MONASH University

MONASH BUSINESS SCHOOL

CENTRE FOR HEALTH ECONOMICS

WORKING PAPERS

DYNAMIC BARGAINING OVER PUBLIC INSURANCE COVERAGE FOR DRUGS IN AUSTRALIA

Discussion Paper no. 2025-09

Jing Jing Li and Anthony Harris

Keywords: dynamic bargaining, pharmaceuticals, drug funding

JEL Classification: I11, H51

Jing Jing Li: Centre for Health Economics, Monash Business School, Monash University (email: jingjing.li@monash.edu); Anthony Harris: Centre for Health Economics, Monash Business School, Monash University (email: anthony.harris@monash.edu).

ABN 12 377 614 012 CRICOS Provider Number: 00008C

AACSB ACCREDITED EQUIS ACCREDITED ASSOCIATION AMBA ACCREDITED

DYNAMIC BARGAINING OVER PUBLIC INSURANCE COVERAGE FOR DRUGS IN AUSTRALIA

Jing Jing Li, Anthony Harris

ABSTRACT

Public funding decisions for pharmaceuticals are the outcomes of a dynamic bilateral bargaining process between the funding agency and a company and can involve considerable delay. Using an empirical duration model of negotiation in Australia from 2005 to 2018, we test if agreement patterns on national public subsidy of pharmaceuticals are consistent with the predictions of dynamic bargaining theory. It took a median of 16 months for the Australian government and companies to reach an agreement, averaging 1.51 rounds of negotiations, with 71% of the rounds failing to reach an agreement. Overall, the results of a process of one-sided offers from companies are consistent with theories of bargaining with incomplete information and delay strategies, where evidence of quality develops over negotiation rounds. Lower value and more risk for the payer delayed agreements and increased the probability of no agreement, while public awareness and interest in a drug reduced the agency's bargaining power and increased agreement rates. Enhanced knowledge about the drug's attributes benefits the government and its constituencies, but pharmaceutical companies have a strong incentive to invest in political alliances to raise awareness of potential benefits to patients and hasten public funding of a drug.

Keywords: dynamic bargaining, pharmaceuticals, drug funding

Author affiliations

[1.] Centre for Health Economics, Monash Business School, Monash University, Melbourne, Australia

Corresponding author

Jing Jing Li,
Centre for Health Economics, Monash Business School, Monash University
Level 5, Building H, Caulfield Campus
Victoria, Australia 3145
Email: jingjing.li@monash.edu Phone: +61399058153

Acknowledgement: We are grateful to Karen Yong for her assistance with data extraction and Duncan Mortimer for his insightful comments on the paper.

Funding statement: A Harris received funding from the Australian Research Council DP 1095691 https://purl.org/au-research/grants/arc/DP1095691

Conflict of interest disclosure: JJ Li and A Harris have a contract through Monash University to conduct independent evaluations of industry submissions to the PBAC.

1.INTRODUCTION

Bilateral bargaining between pairs of agents is pervasive in many economic environments. In the market for pharmaceuticals and other patented medical products, bargaining between 3rd party payers and firms over coverage and the associated per-unit price or subsidy is common. Yet the theoretical and empirical literature on the outcomes of bargaining is sparse. The general theoretical literature in economics has analysed the equilibrium outcomes of bilateral bargaining in a variety of settings in what has been described as the "Nash program" (Binmore *et al.*, 1986). Typically, in this literature the emphasis is on finding equilibrium solutions, and in empirical papers on predicting the effect of changing market conditions or market structure on those equilibria. In this paper, we focus on the features of the bargaining environment that lead to delay in reaching an agreement, and test some of the predictions of dynamic bargaining theory in the context of bilateral agreements (and disagreements) on subsidies to medicines between two players - a public funding agency and a pharmaceutical company using the empirical example of the Australian Pharmaceutical Benefits Scheme.

The last 50 years have seen a dramatic increase in the use, effectiveness, and cost of medicines. Concern about the affordability to consumers and to public insurers began in the 1990s and has been amplified by the rise of high-priced biologic and targeted therapies in the 2000s. Governments and other third-party payers have sought to reduce rising expenditure through a range of direct and indirect price and volume controls, including limits to insurance coverage and requirements to demonstrate value for money (Barnieh *et al.*, 2014; Dylst *et al.*, 2011; Lee *et al.*, 2015; Towse *et al.*, 2012). There has also been concern about the implications of public regulation of drug prices for the share of value going to each party and its effect on market dynamics, particularly on investment incentives for socially valuable innovation (Jena and Philipson, 2008; Woods *et al.*, 2024). Public health agencies and insurers have increasingly been willing to bargain over prices and coverage conditions for medicines in attempts to ensure that the net gains from patented and generic prescription pharmaceuticals accrue more to the community and less to profits (Drummond, 2013). This has resulted in persistent criticism of the timeliness of decision-making (Drummond and Sorenson, 2009; Pearce, 2012) that a delay from the bargaining process, or a failure to agree, reduces not only the payoff to the pharmaceutical company but also reduces consumer surplus from lost therapeutic gains. On the other hand, delays associated with bargaining might increase the benefits to the payer and increase consumer welfare from reduced prices, insurance premia, or taxes and improve quality of care from more targeted therapies.

The paper expands the broader empirical literature, that tests and confirms some of the key predictions of dynamic bargaining theory including (i) the conditions under which a bargain will be struck; (ii) the duration of the process; (iii) the effect of delay on the value to each party; iv) the effect of outside options for each party on the disagreement point and the likelihood of a successful bargain; and (v) the effect of investment in marketing on bargaining power and the consequences for delay in agreement on price. The paper also extends the literature on the factors that influence public funding agreements for health technologies and the revealed

willingness to pay for health (Dakin *et al.*, 2015; Harris *et al.*, 2016).

We find that the results of a process of one-sided offers from companies are consistent with the predictions of bargaining with incomplete information from the theoretical literature that higher available surplus and less uncertainty over value results in a higher rate of agreement and less delay. The value to the payer agency increases with delay as information on quality develops over time. The results are also consistent with the idea that the bargaining power of public payers may be reduced by company and community pressure, but we do not find strong evidence that bargaining outcomes are influenced by outside options such as the availability of substitutes or international price spillovers.

The paper is organised as follows. Section 2 discusses the empirical implications of dynamic bargaining theory that can be tested in our empirical model of public insurance for pharmaceuticals. Section 3 describes the theoretical framework and Section 4 the data used in the empirical model. Section 5 tests the predictions of bargaining models in the context of the Australian market for pharmaceuticals. Section 6 describes the results, which are discussed in Section 7 with conclusions in Section 8.

2.RELATED LITERATURE

Empirical work on bilateral bargaining over health technology pricing has focussed on the effects of competition and price discrimination. For example, Grennan (2013) shows the importance of bargaining power in determining the final price, and the bargaining power of a single purchaser to counteract the effect of lower competition on prices. In the pharmaceutical market, there have been several game-theoretic studies of pricing and access policies, such as reference pricing and performance-based risk-sharing arrangements (Antonanzas *et al.*, 2011), and the impact of a drug manufacturer's marketing decision on coverage, pricing, and social welfare (Wright, 2004). In terms of empirical dynamic bargaining models with one-sided asymmetric information that are more directly relevant to the current paper, Ambrus *et al.* (2011), in very different setting of historical ransom negotiations and Backus *et al.* (2020) in online auctions, find results consistent with incomplete information models, with evidence of common sequences of failure to reach agreement, and find that bargaining power and better outside options improves agents' outcomes. An analysis of the residential housing market in England by Merlo and Ortalo-Magné (2004) reported results consistent with bargaining models (with surprising similarity to our results in terms of how many offers sellers make). We adopt a similar theoretical model to Backus *et al.* (2020) in a setting comparable to that in Critchley and Zaric (2019), where a government funding agency is assumed to maximise expected net social value, and a pharmaceutical company is assumed to maximise profits in negotiation on price and access to public funding.

A related empirical literature has examined the determinants of public willingness to pay for the treatment benefits of pharmaceuticals. In an analysis of the UK National Health Service, Dakin *et al.* (2015) found that

the additional monetary cost per unit of health gain alone predicted 82% of the decisions to fund drugs, while Harris *et al.* (2008) and Harris *et al.* (2016) concluded that cost-effectiveness, clinical efficacy, cost to government and disease severity were significant factors in drug funding decisions in Australia. These analyses considered the likelihood of a subsidy given the expected net benefits of the treatment, but they did not consider the strategic interaction of the parties nor the dynamics of the negotiation. We extend those analyses and focus on what determines the evolution of bids over time and the role of bargaining power in delaying agreement and test if outcomes are consistent with the predictions of the theoretical literature on dynamic bargaining with imperfect information.

3.THEORETICAL FRAMEWORK

Negotiation between government and a pharmaceutical company through a health agency or public insurer[1] over funding a therapy on a national formulary has many of the characteristics of a classic bargaining game in the tradition of Nash (Nash, 1953) and Harsanyi (Harsanyi and Selten, 1972). The agency maximises the expected utility payoff based on the contribution of the medicine to patient wellbeing and the opportunity cost of public funding. A pharmaceutical company maximises profit given its marginal opportunity cost of delivery[2]. A number of authors have expressed this negotiation in terms of a stylised imperfect information axiomatic bargaining game where a new treatment produced by a company at marginal cost c offers uncertain health benefits b for a course of treatment to a group of patients, and where benefits are conceived as extra

[1] In most countries with a national subsidised medicine formulary an independent or semi-independent agency consider bids from pharmaceutical companies to list the drug for an indication or set of indications at an agreed payment per course of treatment. Occasionally an entity other than a pharmaceutical company may propose funding but this is rare.

[2] In some countries the agency has an explicit annual drug budget (e.g. New Zealand), in some, the budget constraint is implied by a stated threshold willingness to pay for health gains (e.g. England and Wales), while in many the budget implications of funding are explicitly part of the decision (e.g. Australia). Elaborate contracts with a variety of components of an agreement (price, administration, indication/population, volume) exist so that bargaining is over feasible utility imputations of the bundle of components. The agreed price may or may not be disclosed publicly and may be a simple constant price per dose perhaps with a volume limit or discount threshold or payment may be conditional on performance. In the paper we summarise all of this simply as an `offer' by the supplier. We assume that the agency attempts to make rational decisions on funding in order to maximise its expected net utility based on a social welfare function that might include efficiency, fairness, risk and time preference parameters. Although the formal negotiation process is one where the company makes offers and the agency accepts or rejects there is sometimes a discussion about acceptable prices or restrictions before or after a formal offer is made that comes closer to an alternating offer mechanism rather than simply one-sided offers. In the empirical analysis we consider some implications of an alternative offer process as well as the possibility that the company has some private information on quality. Quality is used in a broad sense to cover all aspects of the therapy including its effectiveness in practice, side effects, indication in terms of first or subsequent line therapy, and the perceived need for the therapy.

health benefits compared to current treatment (Antonanzas *et al.*, 2011; Barros, 2011; Critchley and Zaric, 2019). The company maximises profits (π) as the difference between the price per unit (p) and the marginal opportunity cost of production (c), and the firm's expected profits are given by π=(p-c). The agency has expected utility from treatment U=V(x)=b where V is the willingness to pay for a multidimensional vector x characteristic of a unit of the therapy (a combination of a drug and an indication). The agency maximises net utility U=(b-p). Where there is uncertainty about the size of the gains and the distribution of the gains, U could be interpreted as the certainty equivalent of the predicted net money value of the average incremental health gains. The classic Nash equilibrium solution says that any equilibrium price satisfies

$$Max\ (b(x) - p)^{\delta}(p - c)^{1-\delta} \qquad (1)$$

The company and the agency share the social gains *(b(x)-c)* according to their bargaining power δ. If no agreement is reached, then each party receives the opportunity cost of their decision *p* or *c* – their disagreement point.

This description of a static equilibrium bargaining outcome, with its assumption of perfect information on the utility of payoffs for each party, does not adequately capture the institutional structure of a typical pharmaceutical funding decision process. In Australia and many other jurisdictions, the pharmaceutical company makes an offer for the funding of a drug at a proposed price and indication, based on a claim of drug quality. The agency can accept or reject the offer, and if there is no agreement, the company can make another offer after a period. The company is unsure of how the agency views the quality of a therapy (the expected value of outcomes in that indication) and how much the agency would be willing to pay for a course of treatment. The value to the public agency is unknown to the company although they may have some knowledge of past negotiation outcomes. The company knows its own net payoff based on the cost of supply and any potential indirect effects on international markets. The agency, while not perfectly informed about the parameters of the company's utility function, may have knowledge from prior pricing of the drug in other jurisdictions[3]. Each party wants to maximise their respective expected payoff over the lifetime of the drug, but each has a disagreement point below which they will not agree to listing on the subsidised formulary and will not continue negotiations. This institutional framework of repeated offers has the structural characteristics of a dynamic bargaining game in the tradition of a screening game (Rothschild and Stiglitz, 1976) with one sided offers from the party who has incomplete information on the value of an agreement to the other party. Rothschild and Stiglitz (1976) showed that a separating equilibrium or no agreement are the two equilibrium outcomes in a two-period screening game. The subsequent bargaining literature, for example Riley (2001), extended this further and specified a structured extensive form for the bargaining process including who

[3] This particularly applies in countries like Australia where bargaining is informed by coverage decisions made by insurers in the leading markets of the U.S. and Europe.

makes an offer and how often, the duration of the process, and who has private information, and then solves for the noncooperative equilibria. Fudenberg *et al.* (1985) is a classic example of a simple infinite horizon dynamic model of noncooperative bargaining that captures two key aspects: i) bargaining involves a succession of steps, and ii) the bargaining parties do not know the value to others of reaching an agreement. In each period, one player makes an offer, which the other player can either accept or reject. Each player has a cost of bargaining, in this case due to impatience, and prefers an agreement today to the same agreement tomorrow. They find that if these, and other conditions are met, a unique equilibrium exists and offers decline over time. The general intuition is that the seller starts with high offers, knowing that if the payoff to the buyer is high, the cost of delay is high, and the buyer will be willing to accede. Each round that the buyer refuses the seller's offer, the seller revises downwards its beliefs about the payoff to the buyer. The seller is uncertain about the buyer's valuation and becomes more pessimistic over time. When the seller becomes sufficiently pessimistic, she prefers the outside opportunity, so she will not bargain indefinitely with the buyer (Fudenberg *et al.*, 1987). The general theme in this literature is that bargaining is substantially a process of communication necessitated by initial differences in information known to the parties separately. Thus, delay may be required to convey private information credibly (Cramton, 1992).

The bilateral drug bargaining environment is one where the seller and the buyer possess some private information on the product's characteristics and their value. Delays in reaching an agreement, separation of agreements by therapy, and the possibility of a complete failure to agree are all characteristics of equilibria in this market. The public agency with outside options in the form of potential substitute treatments has a credible strategy of haggling before discontinuing the negotiation and funding the alternatives. The pharmaceutical company has the option of selling in other markets and avoiding the cost of any spillover effects on prices elsewhere. However, delay risks the entry of competitors with similar therapies, even for patented drugs. Thus, we might expect that 1) the value of the offer to the buyer increases over time[4]; 2) where there are close treatment alternatives the disagreement point for the agency is higher and an agreement is delayed; and (3) where a low price in one country has flow-on effects in other markets the disagreement point is higher for the company and the probability of an agreement in each round of negotiation is lower. The pharmaceutical company has the option of investing in marketing prior to the application for funding to increase its bargaining power in negotiations. Investment may take the form of direct engagement with patient groups or doctors and social media, for example, by offering free early access to the product through clinical trials. Political pressure to fund a new drug is likely to increase the discount rate of the agency and lead to a higher rate of agreement at each round of negotiation. As discussed above, the dynamic bargaining literature suggests where the buyer discounts the future, there are potentially separating equilibria with different prices for products of different

[4] Any rational model of dynamic bargaining with one-sided private information on the buyer side implies declining price offers. (Card, D. (1990). 'Strikes and Wages: A Test of an Asymmetric Information Model*', *The Quarterly Journal of Economics*, vol. **105**(**3**), pp. 625-659).

quality. There may also be a delay in achieving these equilibrium prices in an alternative offer mechanism due to impatience or other bargaining costs (Cramton, 1992; Grossman and Perry, 1986). In our case, where there is asymmetry of information on the quality and the value of treatment for each indication of a drug, this raises the possibility of separate negotiated prices for the same drug as different therapies across clinical areas e.g. a drug used across types of cancer or between stage of cancer of a given type.

The theoretical bargaining literature leaves open the question of whether a particular extensive form description of the game represents a reasonable characterisation of the actual bargaining process, and whether agents behave rationally in terms of maximising expected utility, but in general, screening equilibria arise from a cost of delay on the part of the buyer and where the payoff is high the parties are more likely to agree (Kennan and Wilson, 1993). The result is that the agency agrees to a subsidy after the company offer is high enough to allow some social gain and the expected cost of waiting for another offer (or an alternative competitor product to arrive) is greater than the additional gain. Further, an agreement reached after a negotiation that is costly in time and money to both parties would prompt regret that a similar agreement was not reached earlier, unless the information of one or both parties changed during the negotiation. Our empirical analysis examines what information changes over time on the size of the expected net benefit to the funder and outside options for both parties. All the screening models suggest that if there is enough private information then the 'types' of agents are partially separated in equilibrium. Purchasers with lower values (or suppliers with a high premium over costs), obtain higher payoffs but only after enduring a wait to prove themselves. In our context, this suggests longer waits for therapies with lower or more uncertain value for money to the agency, where companies may attempt to influence the expected utility of the agency by providing information either directly through new evidence of value or indirectly through advocacy. It also implies dividing the market for a drug in time by applying for funding for separate indications at different prices. They may for example start with therapies with a high expected value, before bidding for other indications with lower patient gains at a lower price or when evidence on value is more mature and outcomes more certain.

We examine the implications of theories of structured bargaining with incomplete information for negotiations of prescription medication subsidies in the Australian national public insurance system, using a duration analysis of past decisions on drug funding to test the implied bargaining-related drivers of two key outcomes at each round of negotiation:

1. Delay in agreement for a therapy
2. Failure to agree.

In a second set of analyses, we examine if:

3. There is evidence of a strategy to offer different price-quality combinations for a drug across therapies
4. A high overseas price reduces the company's bargaining power and reduces the probability of an

agreement.

4.DATA

The data for this study is sourced from the Australian national public health insurance scheme, the Pharmaceutical Benefits Scheme (PBS). As the first national body in the world to formally require economic evidence in negotiations with suppliers for subsidy listings on a national formulary, the PBS provides a unique and extensive dataset. Its iterative process for drug subsidy decisions, including well-documented offers and outcomes on agreements and disagreements each round for 30 years makes it the ideal setting for studying the outcomes of bargaining over price and coverage.

In Australia, drug access is primarily through the PBS. While a company is free to set prices for registered prescription drugs on the private market, this is rare due to the significant price differential for consumers, particularly for patented drugs. The government receives proposals from sponsors to fund a medicine on the PBS at a price for a given indication. The government assesses the proposal through a semi-independent agency, the Pharmaceutical Benefits Advisory Committee (PBAC), which recommends to the government if the drug should be funded or not at the price proposed. If a drug is accepted, it becomes available on prescription with a low common fixed contribution from patients. If the committee rejects the proposal, the drug is not funded, but the company may submit a subsequent proposal. Decisions are made three times a year with fixed submission and meeting schedules[5]. The evaluation process from submission to outcome takes 17 weeks, and there are opportunities for pharmaceutical firms to address concerns raised in the evaluation, however, if an agreement cannot be reached between the agency and the firm, the application will be rejected. Although companies can technically resubmit to the next meeting, preparation time is such that it is far more likely that it would need to wait a further 8 months for the next meeting date[6]. There is no limit to the number of times a company can submit a drug for consideration, and resubmissions are common.

The stated criteria for acceptance or rejection include total cost to government of a subsidy, the cost of the therapy to patients without a subsidy, treatment effectiveness, and cost effectiveness in terms of additional costs and health gains over current therapy. The committee also considers risk in terms of their confidence in the evidence provided on each of these quantifiable criteria, as well as what they describe as the less quantifiable aspects of clinical need, severity of illness, the availability of alternative therapies and equity as

[5] There are out of cycle meetings where decisions are made, but these were rare prior to 2019.

[6] Note due to changes to PBS listing process, from January 2021 there are new resubmission pathways that a pharmaceutical firm can follow (provided the drug meets certain criteria) that will allow a reconsideration of the evidence sooner, these changes however do not impact our dataset given the included decisions were prior to 2019.

it relates to patient characteristics such as age, geography and socioeconomic status.[7] Taken together these characteristics of the proposed treatment represent the expected net benefits to the agency of an agreement to fund a drug on the national formulary.

Detailed information on offers made in each submission, the PBAC's views on the evidence presented, and their quality are documented in detailed committee minutes, available as public summary documents (PSDs) from July 2005 (PBAC Decisions, 2024). These documents were the primary data sources. For submissions to the committee between July 2005 and November 2018 (n=1627), we extracted details on comparable submissions or resubmissions with a negotiated price. These were submissions with evidence of a difference in quality-adjusted life years (QALY's) (n=634). The excluded submissions (n=993) were those based on either a cost minimisation analysis with no claim of superiority or where the only evidence of superiority presented was a clinical outcome measure or life years saved. In the first group, any price negotiation was constrained by the price of the equivalent therapy. For the latter group, the lack of a comparable outcome measure made a comparison of net benefits across drugs problematic. All submissions were grouped into drug/indication pairs (therapies), and the date of each submission was recorded. If a drug has more than one distinct indication, these are treated as separate therapies, with each submission representing a round of negotiation. Our final dataset included a total of 634 rounds of negotiations for 400 therapies, with 270 drugs (see Figure 1) and a maximum of 6 rounds of negotiation for each therapy.

Table 1 summarises the variables used in the analyses. The main outcome in the duration analysis is years to an agreement. The PBAC can agree that a product be covered on the PBS at the price requested, recommendation coverage with some criteria, make a binding recommendation to reject a product for listing on that occasion or defer a decision to a later meeting. Recommendation of a product at the price proposed is coded as 1 (agreement) and all other recommendations as 0 (failure to agree)[8].

The measured value of the therapy to the PBAC (the funding agency) depends on their expected health benefits to patients less the opportunity cost of treatment over current therapy, and we characterise this as:

a) The estimated incremental monetary cost per QALY compared to current practice - the incremental cost-effectiveness ratio (ICER), reported in 6 bands. A higher ICER means lower net health benefits for the

[7] Details of the listing process and the guidelines for submissions are available on the Australian Government Department of Health and Aged Care website.

[8] The PBAC may recommend a drug be listed on the PBS pending conditions on coverage. However, as there could be subsequent negotiations between the drug company and the government that could result in a lower than submitted price or an augmented patient population, that would imply that the decision would be based on an unobserved set of characteristics including efficacy outcomes and a lower ICER and overall cost to government. For this reason, these types of recommendations are coded 0. Note that a recommendation not to list precludes a subsidy on the PBS.

agency.

b) The stated incremental cost of the therapy may not represent the true marginal opportunity cost (Claxton *et al.*, 2015). It seems reasonable to suggest that the greater the size of the total expenditure on a therapy, the higher the marginal opportunity cost. We proxy the opportunity cost of an agreement by whether the drug will likely cost more than $10 million per annum (a threshold used by the Australian Government to signal high cost requiring additional cabinet approval before listing) as an additional effect on the likelihood of an agreement.

c) We include three binary variables that measure the buyer's confidence in the quality of the evidence supporting the expected ICER.

   i. Whether the agency believed that the effect on patients was clinically significant

   ii. Whether the agency had confidence in the quality of the clinical evidence, and

   iii. Whether the agency had confidence in the modelled economic evaluation

The agency may not value QALY gains equally and there is a range of potential features of patients that might receive greater weight (such as age, severity or need). While PBAC meeting documentation makes references to severity and need, these are not consistently reported so we use a measure of patient need based on the U.S. Food and Drug Administration's designation of priority review (FDA, 2025). The number of potentially available drugs with the same 5-digit ATC code at the date of negotiation (WHOCC, 2024) is used to characterise the outside options for the agency. We proxy the results of marketing efforts on public awareness, interest and advocacy-driven political pressure for a therapy as the relative rate of change in Google internet searches in the year prior to the submission. Evidence suggests that internet search trends can accurately reflect patient priorities, health-related behaviours as well as voter interest in political studies (Frijters *et al.*, 2013; Reilly *et al.*, 2012; Willard and Nguyen, 2013; Yang *et al.*, 2011). The data was accessed through Google Trends (https://trends.google.com/trends/), which samples a portion of Google web searches to form an estimate of the quantity of searches. For each submission, data was collected by entering the drug name, restricting searches to the "Health" category (the data is available from the authors by request). We are interested in the average change in search data for our drug compared to the "health" category in the year leading up to the PBAC meeting. This data is reported as a percentage change relative to the specified beginning of the time period at regular intervals. For example, for a drug proposal at the November 2012 PBAC meeting, our search was conducted from November 2011 to the start of November 2012, and each data point expressed as a percentage change relative to Google Trends at the start of November 2011. We then average across these data points to calculate the ratio of that change over the year relative to the change within the overall "health" category. We restricted the time of interest to one year prior to the PBAC meeting as we believe this period best captures any drug promotional activities leading up to the committee's decision. This has the added benefit of allowing the measurement of any change in interest if the drug was rejected at a prior meeting, as it generally takes the company approximately a year before it can resubmit if there are major changes.

All data were double-extracted by experienced PBAC evaluators using a pre-specified coding manual. Ratings of committee confidence in the evidence were done blind to the final decision. Any disagreements in the coding were resolved via consensus. Scores were based as much as possible on the objective statements in the PBAC documentation. In the analysis of the spillover effects of pricing in other markets, we use the U.S. prescription drug price reported in the U.S. Veterans Affairs Federal Supply Schedule at each proposal date (US VA FSS, 2024).

5.EMPIRICAL STRATEGY

We use time-to-event analysis to characterise the dynamic nature of the bargaining process in Australia and test the implied drivers of delay in reaching an agreement on coverage and the probability of no agreement being reached. Unlike binary regression models, time-to-event analysis allows us to explicitly model the delay before an agreement, control for censoring, recognise the skewness in the duration, and enhance the statistical power to detect an effect of our measures of bargaining power (Annesi *et al.*, 1989; van der Net *et al.*, 2008). We describe the time to an agreement using the Kaplan-Meier method and assess factors influencing agreement over time using the semi-parametric Cox proportional hazards regression model (Cox, 1972). The Cox model estimates the instantaneous hazard rate (h) of an agreement being reached for a particular drug indication *j* at time *t* as a function using a vector of explanatory variables *X:*

$$h(X_j) = h_0(t)exp(X_j\beta_j)$$

A major advantage of the Cox model over parametric survival models is that it does not require parameterisation of the unknown baseline hazard $h_0(t)$, assuming instead that the hazard ratio between any two individuals remains constant over time. In our context, the relative risk of an agreement for different drugs remains proportional and does not change as time progresses. We verify this assumption and estimate hazard ratios using parametric survival analyses for comparison.

Therapies are followed from the date of their first proposal for funding until an agreement is reached or they are censored at the end of the observation period. Time-varying covariates are included to account for changes in therapy characteristics over rounds of negotiations. We use the Efron approximation to adjust for tied survival times (Efron, 1977).

We test the covariates for all plausible interactions[9]. No significant interactions were found, so they are

[9] ICER x clinically important difference, ICER x budget impact, confidence in clinical x confidence in economic

excluded from the final model. We report hazard ratios for each variable and 95% CIs clustered by therapy. We also report the predicted delay associated with a change in each variable at a given set of values for all others. Model goodness of fit is examined with the Cox-Snell residuals. We applied delayed entry for the time before 1 March 2005 for therapies that have had proposals prior to our observation period. If a therapy is not listed within 4 years of the first proposal, it is censored in the main duration analysis to avoid an outlier effect. Appendix 1 also presents the results of the duration analysis using the full dataset and censoring at 5 years, as well as alternative specifications.

We examine the pattern of value to parties across rounds of bargaining. We do not observe the agreed price of a therapy because a) each drug has a single published subsidised price that is a weighted average of prices across therapies and b) published prices do not take into account confidential price agreements, including discounts. However, as noted above, we would expect the expected value to the agency to rise across rounds of negotiation within a therapy as price and risk fall. If the company initially proposes high quality therapy, we expect to see an adjustment in bid price to compensate for lower quality and higher risk with a fall in the ICER for later therapies (or at least no increase) in a smaller target population with a lower predicted total government expenditure. We use panel data categorical response models to test if the ICER, predicted total government expenditure, and risk changes with each round of negotiation within and across therapies.

We also consider if spillover effects of price in the U.S. market delays agreement. We anticipate that the main effect of a high international price is to increase the bid price for the therapy and increase the ICER. We therefore excluded overseas prices in the duration analysis and use structural equation modelling to test whether the U.S. price indirectly affected the probability of an agreement through mediation of the value of the offer to the payer (Appendix 2).

All analyses were conducted using STATA version 17.0 (StataCorp LP, College Station, TX, U.S.). We report 95% confidence intervals and test for the significance of covariates in all analyses at 1%, 5% and 10% levels.

6.RESULTS

Our final data included 634 rounds of negotiations for 400 therapies (270 unique drugs of which 70 had multiple therapies) (see Table 2). Figure 2 illustrates the Kaplan-Meier curve of time to agreement from the first round. The total time under negotiation for the population was 428 years, with a median time from first submission to agreement of 1.34 years (approximately 16 months) (IQR: 0.67, 2.67).

evidence, Google Trends x ICER, FDA expedited access x clinically important difference, FDA expedited access x ICER, FDA expedited access x Budget impact.

An agreement was reached for 181/400 (45%) therapies, with an average of 1.51 rounds of negotiations (min 1, max 6). Over half (65%, 261/400) had a clinically important effect, and 28% of these (111/400) received a priority designation by the FDA for treating a severe illness and demonstrating significant improvements over existing therapies. Ninety percent of drugs presented efficacy evidence from randomised trials, but the PBAC was not confident in the clinical claims made in 45% of all bids (286/634). The most reported ICER category was between $45,000 and $75,000 (34%). Overall, 91% (155/181) of ICERs for therapies that reached agreement were below $75,000 per QALY gained.

Table 3 summarises the hazard ratios (95% CI) from the Cox proportional hazards regression and Table 4 predicts the impact of each variable on time to agreement compared to a base case. The base case represents the median ICER category ($45,000 to $75,000) with other categorical variables set to zero and continuous variables at their mean values. In the main model, except for the total budgetary cost to government and number of substitutes all variables are significant at the 5% level with the expected direction of effect. Each higher cost per QALY category above $15,000 to $45,000 increases delay, with progressively lower rates of agreement. For proposals at $45,000 to $75,000 cost per QALY, the rate of agreement is 45% less compared to those at <$15,000 per QALY (HR: 0.55, 95% CI: 0.36, 0.84), translating to an additional delay in median time to agreement of 0.66 years (8 months). The presence of considerable economic uncertainty reduces the rates agreement by 64% (HR: 0.36, 95% CI: 0.26, 0.51), delaying median time to agreement by 1.34 years (16 months). In contrast, a clinically important effect increases the rate of agreement by 55% (HR: 1.55; 95% CI: 1.07, 2.24), shortening median time to agreement by 0.33 years (4 months). An FDA priority review designation indicating it would significantly improve the treatment, diagnosis, or prevention of a serious condition increased the rate of agreement by 45% (HR: 1.45, 95% CI: 1.03, 2.04) and reduced time to agreement by 0.33 years (4 months). Conversely, if the drug was associated with significant clinical uncertainty, then parties reached agreement 50% slower compared to those without (HR: 0.50 95% CI: 0.33, 0.75), delaying the time to agreement by 0.67 years (8 months). Each standard deviation increase from the mean in Google Trends in the year leading to the negotiation is associated with 24% faster rate of agreement (HR: 1.24; 95% CI: 1.10, 1.39), and reduces delay in the median time to agreement by 0.33 years (4 months). An increase in the opportunity cost of the drug, as measured by the expected annual total government expenditure of over $10 million, is not associated with a reduced rate of agreement (HR: 0.77, 95% CI: 0.57, 1.05). The availability of potential substitutes does not affect the timing of agreements (HR: 0.95, 95% CI: 0.88, 1.03).

Post-estimation tests support the adherence of the data to the proportionality assumption. The Nelson Aalen cumulative hazard estimator for Cox-Snell residuals also indicates the final model's general goodness of fit. In sensitivity analyses (see Appendix 1), we find the effects of the independent variables were robust when estimated using alternate parametric functions and when data was censored at 5 years or the end of follow-up.

As discussed, we prefer the Cox proportional hazards model over other parametric proportional hazard functions due to the lack of *a priori* knowledge about the baseline hazard of agreement. In post-estimations, we back out the baseline hazard function for the Cox model (Figure 3). The hazard function indicates an initially increasing hazard of a positive recommendation (of up to 1.7 years, which means approximately 3 rounds of negotiation) before the hazard declines. The shape of this function is not consistent with the underlying baseline hazard of parametric proportional hazards models. This inconsistency explains why parametric model estimates were generally less precise, even though point estimates for the HRs are similar to the main model. In order to compare with earlier studies, we re-estimate a logit model of whether an agreement was reached for a therapy at each negotiation using an identical set of covariates with standard errors clustered by therapy. The results are similar to the Cox model estimates in terms of sign and significance, except that need as proxied by FDA priority is not significant (OR=1.16, 95% CI:0.70, 1.92), and the budget impact has a significant effect (OR= 0.5, 95%CI: 0.33,0.75) on the odds of an agreement (Table A1.1 col.8).

Table 5 provides weak evidence that risk to the agency is lower for the first therapy. The odds that confidence in the evidence of value is higher (lower risk) in later therapies is 0.47 (95%CI 0.22, 1.22). In general, the agency's confidence in the value of a therapy increased through negotiation as more information was provided or revealed. Table 5 shows that agency confidence in value increased with each round of negotiation with an odds ratio of at least 2.04 (95% CI: 1.38, 3.00). This may have been due to new evidence from clinical trials or accumulated clinical practice experience over time which confirmed effectiveness and provided reassurance about safety. Later therapies with a drug have lower odds of a budget exceeding $10 million (OR=0.43, 95% CI: 0.19, 0.97), but there is no significant change in the value of the therapy (the ICER). The results in Table 5 are largely robust to respecifying the statistical models using fixed effects and excluding covariates (see Appendix 2) with no change in signs or the size of point estimates and no change in significance of the coefficients. Turning to the potential impact of international price spillover effects on bargaining power, a high price for the drug in the US appears to have a relatively small effect on the ICER proposed, but we do not find evidence of any significant effect on the likelihood of an agreement (see Appendix 2).

7.DISCUSSION

This study extends the application of duration analysis to characterise the determinants of negotiation outcomes and delays in pharmaceutical reimbursement decisions. Bargaining is not costless, and we would expect that the probability of an agreement to increase over time. The estimated hazard function supports this hypothesis at least for up to 2 years. Where the treatment is for a severe condition, the potential for a significant gain over existing therapies appears to add to the payoff for the agency, and delay is reduced. While an agreement is less likely at a lower value to the agency (a higher ICER), improved quality of evidence on the clinical and economic implications of treatment reduces risk for the payer leads to less delay and increases

the probability of agreement. Significant economic uncertainty is a key feature in a majority (68%) of negotiation rounds between manufacturers and the PBAC and a lack of confidence in the estimated ICERs is a key factor in funding delays.

We find agreement to be positively influenced by surges in internet searches leading up to the decisions, suggesting company investment in raising awareness of a new drug will reduce government bargaining power and consequently increase the rate of agreement at a given bid price. While we do not know the drivers of heightened internet searches, they are likely to be a combination of the characteristics of the drug, the disease, and the efforts of patient interest groups and companies. The absence of evidence here of an impact of the budget on time to agreement is surprising. The lack of variation between rounds of negotiation of the $10m threshold cost to government does not allow a precise estimate of its impact on delay in reaching an agreement, but as the logit model results show, it does suggest a significant effect on whether an agreement is ever reached. Conversely, our measure of patient need (an FDA priority review designation) is associated with significantly less delay in reaching an agreement although it does not precisely estimate the effect on the probability that an agreement is ever reached. We also do not find evidence that outside options for either party have a significant effect on bargaining power and the time pattern of agreement. For the agency, the absence of an effect for the number of potential substitutes on delay could be partly due to measurement error, as our measure - the number of drugs with the same mechanism of action - does not fully capture their quality. For the company, we find a small indirect effect of the US price on the probability of an agreement, suggesting that a high overseas price may increase the bid price (and the ICER), perhaps due to a threat of spillover effects on other markets.

A sequence where the company proposes a therapy with a high budget cost but acceptable ICER and then waits for payer confidence in the drug's value to build over time before accepting a lower price for a subsequent therapy is a possible strategy for some drugs. In a dynamic bargaining game with incomplete information, more information is revealed over time and the payer's belief in the value for money changes as the negotiations unfold and as the company negotiates for subsequent therapies. A pattern like this would be consistent with a separating equilibrium with different price/quality combinations across therapies, but the data here give only limited support for the idea of a common equilibrium pattern like this. Note that in only 18% of negotiations was there a prior agreement for the drug, and it may be that any sequential strategy is affected by unanticipated events such as trial results or other discoveries as well as wider strategic considerations that determine the timing of therapy launches or non-linear price effects (Verniers *et al.*, 2011). The results do confirm the importance of risk as a key component of the expected value of a drug to the agency and the rate of agreement. Experience with the negotiation for the drug in any indication gives the agency more familiarity with the evidence, particularly on drug side effects, and a better prediction of value.

There are some limitations of our analysis. First, we have simplified the characterisation of the negotiation

process to allow us to estimate the empirical models. Second, although we allow for multiple rounds of negotiation, we do not vary the determinants of the bargain over time. While some theoretical literature outlines multi-staged funding processes that include the decision to submit, price negotiation, and marketing (Critchley and Zaric, 2019; Wright, 2004), we do not observe drugs that are never submitted for subsidy, nor do we differentiate between types of agreement on price, quality and utilisation. Instead, these elements are treated as one combined bargaining outcome and we focus on the positions of the players conditional on bargaining taking place, which means that we cannot address the broader issue of company choices before negotiation. This has limited what we can say about the outcomes of the bargaining process here and the total delay from patent approval to drug launch in Australia. Nevertheless, our main result is consistent with the theoretical literature: an institutional negotiation process that takes some time to reach an agreement confers bargaining power, giving the less impatient party a greater share of the gains from medicines. In this case, delays appear to benefit the government and its constituencies through improved cost-effectiveness, while pharmaceutical companies have a strong incentive to invest in political alliances to hasten public funding for drugs.

8.CONCLUSION

Using data from public reimbursement decisions for pharmaceuticals in Australia, we have shown that the time to an agreement on price and coverage between a single-buyer and a pharmaceutical company is determined by relative bargaining power, with delay, a feature of the process. Consistent with rational models of bargaining, expected net value to the payer increases with delays in agreement, while a strong perceived `need' over and above the health gains enhances the company's position, reduces delay and increases the rate of agreement on funding. This is clearly observed where the treated condition is severe or where there is heightened public awareness and interest in the therapy. In terms of the policy implications, the results suggest that while longer negotiations may deprive some patients of a clinical benefit, they also might enhance the terms of the agreement in favour of the wider public interest by improving value for money and reducing risk. In a stylised form of dynamic bargaining the company might reduce delay by separating the market for therapies by quality over time, although we did not find strong evidence of this here. Perhaps the most tantalising result in this paper is that increased internet search activity is associated with faster agreement, implying that marketing investment at an early stage is a potential means of lifting profit share in addition to the more usual post-launch marketing to the medical profession. More broadly, to the extent that pre-launch marketing activities could influence political interest in the drug, it is a means to reduce the bargaining power of the funding agency. The results are based on the institutional framework of drug funding in Australia, but they are likely to be applicable to other jurisdictions where a similar process of company-initiated offer followed by negotiation on price and access are a feature of coverage decisions.

REFERENCES

Ambrus, A., E. Chaney and I. Salitskiy (2011). 'Pirates of the Mediterranean: An Empirical Investigation of Bargaining with Transaction Costs'.

Annesi, I., T. Moreau and J. Lellouch (1989). 'Efficiency of the logistic regression and Cox proportional hazards models in longitudinal studies', *Statistics in medicine*, vol. **8**(**12**), pp. 1515-1521.

Antonanzas, F., C. Juarez-Castello and R. Rodriguez-Ibeas (2011). 'Should health authorities offer risk-sharing contracts to pharmaceutical firms? A theoretical approach', *Health Economics, Policy and Law*, vol. **6**(**3**), pp. 391-403.

Backus, M., T. Blake, B. Larsen and S. Tadelis (2020). 'Sequential Bargaining in the Field: Evidence from Millions of Online Bargaining Interactions*', *The Quarterly Journal of Economics*, vol. **135**(**3**), pp. 1319-1361.

Barnieh, L., B. Manns, A. Harris, M. Blom, C. Donaldson, S. Klarenbach, D. Husereau, D. Lorenzetti and F. Clement (2014). 'A synthesis of drug reimbursement decision-making processes in organisation for economic co-operation and development countries', *Value Health*, vol. **17**(**1**), pp. 98-108.

Barros, P. P. (2011). 'The simple economics of risk-sharing agreements between the NHS and the pharmaceutical industry', *Health Econ*, vol. **20**(**4**), pp. 461-470.

Binmore, K., A. Rubinstein and A. Wolinsky (1986). 'The Nash Bargaining Solution in Economic Modelling', *The RAND Journal of Economics*, vol. **17**(**2**), pp. 176-188.

Claxton, K., S. Martin, M. Soares, N. Rice, E. Spackman, S. Hinde, N. Devlin, P. C. Smith and M. Sculpher (2015). 'Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold', *Health Technol Assess*, vol. **19**(**14**), pp. 1-503, v-vi.

Cox, D. R. (1972). 'Regression models and life tables (with discussion)', *Journal of the Royal Statistical Society*, vol. **34**, pp. 187-220.

Cramton, P. C. (1992). 'Strategic Delay in Bargaining with Two-Sided Uncertainty', *The Review of Economic Studies*, vol. **59**(**1**), pp. 205-225.

Critchley, G. J. and G. S. Zaric (2019). 'The impact of pharmaceutical marketing on market access, treatment coverage, pricing, and social welfare', *Health Econ*, vol. **28**(**8**), pp. 1035-1051.

Dakin, H., N. Devlin, Y. Feng, N. Rice, P. O'Neill and D. Parkin (2015). 'The Influence of Cost-Effectiveness and Other Factors on Nice Decisions', *Health Econ*, vol. **24**(**10**), pp. 1256-1271.

Drummond, M. (2013). 'Twenty years of using economic evaluations for drug reimbursement decisions: what has been achieved?', *Journal of health politics, policy and law*, vol. **38**(**6**), pp. 1081-1102.

Drummond, M. and C. Sorenson (2009). 'Nasty or nice? A perspective on the use of health technology assessment in the United Kingdom', *Value in Health*, vol. **12**(**s2**), pp. S8-S13.

Dylst, P., A. Vulto and S. Simoens (2011). 'The impact of reference-pricing systems in Europe: a literature review and case studies', *Expert review of pharmacoeconomics & outcomes research*, vol. **11**(**6**), pp. 729-737.

Efron, B. (1977). 'The efficiency of Cox's likelihood function for censored data', *Journal of the American statistical Association*, vol. **72**(**359**), pp. 557-565.

FDA (2025) *US Food and Drug Administration New Drug Application (NDA) and Biologic License Application (BLA) approvals*. Available at https://www.fda.gov/drugs/drug-and-biologic-approval-and-ind-activity-reports/nda-and-bla-approvals.

Frijters, P., D. W. Johnston, G. Lordan and M. A. Shields (2013). 'Exploring the relationship between macroeconomic conditions and problem drinking as captured by Google searches in the US', *Social science & medicine*, vol. **84**, pp. 61-68.

Fudenberg, D., D. K. Levine and J. Tirole (1985). 'Infinite-Horizon Models of Bargaining with One-Sided Incomplete Information', in (Roth, A. Ed.) *Game Theoretic Models of Bargaining,* pp. 73-98, Cambridge, UK and New York: Cambridge University Press.

Fudenberg, D., D. K. Levine and J. Tirole (1987). 'Incomplete information bargaining with outside opportunities', *The Quarterly Journal of Economics*, vol. **102**(**1**), pp. 37-50.

Google Trends (2024) *Google trends*. Available at https://www.google.com/trends.

Grennan, M. (2013). 'Price Discrimination and Bargaining: Empirical Evidence From Medical Devices', *American Economic Review*, vol. **103**(**1**), pp. 145-177.

Grossman, S. J. and M. Perry (1986). 'Sequential bargaining under asymmetric information', *Journal of Economic Theory*, vol. **39**(**1**), pp. 120-154.

Harris, A., J. J. Li and K. Yong (2016). 'What Can We Expect from Value-Based Funding of Medicines? A Retrospective Study', *Pharmacoeconomics*, vol. **34**(**4**), pp. 393-402.

Harris, A. H., S. R. Hill, G. Chin, J. J. Li and E. Walkom (2008). 'The role of value for money in public insurance coverage decisions for drugs in Australia: a retrospective analysis 1994-2004', *Medical Decision Making*.

Harsanyi, J. C. and R. Selten (1972). 'A Generalized Nash Solution for Two-Person Bargaining Games with Incomplete Information', *Management Science*, vol. **18**(**5**), pp. P80-P106.

Jena, A. B. and T. J. Philipson (2008). 'Cost-effectiveness analysis and innovation', *J Health Econ*, vol. **27**(**5**), pp. 1224-1236.
Kennan, J. and R. Wilson (1993). 'Bargaining with Private Information', *Journal of Economic Literature*, vol. **31**(**1**), pp. 45-104.
Lee, I. H., K. Bloor, C. Hewitt and A. Maynard (2015). 'International experience in controlling pharmaceutical expenditure: influencing patients and providers and regulating industry - a systematic review', *J Health Serv Res Policy*, vol. **20**(**1**), pp. 52-59.
Merlo, A. and F. Ortalo-Magné (2004). 'Bargaining over residential real estate: evidence from England', *Journal of Urban Economics*, vol. **56**(**2**), pp. 192-216.
Nash, J. (1953). 'Two-person cooperative games', *Econometrica: Journal of the Econometric Society*, pp. 128-140.
PBAC Decisions (2024) *Public summary documents by meeting*. Available at https://www.pbs.gov.au/pbs/industry/listing/elements/pbac-meetings/psd.
Pearce, A. (2012). 'Why medicines take so long to get listed on the PBS', in (Editor Ed.)^Eds.), *Book Why medicines take so long to get listed on the PBS*, City.
Reilly, S., S. Richey and J. B. Taylor (2012). 'Using google search data for state politics research: an empirical validity test using roll-off data', *State Politics & Policy Quarterly*, vol. **12**(**2**), pp. 146-159.
Riley, J. G. (2001). 'Silver signals: Twenty-five years of screening and signaling', in (Editor Ed.)^Eds.), *Book Silver signals: Twenty-five years of screening and signaling,* pp. 432-478, City: American Economic Association.
Rothschild, M. and J. Stiglitz (1976). 'Equilibrium in competitive insurance markets: An essay on the economics of imperfect information', *Uncertainty in economics,* pp. 257-280: Elsevier.
Towse, A., M. Drummond and C. Sorenson (2012). 'Measuring value: Pharmacoeconomics theory and practice', *The Economics of the Biopharmaceutical Industry, by Patricia Danzon and Sean Nicholson*, pp. 394-437.
US VA FSS (2024) *Historical VA Pharmaceutical Prices*.
van der Net, J. B., A. C. J. W. Janssens, M. J. C. Eijkemans, J. J. P. Kastelein, E. J. G. Sijbrands and E. W. Steyerberg (2008). 'Cox proportional hazards models have more statistical power than logistic regression models in cross-sectional genetic association studies', *European Journal of Human Genetics*, vol. **16**(**9**), pp. 1111-1116.
Verniers, I., S. Stremersch and C. Croux (2011). 'The global entry of new pharmaceuticals: A joint investigation of launch window and price', *International Journal of Research in Marketing*, vol. **28**(**4**), pp. 295-308.
WHOCC (2024) *WHO Collaborating Centre for Drug Statistics Methodology, ATC classification index with DDD*. Available at https://atcddd.fhi.no/atc_ddd_index/.
Willard, S. D. and M. M. Nguyen (2013). 'Internet search trends analysis tools can provide real-time data on kidney stone disease in the United States', *Urology*, vol. **81**(**1**), pp. 37-42.
Woods, B., J. Lomas, M. Sculpher, H. Weatherly and K. Claxton (2024). 'Achieving dynamic efficiency in pharmaceutical innovation: Identifying the optimal share of value and payments required', *Health economics*, vol. **33**(**4**), pp. 804-819.
Wright, D. J. (2004). 'The drug bargaining game: pharmaceutical regulation in Australia', *Journal of health economics*, vol. **23**(**4**), pp. 785-813.
Yang, A. C., S.-J. Tsai, N. E. Huang and C.-K. Peng (2011). 'Association of Internet search trends with suicide death in Taipei City, Taiwan, 2004–2009', *Journal of affective disorders*, vol. **132**(**1**), pp. 179-184.

FIGURES AND TABLES

Figure 1: Flow Diagram of submissions (i.e. rounds of negotiations) included in the analyses

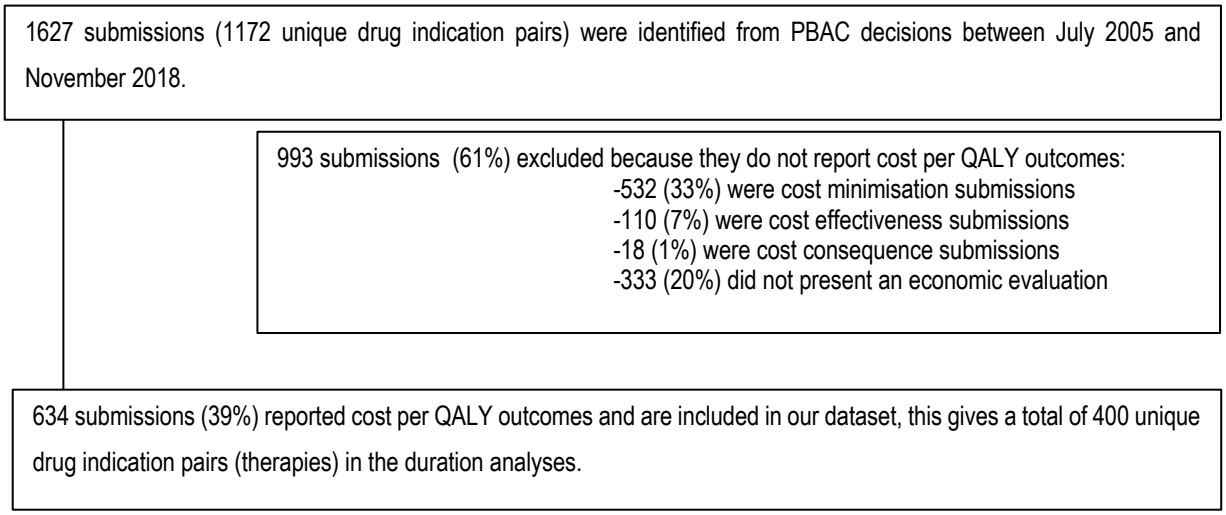


Table 1: Variable Definition

Concept measured	Variable	Variable Definition	Coding	Source
Dependent variable				
Bargaining outcome	Agreement	Whether the PBAC recommended the drug for listing at the requested price and population.	1=agreement 0=no agreement (including decisions by PBAC to not recommend, defer, list at a lower price or list with additional criteria)	PBAC Decisions (2024)
Time to agreement	Years since first proposal	Time to agreement (censored at 4 years in the primary analysis)	Years from the first proposal (proposal date is typically 3 months before the date of the PBAC meeting to allow for independent evaluation)	PBAC Decisions (2024)
Independent variables				
The expected net value	ICER	PBAC accepted ICER (cost/QALY gained) for the drug. This is reported as a categorical variable in the PSD.	1= Less than $15,000 2= $15,000 to $45,000 3= $45,000 to $75,000 4= $75,000 to $105,000 5= $105,000 to $200,000 6= Greater than $200,000	PBAC Decisions (2024)
	Budget impact	Did the expected annual budget for the health system due to funding the drug exceed $AUD10 million?	0=no 1=yes	PBAC Decisions (2024)
	Clinically important difference	Did the committee believe the treatment effect size (relative to the comparator) was clinically important and meaningful?	0=no 1=yes	PBAC Decisions (2024)
	Clinical uncertainty	How confident was the PBAC with the clinical information presented before them?	0=none or limited uncertainty 1=considerable uncertainty	PBAC Decisions (2024)
	Economic uncertainty	How confident was the PBAC with the economic evaluation that generated the ICER relied on in the decision?	0=none or limited uncertainty 1=considerable uncertainty	PBAC Decisions (2024)
	Severity of the condition/ need	Did the drug receive a priority need designation from the FDA, indicating the drug was aimed at treating a serious condition?	0=no 1=yes	FDA (2025)
Outside options buyer: current availability of substitutes	Number of drugs within the same ATC code indicating similar mechanisms of action in the world	How many other drugs were already in the same ATC group at the 5-digit level at the time of the PBAC meeting? This gives an indication of the number of potential substitutes.	Number drugs (1-max 5) within the same 5-digit ATC classification.	WHOCC (2024)
Marketing effort of the firm	Google Trends	Difference in average percentage change in year leading up to the PBAC meeting in Google Trend data for the drug relative to "Health" category searches over the same period.	Change (%) in the year leading up to PBAC meeting	Google Trends (2024)

Concept measured	Variable	Variable Definition	Coding	Source
Outside options and spillover effects	Price of drug in the US market at the time of the submission.	US FSS price (for a month of treatment at the average dosage) at the time of the proposal (or in the nearest year if the drug was not available in the US at the time of the proposal)	Log of price of the drug in US dollars for an equivalent quantity as the requested listing.	US VA FSS (2024)
Separating equilibrium	Separate agreements by therapy with varying quality	Prior agreement	If drug had an earlier agreement to fund a therapy =1, else=0	PBAC Decisions (2024)

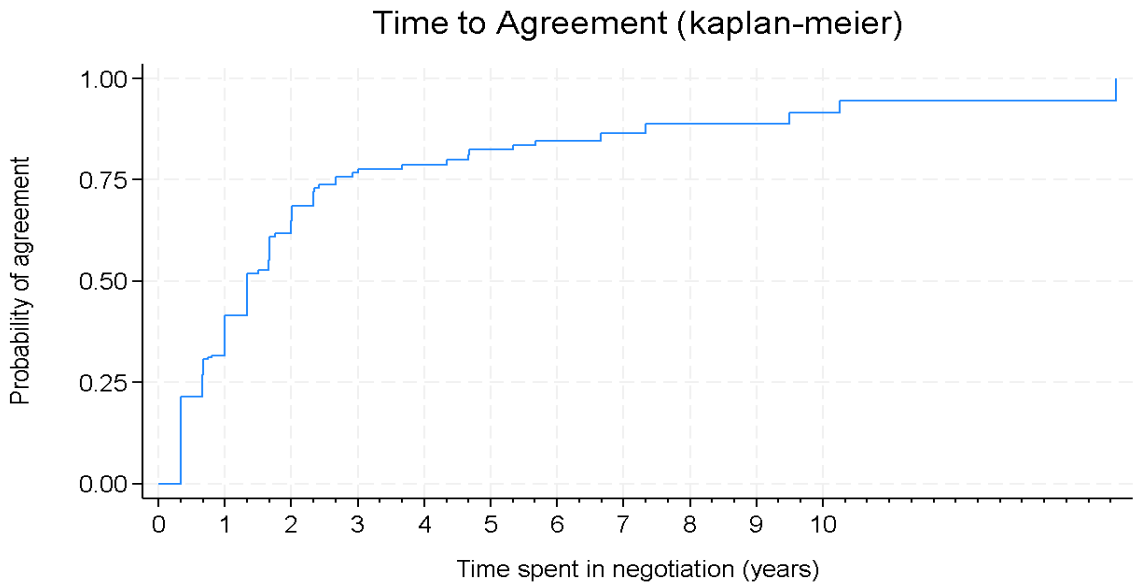
ATC=World Health Organisation Anatomical Therapeutic Chemical Classification, ICER=incremental cost-effectiveness ratio (additional cost/ additional QALYs gained due to the intervention), IQR=interquartile range, PBAC=Pharmaceutical Benefits Advisory Committee, PBS=Pharmaceutical Benefits Scheme, PSD=public summary document which is a public meeting documentation of the PBAC, U.S. VA FSS=United States Veteran Affairs Federal Supply Schedule

Table 2: Descriptive statistics

Characteristics	n (%) of submissions	n (%) of therapies †
Number of negotiations (i.e. number of cost per QALY submissions)	634	-
Total number of drug/indication pairs (therapies)	400	400
Number of rounds of negotiations per therapy, mean (sd)	1.51 (0.78)	-
median(range)	1 (1,6)	
Number that reached agreement §	181/634 (29%)	181/400 (45%)
FDA priority need	158/634 (25%)	111/400 (28%)
Substitutes as measured by the number of drugs in an ATC class, mean (SD)	3.5 (1.8)	-
Evidence from randomised trials	562/634 (89%)	358/400 (90%)
Clinically important difference between drug and comparator	363/634 (57%)	261/400 (65%)
Considerable clinical uncertainty	286/634 (45%)	208/400 (52%)
Considerable economic uncertainty	432/634 (68%)	307/400 (76%)
% change in Google Trends in the year leading up to meeting		
Mean (SD)	7% (55%)	-
Median (range)	-1% (-99%, 332%)	-
Less than 0%	318 (50%)	242 (61%)‡
Between 0% and <50% increase	237 (37%)	196 (49%)‡
50% increase to <100% increase	44 (7%)	44 (11%)‡
100% increase to <150% increase	19 (3%)	19 (5%)‡
Greater than 150% increase	16 (3%)	16 (4%) ‡
ICER ($/QALY gained) category in PSD		-
Less than $15,000	81 (13%)	70 (18%)‡
$15,000 to $45,000	191 (30%)	155 (39%)‡
$45,000 to $75,000	215 (34%)	158 (39%)‡
$75,000 to $105,000	61 (10%)	54 (14%)‡
$105,000 to $200,000	48 (8%)	45 (11%)‡
Greater than $200,000	38 (6%)	30 (8%) ‡
Budget impact >$10Million (AUD) per annum	386/634 (61%)	244/400 (61%)

ICER=incremental cost-effectiveness ratio, IQR=interquartile range; SD=standard deviation; PSD=public summary document
†Therapies are unique drug/indication pairs; the same drug submitted for distinctly different indications were considered to be separate therapies in the analyses. ‡ does not add up to 100% due to the values changing between successive submissions. § agreement is reached when the PBAC recommends listing at the price and population proposed without further restrictions.

Figure 2: Kaplan-Meier curve of time to agreement from date of first proposal to the PBAC



	Total time at risk (years)	Incidence †	no. of therapies	------ Time to agreement (Years)----- 25%	50%	75%
Total	428.26	0.42	400	0.67	1.34	2.67

†number recommended divided by total time at risk.

Table 3: Cox model results

Variables	HR (95% CI)†
FDA priority need	1.45** (1.03, 2.04)
Number of substitutes	0.95 (0.88, 1.03)
Clinical uncertainty	0.50*** (0.33, 0.75)
Clinically important difference	1.55** (1.07, 2.24)
Economic uncertainty	0.36*** (0.26, 0.51)
ICER category (comparisons versus ICER<$15,000)	
$15,000 - $45,000	0.67* (0.43, 1.04)
$45,000 - $75,000	0.55*** (0.36, 0.84)
$75,000 - $105,000	0.47** (0.23, 0.95)
$105,000 - $200,000	0.22** (0.07, 0.71)
$200, 000	0.15*** (0.04, 0.48)
Budget impact >$10million per year	0.77 (0.57, 1.05)
Google Trends (each SD from mean)	1.24*** (1.10, 1.39)
Number of submissions	625

*** p<0.01, ** p<0.05, * p<0.1; confidence intervals adjusted for therapy clusters †Censored at 4 years plus delayed entry (1 March 2005 when PSDs became publicly available)

Table 4: Predicted margins for time to agreement

	Difference in time to agreement from base case prediction of 1 year †		
Variables	**Median**	**25%**	**75%**
FDA priority 1	-0.33	0.00	-0.34
Number of substitutes (1 SD from the mean)	0.00	0.01	0.33
Clinical uncertainty 1	0.67	0.42	NE
Clinically important difference =1	-0.33	0.00	-0.34
Economic uncertainty=1	1.34	0.67	NE
ICER band =1 <$15K	-0.66	0.00	-0.67
ICER band =2 $15-45K	-0.33	0.01	-0.17
ICER band =3 $45-75K	-	-	-
ICER band =4 $75,000 - $105,000	0.00	0.01	0.33
ICER band =5 $105,000 - $200,000	1.00	0.67	NE
ICER band =6 >$200,000	NE	1.01	NE
Budget impact >$10 Million per annum	0.33	0.01	0.66
Google Trends (1 SD from the mean)	-0.33	0.00	-0.33

† base scenario where ICER band= 3 (<$45,000-$75,000), all other categories set to zero and continuous variables set at the mean. The median time to agreement is 1 year (IQR: 0.33,1,67) NE=not estimable.

Figure 3: Baseline hazard for reaching an agreement over time

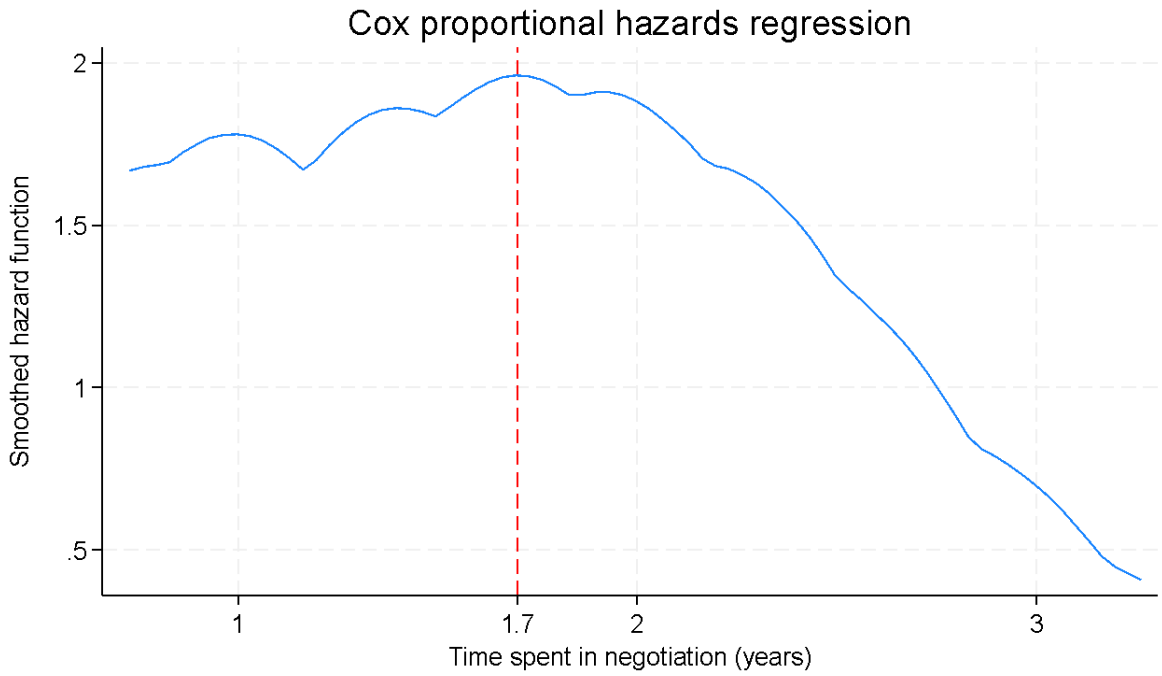


Table 5: ICER, risk in terms of the agency's confidence in value, and budget cost over prior agreement and negotiation rounds

	Odds ratio (95%CI)		
	Risk falls	**ICER**	**Budget impact**
	(1)	(2)	(3)
Prior drug agreement	0.47* (0.22, 1.22)	0.96 (0.44,2.10)	0.43** (0.19, 0.97)
Prior negotiation =1	2.04*** (1.38, 3.00)	1.06 (0.75,1.51)	1.14 (0.69, 1.89)
Prior negotiation =2	2.56*** (1.46, 4.47)	0.65 (0.39,1.09)	1.58 (0.64, 3.87)
Prior negotiation =3	3.62*** (1.95, 6.73)	0.56 (0.16,1.93)	1.28 (0.32, 5.19)

*** p<0.01, ** p<0.05, * p<0.1; Robust or bootstrap confidence intervals n=634

Risk that value will not be realised is a (0-3, high to low risk) score computed as a linear combination of 0-1 scores for clinical effectiveness, confidence in clinical evidence and confidence in economic evidence. Estimates in cols. 1-3 control for FDA priority, Google Trends (SD above the mean), and the number of potential substitutes. The group variable is drug, of which there are 270 with 400 therapies. Full results and other specifications reported in Appendix Tables A2.1 to A2.3.

Col 1 Random effects ordered logit of index (0-3) of greater confidence (indicating falls in risk), where the estimated parameters are the odds of having one level more confidence if there had been a prior agreement for the drug or in a negotiation round for the drug after the first. Includes budget impact as a covariate.

Col 2 Random effects ordered logit of ICER coded high to low where estimated parameters are the odds of being in a higher ICER if there had been a prior agreement for the drug or in a negotiation round for the therapy after the first round. Col 1 includes US drug price as covariate.

Col 3 Random effect logit regression of binary indicator if the cost to government is expected to be over $10m where the estimated parameters are the increased odds of the cost of government being over $10m if there had been a prior agreement for the drug or in a negotiation round for the therapy after the first round.

APPENDIX 1

Table A.1.1: Hazard ratios (HR) for covariates on time to agreement from date of first proposal across different model specifications

	Cox semi-parametric models (HR)				Parametric proportional hazard models (HR)			Logit (OR)
VARIABLES	**primary max 4yr**	**max 4yr no delayed entry**	**all data**	**max 5yr**	**Exponential**	**Weibull**	**Gompertz**	**Logit**
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
FDA priority	1.45**	1.72***	1.46**	1.48**	1.41**	1.53**	1.41**	1.16
	(1.03, 2.05)	(1.22, 2.42)	(1.04, 2.04)	(1.05, 2.08)	(1.04, 1.93)	(1.08, 2.17)	(1.04, 1.91)	(0.70, 1.92)
Number of substitutes	0.95	1.00	0.97	0.95	0.97	0.97	0.97	0.95
	(0.88, 1.03)	(0.91, 1.09)	(0.89, 1.04)	(0.88, 1.03)	(0.89, 1.05)	(0.89, 1.07)	(0.89, 1.05)	(0.85, 1.06)
Clinical uncertainty	0.50***	0.53***	0.52***	0.51***	0.49***	0.46***	0.49***	0.48***
	(0.33, 0.75)	(0.35, 0.80)	(0.35, 0.76)	(0.34, 0.76)	(0.32, 0.73)	(0.29, 0.72)	(0.33, 0.74)	(0.30, 0.76)
Clinically important difference	1.55**	1.37*	1.45**	1.52**	1.51**	1.57**	1.51**	1.72**
	(1.07, 2.24)	(0.94, 1.99)	(1.03, 2.06)	(1.06, 2.19)	(1.05, 2.18)	(1.06, 2.34)	(1.04, 2.17)	(1.05, 2.82)
Economic uncertainty	0.36***	0.39***	0.35***	0.35***	0.40***	0.45***	0.40***	0.12***
	(0.26, 0.51)	(0.27, 0.56)	(0.25, 0.50)	(0.25, 0.50)	(0.29, 0.56)	(0.31, 0.64)	(0.29, 0.55)	(0.08, 0.19)
ICER category (comparisons versus ICER <$15,000/QALY)								
$15,000 - $45,000	0.67*	0.63**	0.67*	0.66*	0.70*	0.61**	0.70*	0.84
	(0.43, 1.04)	(0.41, 0.98)	(0.44, 1.04)	(0.42, 1.02)	(0.47, 1.03)	(0.39, 0.96)	(0.48, 1.04)	(0.45, 1.58)
$45,000 - $75,000	0.55***	0.43***	0.54***	0.55***	0.57***	0.49***	0.58***	0.41***
	(0.36, 0.84)	(0.28, 0.68)	(0.35, 0.82)	(0.36, 0.84)	(0.39, 0.84)	(0.31, 0.77)	(0.39, 0.85)	(0.21, 0.80)
$75,000 – $105,000	0.47**	0.43**	0.52*	0.52*	0.48**	0.43**	0.49**	0.40*
	(0.23, 0.95)	(0.21, 0.87)	(0.27, 1.01)	(0.26, 1.01)	(0.25, 0.95)	(0.21, 0.87)	(0.25, 0.95)	(0.15, 1.03)
$105,000 - $200,000	0.22**	0.21***	0.22**	0.22**	0.22***	0.21***	0.22***	0.11***
	(0.07, 0.71)	(0.06, 0.66)	(0.07, 0.71)	(0.07, 0.71)	(0.07, 0.66)	(0.07, 0.67)	(0.07, 0.66)	(0.03, 0.40)
>$200, 000	0.15***	0.11***	0.18***	0.14***	0.14***	0.12***	0.14***	0.15**
	(0.04, 0.48)	(0.03, 0.37)	(0.06, 0.52)	(0.04, 0.45)	(0.04, 0.45)	(0.03, 0.39)	(0.05, 0.45)	(0.04, 0.65)
Budget impact >$10Mil per annum	0.77	0.80	0.75*	0.79	0.84	0.84	0.84	0.50***
	(0.57, 1.05)	(0.58, 1.11)	(0.55, 1.01)	(0.58, 1.07)	(0.63, 1.13)	(0.60, 1.17)	(0.63, 1.13)	(0.33, 0.75)
Google Trends	1.24***	1.26***	1.23***	1.24***	1.21***	1.26***	1.21***	1.31***
(each SD above mean)	(1.10, 1.39)	(1.11, 1.42)	(1.10, 1.39)	(1.11, 1.40)	(1.09, 1.36)	(1.11, 1.42)	(1.08, 1.35)	(1.07, 1.61)
ln_p						1.24***		
						(1.14, 1.35)		
gamma							0.98	
							(0.84, 1.14)	
Constant					1.34	1.22	1.36	4.28***
					(0.81, 2.20)	(0.70, 2.12)	(0.82, 2.27)	(1.87, 9.81)
Observations	625	629	634	632	625	625	625	634

ICER=incremental cost-effectiveness ratio (expressed as additional cost per QALY gained), Mil=million, QALY=quality adjusted life year,
*** p<0.01, ** p<0.05, * p<0.1; confidence intervals adjusted for therapy clusters

APPENDIX 2

Extended analysis time to agreement and value to the purchaser

Risk as measured by the agency's confidence in the quality of evidence of cost-effectiveness

We test if the agency's confidence in the evidence of cost-effectiveness improves with negotiation in an ordered random effects logit across therapies for a drug (Table A2.1, col 3) and across rounds of negotiation within a therapy (Table A2.1 col 1). Confidence is measured as the linear combined index of uncertainty across economic and clinical uncertainty and the belief in clinical effectiveness. The highest index of confidence (3) is no major clinical or economic uncertainty and confidence in a clinically significant effect. The lowest is a score of 0, with uncertainty in each and no confidence in a clinically significant effect of the therapy.

Table A.2.1 Greater confidence in value before and after first therapy agreement and across rounds of negotiation for a drug: Ordered random effects logit regression of confidence index (0-3; poor-high)

	Ordered random effect logit odds ratio (95%CI)		
	(1)	(2)	(3)
Prior agreement	1.01 (0.54, 1.90)	1.01 (0.53,1.91)	0.47* (0.22, 1.22)
Negotiation			
round=2	1.64*** (1.19, 2.27)	1.63** (1.18, 2.27)	2.04*** (1.38, 3.00)
round=3	2.49*** (1.35, 4.44)	2.45*** (1.36, 4.41)	2.56*** (1.46, 4.47)
round>3	2.41** (1.16, 5.02)	2.55** (1.28, 5.07)	3.62*** (1.95, 6.73)
ICER			
$15,000-$45,000		0.74 (0.32, 1.72)	0.76 (0.39,1.47)
$45,000-$75,000		0.83 (0.35, 1.99)	0.79 (0.39, 1.60)
$75,000-$105,000		0.38** (0.17, 0.85)	0.37** (0.16, 0.86)
$105,000-$200,000		0.71 (0.33, 1.53)	0.63 (0.28,1.39)
>$200,000		0.33** (0.11, 0.98)	0.30** (0.10, 0.94)
FDA priority need		1.30 (0.74, 2.31)	1.34 (0.80, 2.24)
Google Trends (each SD above mean)		1.19** (1.02, 1.40)	1.18** (1.03, 1.37)
Number of substitutes		0.99 (0.88, 1.12)	1.00 (0.88, 1.12)
Budget impact >$10million per annum		0.90 (0.63, 1.28)	0.90 (0.60, 1.34)

* p<0.10, ** p<0.05, *** p<0.01.

634 observations on 400 therapies within the group variable drug (n=270). Area under ROC for random effects logit is >0.6 for poor and high confidence but not significantly different from 0.5 for low and moderate levels, SD=standard deviation.

Col 1 and Col 2 show prior negotiations for a single therapy. In Col 3 prior negotiations for a drug across all therapies

Cost to government

We test if the total cost to government is more likely to be over the $10m threshold in later bids using a logit, linear fixed effects and ordered random effects logit across therapies for a drug and across rounds of negotiation within a therapy.

Table A.2.2 Probability of the projected annual government spending on a therapy exceeding $10m before and after first therapy agreement and across rounds of negotiation for a therapy

	Logit Odds Ratio		Linear fixed effect		Random effects logit Odds Ratios	
	(1)	(2)	(3)	(4)	(5)	(6)
Prior drug agreement (1=yes)	0.75	0.81	-0.16**	-0.17**	0.40**	0.43**
	(0.50, 1.14)	(0.53, 1.24)	(-0.29, -0.03)	(-0.29, -0.04)	(0.18, 0.92)	(0.19, 0.97)
Therapy negotiation						
round=2	1.20	1.21	-0.02	-0.01	1.10	1.14
	(0.83, 1.75)	(0.83, 1.78)	(-0.09, 0.05)	(-0.09,0.06)	(0.67, 1.79)	(0.69, 1.89)
round=3	1.86**	2.03**	-0.03	-0.01	1.40	1.58
	(1.01, 3.43)	(1.09, 3.79)	(-0.14, 0.08)	(-0.15,0.12)	(0.61, 3.23)	(0.64, 3.87)
round>3	2.00	2.12	-0.04	-0.02	1.18	1.28
	(0.61, 6.52)	(0.62, 7.16)	(-0.24, 0.16)	(-0.22, 0.19)	(0.28, 4.90)	(0.32, 5.19)
Confidence						
Low		0.97		-0.05		0.86
		(0.61, 1.53)		(-0.19, 0.09)		(0.39, 1.90)
Medium		1.15		-0.08		0.86
		(0.73, 1.81)		(-0.20, 0.05)		(0.41, 1.81)
High		0.85		-0.10		0.56
		(0.51, 1.42)		(-0.28, 0.07)		(0.22, 1.43)
FDA priority need		0.88		-0.03		0.74
		(0.60, 1.28)		(-0.18, 0.12)		(0.36, 1.53)
Google trends		1.21**		-0.02		1.09
		(1.02, 1.44)		(-0.06, 0.03)		(0.83, 1.42)
Number of substitutes		1.06		-0.06		1.13
		(0.97, 1.16)		(-0.16, 0.05)		(0.92, 1.39)

* p<0.10, ** p<0.05, *** p<0.01. 634 observations on 400 therapies within the group variable drug (n=270). Area under the ROC for (random effects) logit is 0.59 (0.62). N=634. Robust standard errors.

Incremental Cost Effectiveness Ratio

We test if the ICER falls each round for a therapy as the agency gains more value from negotiations and after the first agreement for the drug by estimating a regression of the ICER band at each round before and after a first agreement for the drug in linear fixed effect and random effect ordered logit models. The

advantage of the linear fixed effect model is its ability to control for drug-specific unobservable aspects of bargaining power that do not change between rounds, such as the bargaining ability of a company, that may be correlated with the control variables. However, this is at the expense of efficiency, as it ignores between drug information. Additionally, by assuming continuous outcomes, it risks potential measurement error bias. In the ordered logit regression, we test if the odds of moving to a higher band each round compared to the odds of being in a lower band is greater than one, as the number of indications rises, with more rounds of negotiation for a drug, or with a lower U.S. price.

Table A.2.3: ICER over time before and after first therapy agreement and across rounds of negotiation for a therapy
Fixed effects linear model and random effects ordered logit of ICER band

	Linear fixed effects		Ordered random effects	
	(1)	(2)	(3)	(4)
Prior drug agreement (1=yes)	0.04	0.05	1.00	0.96
	(-0.29, 0.37)	(-0.33,0.43)	(0.51,1.98)	(0.44,2.10)
Therapy negotiation				
round=2	-0.17**	-0.12	0.96	1.06
	(-0.34, -0.01)	(-0.29,0.06)	(0.68,1.36)	(0.75,1.51)
round=3	-0.44***	-0.38**	0.58**	0.65
	(-0.70, -0.18)	(-0.66,-0.09)	(0.35,0.95)	(0.39,1.09)
round>3	-0.41	-0.44	0.58	0.56
	(-1.07, 0.24)	(-1.10,0.22)	(0.16,2.16)	(0.16,1.93)
FDA_priority		-0.22		1.02
		(-0.70,0.26)		(0.51,2.05)
US drug price(log)		0.03***		1.10***
		(0.01,0.04)		(1.05,1.15)
Confidence in evidence				
Low		-0.00		0.92
		(-0.31,0.30)		(0.52,1.62)
Medium		-0.02		0.92
		(-0.36,0.32)		(0.53,1.60)
High		-0.36		0.34***
		(-0.81,0.09)		(0.16,0.73)
Google trends (each SD above the mean)		-0.07		0.88
		(-0.15,0.02)		(0.73,1.06)
Number of substitutes		0.37***		1.41***
		(0.11,0.62)		(1.19,1.67)
Budget impact >$10million per annum		0.19		2.52***
		(-0.09,0.47)		(1.55,4.13)

* p < 0.05, ** p < 0.01, *** p < 0.001. 634 observations on 400 therapies within the group variable drug (n=270). Robust standard errors.
The estimates of the effect of a unit change in each variable; in (1) and (2) on the ICER on a linear scale of 1 to 6 where 6 >$200,000 5=$105,000-$200,000 4 = 75000-104,000 3=$45,000-$74,000 2= 15,000-44,000 to 1=<$15000 per QALY; and in (3) and (4) on the ratio of the odds of being in a higher ICER band. Area under the ROC for random effects ordered logit >0.65 except for category 3=0.57 (95% CI 0.51,0.60)

Spillover effects

Australia is a secondary market, with most drugs launched in the United States and Europe before Australia, with several downstream countries after that. Consequently, the price and value offered may take account of the upstream and downstream implications for future pricing for the company. We expect

that for some drugs, the US price indirectly impacts the probability of an agreement through its effect on a threshold price and, consequently, the ICER in the bid. There may be some direct effect on the company's bargaining power if a low overseas price makes the agency unwilling to accept a high ICER. It is not clear that the agency looks to overseas prices in this way, so we do not expect a large direct effect on the time to listing, which is why we exclude the international price from the duration analysis in the main analysis. We use a mediation analysis of the US price to examine the direct and indirect effect of the US therapy price on the probability of an agreement at each negotiation point.

We used a generalised structural equation model (GSEM) to estimate the direct, indirect, and total effects of the log-transformed price of the therapy on the probability of an agreement mediated by the ordinal variable representing ICER bands. The model is specified as follows:

1. **Mediator Equation (Ordinal Outcome):**

   $ICER_i=\alpha_0+\alpha_1\cdot(\ln)USprice_i+\varepsilon_{1i}$,

   where ICER is treated as an ordinal variable with categories determined by latent thresholds. The equation was estimated using an ordinal logistic regression

2. **Outcome Equation (Binary Outcome):**

   $\text{logit}(\Pr(\text{agreement}=1))=\beta_0+\beta_1\cdot\ln(USprice_i)+\beta_2\cdot ICER+\beta 3\cdot CinicalUncertainty+\beta 4\cdot Clinical Importance+\beta_5\cdot EconomicUncertainty+\beta_6\cdot GoogleTrends+\beta_7\cdot Substitutes+\beta_8\cdot BudgetCost+\varepsilon_{2i}$.

Table A.2.4 The direct effect of US price(log) on the probability of an agreement (logit) and the effect mediated through the ICER (ordered logit)

Panel 1: US price(log) mediation analysis GSEM

ICER	Coefficient (95%CI)
US Price(log)	0.08*** (0.05, 0.11)
Agreement (yes=1)	
ICER	-0.49*** (-0.69, -0.29)
US Price(log)	0.04 (-0.02, 0.09)
Clinical Uncertainty	-0.74*** (-1.21, -0.28)
Clinical effectiveness	-0.43* (-0.88, 0.02)
Economic Uncertainty	-2.06*** (-2.50, -1.63)
Google trends (each SD above mean)	0.28***(0.07, 0.49)
FDA priority	0.08 (-0.41, 0.57)
Number of substitutes	-0.06 (-0.17, 0.06)
Budget impact >$10million per annum	-0.69*** (-1.12, -0.25)
Constant	2.40*** (1.64, 3.15)

Panel 2: Direct and Indirect Effect of a change in US price of $5000 from mean of $9210 on Agreement

	Change in probability of an agreement
Indirect	-0.005*** (-0.007, -0.002)
Direct	0.004 (-0.0003, 0.009)
Total	0.0003 (-0.005, 0.005)

* p < 0.05, ** p < 0.01, *** p < 0.001. n=634

The total effect of the US price on the probability of an agreement is the combination of the direct and indirect pathways. Table A2.4 shows that the indirect effect, while small, is statistically significant, suggesting that the ICER plays a role in mediating the small effect of a higher US price on the probability of an agreement. After accounting for this mediation, the direct relationship between price and agreement is weak and not statistically significant. In summary, higher US drug prices indirectly decrease the probability of recommending the drug through their influence on reducing the agency's value of the therapy (moving into less favourable ICER categories), but this effect is very small. For example, an increase in the US price of $5000 from the mean price of $9210 would result in a fall in the probability of agreement of 0.005 points, if not counteracted by a positive direct effects on agreement or confounded by any unobserved characteristics of the drug that are correlated with the US price but not with the ICER.