resp. $\Pi^{IBP}_{\text{manufacturer}}-I>\Pi^{UA}_{\text{manufacturer}}-I$), the drug manufacturer is

better off under indication-based pricing. If $\tilde{I} < I < \bar{I}$ (resp. $\hat{I} < I < \bar{I}$), indication B receives investment under indication-based pricing but not under uniform pricing. We have $\Pi^{IBP}_{\text{manufacturer}} - I > \Pi^{IBP}_{\text{manufacturer}} - \bar{I} = \Pi^{A}_{\text{manufacturer}}$. Hence, the drug manufacturer is better off under indication-based pricing. *Q.E.D.*

Proof of Proposition 2. The demand for a given indication $l \in \{A, B\}$ priced at p is given by $(n_l/v_l)(v_l - \bar{\beta}_l p)^+$. Under indication-based pricing, the demand for indication $l \in \{A, B\}$ is

$$D_l^{IBP} = \begin{cases} \frac{n_l}{2} & k+1 \le \frac{2}{\beta+1} \\ 2n_l \frac{\frac{1}{k+1} - \beta}{X} & \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ \frac{n_l}{2} & \text{else.} \end{cases}$$

Under UN, $D_A^{UN} = D_A^{IBP}$. Moreover,

$$D_B^{UN} = \begin{cases} n_B(1 - \frac{v_A}{2v_B}) & \text{if } k+1 \le \frac{2}{\beta+1}, 2v_B > v_A \\ n_B(1 - \frac{v_A}{v_B}\frac{\beta}{X}) & \text{if } \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta}, v_A < v_B \\ n_B(1 - \frac{v_A}{2v_B}) & \text{if } \left\{ \frac{2}{3\beta} < k+1 \le \frac{1}{\beta} \text{ and } \frac{v_A}{2\beta} < \frac{v_B}{X} \right\} \text{ or if } \left\{ k+1 > \frac{1}{\beta} \text{ and } v_A < 2v_B \right\} \\ 0 & \text{else.} \end{cases}$$

It is straightforward to show that in each case of range of $k+1$, we have $D_B^{UN} > D_B^{IBP}$ iff $v_B > v_A$. As a result, the total demand is higher under UN iff $v_B > v_A$ as well.

Under UA,

$$D_i^{UA} = \begin{cases} \frac{n_i}{v_i} \frac{n_i + n_j(2\frac{v_i}{v_j} - 1)}{2\left(\frac{n_i}{v_i} + \frac{n_j}{v_j}\right)} & (a1), (c1), (d1) \\ 0 & (a2), (b2), (c3), (d2) \\ 2n_i \frac{\frac{1}{k+1} - \beta}{X} & (b1), (c2) \end{cases}$$

$$D_j^{UA} = \begin{cases} \frac{n_j}{v_j} \frac{n_j + n_i(2\frac{v_j}{v_i} - 1)}{2\left(\frac{n_i}{v_i} + \frac{n_j}{v_j}\right)} & (a1), (c1), (d1) \\ \frac{n_j}{2} & (a2), (c3), (d2) \\ 2n_j \frac{\frac{1}{k+1} - \beta}{X} & (b2) \\ n_j \left(1 - \frac{\beta}{X}\frac{v_i}{v_j}\right) & (b1), (c2). \end{cases}$$

It is straightforward to show that in case (a1), (c1), (c2) and (d1), $D_i^{UA} < D_i^{IBP}$ and $D_j^{UA} > D_j^{IBP}$.
In case (a2), (b2), (c3) and (d2), $D_i^{UA} = 0 < D_i^{IBP}$ and $D_j^{UA} = D_j^{IBP}$.
In case (b1), $D_i^{UA} = D_i^{IBP}$ and $D_j^{UA} > D_j^{IBP}$. The total demand is

$$D_A^{UA} + D_B^{UA} = \begin{cases} (n_A + n_B)/2 & (a1), (c1), (d1) \\ n_j/2 & (a2), (c3), (d2) \\ 2n_j \frac{\frac{1}{k+1} - \beta}{X} & (b2) \\ 2n_i \frac{\frac{1}{k+1} - \beta}{X} + n_j \left(1 - \frac{\beta}{X}\frac{v_i}{v_j}\right) & (b1), (c2) \end{cases}$$

In case (c2), the total demand under UA is higher than under IBP iff

$$n_i\left(1 - \frac{\beta}{X}\right) + n_j\left(1 - \frac{\beta}{X}\frac{v_i}{v_j}\right) > \frac{n_i + n_j}{2} \Leftrightarrow \frac{n_j}{2}\left(1 - \frac{2\beta}{X}\frac{v_i}{v_j}\right) > \frac{n_i}{2}\left(\frac{2\beta}{X} - 1\right) \Leftrightarrow X - 2\beta\frac{v_i}{v_j} > \frac{n_i}{n_j}(2\beta - X)$$
$$\Leftrightarrow \frac{2}{k+1} - \left(2\frac{v_i}{v_j} + 1\right)\beta > \frac{n_i}{n_j}\left(3\beta - \frac{2}{k+1}\right),$$

which is valid in case (c2).

Therefore, the total demand is the same as under IBP in cases (a1), (c1) and (d1); it is lower than under IBP in cases (a2), (b2), (c3) and (d2); it is higher than under IBP in cases (b1) and (c2). *Q.E.D.*

Proof of Proposition 3.

(i) Under both indication-based pricing and uniform pricing with non-adjustable price, indication A is priced the same way and thus the coverage is the same and the patient utility from indication A is the same. Therefore, patients are better off under the pricing scheme leading to the highest patient utility derived from indication B.

Under indication-based pricing, indication B is priced and covered as described in Lemma 3 and thus, using eq. (1) the patient utility is given by

$$\Pi^{IBP}_{\text{patient}} = \begin{cases} \frac{n_B v_B}{8} & k+1 \le \frac{2}{\beta+1} \\ \frac{n_B v_B}{2}\left(1-\frac{\beta}{X}\right)^2 = 2n_B v_B \frac{\left(\frac{1}{k+1}-\beta\right)^2}{X^2} & \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ \frac{n_B v_B}{8} & \text{else.} \end{cases}$$

Under uniform pricing with non-adjustable price, indication B is priced at the indication A price which can be obtained from Lemma 3. We obtain the resulting payer coverage decision from Lemma 2 and the patient utility from eq. (1):

$$\Pi^{UN}_{\text{patient}} = \begin{cases} \frac{n_B}{2v_B}\cdot\left(v_B-\frac{v_A}{2}\right)^2 & \text{if } k+1 \le \frac{2}{\beta+1} \text{ and } 2v_B > v_A \\ \frac{n_B}{2v_B}\cdot\left(v_B-\frac{\beta v_A}{X}\right)^2 & \text{if } \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \text{ and } v_A < v_B \\ \frac{n_B}{2v_B}\cdot\left(v_B-\frac{v_A}{2}\right)^2 & \text{if } \left\{\frac{2}{3\beta} < k+1 \le \frac{1}{\beta} \text{ and } \frac{v_A}{2\beta} < \frac{v_B}{X}\right\} \text{ or if } \left\{k+1 > \frac{1}{\beta} \text{ and } v_A < 2v_B\right\} \\ 0 & \text{else.} \end{cases}$$

When $k+1 \le 2/(\beta+1)$ and $2v_B > v_A$, we have

$$\Pi^{IBP}_{\text{patient}} < \Pi^{UN}_{\text{patient}} \quad \Leftrightarrow \quad \frac{1}{4} < \left(1-\frac{v_A}{2v_B}\right)^2 \quad \Leftrightarrow \quad 1-\frac{v_A}{2v_B} > \frac{1}{2} \quad \Leftrightarrow \quad v_A < v_B.$$

When $2/(\beta+1) < k+1 \le 2/(3\beta)$ and $v_A < v_B$, we have

$$\Pi^{IBP}_{\text{patient}} < \Pi^{UN}_{\text{patient}} \quad \Leftrightarrow \quad \left(1-\frac{\beta}{X}\right)^2 < \left(1-\frac{\beta v_A/v_B}{X}\right)^2 \quad \Leftrightarrow \quad v_A < v_B.$$

When $2/(3\beta) < k+1 \le 1/\beta$ and $v_A/(2\beta) < v_B/(2/(k+1)-\beta)$ (which implies $v_A < 2v_B$), we have

$$\Pi^{IBP}_{\text{patient}} < \Pi^{UN}_{\text{patient}} \quad \Leftrightarrow \quad \frac{1}{4} < \left(1-\frac{v_A}{2v_B}\right)^2 \quad \Leftrightarrow \quad v_A < v_B.$$

This inequality is possible in this case because $2/(3\beta) < k+1 \le 1/\beta$ implies $2 \ge 2\beta/(2/(k+1)-\beta) > 1$.

When $k+1 > 1/\beta$ and $v_A < 2v_B$, we have

$$\Pi^{IBP}_{\text{patient}} < \Pi^{UN}_{\text{patient}} \quad \Leftrightarrow \quad v_A < v_B.$$

Therefore, for all possible values of k, we have $\Pi^{IBP}_{\text{patient}} < \Pi^{UN}_{\text{patient}}$ iff $v_A < v_B$.

(ii) Under indication-based pricing, the patient utility is given by

$$\Pi^{IBP}_{\text{patient}} = \begin{cases} \frac{n_A v_A + n_B v_B}{8} & k+1 \le \frac{2}{\beta+1} \\ \frac{n_A v_A + n_B v_B}{2}\left(1-\frac{\beta}{X}\right)^2 = 2(n_A v_A + n_B v_B)\frac{\left(\frac{1}{k+1}-\beta\right)^2}{X^2} & \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ \frac{n_A v_A + n_B v_B}{8} & \text{else.} \end{cases}$$

Under uniform pricing with adjustable price, the price and coverage are set as described in Lemma 4 and the patient utility is obtained by summing the utility from each indication.

If $k+1 \le 2/(\beta+1)$, then

$$\Pi^{UA}_{\text{patient}} = \begin{cases} \frac{n_A v_A + n_B v_B}{2} - \frac{3(n_A+n_B)^2}{8(r_A+r_B)} & \text{if } \frac{n_i}{n_j} \ge \frac{v_j}{v_i} - 2 \\ \frac{n_j v_j}{8} & \text{else,} \end{cases}$$

where the first expression is obtained after simplifying $(n_A/2v_A)(v_A-p)^2 + (n_B/2v_B)(v_B-p)^2$ with $p = (n_A+n_B)/(2(n_A/v_A + n_B/v_B))$. When $n_i/n_j \ge v_j/v_i - 2$, we have

$$\Pi^{IBP}_{\text{patient}} < \Pi^{UA}_{\text{patient}} \quad \Leftrightarrow \quad \frac{n_A v_A + n_B v_B}{8} < \frac{n_A v_A + n_B v_B}{2} - \frac{3(n_A+n_B)^2}{8(r_A+r_B)} \quad \Leftrightarrow \quad n_A v_A + n_B v_B > \frac{(n_A+n_B)^2}{r_A+r_B}$$
$$\Leftrightarrow \quad \frac{v_B}{v_A} + \frac{v_A}{v_B} > 2 \quad \Leftrightarrow \quad (v_B - v_A)^2 > 0.$$

Hence, for $k+1 \le 2/(\beta+1)$, the patient is better off under uniform pricing with adjustable price iff $n_i/n_j \ge v_j/v_i - 2$.

If $2/(\beta+1) < k+1 \le 2/(3\beta)$, then, when the price is $v_j/X - \epsilon$ ($> v_j \ge v_i$) (case (b2)), we have

$$\Pi^{UA}_{\text{patient}} = \frac{n_j}{2v_j}\left(v_j - \beta\frac{v_j}{X}\right)^2 = \frac{n_j v_j}{2}\left(1 - \frac{\beta}{X}\right)^2 < \Pi^{IBP}_{\text{patient}}.$$

When the price is $v_i/X - \epsilon$ (case (b1)), we have

$$\Pi^{UA}_{\text{patient}} = \frac{n_i}{2v_i}\left(v_i - \beta\frac{v_i}{X}\right)^2 + \frac{n_j}{2v_j}\left(v_j - \beta\frac{v_i}{X}\right)^2 = 2n_i v_i \frac{\left(\frac{1}{k+1} - \beta\right)^2}{X^2} + \frac{n_j v_j}{2}\frac{\left(X - \beta\frac{v_i}{v_j}\right)^2}{X^2}$$

$$\Pi^{UA}_{\text{patient}} - \Pi^{IBP}_{\text{patient}} = \frac{n_j v_j}{2}\frac{\left(X - \beta\frac{v_i}{v_j}\right)^2}{X^2} - 2n_j v_j \frac{\left(\frac{1}{k+1} - \beta\right)^2}{X^2} = \frac{n_j v_j}{2X^2}\beta\left(1 - \frac{v_i}{v_j}\right)\left(\frac{4}{k+1} - 3\beta - \beta\frac{v_i}{v_j}\right) > 0,$$

where the last inequality is due to $v_i/v_j < 1$ and $4/(k+1) - 4\beta > 0$ in this range of $k+1$.

If $k+1 > 2/(3\beta)$, the patient utility in case (c1) and (d1) (resp. (c2), (c3), (d2)) is the same as in case (a1) (resp. (b1), (a2), (a2)). Therefore, the patient is better off under uniform pricing with adjustable price in cases (c1), (d1) and (c2).

Q.E.D.

Proof of Proposition 4.

(i) The payer's objective from a given indication i when priced at p is

$$W_i = \frac{n_i}{v_i}(v_i - \bar{\beta}_i p)^+ \left[\frac{k+1}{2}(v_i + \bar{\beta}_i p) - p\right].$$

Under both indication-based pricing and uniform pricing with non-adjustable price, the payer's objective from indication A is the same. Therefore, it suffices to compare the payer's objective derived from indication B. We find that under indication-based pricing, the payer's objective derived from indication B is

$$\begin{cases} n_B v_B \frac{3k+1}{8} & k+1 \le \frac{2}{\beta+1} \\ 0 & \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ n_B v_B \left(\frac{3(k+1)}{8} - \frac{1}{4\beta}\right) & \text{else.} \end{cases}$$

Under uniform pricing with non-adjustable price, the payer's objective derived from indication B is

$$\begin{cases} \frac{k n_B}{2v_B}\left(v_B^2 - \frac{v_A^2}{4}\right) + \frac{n_B}{2v_B}\left(v_B - \frac{v_A}{2}\right)^2 & k+1 \le \frac{2}{\beta+1} \text{ and } \frac{v_A}{2} < v_B \\ \frac{n_B}{v_B}\left(v_B - \beta\frac{v_A}{X}\right)\left[\frac{k+1}{2}\left(v_B + \beta\frac{v_A}{X}\right) - \frac{v_A}{X}\right] & \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \text{ and } v_A < v_B \\ \frac{(k+1)n_B}{2v_B}\left(v_B^2 - \frac{v_A^2}{4}\right) - \frac{n_B v_A}{2\beta v_B}\left(v_B - \frac{v_A}{2}\right) & \left\{\frac{2}{3\beta} < k+1 \le \frac{1}{\beta} \text{ and } \frac{v_A}{2\beta} < \frac{v_B}{X}\right\} \text{ or } \left\{k+1 > \frac{1}{\beta} \text{ and } \frac{v_A}{2} < v_B\right\} \\ 0 & \text{else.} \end{cases}$$

When $k+1 \le 2/(\beta+1)$ and $r = v_A/v_B < 2$, we have

$$W^{IBP} < W^{UN} \quad \Leftrightarrow \quad \frac{3k+1}{8} < \frac{k}{2}\left(1-\frac{r^2}{4}\right)+\frac{1}{2}\left(1-\frac{r}{2}\right)^2 \quad \Leftrightarrow \quad r^2(1-k)-4r+k+3>0$$
$$\Leftrightarrow \quad (r-1)((1-k)r-k-3)>0.$$

Note that $k+1 \le 2/(\beta+1)$ implies $k \le 2/(\beta+1)-1 < 1$. Hence both roots 1 and $(k+3)/(1-k)$ are positive. Moreover, since $1-k<1$ and $k+3>3$, we have $(k+3)/(1-k)>3$. Therefore, on the domain $0<r<2$, $W^{IBP} < W^{UN}$ iff $r<1$.

When $2/(\beta+1) < k+1 \le 2/(3\beta)$ and $v_A/v_B < 1$, we have

$$W^{IBP} < W^{UN} \quad \Leftrightarrow \quad \frac{k+1}{2}\left(v_B+\beta\frac{v_A}{X}\right)-\frac{v_A}{X}>0 \quad \Leftrightarrow \quad \frac{k+1}{2}\left(v_B X+\beta v_A\right)-v_A>0$$
$$\Leftrightarrow \quad \left(1-\beta\frac{k+1}{2}\right)(v_B-v_A)>0.$$

The last inequality is automatically satisfied due to $v_B > v_A$ and $k+1<2/(3\beta)$.

When either $2/(3\beta) < k+1 \le 1/\beta$ and $v_A/(2\beta) < v_B/X$ or $k+1>1/\beta$ and $v_A/2 < v_B$ we have

$$W^{IBP} < W^{UN} \quad \Leftrightarrow \quad \frac{3(k+1)}{8}-\frac{1}{4\beta} < \frac{k+1}{2}\left(1-\frac{r^2}{4}\right)-\frac{r}{2\beta}\left(1-\frac{r}{2}\right)$$
$$\Leftrightarrow \quad r^2\left(k+1-\frac{2}{\beta}\right)+\frac{4}{\beta}r-\left(k+1+\frac{2}{\beta}\right)<0$$
$$\Leftrightarrow \quad (r-1)\left[r\left(k+1-\frac{2}{\beta}\right)+k+1+\frac{2}{\beta}\right]<0.$$

If $2/(3\beta) < k+1 \le 1/\beta$, then $k+1<2/\beta$, so the two roots are 1 and $(k+1+2/\beta)/(2/\beta-k-1)>0$ and the polynomial is negative outside the roots. Moreover, $2/(3\beta)<k+1$ implies that the second root is greater than 2, while the bound on v_A/v_B in this case is lower than 2. It follows that in this case, $W^{IBP} < W^{UN}$ iff $r<1$.

If $k+1>1/\beta$, we need to distinguish two cases: $k+1<2/\beta$ and $k+1 \ge 2/\beta$. When $k+1<2/\beta$, as above both roots are positive, the second root is larger than 2, and the polynomial is negative outside the roots. The constraint $r<2$ implies that $W^{IBP} < W^{UN}$ iff $r<1$. When $k+1 \ge 2/\beta$, one root is negative (the other root is 1) and the polynomial is negative between the roots. It follows that in this case, $W^{IBP} < W^{UN}$ iff $r<1$.

(ii) Under indication-based pricing, the payer's objective is

$$\begin{cases} (n_A v_A + n_B v_B)\frac{3k+1}{8} & k+1 \le \frac{2}{\beta+1} \\ 0 & \frac{2}{\beta+1} < k+1 \le \frac{2}{3\beta} \\ (n_A v_A + n_B v_B)\left(\frac{3(k+1)}{8}-\frac{1}{4\beta}\right) & \text{else.} \end{cases}$$

Under uniform pricing with adjustable price, the payer's objective is as follows. When $k+1 \le 2/(\beta+1)$, then

$$W^{UA} = \begin{cases} \frac{(k+1)(n_A v_A+n_B v_B)}{2}-\frac{k+3}{8}\frac{(n_A+n_B)^2}{\frac{n_A}{v_A}+\frac{n_B}{v_B}} & \frac{n_i}{n_j} \ge \frac{v_j}{v_i}-2 \\ \frac{3k+1}{8}n_j v_j & \text{else.} \end{cases}$$

When $n_i/n_j \ge v_j/v_i - 2$, we have

$$W^{IBP} < W^{UA} \quad \Leftrightarrow \quad \frac{(n_A+n_B)^2}{\frac{n_A}{v_A}+\frac{n_B}{v_B}} < n_A v_A + n_B v_B \quad \Leftrightarrow \quad 0<(v_A-v_B)^2.$$

Hence, for $k+1 \leq 2/(\beta+1)$, the payer's objective is higher under uniform pricing with adjustable price iff $n_i/n_j \geq v_j/v_i - 2$.

If $2/(\beta+1) < k+1 \leq 2/(3\beta)$, then we have either (in case (b2)) $W^{UA} = 0 = W^{IBP}$ or, in case (b1),

$$W^{UA} = \frac{n_j}{v_j}(v_j - \beta\frac{v_i}{X})\left[\frac{k+1}{2}\left(v_j + \beta\frac{v_i}{X}\right) - \frac{v_i}{X}\right] = \frac{n_j}{v_j}(v_j - \beta\frac{v_i}{X})\frac{k+1}{2}(v_j - v_i) > 0.$$

Hence, for $2/(\beta+1) < k+1 \leq 2/(3\beta)$, the payer's objective is indifferent in case (b2) and is better off under UA in case (b1).

When $k+1 > 2/(3\beta)$, then

$$W^{UA} = \begin{cases} \frac{(k+1)(n_A v_A + n_B v_B)}{2} - \left(\frac{k+1}{8} + \frac{1}{4\beta}\right)\frac{(n_A+n_B)^2}{\frac{n_A}{v_A}+\frac{n_B}{v_B}} & (c1) \text{ or } (d1) \\ \frac{n_j}{v_j}(v_j - \beta\frac{v_i}{X})\frac{k+1}{2}(v_j - v_i) & (c2) \\ n_j v_j\left(\frac{3(k+1)}{8} - \frac{1}{4\beta}\right) & (c3) \text{ or } (d2). \end{cases}$$

In case (c1) and (d1), we have

$$W^{IBP} < W^{UA} \quad \Leftrightarrow \quad \frac{(n_A+n_B)^2}{\frac{n_A}{v_A}+\frac{n_B}{v_B}} < n_A v_A + n_B v_B \quad \Leftrightarrow \quad 0 < (v_A - v_B)^2.$$

In case (c2),

$$\begin{aligned} W^{UA} - W^{IBP} &= \frac{k+1}{2}\frac{n_j}{v_j}(v_j - \beta\frac{v_i}{X})(v_j - v_i) - (n_i v_i + n_j v_j)\left(\frac{3(k+1)}{8} - \frac{1}{4\beta}\right) \\ &= n_j v_j\left(\frac{k+1}{8} + \frac{1}{4\beta}\right) - \frac{k+1}{2}\frac{n_j v_i}{v_j}\left(v_j(1+\frac{\beta}{X}) - v_i\frac{\beta}{X}\right) - n_i v_i\left(\frac{3(k+1)}{8} - \frac{1}{4\beta}\right) \\ &= n_j v_i \frac{k+1}{8\beta}\left[\frac{v_j}{v_i}\left(\beta + \frac{2}{k+1}\right) - 4\beta\left(1 + \frac{\beta}{X}(1 - \frac{v_i}{v_j})\right) - \frac{n_i}{n_j}(3\beta - \frac{2}{k+1})\right] \\ &\geq n_j v_i \frac{k+1}{8\beta}\left[\frac{v_j}{v_i}\left(\beta + \frac{2}{k+1}\right) - 4\beta\left(1 + \frac{\beta}{X}(1 - \frac{v_i}{v_j})\right) - \frac{2}{k+1} + \left(2\frac{v_i}{v_j} + 1\right)\beta\right] \\ &= n_j v_i \frac{k+1}{8\beta}\frac{v_i}{v_j}\left[u^2\left(\beta + \frac{2}{k+1}\right) - u\left(3\beta + 4\frac{\beta^2}{X} + \frac{2}{k+1}\right) + 2\beta(\frac{2\beta}{X} + 1)\right], \quad u \equiv v_j/v_i > 1 \\ &= n_j v_i \frac{k+1}{8\beta}\frac{v_i}{v_j}\left(\beta + \frac{2}{k+1}\right)\left[u^2 - \frac{u}{X}\left(\beta + \frac{2}{k+1}\right) + \frac{2\beta}{X}\right] \\ &= n_j v_i \frac{k+1}{8\beta}\frac{v_i}{v_j}\left(\beta + \frac{2}{k+1}\right)(u-1)(u - \frac{2\beta}{X}) \geq 0, \end{aligned}$$

where both inequalities above result from the conditions defining case (c2).

In case (c3) and (d2), we have $W^{IBP} > W^{UA}$. Hence, for $k+1 > 2/(3\beta)$, the payer's objective is higher under uniform pricing with adjustable price iff case (c1) or (c2) holds.

Q.E.D.