

Beyond Independent Shots on Goal: Risk Capacity, Synergy, and Concentration in Pharmaceutical R&D Portfolios

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Research Article

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Abstract

Background: Pharmaceutical portfolios may develop one asset across indications or several assets against shared biology. These strategies offer synergies but can concentrate failures and reduce revenue through overlap.

Methods: Six matched programs were compared as independent assets, pipeline in a pill (PIAP), or multiple shots on goal (MSOG). Monte Carlo simulation and Gaussian-factor integration estimated expected net present value (eNPV), productivity, downside risk, financial-capacity breaches, effective breadth, and launch-count probabilities. Robustness was assessed across 1,000 matched portfolios.

Results: With individual success probabilities and additive economics held constant, dependence preserved mean value but increased downside risk. Six PIAP programs supplied the diversification benefit of 3.19 independent programs. In the central benchmark, PIAP needed 20% research and development (R&D) savings on additional indications to meet high-capacity value and risk limits. Across varied portfolios, median required savings among feasible solutions were 23% (10th–90th percentile, 15%–29%); 17% had no solution through 30%. Staging reduced expected discounted development costs by a median \$114 million but lowered eNPV by a median \$428 million. An 80% chance of at least two eventual launches required 19 independent or 25 PIAP starts. Ignoring 25% revenue cannibalization at 10% R&D savings produced median eNPV regret of \$59 million.

Conclusions: Concentration can improve efficiency while increasing downside exposure. The framework estimates the savings needed to justify concentration within a company's value and financial limits, with launch-count targets reported alongside these criteria.

Introduction

Pharmaceutical portfolio teams often tackle concepts such as pipeline diversification, and the option to take multiple shots on goal for a given indication. Six "programs" may represent six unrelated assets, one asset developed in six indications, or several assets directed at a common target, pathway, or indication [1]. Each structure can produce the same expected number of launches, but they do not provide the same distribution of outcomes. Shared asset, biology, execution, or safety risks cause successes and failures to cluster [2,3]. Meanwhile, commercial overlap (often from multiple shots on goal) can further make the value of additional launches non-additive [4].

This distinction can be studied empirically. Dai et al. estimated dependence across more than 25,000 clinical trials and reported approximately 10% correlation within therapeutic areas and correlations approaching 40% for trials sharing phase or mechanism [5]. Though valuable for portfolio analysis, these estimates do not, by themselves, indicate whether a particular level of concentration is economically justified, or even survivable for a particular sponsor. The appropriate decision depends on the value of operational synergy, commercial revenue overlap, and the organization's ability to endure poor outcomes.

An illustrative example: A mid-sized company has the option to launch Phase 2 development across several indications in parallel to preserve revenue prior to patent expiry. Doing so may allow for sharing of platform knowledge, manufacturing, evidence generation, and commercial activities, but also places more capital at risk before information from readouts arrives. A late safety finding can terminate several programs together, after enormous sums have been spent on clinical trials. A staged strategy (sequencing pivotal trials until a first approval) spends less up front, but delayed follow-on indications can surrender years of protected revenue and weaken

launch momentum. True diversification with independent assets sacrifices synergy but delivers more predictable outcome sets.

Conventional expected net present value (eNPV) sums an investment's expected discounted cash flow and is indispensable in portfolio analysis. But mean eNPV from a Monte Carlo simulation cannot differentiate two portfolios with similar means and different variances [6]. Productivity indices are also common because capital is constrained. In this analysis, expected productivity index (ePI) is defined as eNPV divided by expected discounted development cost, and is analogous to the expected return on investment in development [7]. Lower-tail net present value (NPV), conditional value at risk (CVaR), liquidity breach, and launch-service probability then describe the distributional features that eNPV and ePI cannot describe.

This work asks four decision questions. First, how much research and development (R&D) or timing synergy must a concentrated portfolio generate to compensate for its tail risk and still remain noninferior to the value of a diversified portfolio? Second, can the sponsor carry the resulting cash flow within stated risk tolerances and spending capacity? Third, how much does delaying pivotal trials for additional indications reduce discounted development costs, and how much value is lost through later launches and fewer years before loss of exclusivity? Fourth, how much value is lost when portfolio decisions overlook shared risks or competition between the company's own products? The primary contribution is a synergy-versus-risk-capacity frontier that answers these questions in money, tail loss, and launch reliability.

Materials and Methods

Portfolio strategies and analysis

This analysis centered on a six-program development portfolio. The diversified strategy assigned each program to an independent asset and biological target/pathway cluster. The pipeline-in-a-pill (PIAP) strategy assigned all six programs to one asset, while the multiple-shots-on-goal (MSOG) strategy assigned all six programs to one shared-biology cluster for the economic analyses. Programs began in Phase 2 and could progress through Phase 3 and regulatory review to launch. Phase probabilities, benchmark cost and revenue, and discount rates were identical across strategies for the primary analysis. Using the same program assumptions across strategies allowed the effects of portfolio structure to be isolated.

The six-program design is intentionally small enough to allow for thorough inspection and large enough to illustrate a realistic, concentrated portfolio. It does not reproduce any particular company's portfolio. All monetary values are constant 2026 US dollars (Table 1).

Table 1. Benchmark assumptions, strategies, and risk policies

Domain	Assumption	Primary value
Portfolio	Programs and topologies	6; independent assets, PIAP one asset, MSOG one biology cluster; launch analysis uses PIAP sixes and MSOG trios
Technical	Phase 2 / Phase 3 / regulatory pass	0.289 / 0.578 / 0.906; cumulative pTRS 0.151
Development	Duration and cost	2 y and \$100M; 3 y and \$400M; 1 y and \$50M
Commercial	Peak sales, margin, support	\$1,000M; 80%; \$100M/y
Timing	Discount rate and base LOE	10%; year 15
Dependence	PIAP and MSOG latent-factor ρ	0.415 and 0.250
Balanced tolerance	P5 NPV / capacity-breach maximum	At least -\$1,000M / at most 10%
Growth tolerance	P5 NPV / capacity-breach maximum	At least -\$1,500M / at most 20%
Capacity	Base / high liquidity plus financing less reserve	\$2,500M / \$6,500M available headroom
Launch service	Primary operational target	At least 2 eventual launches with 80% probability; mature-period planning approximation

Abbreviations: CVaR5, conditional value at risk in the worst 5% of outcomes; eNPV, expected net present value; LOE, loss of exclusivity; MSOG, multiple shots on goal; P5, fifth-percentile NPV; PIAP, pipeline in a pill; pTRS, probability of technical and regulatory success.

Technical dependence

Dependence was generated with Gaussian latent factors. For program i in cluster g , latent technical performance was

$$Z_{ig} = \sqrt{\rho_g} \cdot F_g + \sqrt{1 - \rho_g} \cdot \varepsilon_{ig} \quad (1)$$

where F_g is the shared group factor and ε_{ig} is the program-specific factor. Both are independent standard normal variables. Each program's probability of advancing through each development phase remained unchanged throughout. Programs were more likely to succeed or fail together due to shared risks, but the expected success rate was preserved. The analysis used dependence parameters of $\rho=0.415$ for indications sharing one asset (PIAP) and $\rho=0.250$ for programs sharing biological mechanisms (MSOG). These scenario assumptions were informed by the size and pattern of binary outcome correlations reported by Dai et al.; the latent-Gaussian parameters were not empirically calibrated [5].

By holding individual success probabilities constant, the analysis was able to examine technical dependence separately from cost savings and development speed. R&D synergies reduced development costs for complementary programs, while acceleration brought their milestones and launches forward. Cannibalization reduces revenue when related products are on the market simultaneously, while commercial synergy reduces post-launch operating cost. The model included shared events that could cause several Phase 3 programs to fail together, while keeping each program's overall probability of success unchanged. Each mechanism was modeled separately so its economic impact could be assessed.

Cash flows and value metrics

Development costs were assigned over phase-specific durations. Approved programs generated a five-year ramp to peak sales, an 80% contribution margin, and annual commercial support cost through the modeled horizon. Generic entry can sharply reduce a brand's market share [8]. At loss of exclusivity, sales fell to 10% of the pre-expiry level, while support costs continued. Cash flows were discounted at a rate of 10%. The model included an existing product franchise that generated cash flow before losing exclusivity in year 8. Its cash flow then declined to 15% of its pre-expiry level. Fixed operating costs were \$1.25 billion per year. Including these company-level cash flows demonstrated how portfolios with the same project NPVs could differ in their need for financing.

The primary metrics of evaluation were eNPV, ePI, the fifth percentile of portfolio NPV (P5), and CVaR5, defined as the mean NPV among the worst 5% of outcomes [9,10]. The analysis measured effective breadth as the number of independent programs producing the same variance in the proportion launched. Under both the base and high financial-capacity profiles, a capacity breach occurred when cumulative enterprise cash deficits exceeded starting cash plus available financing after setting aside the required reserve. These measures linked portfolio outcomes to traditional risk management: appetite, tolerance, and capacity. Risk appetite was the amount of risk the organization was willing to accept for a potential benefit; risk tolerance was expressed as limits on P5 NPV, the probability of exceeding financial capacity, and the reliability of meeting launch targets. Risk capacity reflected the company's ability to fund operations in cases of severely poor outcomes [11,12].

Decision rules

The analysis identified the minimum R&D cost saving on additional programs needed to make a concentrated strategy acceptable under three criteria: eNPV had to be at least as high as diversification, P5 NPV had to meet the selected risk limit, and the probability of exceeding financial capacity had to remain below the policy maximum. Scenarios that failed to meet all three criteria with savings of up to 30% were classified as having no feasible solution within the tested range. The primary analysis combined high financial capacity with balanced risk tolerances, and a secondary stress test combined base capacity with growth-oriented tolerances. For each portfolio structure, the analysis estimated how many program starts were needed to provide an 80% chance of at least two eventual launches. This launch-count approximation assigns approvals to a mature three-year planning period; it does not simulate launch dates or rolling calendar windows. This calculation used independent MSOG clusters of three and PIAP clusters of six. Delaying trials may still allow a portfolio to meet its launch target, but leaves fewer years to earn revenue before loss of exclusivity.

Experiments and precision

An initial pilot used 10,000 simulations per scenario to examine each mechanism separately. The main analysis increased this to 100,000 simulations, with 250,000 near the thresholds where the preferred decision changed. Strategies and economic assumptions were compared using the same underlying random draws to reduce simulation noise [13]. Scenarios covered R&D savings of 0%–30%, development acceleration of up to 1.5 years, loss of exclusivity in years 12, 15, or 18, and revenue cannibalization of 0%–50%. Both PIAP strategies started all six Phase 2 programs together. Staged PIAP advanced eligible programs through Phase 3 and regulatory review one at a time until the first approval, then advanced the remaining programs in parallel. If a program

failed, the next eligible program was attempted. Parallel PIAP advanced eligible programs without waiting. Finally, the analysis measured the value lost when a strategy chosen under assumptions of independent outcomes and fully additive revenues was evaluated with shared technical risks and revenue cannibalization. The assumed choice switched to concentration when its estimated eNPV advantage exceeded \$25 million.

Matched-heterogeneity robustness

The robustness analysis generated 1,000 sets of opportunities using Latin hypercube sampling [14]. Each portfolio structure received the same six programs with the same assignments. Cumulative probability of technical and regulatory success (pTRS) was drawn from a triangular distribution ranging from 0.075 to 0.227, with a most likely value of 0.151.

Development costs ranged from 70% to 130% of the benchmark, and peak sales from 50% to 150%. Timelines were varied within prespecified ranges.

Each of the 4,096 possible combinations of program outcomes was evaluated for each set, then the shared Gaussian factor was integrated using 32-point Gauss-Hermite quadrature [15]. This avoided random simulation noise when estimating the required level of synergy across the 1,000 portfolios. There were eight borderline scenarios where small changes in estimated value or risk could change whether the concentrated strategy met the acceptance criteria. These were checked with 250,000 Monte Carlo simulations each [16]. The intervals could extend no more than \$25 million on either side of the estimated eNPV difference, or 0.25 percentage points on either side of an estimated decision probability (Supplementary Material, Tables S1–S2).

Generative AI tools from OpenAI were used under the author's direction to assist with code generation and language editing. All analytical specifications, code review, verification,

interpretation, and final text were controlled and approved by the author. No generative AI was used to create simulated data or images.

Results

Dependence preserves means while consuming capacity for tail-risk

Under flat economics, the three six-program strategies had nearly identical expected value.

Diversification produced eNPV of \$84.2 million and ePI of 0.077, while PIAP without cost synergy produced eNPV of \$84.6 million and ePI of 0.077. But the distribution and tail risk were quite different. PIAP standard deviation was \$1.223 billion compared with \$0.938 billion under diversification; P5 declined from -\$1.148 billion to -\$1.179 billion, and CVaR5 declined from -\$1.307 billion to -\$1.625 billion. The probability of zero launches increased from 37.4% to 51.1%. Six PIAP programs supplied 3.19 variance-equivalent independent shots (Table 2).

Table 2. Flat-benchmark portfolio scorecard at the selected dependence scenarios

Strategy	eNPV	ePI	P5 NPV	CVaR5	SD NPV	P(0 launches)	Base breach	Eff. breadth
Diversified	\$84M	0.077	-\$1,148M	-\$1,307M	\$938M	37.4%	60.9%	5.98
PIAP, 0% saving	\$85M	0.077	-\$1,179M	-\$1,625M	\$1,223M	51.1%	63.9%	3.19
PIAP, 20% saving	\$268M	0.292	-\$996M	-\$1,356M	\$1,273M	51.1%	60.3%	3.19
MSOG, 0% saving	\$82M	0.075	-\$1,148M	-\$1,464M	\$1,094M	45.7%	62.1%	4.06
MSOG, 20% saving	\$266M	0.290	-\$996M	-\$1,228M	\$1,136M	45.7%	56.8%	4.06

All monetary values are constant 2026 US dollars. Abbreviations: CVaR5, conditional value at risk in the worst 5% of outcomes; ePI, expected productivity index; eNPV, expected net present value; MSOG, multiple shots on goal; P5, fifth-percentile NPV; PIAP, pipeline in a pill.

The synergy threshold depends on runway and organizational capacity

With $\rho=0.415$, loss of exclusivity (LOE) in year 15, and no development acceleration, PIAP required a 20% reduction in R&D costs for the five additional indications to meet the high-capacity policy criteria. At that point eNPV exceeded diversification by \$184 million, P5 was -\$996 million, and high-capacity breach probability was 4.66%. The frontier was dictated by the simultaneous constraints rather than value alone. Moving LOE to year 12 raised required savings to 27%. A base-capacity sponsor remained infeasible even at 30% savings, and the probability of breaching financial capacity was 57.9%. The economic attractiveness of concentration and the ability to survive its cash-flow path were separate considerations (Figures 1 and 2).

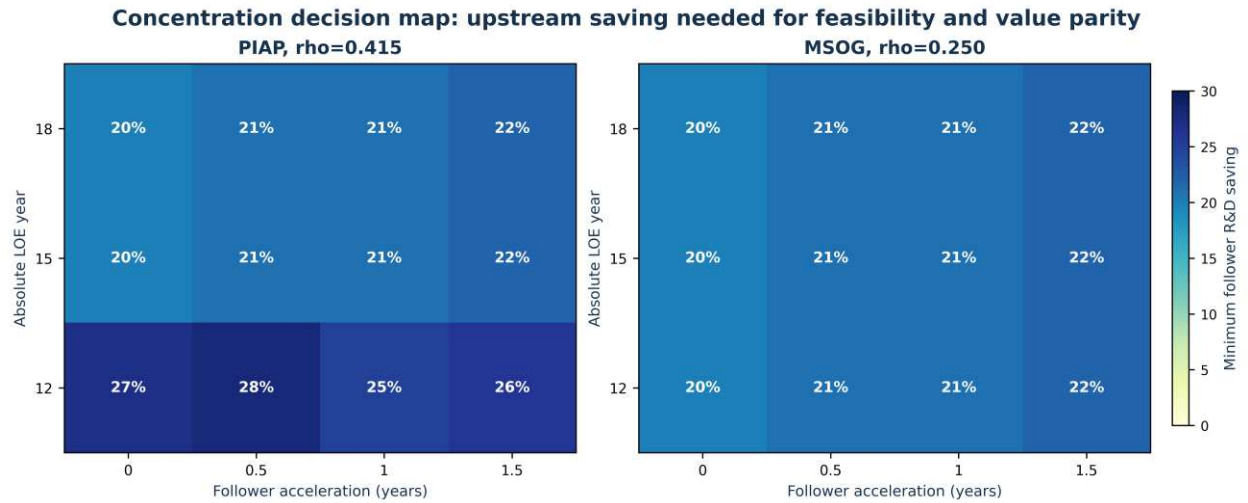


Figure 1. Concentration decision map under flat benchmark economics. The frontier is the minimum follower R&D saving that makes a concentrated strategy value-noninferior to diversification and compliant with the selected fifth-percentile NPV and financing-capacity limits. PIAP, pipeline in a pill; MSOG, multiple shots on goal; LOE, loss of exclusivity.

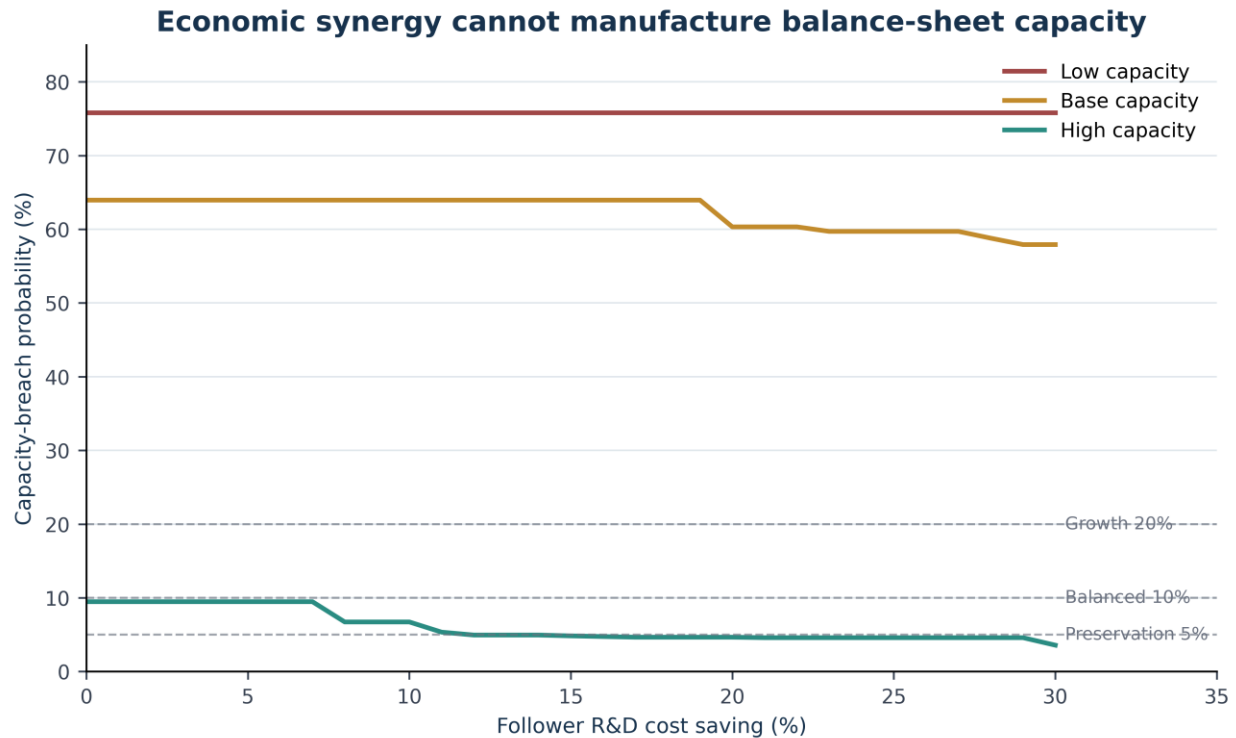


Figure 2. Risk capacity changes the feasible set. Expected synergy can satisfy value and tail criteria while the strategy remains outside the organization's financing capacity. The base-capacity PIAP case remains infeasible at 30% follower R&D saving.

Cannibalization also changed expected economics. At 25% overlap, the flat PIAP frontier still occurred at 20% savings, yet its eNPV advantage over diversification fell to \$5.4 million. At 50% overlap, no viable PIAP solution existed through 30% savings. Even a 40% reduction in commercial support costs was insufficient for PIAP to meet the financial and risk limits. These savings began only after launch, too late to reduce development spending or protect against losses when several programs failed.

Staging lowers discounted development cost and can reduce value through delay

In the flat benchmark, staging pivotal trials reduced expected discounted development costs by \$115.9 million, primarily by deferring spending. However, these launches made later, under

staged development, had only an average of 6.3 years before loss of exclusivity, compared with 9.0 years under parallel development. As a result, eNPV fell by \$440.6 million and P5 NPV by \$151.6 million. Despite the lower early development spending, the probability of a funding shortfall rose by 6.38 percentage points under the base financial-capacity assumptions. The chance of at least two launches by year 9 also fell from 24.1% to zero. Average NPV in the worst 5% of outcomes (CVaR5) improved because development spending was deferred in poor-outcome paths. Those savings were insufficient to offset the effect of later revenue on eNPV and P5 NPV (Figure 3).

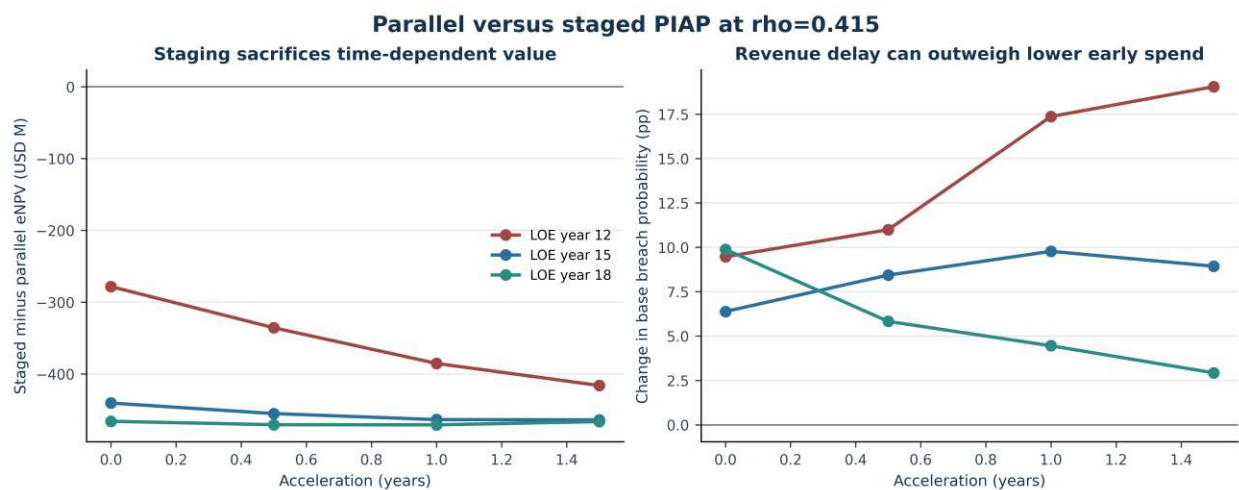


Figure 3. Parallel versus staged pipeline-in-a-pill development. Staging reduces expected discounted development cost and peak R&D spending by deferring pivotal development. Delayed launches reduce expected net present value, protected runway, and near-term launch reliability. PIAP, pipeline in a pill; LOE, loss of exclusivity.

The comparison demonstrates why launch counts need to be considered alongside timing and value. Parallel development commits more money before results are available, while staging reduces early spending but leaves successful programs fewer years to earn revenue before loss of

exclusivity. Comparing the strategies therefore requires launch dates, remaining exclusivity, eNPV, ePI, and funding needs.

Launch-service targets reveal hidden concentration

Under identical program assumptions, an 80% probability of at least two eventual launches required 19 diversified starts, 20 MSOG starts, or 25 PIAP starts. With varied program assumptions and a single dependence factor on cumulative pTRS, the corresponding breadths were 19, 21, and 25; the fixed benchmark used phase-specific factors. PIAP therefore required 32% more nominal starts than diversification to provide the same launch target. The launch target demonstrated how shared risks affected the number of program starts needed to sustain new launches. Meeting that target, however, does not guarantee sufficient value. Waiting for the first approval before starting the remaining pivotal trials together can delay launches, which reduces runway prior to LOE and erodes the NPV that can be realized. Because of that, expected numbers of launches should not be examined in a vacuum, and instead should be considered along with expected value and pre-LOE runway (Figure 4).

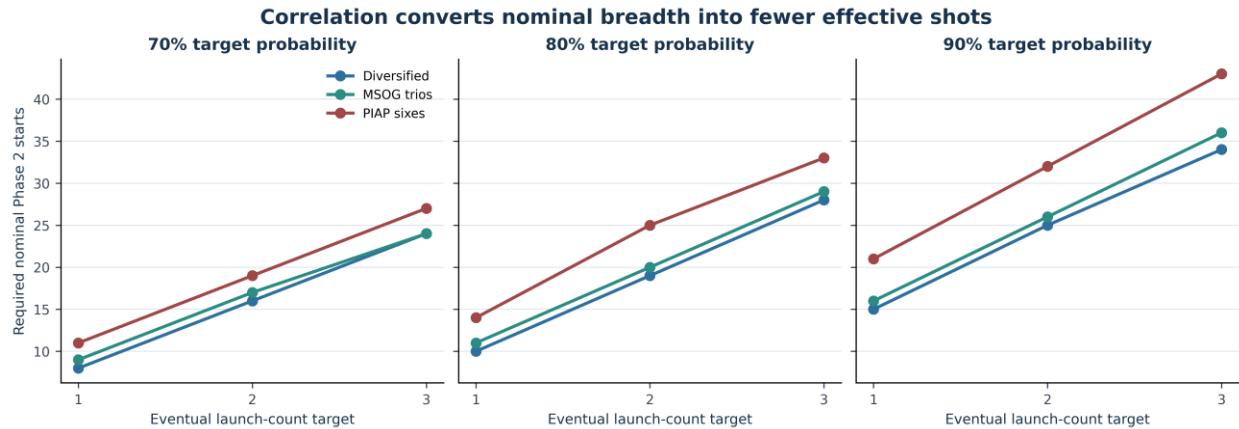


Figure 4. Nominal breadth required to satisfy eventual launch-count targets under diversified, multiple-shots-on-goal, and pipeline-in-a-pill geometries. Counts approximate a mature three-year planning period; launch dates and rolling calendar windows are not simulated. Technical dependence requires more nominal starts to provide the same launch reliability. MSOG, multiple shots on goal; PIAP, pipeline in a pill.

Matched heterogeneity converts a point estimate into a decision distribution

Across 1,000 matched portfolios with varying program characteristics, PIAP met the value and risk criteria in 83.0% of scenarios with R&D cost savings of up to 30%. Among feasible portfolios, the median required R&D saving was 23%, with a 10th-90th percentile range of 15%-29%. Only 25.6% of all cells cleared by 20% saving, and 57.5% cleared by 25%. MSOG was more frequently feasible: 94.1% of cells had a solution and the median frontier was 20% (Table 3; Figure 5).

Table 3. Decision outputs from matched-heterogeneity robustness

Decision output	PIAP	MSOG or comparator	Interpretation
Median R&D saving frontier	23%	20%	Compensating synergy differs by concentration geometry
10th-90th percentile	15%-29%	12%-27%	A benchmark is a distribution across opportunity sets
No solution through 30%	17.0%	5.9%	Some portfolios remain outside policy limits
Clear by 20% saving	25.6%	49.6%	The flat 20% result is not a universal threshold
Base-capacity growth solution	0 of 1,000	0 of 1,000	Capacity can bind across the full sampled opportunity space
Starts for 80% launch-count target	25	21 MSOG; 19 diversified	Nominal breadth understates concentration
Staged minus parallel eNPV	Median - \$428M	10th-90th: -\$559M to - \$313M	Discounted cost reduction did not offset delayed revenue
Ignored-overlap regret	Median \$59M	90th percentile \$94M	Assumption error is economically material

All monetary values are constant 2026 US dollars. Abbreviations: eNPV, expected net present value; MSOG, multiple shots on goal; PIAP, pipeline in a pill.

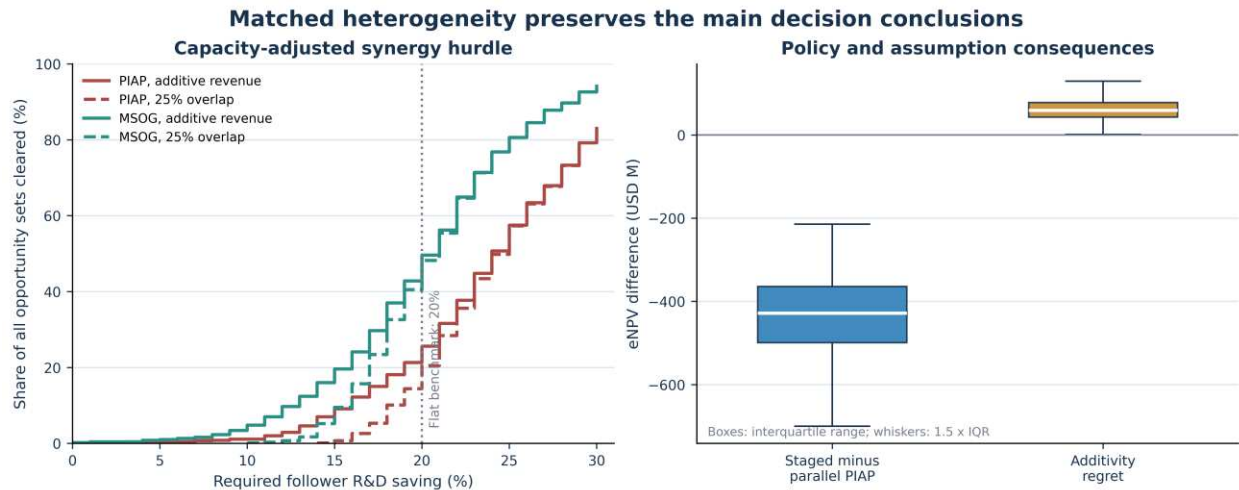


Figure 5. Matched-heterogeneity robustness. The left panel shows the cumulative distribution of minimum R&D saving needed to clear the high-capacity balanced frontier. The right panel shows staged-minus-parallel PIAP eNPV differences and the eNPV regret from assuming additive revenue at 10% R&D saving and 25% cannibalization. Boxes show interquartile ranges, white lines mark medians, and whiskers use the 1.5-times-interquartile-range rule; outliers are hidden. PIAP, pipeline in a pill; MSOG, multiple shots on goal.

Among portfolios with feasible frontiers, looking at these factors individually, average development cost had the strongest association with the cost savings required to justify concentration (Spearman $\rho=0.72$ for PIAP and 0.83 for MSOG). As expected, higher pTRS programs tended to require less R&D saving to justify concentration ($\rho=-0.13$ for PIAP and -0.14 for MSOG). Variation in sales potential across programs had little association with the required savings.

Wrong dependence and revenue assumptions create measurable regret

At 10% R&D saving and 25% true cannibalization, an additive model selected PIAP in all 1,000 heterogeneous cells. The true oracle selected diversification in all cells. Median eNPV regret was \$59 million, the 90th percentile was \$94 million, with a maximum of \$160 million. Regret

exceeded \$50 million 64% of the time, and exceeded \$100 million in 7%. In the separate flat grid restricted to cannibalization of 25% or less, selecting a strategy without considering shared risks or revenue cannibalization lost up to \$135.6 million in eNPV compared with the value-optimal choice under the modeled conditions. Compared with diversification, P5 NPV was up to \$279.8 million lower and the probability of a funding shortfall rose by as much as 14.2 percentage points. These maxima occurred in different scenarios (Figure 6).

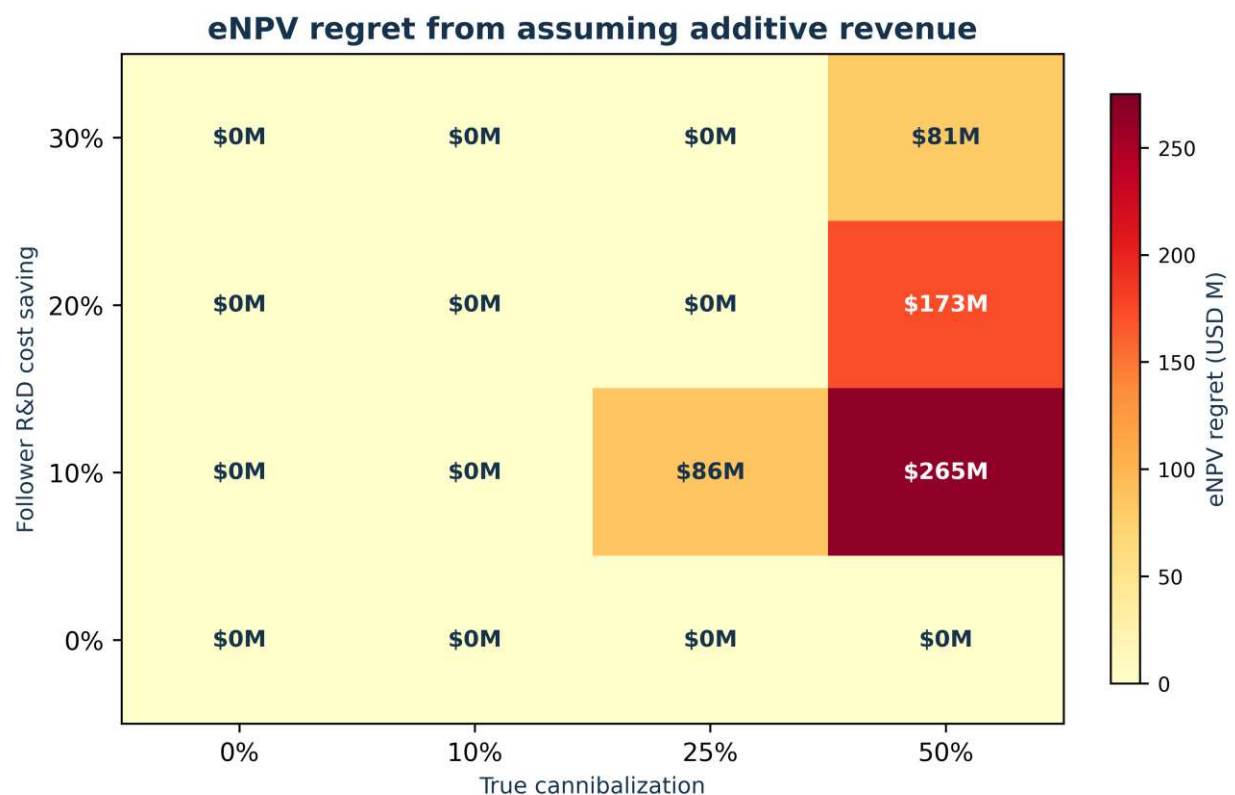


Figure 6. Decision regret when concentration is selected under independence and additive revenue, then evaluated under technical dependence and cannibalization. Values show expected NPV regret across follower R&D-saving and true-cannibalization assumptions. The figure uses parallel PIAP with fixed benchmark inputs, $p=0.415$, LOE in year 15, and no acceleration. Cannibalization extends to 50%, beyond the 25% maximum used in the restricted grid summarized in the text. NPV, net present value; PIAP, pipeline in a pill; LOE, loss of exclusivity.

Discussion

Principal finding

The primary output of this analysis is a decision frontier that allows the user to understand the minimum cost saving or development acceleration needed for a concentrated portfolio to meet the selected value and risk criteria. Pipeline-in-a-pill (PIAP) and multiple shots on goal (MSOG) can reduce costs and shorten development timelines through resource and knowledge synergies. However, they also tie several programs to the same potential sources of failure (safety, wrong target), and parallel development can commit substantial resources to an asset before any definitive results are available to de-risk the work. This may pay off in the end for the company, but whether those benefits justify concentration depends on both the portfolio and the company's ability to potentially survive poor trial outcomes.

In the central benchmark, a 20% reduction in R&D costs for the additional indications was sufficient for PIAP to meet the criteria of a sponsor with high financial capacity and balanced risk tolerances. When program characteristics varied, only 25.6% of sampled portfolios met the criteria with savings of 20% or less. The remaining 74.4% required greater savings or had no feasible solution; 17.0% did not meet the criteria even at 30% savings. The central estimate therefore provides a useful benchmark, but its applicability depends on the programs being considered.

Correlation estimates provide inputs for this type of decision analysis, and were used to guide the dependence assumptions, including ρ and the grouping of programs by shared risks [5]. The model then estimates how those risks affect effective breadth, downside NPV, launch reliability, funding needs, and the savings required to justify concentration. A company can apply the same approach using its own assumptions and constraints.

Risk appetite, tolerance, and capacity

A sponsor may decide to accept concentrated technical risk to accelerate a candidate, or to preserve revenue before loss of exclusivity. That willingness reflects its risk appetite. Risk tolerance gives the portfolio team specific limits against which to assess the strategy, such as a maximum 10% probability of a funding shortfall or a minimum P5 portfolio NPV. Risk capacity depends on the funds available to keep the company operating if several programs fail together [11,12]. Under the base-capacity stress test, no PIAP strategy met the criteria within the tested R&D-savings range.

This suggests a practical sequence for portfolio analysis and review. The team can estimate the expected cost savings and development acceleration due to synergies, while finance determines the available funding and reserves. Strategic alternatives analysis can be used to identify which strategies meet the risk limits. If a development team chooses to pursue a strategy outside these limits, that would require an explicit decision to accept greater risk or obtain additional financial capacity.

Synergies can sometimes justify the concentration risk. Shared knowledge can improve research productivity [17]. PIAP and MSOG strategies can increase efficiency, including manufacturing and trial infrastructure, and may reduce development costs or timelines. Related indications may also share medical affairs and commercial infrastructure. But these tradeoffs must be considered quantitatively in order to determine which path best aligns with the company's approach to risk. Concentration can be justified when the expected savings are significant and adverse outcomes stay within the sponsor's financial and risk limits. A portfolio that meets these conditions for a well-funded company may be unaffordable for a company with less cash or limited financing access. Large companies can also better endure a concentration of N indications assigned to an

individual asset, since the size of their existing development and commercial portfolios dilutes this impact from a risk perspective. And the balance of these risks can be modulated through acquisition, partnering, indication sequencing, and discontinuation of other programs.

Practical output for readers

This framework and accompanying code provide five components that a portfolio team can reproduce with internal data: a specification of programs sharing asset or biological risks, a cash-flow model, estimates of the savings needed to meet value and risk criteria, a summary of downside and launch outcomes, and an analysis of losses from incorrect assumptions. This framework allows the team to determine how much R&D saving or acceleration is required to justify a given concentration strategy, and its probability of exceeding the available funding. These simulation outputs support better contextualized reporting of several metrics. Expected launches can be accompanied by effective breadth, since six programs sharing one asset may provide substantially less diversification than six independent assets. eNPV and ePI should be presented with P5 NPV or CVaR and the distribution of funding needs. Launch targets can include the time remaining before loss of exclusivity or the expected value per launch. For MSOG, it is important for assumptions to capture the percentage of revenue that would be lost due to overlap, which is not always straightforward since a new asset may have patent protection for longer than the asset it would be siphoning revenue from. Recommendations can identify the requirement/limiting factor that determined the decision.

Relation to prior work

Portfolio optimization and risk-adjusted valuation have long been applied to pharmaceutical R&D [2,3,18,19,20]. Previous studies have estimated pTRS [21,22,23] and development

costs [24,25,26], and recent Therapeutic Innovation & Regulatory Science (TIRS) analyses have used eNPV to characterize development efficiency [27,28] as well as the financial value of time [29]. This analysis uses dependence scenarios informed by empirical studies to examine the cost and timing benefits needed to justify concentration within portfolios [5].

The main contribution is the estimated savings that would be required for concentration to be justified. Launch reliability provides an additional operational measure.

Limitations

The analysis uses a simplified portfolio model. The probabilities, costs, sales, and timelines used here are basic assumptions, so end-users should use their own company values rather than over-extrapolating from this example. The fixed benchmark holds program characteristics constant to isolate the effects of portfolio structure. Allowing those characteristics to vary tests the stability of the findings, but the sampling distributions do not represent a jointly estimated distribution from historical portfolios.

The Gaussian factor model makes shared technical risk easier to represent and calculate.

Alternative copulas, or models that represent common events explicitly, may be needed to produce stronger clustering of shared hazards [30]. Detailed forecasts for individual clinical programs would require additional information.

Cannibalization was varied as a scenario assumption and was not estimated from actual market share or other data. The launch-count analysis approximates a mature planning period using eventual approvals and does not model rolling calendar windows. Acquisitions, partnerships, reprioritization, and program termination in response to new information would change the results and takeaways [31].

The risk policies illustrate how organizational limits affect the available choices; they should not be interpreted as recommended limits for sponsors. Fractional Kelly or utility-based methods could extend the analysis to determine how much capital to allocate to concentrated opportunities [32]. Such extensions would require additional information about risk preferences and future access to capital. Applying the current framework to an individual company's specific revenue and funding projections would be a more immediate next step.

Conclusion

PIAP and MSOG strategies seek to combine potential efficiencies with shared technical risks in an advantageous manner. Outcome dependence/correlation introduces variance and changes downside value and launch reliability, which can be difficult to notice since expected value remains unchanged under matched success probabilities and additive economics. Cost savings, synergies, staging, and cannibalization then determine how much benefit can be derived from this construction.

The analysis estimates the benefit that would be needed to justify concentration within the company's risk limits, with launch reliability reported alongside those criteria. These estimates depend on the programs and the organization evaluating them. Expressing the tradeoffs in dollars, probability of funding shortfall, and launch outcomes gives portfolio committees a basis for deciding whether the expected benefits are sufficient and whether the company would be able to tolerate negative potential outcomes.

Funding

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Conflict of Interest

The author is employed by Iambic Therapeutics. This work was conducted independently and does not represent the views of Iambic Therapeutics. The author declares no other competing interests relevant to this work.

Author Contributions

Michael R. Doane: Conceptualization, Methodology, Software, Validation, Formal Analysis, Investigation, Data Curation, Visualization, Writing - Original Draft, Writing - Review and Editing, and Project Administration. The author approved the submitted version and accepts responsibility for the accuracy and integrity of the work.

Data Availability

The original code, machine-readable configuration files, simulated data, decision-cell outputs, validation reports, and figures supporting this study are publicly available at <https://github.com/MRDOANE/prism-portfolio-concentration> and archived in Zenodo at <https://doi.org/10.5281/zenodo.22649794>. The archived release includes the corrected CVaR implementation and results, revised launch-figure labels, and change log.

Ethics Approval and Consent to Participate

Not applicable. This study used simulated data and published aggregate parameters. No human participants, identifiable records, animals, or clinical interventions were involved.

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