1. **Framing the portfolio selection problem**
   1. What is the mathematical formulation of the drug development portfolio selection problem?

**Objective Function**: max   
**Decision Variables:**  **Constraints:**

* **Therapeutic area budget constraints**
* **Pipeline constraints**
* where
  1. Make a recommendation on which drugs to continue developing and which drugs to put on hold
* **Developing drugs:** 
  + 3,4,6,13,15,17,18,20,21,22,24,25,27,28,29,30,39,40,42,43,44,47,48,50,57,58,62,66,69,72,76,77,78,86,91,98,99,101,102,104,105,106,109,110,111,112
* **On hold:** all the remaining 68 drugs
  1. What percent of the overall budget is used for drug development?
* Total Cost: $874.48 M
* 87.448 % of the total budget is used for the drug development

1. **Incorporating risk management in the analysis**
   1. How does the mathematical formulation for the drug development need to be appended to incorporate a constraint on the portfolio’s variance?

**Portfolio Variance:**  (= )

**Add a constraint on variance:**

* 1. Illustrate an efficient frontier
* **(Figure1) in Appendix page**
* Minimum allowed variance: 0
* Maximum allowed variance: the possible maximum variance when developing all the 114 drugs
  1. make a recommendation on how much risk to take and what drugs will be developed under this scenario

**Steps for deriving a recommendation from the efficient frontier, the returns of which continuously go up as risks increase**

1. **Calculate the slope of the frontier curve (Figure 2) by each range of standard deviation**
   * a slope refers to the marginal increase in returns as risks increase
   * **the slope graph (Figure 3)** shows that every slope of the frontier curve is positive
   * the slope becomes exponentially steeper at the standard deviation of 737.895 and then the overall trend gradually decreases with multiple fluctuations
   * the slope rebounds up at the point where the standard deviation is 3841.543 and goes up slightly more and then decreases again with big volatility
   * It implies that it is hard to find a specific point where we can minimize the loss of returns reducing risks significantly since there's no range of standard deviation where the slope of frontier line turns to the negative direction or at least flatten
2. **Create “peak\_df” data frame (Figure 4) consisting of only the standard deviations where the slopes of the frontier curve increase (positive second derivative values).** 
   * such points can give more efficiencies in reducing the loss of returns when reducing risks compared to the points where the slopes decrease
3. **Calculate the percentage changes from the risk neutral point to each point in peak\_df** 
   * risk neutral point (no variance constraint): Standard Deviation = 23142.146, Return = 4480.672
   * calculate the percent change of risk and return from the risk neutral point to each of the points in peak\_df
4. **Compare the efficiency of each point based on the marginal percent change of risk with respect to returns (Figure 5)**
   * percent change of risk / percent change of return.
   * it represents how much percent of risks decrease at a specific point as returns decrease by 1% from the risk neutral point.
   * when taking risk by about 4,463 standard deviation, we get the highest marginal percentage change of risk which 4.88.
   * returns at the risk neutral - returns at the most efficient point = 23142.146 - 23122.969 = 19.177 which means $19.177M should be forgone.
   * stdDev at the risk neutral - stdDev at the most efficient point = 4480.672 - 4463.391 = 17.281 (reduced).
5. **Recommendation with summary**
   * the goal is to maximize returns, but the company should forgo some returns if the loss of returns reduces risks significantly.
   * the term "significantly" is ambiguous, so I found a point that offers relatively more efficiency in a sense that more risks are reduced given the same reduction in returns compared to the risk neutral point.
   * the standard deviation (risk) which the company should take is about 4463.391.
   * the company should sacrifice returns by $19.177M then they can reduce risks by 17.281 (standard deviation).
   * Developing drugs: 3,4,6,13,17,18,20,21,22,24,25,27,28,29,30,39,40,42,43,44,45,47,48,50,57,58,62,66,69,72,76,77,78,86,91,98,99,101,102,104,105,106,109,110,111,112
   1. If the portfolio risk were to be minimized, what drugs would be chosen for development?

* **Objective Function:** min
* **Selected Drugs:** No drug is invested, and only risk-free return is earned ($1030M)
* **Portfolio Variance:** 0
  1. Which therapeutic area you would recommend allocating the additional $50 million if the goal is to maximize return?
* Add an auxiliary variable
* Each budget constraint ), (only one area must be selected)
* Recommending therapeutic area: = Oncology  
  1. How does the allocation of the additional $50 million depend on the willingness to take risk at Zinca? **(Figure 6)**
* when posing a variance constraint from minimum to maximum, the donation tends to be allocated to "Central nervous system", "Transplantation", and "Cardiovascular" at the very beginning.
* within the most part of the initial range of the allowed variance, the donation tends to be allocated to "Transplantation".
* as the variance constraint becomes looser, "Respiratory and dermatology" and "Rheumatology and hormone therapy" are more likely to be targeted for the additional donation.
* when the variance constraint is very close to (and even arrives at) the risk neutral point, "Oncology" is the optimal area to which the donation should be allocated.
* "Ophtalmics" has never been selected across all the range of the variance constraints.

1. **Company-Wide budgeting**
   1. How does the mathematical formulation change when the therapeutic area budget constraints are replaced by the company-wide budget?

* The original budget constraint is replaced by:
  1. What changes does the company-wide budget imply in terms of

1. **Selected projects**

* Added drugs: 5, 11, 16, 26, 53, 68, 73, 74, 75
* Removed drugs: 15, 29

1. **Portfolio’s return**

* $23142.1 M -> $24675.3 M
* Increased by $1533.2 M compared to the department-wide budget constraint

1. **Standard Deviation of portfolio’s return**

* 4480.6722 -> 4742.2596
* Increased by 261.5874

1. **Percent of funds allocated on projects**

* 87.448% -> 98.695%
* Increased by 11.247%
  1. How does the efficient frontier change if the company-wide budget is used?
* the EF charts **(Figure 7)** have highly similar trend and patterns over the two models
* CW model can afford to take more risks earning more corresponding returns. In detail, when posing the same variance constraints, the DW model stops taking risks at the 75th constraint with 4480 stdDev and 23142 return, whereas the CW model keeps taking risks with more return and stops at the 84th constraint with 4742 stdDev and 24675 returns.
  1. Would you recommend Zinca to use therapeutic area budgets or the company-wide budget? Explain your reasoning.
* **I would recommend Zinca takes the company-wide budget constraint.**
* according to the diff\_df **(Figure 8)**, from the 6th constraint, the CW model always makes higher returns taking bigger or smaller risks than the DW model within the same range of variance constraints.
* the CW model tends to make increasingly higher returns as the variance constraint becomes looser.

1. **Managing extreme risks**

4-1) Assess the maximum risk at the 95% VAR (if the portfolio is selected using a risk-neutral approach) and the minimum possible risk attainable at the 95% VAR for the drug portfolio. What are the expected returns of these portfolios? Compare these results to the 95% VAR and expected return obtained from model “drug1.ipynb”

* Maximum risk (variance): 20076423.45
  + The maximum risk is the variance of the portfolio created by the minimum r.
  + Min r ranges from 0 to 15771.4398 which is the 95% VaR of the selected portfolio.
    - h can exceed the standard deviation of the portfolio, as h is an auxiliary variable where
    - It results in the min r can be stretched to 0 from the 95% Var of the highest risk portfolio.
  + Expected return: $23,142 (M)
  + 95% VaR = $15,771.4398 (M)
* Minimum risk (variance): 19921861.5
  + The minimum risk is the variance of the portfolio created by the possible maximum r.
  + Max r = 15780.69028 which is the 95% VaR of the lowest risk portfolio
  + Expected return: $23,123 (M)
  + 95% VaR = $15,780.6903 (M)
* The maximum risk portfolio selected based on the possible minimum r is the as the one selected in “drug1”.
  + As the exact same drugs are selected, the variance, expected return of the two models are the same
  + the 95% VaR of the two models (drug1 & max risk portfolio): – 1.645(4480.6722) = 15771.44

4-2) Explain whether Zinca should be concerned about the extreme risk of its drug development portfolio?

* I would recommend that Zinca incorporates the constraint on the 95% VaR because they are willing to sacrifice some returns if it reduces risks. Even though it is only 5% confidence that they get the return at the extreme risk range, it will enable them to reduce the overall risk at an efficient point when it comes to the extreme risk. And the resulting portfolio with the largest return at the 95% VaR is equal to the portfolio I recommend in “drug2”, which implies that the portfolio is composed at the most efficient point in terms of the reduction in the marginal percent change of risk with respect to reduction of returns.

Chart, line chart

Description automatically generated**Appendix**

[ Figure 1]

Efficient Frontier for Part2

Table

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Description automatically generated[Figure 2]

Table for the slopes of the efficient frontier by its standard deviation

Chart, line chart

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[Figure 3]

Chart for the slopes of the efficient frontier (first derivative)

Table

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[Figure 4]

Table

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Peak df:  
Data frame for the standard deviation the slope of which increases (second derivative is positive value)

Table

Description automatically generated[Figure 5]

Table for the percentage change of returns and stdDev from the risk neutral point to each point the slope of which increases and the marginal percent change of stdDev with respect to returns

Table

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Description automatically generated[Figure 6]

Therapeutic areas to which the additional $50M donations assigned by different variance constraints

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Chart, line chart

Description automatically generated[Figure 7]   
Efficient frontier charts for the two different constraints on budget

Table

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[Figure 8]

Diff\_df:

Table

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Description automatically generatedDifferences in return and stdDev between Company-Wide budget constraint and Department-Wide budget constraint