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Innovative applications of O.R.

Optimal co-development contracts for companion diagnostics

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ABSTRACT

The market for companion diagnostics is expected to be a US$10.07 billion by 2026. Companion diagnostics have the potential to make expensive drugs cost-effective by identifying patients who would benefit from them. We consider the contract design problem between a pharmaceutical company which owns a drug that is effective for a particular subset of the patient population and a biotech company which owns some technology that could facilitate the development of a companion diagnostic. We obtain theoretical and practical results. We determine when both parties enter such a contract and fully characterize the optimal solutions in closed-form. We find sufficient conditions under which the optimal contract exhibits a particular structure. We show that the first-best can be achieved in some cases and identify sufficient conditions under which the biotech company would not work alone but participates in the project with the pharmaceutical company's subsidy. We find that heuristics based on practical preferences could be costly to the pharmaceutical company and hence the principal should use the second-best solution; and contract type depends heavily on the biotech company's workforce level, unit cost of workforce and information level.

1. Introduction

In recent years a number of biologics and targeted therapies have been developed that are expensive and not effective in the entire patient population. In some cases the effectiveness is related to a gene or other biomarker, in which case use of the drug can be restricted to those individuals who are most likely to benefit. For example, trastuzumab is only used to treat breast cancer that is HER2 positive, and panatimumab is not effective in people who have a mutation in the KRAS gene (Amado et al., 2008). This can have implications for formulary listings and hence also on the profits of pharmaceutical firms. For example, in Ontario, Canada, Amgen agreed to pay for KRAS testing for all individuals who might be eligible for treatment as a condition for formulary listing (MAS, 2010).

In cases where it is reasonable to suspect that a biomarker can be found (CBC, 2013a, 2013b; Lougheed, 2013), interest has developed in finding "companion diagnostics" to help identify individuals most likely to benefit from a drug (Agarwal, 2012; Agarwal, Ressler, & Snyder, 2015; Atherly & Camidge, 2012; Desiere, Gutjahr, & Rohr, 2013; FDA, 2013a, 2013b; LeapTherapeutics, 2020; Pharmafile, 2018; Tufts-CSDD, 2013; Watson, 2013). For example, in 2011 the FDA approved the use of crizotinib (Xalkori) alongside a companion diagnostic test for late-stage, non-small cell lung cancer in patients with an abnormal ALK gene (JHOP, 2015), and then in 2016 the FDA approved expanded use of the drug in patients with a ROS-1 gene alternation while a companion diagnostic was still being developed (Navarro, 2016).

The development of companion diagnostic tests often involves partnerships between drug companies and diagnostic test manufacturers, in a process known as co-development. A review article examined partnerships between pharmaceutical companies and diagnostics test companies for the development of companion diagnostics (Leamon & Sherman, 2012). The article identified 44 partnerships between pharmaceutical companies and companion diagnostics firms between 2008 and 2010, and a more recent forecast suggests that the market for companion diagnostics will grown to US$10.07 billion industry by 2026 (Bloomberg, 2019). Several models for the development of companion diagnostics were defined. These include partnerships and licensing, in which a pharmaceutical company will "collaborate with a diagnostics company to develop a test", (Leamon & Sherman, 2012). We use the term "co-development" to refer to any interaction between a pharmaceutical company and a diagnostics developer in which there is collaboration to develop a companion diagnostics test.

There are recent examples of co-development. For example, Merck and Agilent Technologies collaborated on the development of the PD-L1 IHC 22C3 pharmDx companion diagnostic for Merck's cancer drug Keytruda (Businesswire, 2023; RTTNews.com, 2023). Bristol-Myers Sqibb and Qiagen have developed a partnership to develop

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several companion diagnostics (Qiagen, 2017). As noted in the press release, the partnership "will leverage the combination of Bristol-Myers Squibb's portfolio of [immuno-oncology] therapies with QIAGEN's proven track record in developing and commercializing companion and complementary diagnostics". This suggests a relationship in which both companies bring unique competencies to the development process.

The motivation for a pharmaceutical company to engage in a co-development partnership can be illustrated by the case of ipilimumab, which can be used to treat malignant melanoma and costs approximately £80,000 per year in the UK. In 2011 the drug received an unfavorable review from NICE (The UK National Institute for Health and Care Excellence). In his comments on the negative evaluation of ipilimumab, Sir Andrew Dillon, CEO of NICE, said "We need to be sure that new treatments provide sufficient benefits to patients to justify the significant cost the NHS is being asked to pay" (Nordqvist, 2011). He also noted that "Only around 30% of people treated with ipilimumab would have improved survival, with only 10% potentially experiencing long-term benefits", and also said "unfortunately, no patient characteristics or biomarkers have *yet been identified* to help identify this small group of people most likely to gain long-term benefit from receiving ipilimumab". This situation is not unique. One article asserted that "90% of all conventional remedies are not efficacious in 50%–70% of cases" (Akhmetov, Ramaswamy, Akhmetov, & Thimmaraju, 2015) Since drug development costs are sunk, discovery of an appropriate biomarker in a case like this could have enormous value to a drug manufacturer if it facilitates formulary listing. A formal partnership with a diagnostic test developer would ensure that the test developer directs scarce resources to a project valued by a pharmaceutical company, increasing the likelihood of regulatory or payer approval.

For a small lab or diagnostics company, partnership with a larger pharmaceutical company may serve as an additional source of investment capital, ensure that there is a market for the new product and, depending on the contract, provide a recurring source of revenue associated with the test. The recurring source of revenue can be a particularly important consideration for many diagnostic tests. A test for a particular gene abnormality only needs to be used once, and test procedures are often reimbursed based on lab steps as opposed to the underlying value of the intellectual property of the test (Agarwal, 2012). A co-development contract may provide financial incentives to a diagnostic developer to take on the risks necessary to pursue innovation. In addition to the factors just described, there may be benefits to both parties in the form of risk sharing, resource sharing, and shared expertise, particularly relating to the regulatory environment.

We investigate co-development contracts for companion diagnostics between a large pharmaceutical company that owns a potentially valuable drug (i.e., drug has been developed and regulatory approval but not formulary listing has been obtained), and a biotech firm that owns technology which could lead to a companion diagnostic test following additional research and development effort. Our research seeks to answer three questions. First, under what conditions should a pharmaceutical company partner with a test developer, and are there conditions under which co-development partnerships are not beneficial to either party? Second, when it is optimal for both parties to enter a co-development contract, what are the structural properties of the contract? And third, how well do several simple and intuitively appealing contracts perform in this setting?

Despite the potential benefits of co-development contracts, there are potential drawbacks: the project could be costly; the project could fail; and, if the project fails, it may be difficult to determine the cause of the failure. We summarize motivation and trade-offs for a co-development partnership between a pharmaceutical company and a biotech firm for a companion diagnostic as follows:

- Enable market access for potentially profitable drugs that only work on a small segment of the population.
- From the biotech firm's perspective, a companion diagnostic project with a large pharmaceutical company could bring capital to the biotech firm and potentially recurring revenue from a successful test co-development.
- If a successful test can be developed, then the drug would be more widely available for patients and hence medical benefits would be more accessible to those who could not afford it in the first place.
- The pharmaceutical firm may not have the specialized skills needed to develop a companion diagnostic test, while the biotech firm might not have the resources needed for development.

We formulate the problem using a principal–agent (PA) framework, in which the pharmaceutical company acts as the principal and offers a contract with specific terms, and the companion diagnostics company acts as the agent and chooses the level of effort to invest in development for a given contract. The PA framework captures the sequential nature of the problem in which there are distinct stages. The contract is described by the amount of initial investment to be made by both companies and a royalty share of the revenue from sales of the companion diagnostic test if it is successfully developed. We characterize contracts as being one of three general types: licensing, royalty incentive or joint effort. We derive sufficient conditions under which the optimal contract exhibits a particular structure. We find that first-best results can be achieved in a few royalty incentive or joint effort contract types but never in a licensing type of contract. There are cases in which the agent would not work alone to develop a diagnostic test but is willing to participate in the project with the principal, and in this case the agent will require a subsidy, i.e., a royalty share that exceeds 100%. We illustrate the commonly observed contract structures and show the effect of problem parameters on the optimal contract structure by conducting numerical analysis.

In particular, we find the following managerial insights:

- The principal should use solution of the second-best problem (which is readily available in closed-form and can be implemented easily in a spreadsheet) since intuitively appealing contract heuristics that are motivated by practice could be costly for the principal.
- The problem parameters related to the agent such has his workforce level, unit cost of workforce, and information level about the project's potential (which plays a crucial role in deter- mining his reservation utility) have significant impact on the optimal contract type. Therefore, the principal should gather as much and accurate information as possible about these parameters before she designs the contract.

We provide a literature review in the next section. In Section 3 we formulate the problem and discuss how we model the agent's utility. We characterize the complete solutions in closed-form and provide structural properties of first-best and second-best in Section 4. Section 5 presents numerical analysis and heuristics. We conclude the paper and give our managerial insights in Section 6. All proofs are provided in the appendix of the paper.

2. Literature review

As our work relates primarily to literature on contracting and co-development in R&D activities, particularly R&D of one product, we review such studies. These studies can be classified as either focusing on single-stage contracts or on multi-stage contracts. We review the work in each category by briefly outlining the problem setting, the participants in the alliance, the contract components, the modeling approach, and the research questions.

2.1. Single-stage contracts

Crama, De Reyck, and Degraeve (2008) studied the problem of designing optimal licensing contracts for collaborative R&D projects between an innovator (licensor) and a marketer (licensee). They considered a setting where the innovator has the higher bargaining power, there is incomplete information about the licensee's valuation of the project, and limited control over the level of licensee's effort in the project. They focused their attention on three-part contracts which are composed of an upfront payment, a milestone payment upon the successful completion of the project, and a royalty percentage of sales. They formulated the problem as a PA model where the innovator is the principal and the licensee is the agent, and they analyzed the properties of the optimal contract under adverse selection (due to hidden information) and moral hazard (due to hidden action).

Yoon, Rosales, and Talluri (2018) considered the contract design problem for the partnership between a small biotech company and a large pharmaceutical company to develop and commercialize a new drug. They formulated the problem as a sequential game where the likelihood of the success of the innovation is decided by the biotech company given the contract parameters that are set by the pharmaceutical company. Unlike in our study, the likelihood of the success is not a function of the contributions of both parts, is instead a value directly determined by the biotech company. The authors considered three different types of contract structures: licensing agreement with milestone payment and the option to include an upfront payment, licensing agreement with royalties and the option to include an upfront payment, and acquisition contract. They characterized the optimal solution for each contract structure, and they illustrated how problem parameters affect the best contract type by using numerical examples. In our study, we consider the problem in an integrated manner and find the best contract structure, rather than obtaining the best solution for each prespecified structure.

Taneri and De Meyer (2017) classified the R&D alliances associated with the development of a new product into two groups: (1) sequential alliance, where an innovator mainly performs the initial set of tasks and the partner carries out the further development or marketing, (2) collaborative alliance, where both parties exert efforts mostly concurrently throughout the process. With their empirical analysis based on a data set consisting of single-stage biopharmaceutical licenses, the authors examined whether considerations rooted in contract theory affect the choice of the alliance structure (sequential or collaborative), and whether the alliance structure has an impact on the performance of the alliance. In our study, we consider the R&D process of a diagnostic test where the outcome is affected by joint contribution of the parties in the alliance, which corresponds to the collaborative alliance structure defined by Taneri and De Meyer (2017).

2.2. Multi-stage contracts

Savva and Scholtes (2014) analyzed the effects of opt-out in a two-stage co-development between a relatively small innovator and a large pharmaceutical company. They define co-development as a partnership for developing a product. They modeled the market value of the product over time as a nonnegative random process under the assumption that both companies are risk-neutral. They compared the value of the project under different settings including standard co-development, standard licensing, and co-development with the option of opting out after the first phase of the project. They characterized the range of the milestone and royalty payments for which the co-development partnership with opt-out options generates the maximum attainable project value.

Xiao and Xu (2012) investigated the impact of royalty revision on the value of a two-stage research and development alliance between two risk-neutral companies (marketer and innovator) in the presence of adverse selection and moral hazard. The opportunity to renegotiate over the royalty rate improves the marketer's profit by providing a flexibility in setting the contract terms. However it also causes the innovator to reveal less of her private information and hence makes it harder for the marketer to design more profitable contracts. The authors analyzed this double-sided effect and identified the conditions under which the marketer could benefit from renegotiating over the royalty payments.

Bhattacharya, Gaba, and Hasija (2015) explored the structure of optimal contracts in a two-stage partnership between a pharmaceutical company and a biotech company under double-sided moral hazard. They formulated the problem by using two different PA models where each party serves as the principal. For both models, the authors showed that the first-best solution can be attained by using dynamic contracts that are renegotiated before observing the outcome of the first-stage.

Crama, De Reyck, and Taneri (2017) considered the R&D collaboration between an innovator and a marketer, where the innovator owns an invention and intends to contract with the marketer. They assumed that both parties are risk neutral, and examined the innovator's problem of jointly determining the contract timing, structure (allocation of control rights and options) and parameters (payment terms) to maximize the value extracted from the collaboration. They investigated the timing decisions by considering three different scenarios: up-front contracting (i.e., single-stage structure), up-front contracting with renegotiation, and delayed contracting. In their model, the authors explicitly included the efforts of both parties in the relevant parts of the process by considering both the R&D and marketing phases in their timeline. The aspect of timing decisions in R&D alliances, which falls outside the scope of our problem setting, has also been considered in other studies including Crama, De Reyck, and Degraeve (2013), Lútkemeyer, Heese, and Wuttke (2021), Lútkemeyer, Heese, Wuttke, and Gernert (2022) and Morreale, Robba, Lo Nigro, and Roma (2017).

Wang, Schmidt, and van der Rhee (2018) considered the contract design problem in a setting where a principal outsources a two-stage R&D project to an agent whose type and effort level are unobservable by the principal. The probability of success in each stage depends on the agent's type and effort level, the second stage can be initiated only if the first stage is successfully completed. The authors considered various contract structures where money transfers are allowed at three points throughout the project timeline: at the start of the project, at the end of the first stage upon its successful completion, at the end of the second stage upon its successful completion. They investigated the price of not knowing the agent's type, the role of money transfers at different time points, the value of offering a menu of contracts rather than a single contract, the impact of including penalties upon failure (besides the money transfers upon success) in the contracts.

2.3. Contributions of this paper

We investigate the problem of designing a single-stage contract to form an alliance between a pharmaceutical company and a biotech company during the development of a companion diagnostics. There are several distinguishing features of our study from the literature reviewed in this section.

- The product jointly developed (i.e., the diagnostic test) has value to both parties but the value may be orders of magnitude greater to the principal.
- We explicitly model the agent's outside option. Thus, the agent's reservation utility is endogenous.
- We model the probability of success as a function of the agent's effort level and the initial investments made by both parties.
- We propose and evaluate the performance of several practical and simple heuristics.
- We conduct a numerical study to identify the most observed contract types and show how they change with parameter values.

3. Formulation

Our focus is on inter-firm interactions during the initiation phase of a collaborative research and development project between a pharmaceutical company (she) and a diagnostics developer (he). She owns a potentially valuable drug which is effective in a subset of the patient population and can only be sold with a companion diagnostic test, and he owns the required technology and knowledge, which she does not have, to develop a companion diagnostic for this drug. We formulate the problem as a principal–agent (PA) model in which the pharmaceutical company is the principal and the diagnostics company is the agent. The pharmaceutical company approaches the diagnostics company and proposes a contract to the diagnostic developer, which is common in personalized medicine practice (Cotter, Babu, & Moore, 2012). As is common in biopharmaceutical partnerships, the contract may include a combination of upfront payments and royalties, which are contingent on the success of the project (LeapTherapeutics, 2020). We do not model repeated interactions, meaning our focus is on designing a single-stage contract. Thus, the diagnostic developer can either accept the contract; reject the contract and pursue development of the companion diagnostic on its own; or not develop the companion diagnostic. Let R_D and R_T be the sales of the drug and companion diagnostic if the companion diagnostic is successfully developed. We assume there are no drug sales if the companion diagnostic is not developed.

We assume that the diagnostics company is a well-established research lab that already owns the required technology to develop the test. The initial investment made in the project is therefore used to cover operational expenses only, and both parties finance their investments through borrowing. Let b_a and b_p be the debt repayment factor of the diagnostics company and the pharmaceutical company (i.e., $b_a - 1$ and $b_p - 1$ are the effective interest rates over the planning horizon), respectively. Since the diagnostics company is a smaller firm, it has a higher debt repayment factor, i.e., $b_a > b_p \geq 1$.

The principal proposes a contract which is described by the amount of initial investment to be made by the agent and the principal (m_a and m_p, respectively) and a royalty percentage (r) of the revenue from the test sales to be given to the agent. Note that m_a is determined by the principal and can be considered as the agent's minimum participation fee requirement by the principal (i.e., the agent's "skin in the game"). A contract where $r > 1$ indicates that the agent receives a portion of the revenue from the drug sales besides the whole revenue from the test sales. Based on the offered contract, the agent chooses the level of effort (f_a) he is going to put into the development of the test. The probability of success for the project ($p(f_a, m_a, m_p)$) depends on the initial investment made in the project and the agent's effort level. The agent incurs a cost ($c_a f_a$) associated with his effort. If the project is successfully completed, then the agent receives his share of the revenue from the test sales (rR_T), and the principal receives revenue from the drug sales in addition to her share of the revenue from the test sales ($(1-r)R_T + R_D$).

Note that in this contract structure the agent is incentivized to work through the use of the royalty percentage (r) of the revenue from the test sales (R_T). It is also possible to achieve this using different, yet mathematically equivalent, structures. For example, the royalty share can be defined as a percentage of the revenue from test and drug sales, rather than test sales only. This would correspond to a contract where the royalty percentage is $r' = \frac{rR_T}{R_T+R_D}$. Another example would be designing a contract that involves a fixed payment of rR_T to be made to the agent upon the successful completion of the project instead of working with royalty shares.

The level of effort that can be provided by the agent (or his existing workforce) is bounded by f_L. We can think of f_L as an upper bound on the workforce of the biotech firm. This could be due to limited availability to such workers with desired expertise, financial constraints, market conditions and other factors. He can expend additional effort using the invested amounts m_a and m_p to hire additional workers. Let c_a and c_h be the unit costs of the agent's existing (internal) workforce and the newly hired (external or subcontracted) workforce, respectively. We assume that newly hired individuals are less efficient (perhaps because of less training and experience with the agent's processes) or more expensive (or both), resulting in $c_h > c_a$.

We model uncertainty in the development process with two independent Bernoulli random variables. Let S be the controllable portion of uncertainty that depends on the initial investment and the agent's effort level, where S=1 indicates success, which occurs with probability $p(f_a, m_a, m_p)$, and S=0 indicates failure There is also uncontrollable exogenous uncertainty in the development process such as scientific and regulatory uncertainty, which can influence the overall outcome of the project. This uncontrollable variable is represented by θ, where θ=1 indicates success, which occurs with probability μ, and θ=0 indicates failure. The project is a success when both of the values are 1; i.e., $S\theta$=1.

We assume that $p(f_a, m_a, m_p) = 1 - e^{-k\left(f_a + \frac{m_a+m_p}{c_h}\right)}$ where k is a positive scalar that we refer to as the coefficient of total effort. This function has three desirable properties: (1) The probability of success is zero if there is no initial investment and the agent does not work. (2) The probability of success is increasing in f_a, m_a and m_p. (3) f_a, m_a and m_p have diminishing marginal contribution to the probability of success (i.e., the probability of success is concave in these components). The value of k represents the skill level of the agent, where a higher value of k represents a more skilled agent.

Given m_a, m_p and r, the agent's effort level (f_a^*) is the value that maximizes his expected utility ($E[U_a]$). He accepts the offered contract only if the maximum expected utility he could receive from the project is higher than his reservation utility (u_r), which we define as the utility level he could achieve without contracting. The principal's goal is to design a contract (m_a, m_p, r) that maximizes her expected profit ($E[\Pi]$).

Based on the above setting and notation, we formulate the co-development problem (D) as follows:

$$\max_{m_p \geq 0, m_a \geq 0, r \geq 0} \quad E[\Pi] = E_{S,\theta}[S\theta((1-r)R_T + R_D) - b_p m_p | f_a = f_a^*] \tag{1}$$

s.t.

$$f_a^* = \arg\max_{f_a \leq f_L} \{E[U_a] = E_{S,\theta}[S\theta u_a(rR_T - c_a f_a - b_a m_a) + (1 - S\theta)u_a(-c_a f_a - b_a m_a)]\}, \tag{2}$$

$$E_{S,\theta}[S\theta u_a(rR_T - c(f_a^*) - b_a m_a) + (1 - S\theta)u_a(-c(f_a^*) - b_a m_a) | f_a = f_a^*] \geq u_r. \tag{3}$$

The objective function (1) represents the principal's expected profit. Since θ is independent of the other random variable S, by multiplying it with S and other terms $(1-r)R_T$, we are simply taking expectation and calculate the expected revenue from the test for the pharmaceutical company. Constraint (2) is the incentive compatibility (IC) constraint and ensures that the agent chooses his optimal effort level. Constraint (3) is the individual rationality (IR) constraint and ensures that the agent's expected utility is no less than his reservation utility.

The value $u_a(.)$ is the utility function of the biotech firm, i.e., the function that links monetary values and risk into utility and helps us to model expected benefit of the biotech firm and determine the effort level that the biotech would choose to maximize its expected utility as well as making sure the agent receives at least his reservation utility. We focus our attention on the case where the agent is risk-neutral (i.e., $u_a(x) = x$). This is reasonable if the biotech firm is publicly listed or backed by external investors who view the company as part of their portfolio of investments, and is consistent with other related work (e.g., Xiao and Xu (2012)), which is aligned with our setting where the agent is described to be a well-established research lab. Substituting $u_a(x) = x$ and evaluating the expectation with respect to θ and S we rewrite D as:

$$(D) \quad \max_{m_p \geq 0, m_a \geq 0, r \geq 0} \quad E[\Pi] = (1 - e^{-k\left(f_a^* + \frac{m_a + m_p}{c_h}\right)})\mu((1-r)R_T + R_D) - b_p m_p \tag{4}$$

s.t.

$$f_a^* = \arg\max_{f_a \leq f_L} \left\{ (1 - e^{-k\left(f_a + \frac{m_a + m_p}{c_h}\right)})\mu r R_T - c_a f_a - b_a m_a \right\}, \tag{5}$$

$$(1 - e^{-k\left(f_a^* + \frac{m_a + m_p}{c_h}\right)})\mu r R_T - c_a f_a^* - b_a m_a \geq u_r. \tag{6}$$

We assume that all parameters are known to both parties, meaning there is no hidden information (asymmetric information) regarding the problem parameters. The only exception is the potential drug sales (R_D). The agent may have limited information about R_D, which is not a direct component of the agent's problem and, therefore, does not affect the solution. We further discuss the impact of R_D on the problem in Section 3.1.

Although the agent's effort level is not observable, as a rational decision maker, he would not work at any level other than f_a^* since it would reduce his expected utility, and this is captured in the model by the IC constraints. Prior to presenting our approach to solve D, we discuss methods for determining reasonable values for u_r.

3.1. The agent's reservation utility

Since successful development of the companion diagnostic facilitates revenue generation from two sources (the drug and the test), the agent can consider both revenue streams when determining his reservation utility (u_r). In this section, we describe a lower and an upper bound on u_r.

3.1.1. A lower bound on the agent's reservation utility (U_{min}):

Since the drug already exists, the maximum expected utility that the agent could receive by developing the test without collaborating with the principal is a lower bound, U_{min}, on his reservation utility. This definition of lower bound would not be true in a simultaneous development scenario where the outside alternative is zero.

Thus, U_{min} is the optimal objective function value of the following model, which we refer to as *the agent-only model* ($\mathcal{A}$).

$$(\mathcal{A}) \quad \max_{m_a \geq 0, 0 \leq f_a \leq f_L} \quad E[U_a] = (1 - e^{-k\left(f_a + \frac{m_a}{c_h}\right)})\mu R_T - c_a f_a - b_a m_a \tag{7}$$

Let $M_h^T = \dfrac{k\mu R_T}{b_a c_h}$ and $M_a^T = \dfrac{k\mu R_T}{c_a}$. We can interpret M_h^T as the ratio of the maximum expected revenue from the project to the unit cost of the contribution of external workforce when the agent acts alone. The interpretation for M_a^T is similar and in this case the denominator of the ratio becomes related to the internal workforce. Note that $M_a^T > M_h^T$ since $c_a < b_a c_h$. Proposition 1 characterizes the solution of $\mathcal{A}$.

All proofs are given in the appendix.

Proposition 1. *The optimal solution of $\mathcal{A}$ is:*

$$m_a^{\mathcal{A}} = \max\left\{0, c_h\left(\frac{1}{k}\ln(M_h^T) - f_L\right)\right\}, \tag{8}$$

$$f_a^{\mathcal{A}} = \min\left\{f_L, \max\left\{0, \frac{1}{k}\ln(M_a^T)\right\}\right\}. \tag{9}$$

Proposition 1 provides optimal values of biotech's investment level and effort level for the agent only model. This result will be useful to determine what the agent can do on his own and hence help us find a lower bound on his utility.

Substituting (8)–(9) into (7) yields $U_{min} = E[U_a | m_a = m_a^{\mathcal{A}}, f_a = f_a^{\mathcal{A}}]$, which is the expected profit that the agent could make by using his own resources, and hence a lower bound on u_r.

Observe that the agent will use external workforce ($m_a^{\mathcal{A}} > 0$) in addition to internal workforce ($f_a^{\mathcal{A}} > 0$) only if $\frac{1}{k}\ln(M_h^T) > f_L$.

3.1.2. An upper bound on the agent's reservation utility (U_{max}):

We define *the coordinated problem* (C) as one where the principal determines f_a and does not need to consider the agent's reservation utility, as though the entire system is one coordinated entity. The principal would maximize her expected profit by solving the following problem:

$$(C) \quad \max_{m_p \geq 0, m_a \geq 0, 0 \leq f_a \leq f_L} \quad E[\Pi] = (1 - e^{-k\left(f_a + \frac{m_a + m_p}{c_h}\right)})\mu(R_T + R_D) - c_a f_a - b_a m_a - b_p m_p \tag{10}$$

Let $M_h^{TD} = \dfrac{k\mu(R_T + R_D)}{b_p c_h}$ and $M_a^{TD} = \dfrac{k\mu(R_T + R_D)}{c_a}$. We can interpret M_h^{TD} as the ratio of the maximum expected revenue from the project to the unit cost of the contribution of external workforce when both the principal and the agent participates to the project. The interpretation for M_a^{TD} is similar and in this case the denominator of the ratio becomes related to the internal workforce. Note that $M_a^{TD} > M_h^{TD}$ since $c_a < b_p c_h$. The next proposition characterizes the solution of C.

Proposition 2. *The optimal solution of the coordinated problem (C) is:*

$$m_p^C = \max\left\{0, c_h\left(\frac{1}{k}\ln(M_h^{TD}) - f_L\right)\right\}, \tag{11}$$

$$m_a^C = 0, \tag{12}$$

$$f_a^C = \min\left\{f_L, \max\left\{0, \frac{1}{k}\ln(M_a^{TD})\right\}\right\}. \tag{13}$$

Proposition 2 provides optimal values for the coordinated problem in which the pharmaceutical company can set the biotech's effort level and it is not required to consider a minimum utility value (u_r) for it. Then we use these values to find an upper bound on the biotech's utility.

Substituting (11)–(13) into (10) yields $U_{max} = E[\Pi | m_p = m_p^C, m_a = m_a^C, f_a = f_a^C]$, which is the maximum expected return that could be achieved from the project and hence is a natural upper bound on u_r. Combining the results presented in Propositions 1 and 2, we have $m_p^C \geq m_a^{\mathcal{A}}$, $m_a^C = 0$, and $f_a^C \geq f_a^{\mathcal{A}}$. Since the objective functions of C and $\mathcal{A}$ are concave (see the proofs in the appendix), $U_{max} \geq U_{min}$. Clearly, a feasible solution to D with positive expected return does not exist when $u_r > U_{max}$. Even when $u_r \leq U_{max}$, there is no guarantee that a contract in D with positive expected return can be found since a large enough value of u_r could violate the IR constraint.

Note that if $M_a^{TD} \leq 1$ then $M_h^{TD} \leq 1$ and $m_p^C = m_a^C = f_a^C = 0$, which also implies that there is no solution to D with positive expected return. Accordingly, we have the following corollary.

Corollary 1. *$M_a^{TD} > 1$ is a necessary condition for the existence of a solution with positive expected return to the co-development problem D.*

Corollary 2. *If $M_a^T < 1$ and $M_a^{TD} > 1$, then $m_a^{\mathcal{A}} = f_a^{\mathcal{A}} = 0$. However, there may still be a feasible solution to D where $m_p > 0$.*

Corollary 1 is intuitive and involves a threshold condition which implies an instance where either the project success chance (μ) is high, or the total project value ($(R_T + R_D)$) is high, or labor cost is (c_a) is low. Corollary 2 is also intuitive and states that if R_T is not large but R_D is, then agent would not do the project himself but he may participate in the project with a partnership with the principal. In that case, the principal would use her expected returns on a successful project to provide funds to incentive participation from the agent.

3.1.3. Choosing the reservation utility

We express the reservation utility as $u_r = U_{min} + \beta(U_{max} - U_{min})$ where $\beta \in [0, 1]$ a bargaining power parameter. $\beta = 0$ (i.e., $u_r = U_{min}$) describes the case where the agent is uninformed about the potential revenue

from the drug sales and/or has limited bargaining power and hence sets his reservation utility considering only the value of his time and the potential revenue from test sales. $\beta = 1$ (i.e., $u_r = U_{max}$) represents the case where the agent is fully informed about the potential revenue from the drug sales and the role of the diagnostic test in achieving those sales, and/or has high bargaining power and sets his reservation utility in a "greedy" manner that the principal gets nothing from the project.

4. Structural properties of first-best and second-best solutions

We characterize and analyze the first-best and second-best solutions, and highlight when a solution achieves first-best performance and takes one of the three special contract types. Before proceeding, we formally define these potential contract types:

- Licensing (L): The workforce and the financial resources of the agent are not used. Therefore, the contribution to the probability of success comes from the investment made by the principal only (i.e., $m_p > 0, m_a = 0$, and $f_a^* = 0$). A royalty share is paid to the agent to meet his reservation utility.
- Royalty Incentive (RI): The contribution to the probability of success comes from the agent's workforce and financial resources (i.e., $m_p = 0, m_a \geq 0$, and $f_a^* > 0$). A royalty share is paid to incentivize the agent to work and to compensate for his expenses as well as his reservation utility.
- Joint Effort (JE): Both the principal's financial resources and the agent's workforce and financial resources are utilized for the development of the test (i.e., $m_p > 0, m_a \geq 0$, and $f_a^* > 0$). A royalty share is paid to incentivize the agent to work and to compensate for his expenses and his reservation utility.

4.1. First-best solution

We define the first-best case ($\mathcal{DF}$) where f_a is determined to maximize $E[\Pi] = (1-e^{-k\left(f_a+\frac{m_a+m_p}{c_h}\right)})\mu[(1-r)R_T+R_D]-b_p m_p$ by the principal as follows:

$$(\mathcal{DF}) \quad \max_{0\leq f_a\leq f_L, m_a\geq 0, m_p\geq 0, r\geq 0} \quad E[\Pi] \tag{14}$$

s.t.

$$(1-e^{-k\left(f_a+\frac{m_a+m_p}{c_h}\right)})\mu r R_T - c_a f_a - b_a m_a \geq u_r. \tag{15}$$

We characterize the closed-form solution for the first-best ($\mathcal{DF}$) case in the following proposition.

Proposition 3. *The optimal solution of $\mathcal{DF}$ is:*

$$f_a^{\mathcal{DF}} = \min\left\{f_L, \max\left\{0, \frac{1}{k}\ln(M_a^{TD})\right\}\right\}, \tag{16}$$

$$m_a^{\mathcal{DF}} = 0, \tag{17}$$

$$m_p^{\mathcal{DF}} = \max\left\{0, c_h\left(\frac{1}{k}\ln(M_h^{TD}) - f_L\right)\right\}, \tag{18}$$

$$r^{\mathcal{DF}} = \frac{u_r + c_a f_a^{\mathcal{DF}}}{(1-e^{-k\left(f_a^{\mathcal{DF}}+\frac{m_p^{\mathcal{DF}}}{c_h}\right)})\mu R_T}. \tag{19}$$

Proposition 3 gives optimal values for agent's effort level, investment amounts for both the agent and the principal and royalty percentage for the first best problem in which the principal can set the agent's effort level, but agent is also provided a minimum utility level.

In the optimal solution of $\mathcal{DF}$ the agent's investment is always zero, i.e., $m_a^{\mathcal{DF}} = 0$, since it is less expensive for the principal to borrow than it is for the agent. When $M_a^{TD} > 1$ we have $f_a^{\mathcal{DF}} > 0$, and the remaining workforce requirement (if any) will be obtained from $m_p^{\mathcal{DF}}$.

We can interpret the royalty percentage $r^{\mathcal{DF}}$ as the ratio of agent's cost (labor + reservation utility) and expected benefit from the test.

The objective function value of the optimal solution to $\mathcal{C}$ (i.e., U_{max}) is always nonnegative (since $(f_a, m_p, m_a) = (0,0,0)$ is a feasible solution) and the objective function value of the optimal solution to $\mathcal{DF}$ is $E[\Pi^{\mathcal{DF}}] = U_{max} - u_r \geq 0$ (see the proof of Proposition 3 in the appendix). Therefore, there exists a feasible solution to $\mathcal{DF}$ with a nonnegative objective function value for the instances of our concern since we assume that $u_r \in [U_{min}, U_{max}]$.

4.2. Second-best solution

We derive the second-best solution, the optimal solution of $\mathcal{D}$, by partitioning the solution space with respect to the agent's effort level f_a^*. The second-best solution falls into one of the following regions: $f_a^* = 0$ (Cases 1a-1b in Table 1), $0 < f_a^* < f_L$ (Cases 2a-2b.ii in Table 1), and $f_a^* = f_L$ (Cases 3a.i-3c.iii in Table 1). By considering the subproblems associated with each region, we characterize all candidate solutions, one being the optimal solution of $\mathcal{D}$.

Proposition 4. *If there exists a feasible solution of $\mathcal{D}$ with positive expected profit, then the second-best solution is the one with the maximum expected profit among the candidate solutions summarized in Table 1.*

Proposition 4 shows that the second-best problem is feasible and fully characterizes its solution. So, implementation of this result is easy and it comes to calculating all possible solutions for a given set of parameters and choosing the highest value. This can be implemented easily in a spreadsheet or in any other programming environment.

From Table 1 it is clear that there are many candidate solutions and the best among them will depend on the parameter values. Nonetheless, we are able to describe several important structural properties of $\mathcal{D}$, which are summarized in the following statements.

Corollary 3. *The following properties are true for the optimal solution of $\mathcal{D}$.*

- *If $M_a^{TD} \leq 1$, or if both $M_h^{TD} \leq 1$ and $f_L = 0$ hold, then there is no feasible contract with positive expected profit.*
- *If $M_h^{TD} < \frac{ku_r}{c_a} + 1$ and $f_L > 0$, then $f_a^* > 0$ (i.e., licensing is not optimal).*
- *$m_a^*(f_L - f_a^*) = 0$. Thus, the agent will only invest if he has used his full workforce.*

The first item of Corollary 3 imposes some threshold conditions on the project's potential, reflected in M_a^{TD} and M_h^{TD}, for identifying the infeasible cases. The second item states that, when the project's potential is low, the principal prefers a contract where the agent utilizes his workforce (if he has any) rather than a licensing contract. Finally, the last item gives an intuitive result for the agent's investment: the agent will invest only after using all his internal workforce.

Proposition 5. *If there exists a feasible solution of $\mathcal{D}$ with positive expected profit, then $f_a^* \leq f_a^{\mathcal{DF}}$.*

Proposition 5 shows that the agent's effort level in the first-best solution is an upper bound on that in the second-best solution.

The following proposition states sufficient conditions under which the optimal solution is a royalty incentive contract.

Proposition 6. *If $1 < \sqrt{M_a^{TD}} < e^{kf_L}$ and $\sqrt{M_a^{TD}} - \ln(\sqrt{M_a^{TD}}) \geq \frac{ku_r}{c_a} + 1$, then the second-best solution is a royalty incentive contract with $m_a^* = m_p^* = 0$ and $r^* = \sqrt{\frac{R_T + R_D}{M_a^T R_T}}$.*

Table 1
The set of solutions which includes the optimal solution of the co-development model (D).

Solution #	Feasibility conditions	m_a	m_p	r	f_a^*	Type
1a	$u_r = 0$	0	0	0	0	–
1b	$M_h^{TD} > 1$ $M_h^{TD} \geq \frac{ku_r}{c_a} + 1$	0	$\frac{c_h}{k}\ln(M_h^{TD})$	$\frac{u_r}{\left(1-\frac{1}{M_h^{TD}}\right)\mu R_T}$	0	L
2a	$1 < \sqrt{M_a^{TD}} < e^{kf_L}$ $\sqrt{M_a^{TD}} - \ln(\sqrt{M_a^{TD}}) \geq \frac{ku_r}{c_a} + 1$	0	0	$\sqrt{\frac{R_T+R_D}{M_a^T R_T}}$	$\frac{1}{k}\ln(\sqrt{M_a^{TD}})$	RI
2b.i	$e^{kf_L} > \frac{ku_r}{c_a} + kf_L + 1$	0	0	The r value such that $r > \frac{1}{M_a^T}$ and $rM_a^T - \ln(rM_a^T) = \frac{ku_r}{c_a} + 1$.	$\frac{1}{k}\left[rM_a^T - \left(\frac{ku_r}{c_a}+1\right)\right]$	RI
2b.ii	$\Delta_1 > 0$ $\varphi - \ln(\varphi) < \frac{ku_r}{c_a} + 1 < \varphi < \frac{ku_r}{c_a} + kf_L + 1$ where $\varphi = \frac{2k\mu(R_T+R_D)}{b_p c_h + \sqrt{\Delta_1}}$ and $\Delta_1 = (b_p c_h)^2 - 4k\mu(R_T+R_D)(b_p c_h - c_a)$.	0	$\frac{c_h}{k}\left[\left(\frac{ku_r}{c_a}+1\right) - (\varphi - \ln(\varphi))\right]$	$\frac{2c_a(R_T+R_D)}{R_T(b_p c_h + \sqrt{\Delta_1})}$	$\frac{1}{k}\left[\varphi - \left(\frac{ku_r}{c_a}+1\right)\right]$	JE
3a.i	$1 < e^{kf_L} \leq \frac{ku_r}{c_a} + kf_L + 1$	0	0	$\frac{u_r + c_a f_L}{(1-e^{-kf_L})\mu R_T}$	f_L	RI
3a.ii	$e^{kf_L} < M_h^{TD} \leq \frac{ku_r}{c_a} + kf_L + 1$	0	$c_h\left[\frac{1}{k}\ln(M_h^{TD}) - f_L\right]$	$\frac{u_r + c_a f_L}{\left(1-\frac{1}{M_h^{TD}}\right)\mu R_T}$	f_L	JE
3b.i	$e^{kf_L} \geq \frac{ku_r}{c_a} + kf_L + 1$	0	0	$\frac{e^{kf_L}}{M_a^T}$	f_L	RI
3b.ii	$\sqrt{M_a^{TD}} > e^{kf_L}$ $\sqrt{M_a^{TD}} \geq \alpha + \frac{kb_a c_h}{c_a}\left[\frac{1}{k}\ln(\sqrt{M_a^{TD}}) - f_L\right]$ where $\alpha = \frac{ku_r}{c_a} + kf_L + 1$.	$c_h\left[\frac{1}{k}\ln(\sqrt{M_a^{TD}}) - f_L\right]$	0	$\sqrt{\frac{R_T+R_D}{M_a^T R_T}}$	f_L	RI
3c.i	$c_h\left[\frac{1}{k}\ln\left(\alpha + \frac{kb_a m_{a2}}{c_a}\right) - f_L\right] - m_{a2} > 0$ $m_{a2} > 0$ where $m_{a2} = \frac{c_a}{kb_a}\left[\frac{-b_a b_p c_h + \sqrt{\Delta_2}}{2c_a(b_a - b_p)} - \alpha\right]$, $\alpha = \frac{ku_r}{c_a} + kf_L + 1$, and $\Delta_2 = (b_a b_p c_h)^2 + 4c_a(b_a - b_p)b_a k\mu(R_T + R_D)$.	m_{a2}	$c_h\left[\frac{1}{k}\ln\left(\alpha + \frac{kb_a m_{a2}}{c_a}\right) - f_L\right] - m_{a2}$	$\frac{1}{M_a^T}\left(\alpha + \frac{kb_a m_{a2}}{c_a}\right)$	f_L	JE
3c.ii	$e^{kf_L} < \frac{ku_r}{c_a} + kf_L + 1$	0	$c_h\left[\frac{1}{k}\ln\left(\frac{ku_r}{c_a} + kf_L + 1\right) - f_L\right]$	$\frac{1}{M_a^T}\left(\frac{ku_r}{c_a} + kf_L + 1\right)$	f_L	JE
3c.iii	-	The m_a value such that $m_a \geq 0$ and $m_a = c_h\left[\frac{1}{k}\ln\left(\alpha + \frac{kb_a m_a}{c_a}\right) - f_L\right]$ where $\alpha = \frac{ku_r}{c_a} + kf_L + 1$.	0	$\frac{1}{M_a^T}\left(\alpha + \frac{kb_a m_a}{c_a}\right)$	f_L	RI

Note that the optimal royalty share exceeds 100% when the conditions in Proposition 6 are satisfied and $M_a^T < 1$ (i.e., if the agent would not consider doing the project himself). In such cases, even though the pharmaceutical company has subsidized the development of the companion diagnostic test, it is optimal to allow the test developer to keep all revenues from the test, and to also supplement test sales with a portion of drug sales. This could be achieved by pharmaceutical company sending funds to the test developer every time a test is used.

The following proposition states a sufficient condition under which the second-best solution achieves first-best results and the optimal solution is a joint effort contract.

Proposition 7. *If* $e^{kf_L} < M_h^{TD} \leq \frac{ku_r}{c_a} + kf_L + 1$, *then the second-best solution is the same as the first-best solution. In all such cases, the contract exhibits a joint effort structure with* $m_a^* = 0$, $m_p^* = c_h\left[\frac{1}{k}\ln(M_h^{TD}) - f_L\right]$ *and* $r^* = \dfrac{u_r + c_a f_L}{\left(1 - \frac{1}{M_h^{TD}}\right)\mu R_T}$.

Thus, in some cases where the optimal solution is a joint effort contract, the first-best solution is achieved under the second-best setting.

Corollary 4. *First-best results can be achieved in all cases given in Table 1 except for 1a, 1b, 2a and 3b.ii. Thus, first-best results can never be achieved with a licensing type of contract (1b) and with certain types of royalty incentive contract (2a and 3b.ii).*

This corollary shows that the first-best can actually be achieved in most of the cases of the second-best.

As shown in Table 1, there may be optimal contracts where $m_a > 0$ or $r < 1$. The principal can impose a positive m_a value as long as the agent's reservation utility is met. An optimal contract where $r < 1$ indicates that the agent's reservation utility is low, which may be caused by several factors including low workforce level, high unit cost of workforce, high debt repayment factor, and limited bargaining power.

5. Numerical analysis and results

We illustrate the results using the parameters listed in Table 2. We use k as a "tuning parameter", whose value depends on f_L and p_a, which is defined as the probability of success with agent's effort only. We generate and solve 10,000 problem instances considering p_a to be uniformly distributed between 0 and 0.5 ($U(0, 0.5)$), f_L to be uniformly distributed between 4000 and 12,000 (which roughly corresponds to 2–6 person-years of full time effort) and generating k values accordingly. U_{min} and U_{max} are derived from other parameters, as described in Section 3.

The parameter values in our problem instances are generated from distributions with reasonably large ranges and/or are consistent with the values in practice. For example, Agarwal et al. (2015) suggests that the potential revenue from a drug with a companion diagnostic can easily reach ten times the revenue from the diagnostic or more, which is already in the range that we consider.

5.1. Optimal contract type

For each problem instance, we find the first- and second-best solutions using Propositions 3 and 4. For each contract type, Table 3 summarizes the number of instances for which the contract type is optimal under the second-best setting. We also report the average values of problem parameters and several other important measures including the maximum and average percentage gap between the objective values of first- and second-best solutions.

There is no feasible contract with positive expected profit for only three of the 10,000 instances. In these three instances the average β is 0.95 indicating that the agent has extremely high bargaining power and almost full information about the potential of the project and wants to extract this amount from the principal. In 65.15% and 33.12% of the problem instances, the optimal contract type is joint effort and licensing, respectively. In only 1.70% of the instances is the optimal contract a royalty incentive type contract. The percentage gap between the objective function values of the first- and second-best solutions is relatively high when the second-best solution is a royalty incentive type of contract. On the other hand, when the second-best solution is a joint effort or licensing contract the percentage gap from the first-best solution is less than 1% on average. We observe that $r^* < 1$ in only 0.02% of problem instances and $r^* \geq 1$ in all instances where the optimal solution is a royalty incentive type contract. This is intuitive for two main reasons. First, r is defined as a percentage of the value to be generated through test sales whereas the total project value is based on test and drug sales. Second, we consider U_{min} as a lower bound when generating the agent's reservation utility. Since r is the only compensation in a royalty incentive type contract, values of $r^* \geq 1$ should be expected to motivate the agent based on the total project value.

Table 2
Parameter setting used to generate problem instances for the numerical study.

p_a	$U(0, 0.5)$
k	$\frac{-\ln(1-p_a)}{f_L}$
μ	$U(0, 1)$
R_T	25,000,000
R_D	$U(2100) \cdot R_T$
c_a	$U(10, 110)$
c_h	$U(1, 3) \cdot c_a$
b_a	$b_p + U(0, 0.3)$
b_p	$U(1, 1.2)$
f_L	$U(4000,\ 12{,}000)$
u_r	$U(U_{min}, U_{max})$

The average value of some parameters across instances tends to be different for each contract type. For example, the average β is 0.64 in instances for which the optimal contract type is joint effort whereas it is 0.22 in the instances where a licensing contract is optimal. This is intuitive because when the agent is more informed about the potential of the project and has more bargaining power he is more likely to enter into a joint effort deal rather than licensing. On the other hand, when the agent is not informed about the project and has limited bargaining power but the project has high potential, the principal would prefer a licensing contract rather than not performing the project at all. The average value of the ratio R_D/R_T and the average μ for royalty incentive contracts are considerably smaller values compared to those of joint effort and licensing contracts, and this indicates that royalty incentive contracts tend to be optimal for instances where the potential drug sales and the likelihood of success are low. The average value of the M_{TD}^h. M_{TD}^h. M_T^h and M_T^a ratios are also related to the optimal contract type. The infeasible instances (three out of 10,000 instances) are the ones where these ratios are very low, indicating that the maximum expected value attained with the test is not positive. As these ratios increase, the value of using the agent's workforce and the additional workforce becomes higher. Therefore, the highest values of these ratios are observed for the joint effort type of contracts. When we analyze our results in detail, we observe for 14.20% of the problem instances that the agent would not develop the test by himself (i.e., $M_T^a < 1$) and positive expected return is only achieved through collaborating with the principal.

To explore the impact of problem parameters further, we analyze the distribution of optimal contract types across problem instances at various levels of problem parameters. By considering one parameter at a time, we classify the instances into twenty groups based on the

Table 3
Average values of problem parameters and average/maximum/minimum percentage difference between FB and SB solutions for each contract type.

				Optimal contract type		
		Infeasible	Feasible	JE	L	RI
	Number of instances (out of 10,000)	3	9997	6515	3312	170
Average values of parameters/ratios	u_r	28,635,896	305,562,469	401,055,876	132,773,889	12,246,176
	β	0.95	0.50	0.64	0.22	0.44
	f_L	9357	8005	7989	8009	8521
	c_h/c_a	2.45	2.01	2.13	1.75	2.20
	b_p/b_a	0.89	0.88	0.89	0.88	0.90
	R_D/R_T	37.29	51.11	50.96	52.30	33.91
	μ	0.51	0.50	0.50	0.51	0.19
	k	0.00000090	0.00004250	0.00004618	0.00003614	0.00002549
	M_h^{TD}	1.41	324.90	331.24	328.31	15.49
	M_a^{TD}	3.97	646.89	706.10	561.66	38.45
	M_h^{T}	0.05	5.59	5.73	5.56	0.52
	M_a^{T}	0.14	12.60	13.85	10.72	1.26
$\frac{E[\Pi^{DF}]-E[\Pi]}{E[\Pi^{DF}]}$	Average	–	0.41%	0.23%	0.65%	2.63%
	Maximum	–	90.34%	83.19%	90.34%	49.46%
	Minimum	–	0.00%	0.00%	0.00*%	0.00%

* The minimum gap across the licensing type of contracts is 0.0006%.

parameter value. Each group is associated with a certain portion of the parameter range, and the groups are sorted accordingly. For instances in the first and last groups, the value of the parameter (not the number of observations) is in its lowest 5% range and highest 5% range, respectively. For each group, we analyze how the optimal solution of the related instances is distributed among the three different contract types. Fig. 1 summarizes the results of our analysis for the parameters $k, c_h/c_a, u_r$ and β, which are found to have a significant impact on the optimal contract type. The nonsmooth parts in Fig. 1(b) are due to the small number of instances in the last two bins. At all levels of these parameters, the optimal solution is a royalty incentive contract only for a small number of instances. As any of $k, c_h/c_a, u_r$ and β increases, the proportion of instances for which a joint effort contract is optimal increases and the proportion of instances for which a licensing contract is optimal decreases. This intuitive result can be explained by a number of reasons. When c_h/c_a increases, agent's workforce become more attractive and the principal takes advantage of the agent's workforce. For higher values of k, the agent becomes more efficient and the principal takes advantage of the agent's skills. As β increases, the agent becomes more informed about the project's potential and thus is more able to contribute significantly to the development of the test. A high u_r value usually indicates high U_{min} and U_{max} values (i.e., high potential for the project). Therefore, as u_r increases, the contribution from both parties becomes reasonable to extract more from the project's potential and hence joint effort type of contract is typically preferred to licensing in such cases.

The impact of problem parameters discussed here indicates that the problem parameters related to the agent have a significant impact on the optimal contract type. Therefore, it is important for the principal to know what the agent's situation is before designing the contract.

5.2. Heuristic methods

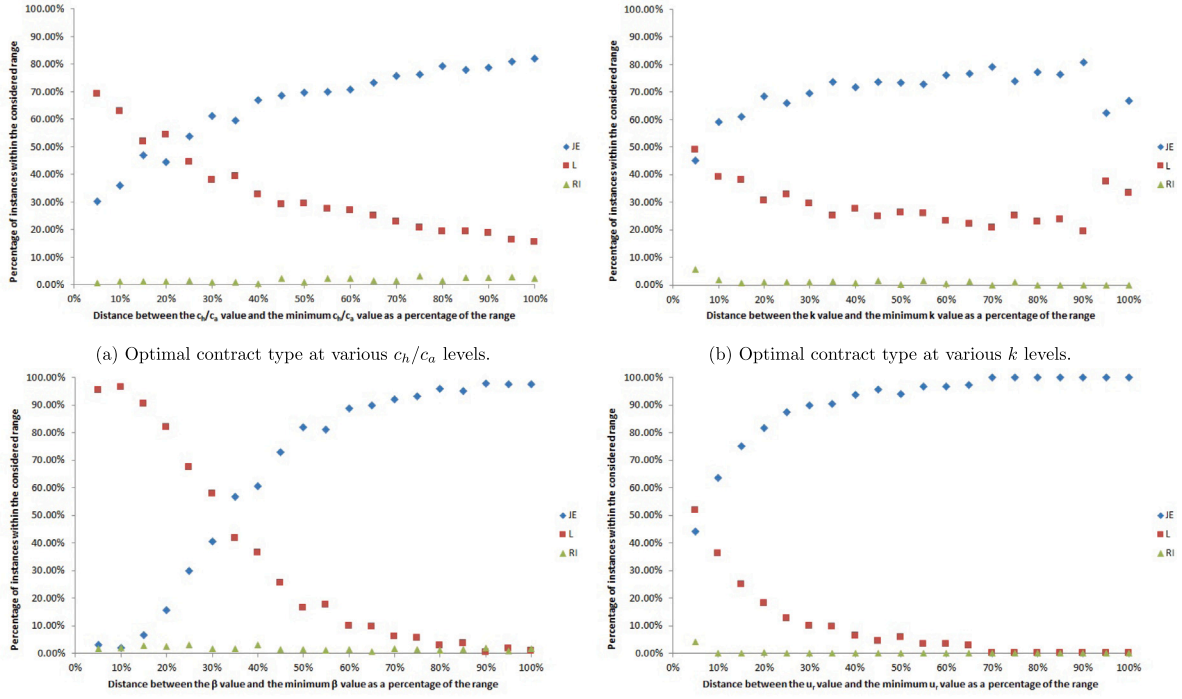
Although we have closed-form solutions for the second-best case, we develop three heuristics in this section. The reason we are interested in these heuristics is that they are motivated by common practice. For example, the Q-heuristic enables the principal to ensure that the agent has "skin in the game" by requiring a "participation fee" (a minimum level of investment) from the agent for the project. We would like to see how the contract structures obtained by these heuristics perform compared to our optimal solutions (i.e., the second-best solutions). The gap between these heuristics and the optimal second-best solution can be interpreted as the principal's cost of using these methods.

We describe the heuristics below. These methods are based on common and hence practically relevant contract structures (Agarwal et al., 2015).

- **Q-Heuristic:** The principal may prefer to design a contract where the agent is required to make a minimum level of investment to the project. To construct this type of solution we solve a modified version of D with $m_a = Q$ as an additional constraint where Q represents the amount of investment to be made by the agent. We set Q as 5% of u_r for our analysis.
- **L-Heuristic:** This forces a licensing contract and would be appropriate if the principal only wants to utilize the technology of the agent and is not interested in using any effort given or investment made by the agent. To obtain the solution of the L-Heuristic, we solve a modified version of D where $m_a = 0$ is added as a constraint and the IC constraint is replaced with $f_a^* = 0$.
- **RI-Heuristic:** This forces a royalty incentive contract and would be appropriate if the principal is not willing to make any upfront investment but may be willing to subsidize future sales of the test. To obtain the solution of the RI-Heuristic, we add $m_p = 0$ to D and solve the resulting constrained problem. Note that this will typically result in $r^* \geq 1$, so that the RI-heuristic is a subsidy on future sales, and the subsidy provides the incentive for the agent to participate.

The heuristic methods described above do not necessarily yield a feasible solution with positive expected profit for all instances since they involve changing some of the existing constraints and/or adding other constraints.

Table 4 summarizes the performance of heuristic methods across the 10,000 problem instances considered in Section 5.1. In the first column, the relevant measures are summarized across all problem instances for which a feasible contract with positive expected profit exists. According to the performance across all feasible instances, the L-Heuristic performs well; it generates the optimal solution for 33.13% of the instances and the average gap from the optimal solution is less than 2% on average. Both the Q-Heuristic and the RI-Heuristic perform relatively poorly with average optimality gap values of 5.68% and 4.51% of the principal's expected profit, respectively. For all of the heuristic methods considered, the gap values are enormous for the worst cases, exceeding 95% of the principal's profits. While the occurrence of these worst-case scenarios is infrequent (as can be seen from Table 5), the corresponding gaps represent the scale of losses that could be incurred if common and practical structures are used instead



(a) Optimal contract type at various c_h/c_a levels.

(b) Optimal contract type at various k levels.

(c) Optimal contract type at various β levels.

(d) Optimal contract type at various u_r levels.

Fig. 1. Distribution of optimal solutions across different contract types at various levels of problem parameters.

Table 4
Performance of the heuristic methods.

			Optimal contract type		
		All feasible	JE	L	RI
	Number of instances (out of 10,000)	9997	6515	3312	170
Q-Heuristic	% Feasible	97.64%	96.50%	99.91%	97.06%
	% Optimal	0.10%	0.00%	0.00%	5.88%
	Average Gap	5.68%	8.35%	0.58%	5.94%
	Maximum Gap	99.82%	99.82%	58.07%	85.50%
L-Based Heuristic	% Feasible	98.02%	98.89%	100.00%	25.88%
	% Optimal	33.13%	0.00%	100.00%	0.00%
	Average Gap	1.85%	2.74%	0.00%	10.30%
	Maximum Gap	98.79%	98.79%	0.00%	97.39%
RI-Based Heuristic	% Feasible	98.33%	97.90%	99.09%	100.00%
	% Optimal	1.70%	0.00%	0.00%	100.00%
	Average Gap	4.51%	5.37%	3.06%	0.00%
	Maximum Gap	99.76%	99.66%	99.76%	0.00%

Table 5
Relative frequency of the optimality gap values for the heuristic methods.

Optimality gap interval	Q-Heuristic	L-Based heuristic	RI-Based heuristic
0–10%	85.23%	96.01%	89.29%
10–20%	7.00%	1.93%	5.44%
20–30%	2.89%	0.77%	1.95%
30–40%	1.62%	0.34%	0.97%
40–50%	1.04%	0.23%	0.76%
50–60%	0.91%	0.20%	0.49%
60–70%	0.46%	0.14%	0.50%
70–80%	0.34%	0.13%	0.18%
80–90%	0.24%	0.07%	0.27%
90–100%	0.28%	0.17%	0.14%

of the optimal contract. These are potentially significant amounts when sale of individual drugs can be hundreds of millions to billions of dollars annually.

In Table 4, we also report the performance of heuristics for three different groups of instances which are formed based on the optimal contract type. Each heuristic method performs well only for particular groups of instances, which indicates that the price of preferences associated with those methods can be very high for some groups of instances. For example, the Q-Heuristic performs poorly on average for the instances whose optimal solution is a joint effort or royalty incentive contract.

To investigate the impact of problem parameters on the performance of the heuristic methods described in this section, we analyze the percentage of instances for which the optimal solution is found by using the heuristic methods. We find that the parameters $k, c_h/c_a, u_r$ and β have significant impact on this measure. The Q-Heuristic and the RI-Heuristic are significantly outperformed by the L-Heuristic at all levels of these parameters.

6. Conclusion

We considered the problem of designing an optimal contract for the partnership between a pharmaceutical company that owns a potentially valuable drug and a biotech company that owns a technology that could be used to develop a companion diagnostic for the drug. We assumed that the agent's information level about the project's potential could vary. We provided full characterizations of the first-best and second-best solutions in closed-form. We derived sufficient conditions under which the optimal contract exhibits a particular structure (licensing, royalty incentive or joint effort). We proposed heuristics that might be appealing for the principal due to ease-of-implementation or some practical preferences. We conducted numerical analysis to illustrate the commonly observed contract types, and to show the impact of problem parameters on the optimal contract type and on the performance of the proposed heuristic methods.

We found that first-best results can be achieved by royalty incentive or joint effort contract types but not by a licensing contract. Depending on the relative value of the test with respect to the value of drug, there are cases when the agent would not work alone but participates the project with the principal, and in these cases, the agent will require a subsidy (i.e., the optimal royalty share exceeds 100%). The agent will only invest to the project after he has used all of his workforce.

We found that the optimal solution is a licensing contract or a joint effort contract for more than 98% of the problem instances, and royalty incentive type of contract is optimal only in less than 2% of the problem instances. In addition, the gap between the first-best and the second-best solution is less than 1% on average when the optimal solution is a licensing or a joint effort contract. We observed that the coefficient of effort in the probability of success function, the relative cost of extensive workforce with respect to the internal workforce, the agent's reservation utility and the agent's information about the potential value of the drug and bargaining power level are the most significant parameters in terms of their impact on the optimal contract type. For low and high values of these parameters, the optimal contract type in the majority of the instances is licensing and joint effort, respectively.

We studied an important problem which has economic and societal implications. As noted in the Introduction, there are many recent examples of companies engaging in this type of partnership. We provided a model and found its closed-form solution which gave insights on the structure of the contacts and when they can happen. We also ran some experiments to gain further insights. We can summarize our managerial insights as follows:

- Instead of using intuitively appealing contract heuristics that are motivated by practice, the principal should use solution of the second-best problem because heuristic solutions can be too far away from optimal (second-best) solutions and too costly for the principal. Furthermore, these optimal (second-best) solutions are readily available in closed-form and can be implemented easily in a spreadsheet.
- The principal should gather as much and accurate information as possible about agent related problem parameters (e.g., his workforce level, unit cost of workforce, and information level about the project's potential which plays a crucial role in determining his reservation utility) because these parameters play a significant role in setting contract type.

The problem considered in this paper can be extended in several ways. Considering risk-sensitive partners to explore the impact of different risk attitudes on the optimal contract type would be an immediate extension. Another extension could be considering the asymmetric information case where one side in the principal–agent framework possesses some information that the other side does not. Successful completion time of the research and development project may have an impact on the return that could be generated by the test and the drug sales. Therefore, modeling the time component (e.g., patent expiry, project timeline) would also be a practically relevant future research direction. Modeling the development of the companion diagnostics together with the drug throughout a partially overlapping timeline could be another interesting future research direction as the structure of the projects regarding research and development of drugs and companion diagnostics seem to evolve in that direction (Agarwal et al., 2015; Cotter et al., 2012).

CRediT authorship contribution statement

Sakine Batun: Conceptualization, data curation, formal analysis, investigation, methodology, software, validation, visualization, writing – original draft, writing – review & editing. **Mehmet A. Begen:** Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, supervision, validation, visualization, writing – review & editing. **Gregory S. Zaric:** Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, supervision, validation, visualization, writing – review & editing.

Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.ejor.2024.11.031.

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