

Case Study B

Pain Relief Medication

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First objective

*Determine the minimum dosage amount of the drugs that achieves **efficacy**.*

The dosage of a drug is said to be **efficient** if at least 50% of the subjects are responding.

Second objective

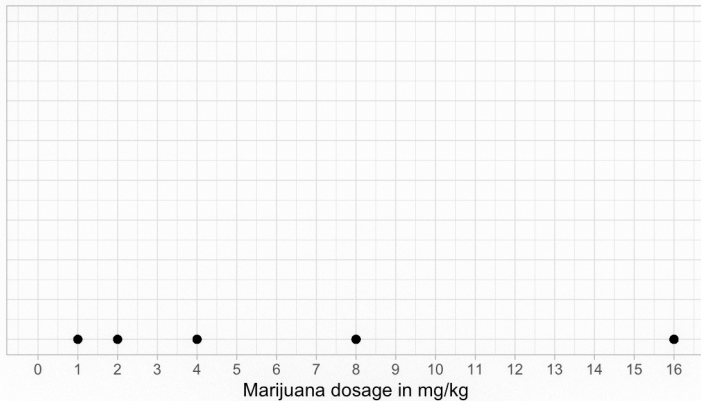
*Detect whether a **synergy** exists between the two drugs.*

If the combined efficacy of the two drug dosages is greater than the sum of the individual efficacy of each drug for its respective dosage, there is **synergy**.

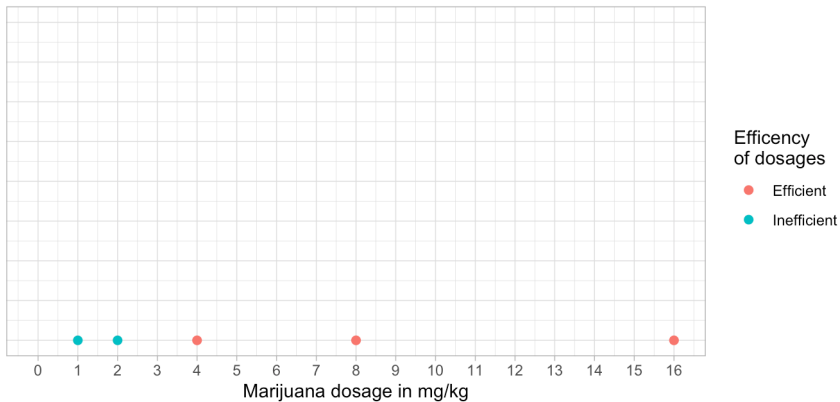
Identifying synergy with the isoboles method

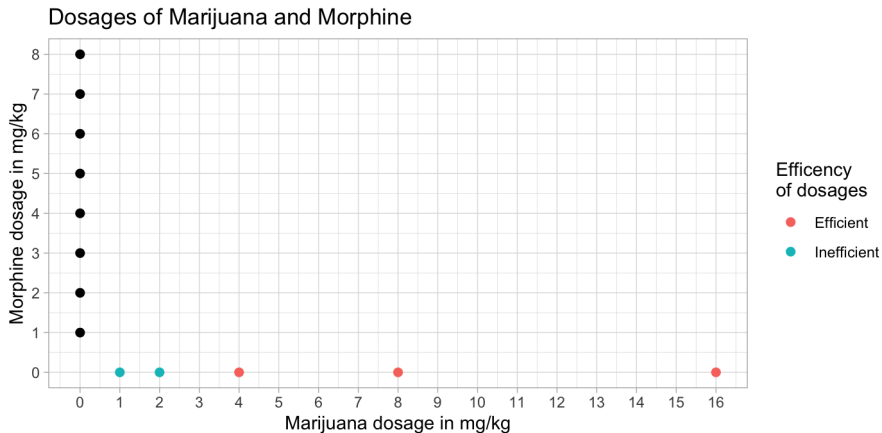
The isoboles method is a graphical representation which allows to identify synergy and helps to better understand the concept.

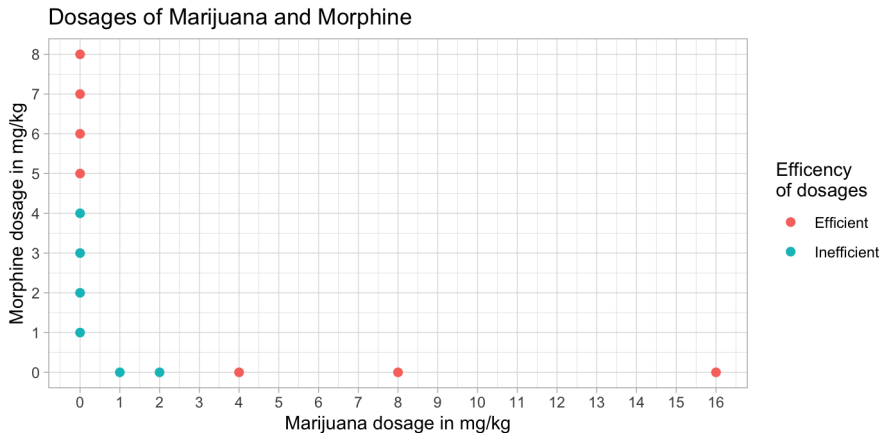
Dosages of Marijuana

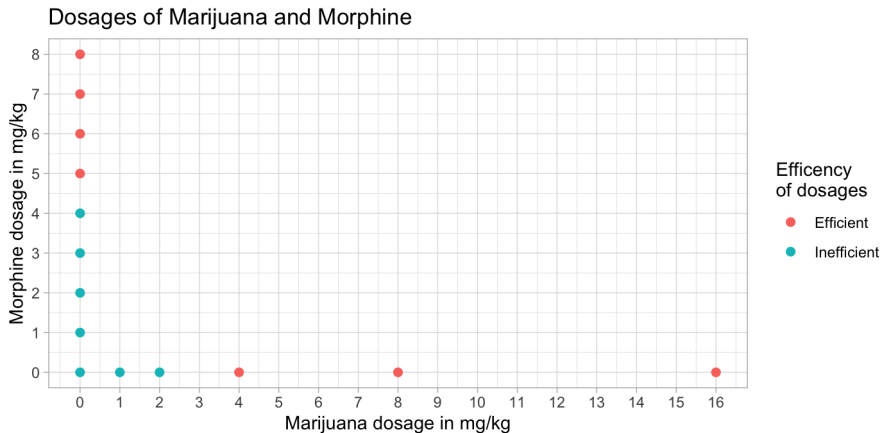


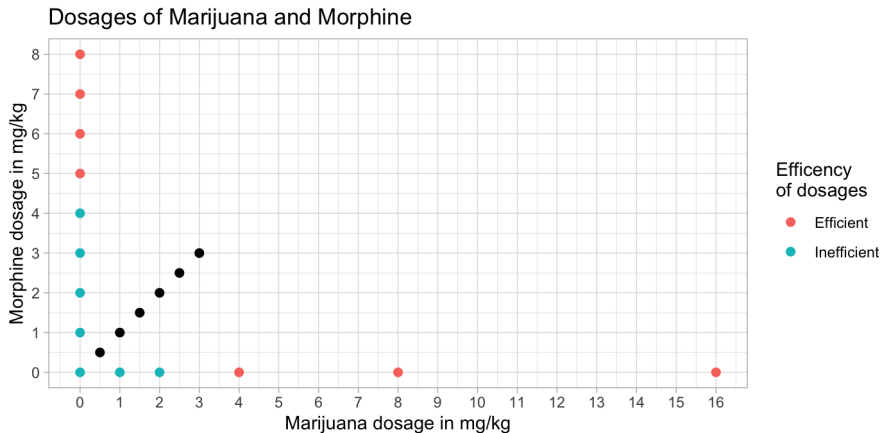
Dosages of Marijuana

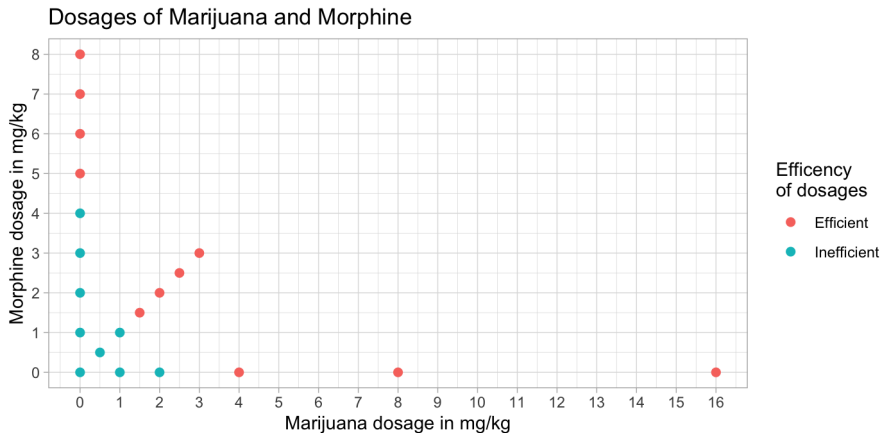


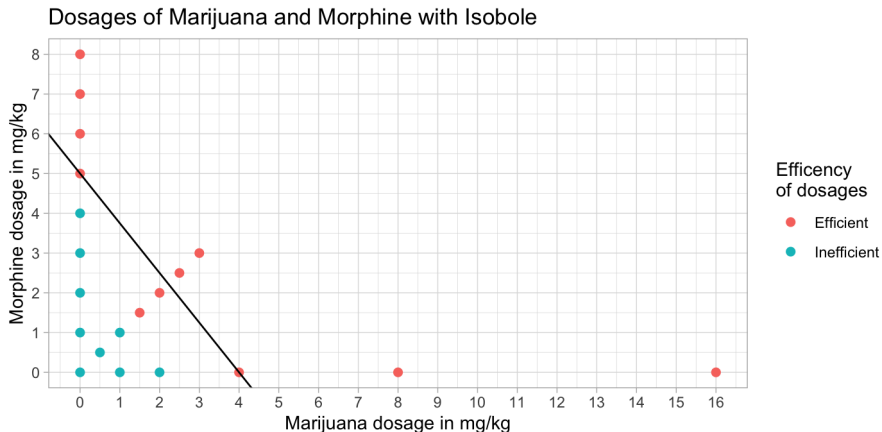












Isobole insights

- ▶ Using 4 mg/kg of marijuana gives an equivalent effect ($\geq 50\%$ of mice responding) to using 5 mg/kg of morphine.
- ▶ Combined dosages of the two drugs which are on the isobole have an equivalent effect to the ones mentioned above.
- ▶ A combined dosage which is under the isobole but is still efficient is synergic.

Isobole conclusion

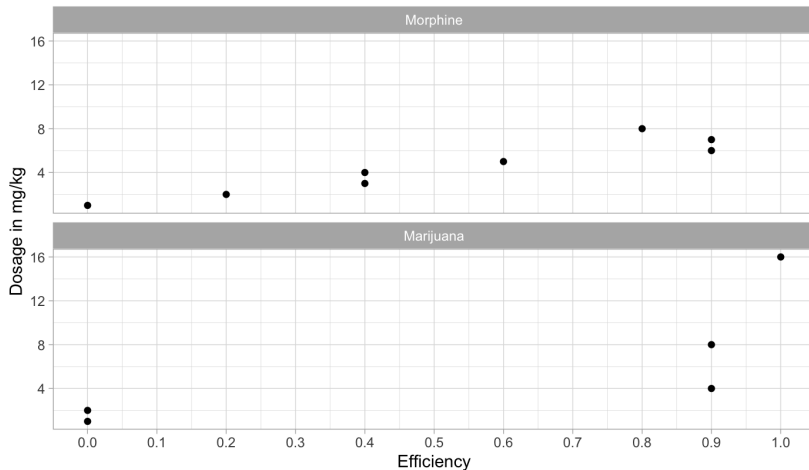
- ✓ **First objective, minimal efficient dosage:**
 - ▶ 4.0 mg/kg for marijuana alone;
 - ▶ 5.0 mg/kg for morphine alone;
 - ▶ 1.5 mg/kg of each for both drugs.
- ✓ **Second objective, synergy:**

Dosages of 1.5 mg/kg and 2.0 mg/kg each are synergic.

Isoboles method assumption

The ratio between dosages of morphine and marijuana when they give the same efficiency level is constant.

Dosages of Marijuana and Morphine vs Efficiency



- ▶ Only two common efficiency levels, 0.0 and 0.9
- ▶ This is not enough to verify the assumption for this experiment.
- ▶ This weakness is due to dosage choices for marijuana.
- ▶ However, the linear isobole method is used in multiple experiments which are extremely similar.