

Pain-Selective Epidural Analgesia: Isobolographic Analysis of co-application of Lidocaine and Chloroprocaine

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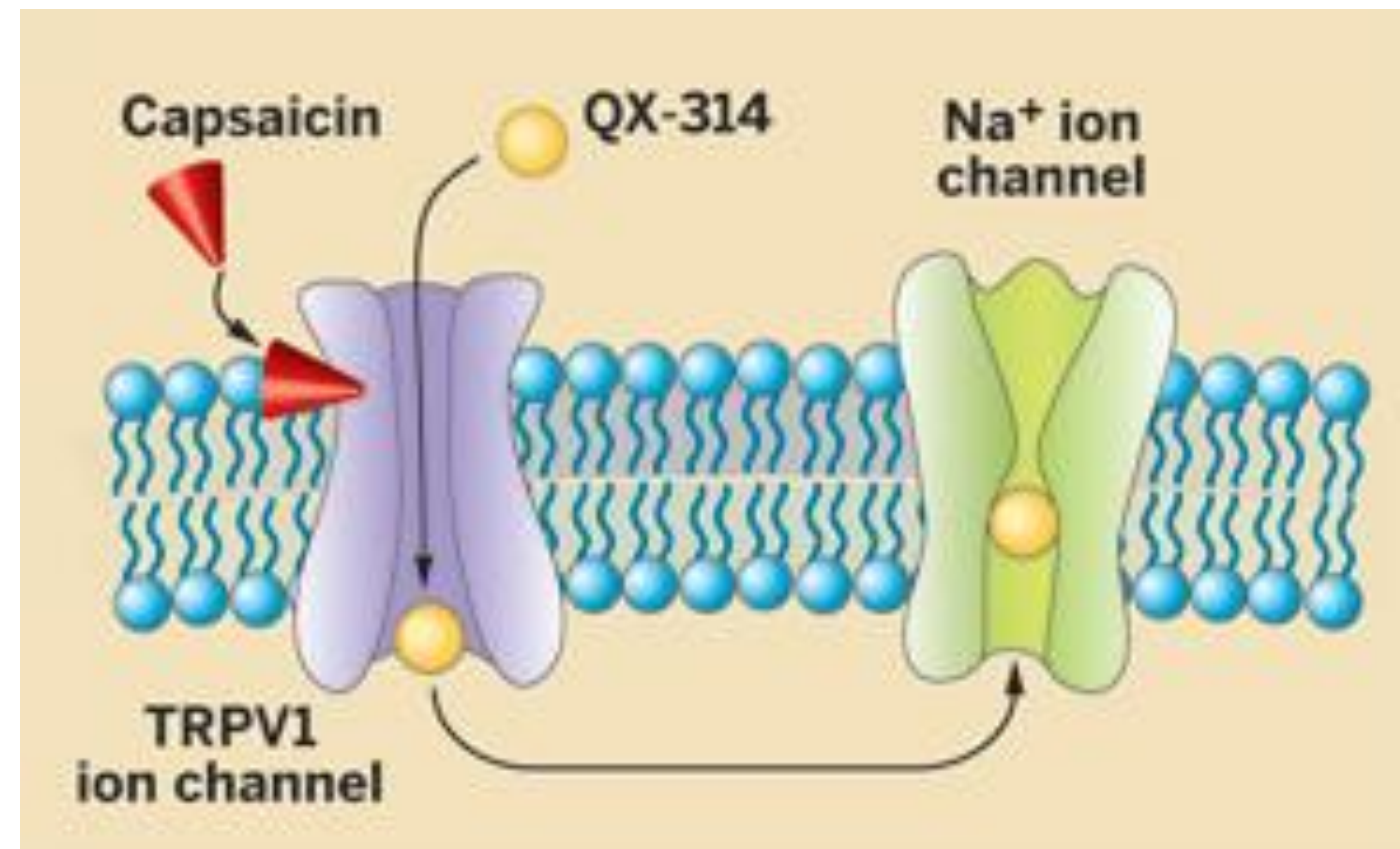
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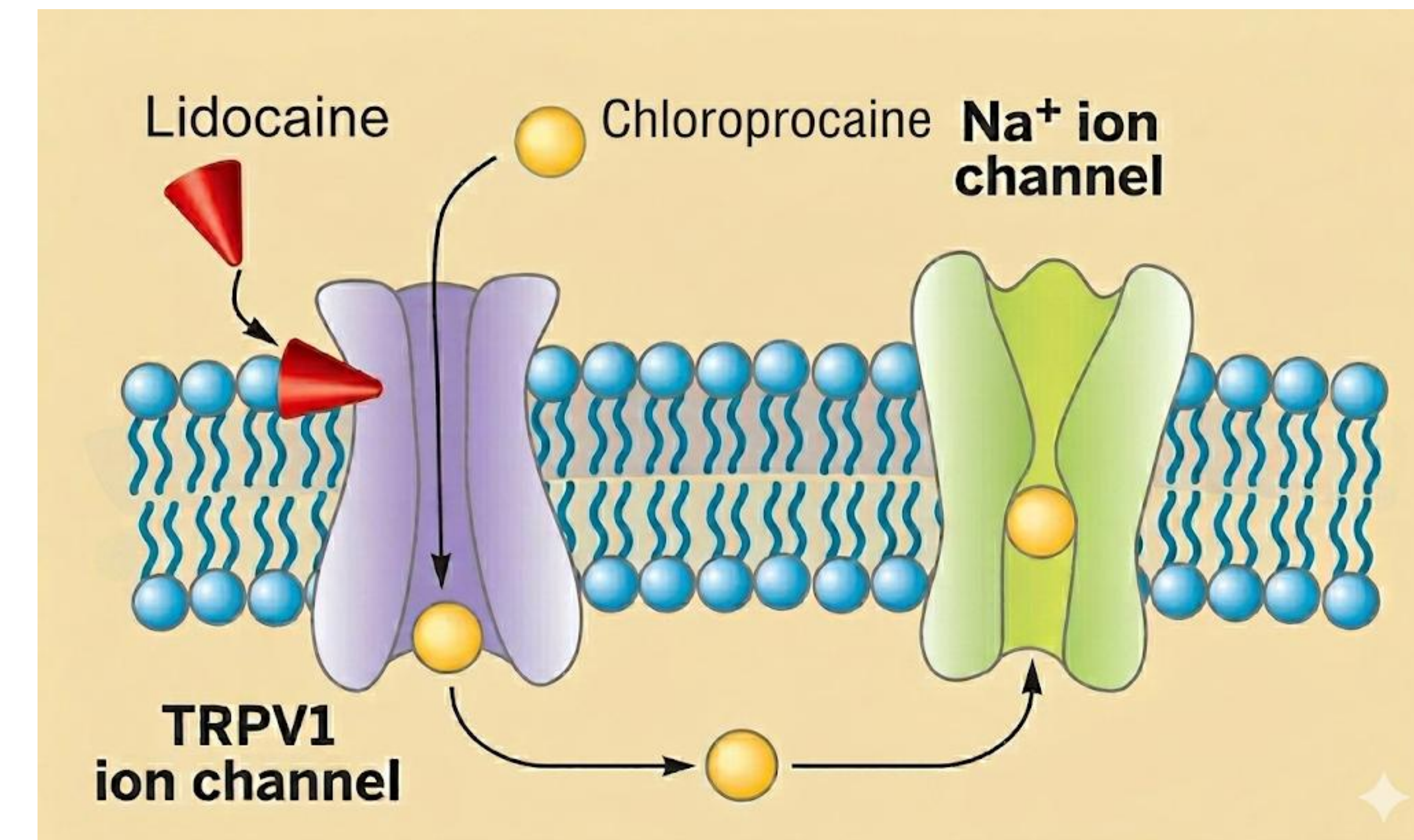


Introduction and Hypothesis

- Epidural analgesia provides excellent pain relief during labor but is commonly limited by motor block and sympathectomy
- A long-standing goal has been to achieve nociceptor-specific local anesthesia without other side effects
- TRPV1 - noxious heat-sensitive channels - are expressed exclusively on nociceptors
- In mice, co-administration of capsaicin (a TRPV1 agonist) with QX-314 (a polarized lidocaine derivative) produced profound nociceptor-selective anesthesia without motor or sympathetic block
- However, burning injection pain from capsaicin and QX-314 neurotoxicity prevented clinical translation.
- Here we use **lidocaine** as the TRPV1 agonist and **chloroprocaine** as the most polarized local anesthetic used in clinical settings.
- **We hypothesize that this co-administration will be synergistic, as the polarized fraction of chloroprocaine will enter nociceptive neurons via TRPV1 channels**



Binshtok et al., *Nature*, 2007

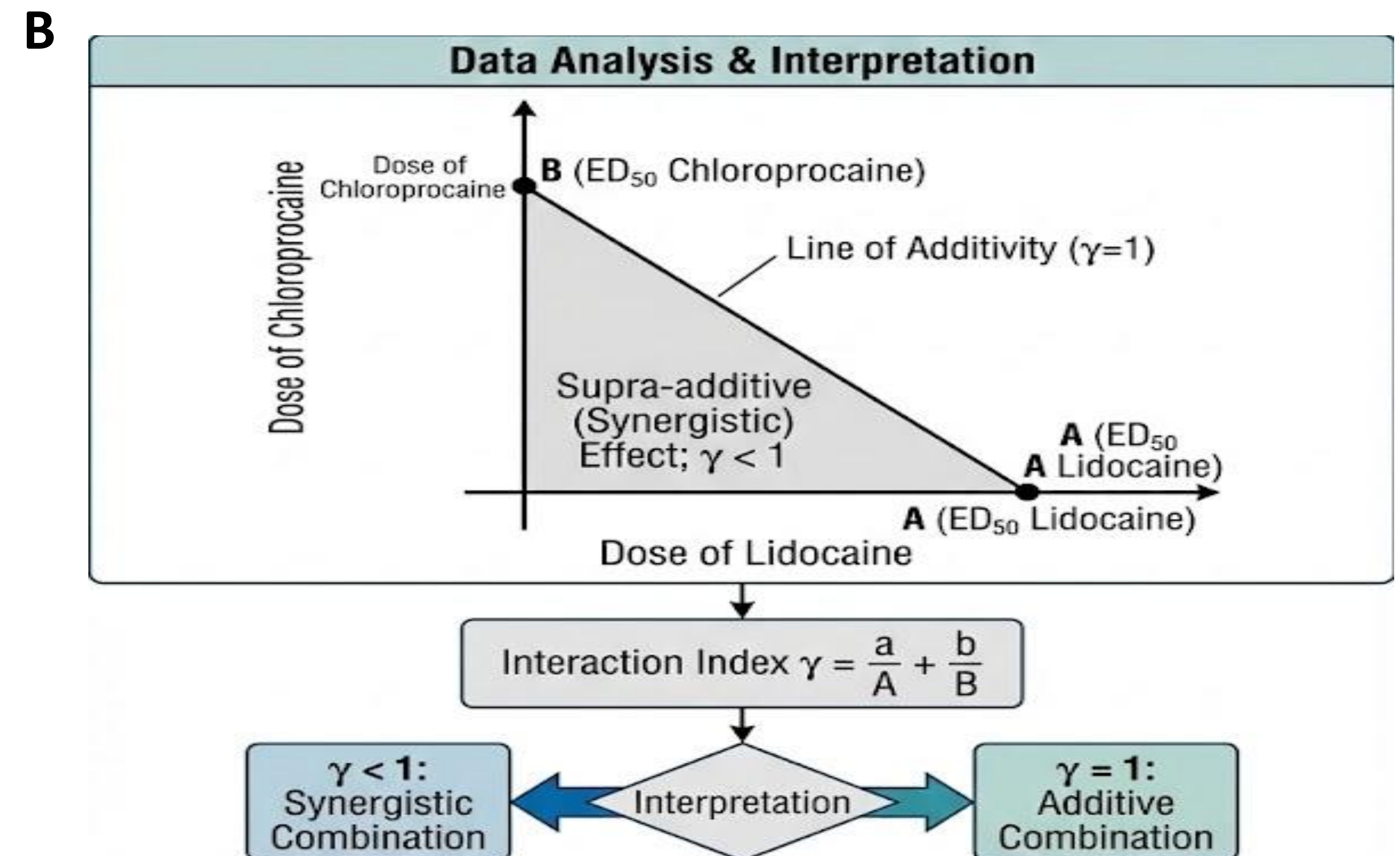
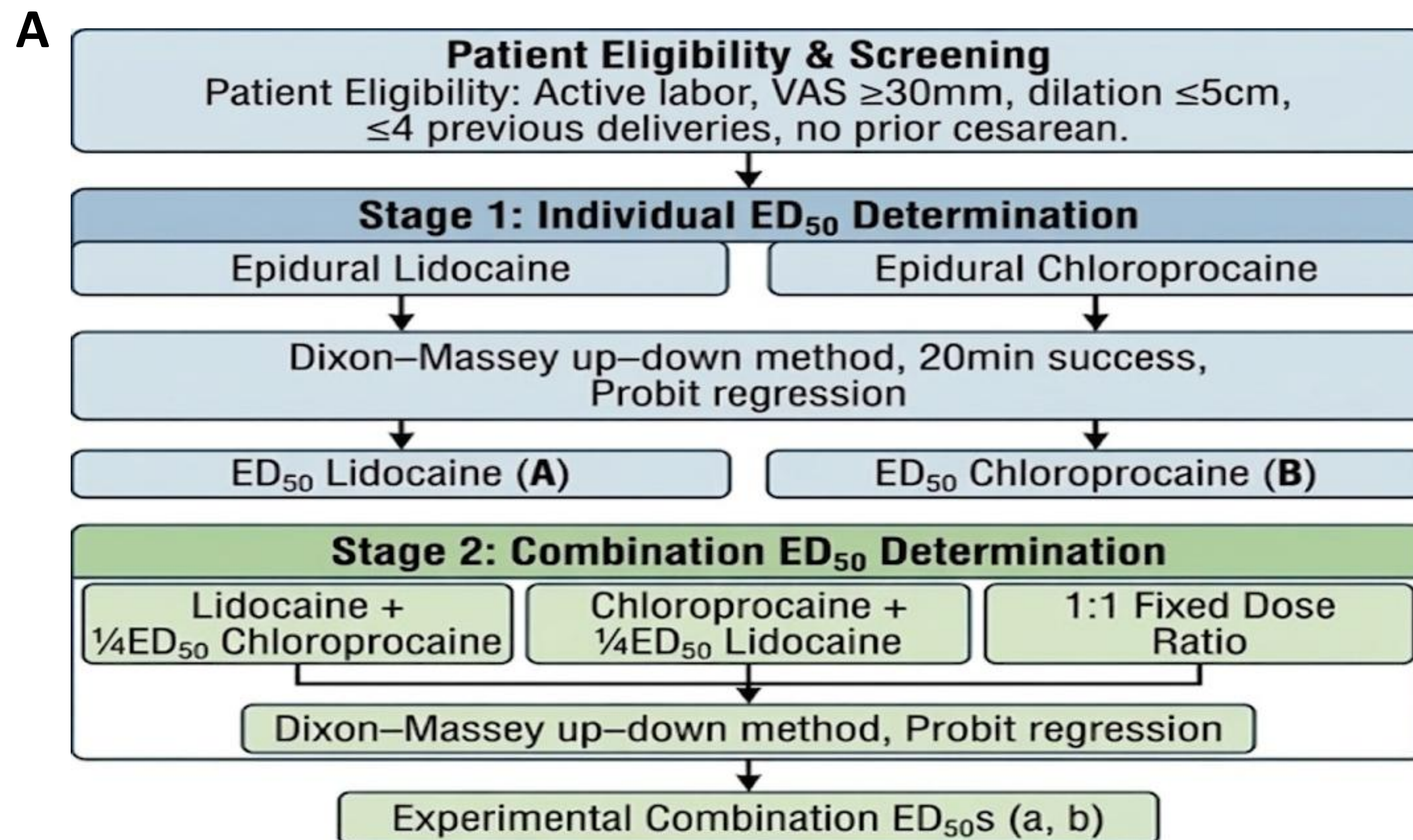


Binshtok et al., *Anesthesiology*, 2009
Kushnir et al. *submitted*

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Methodology

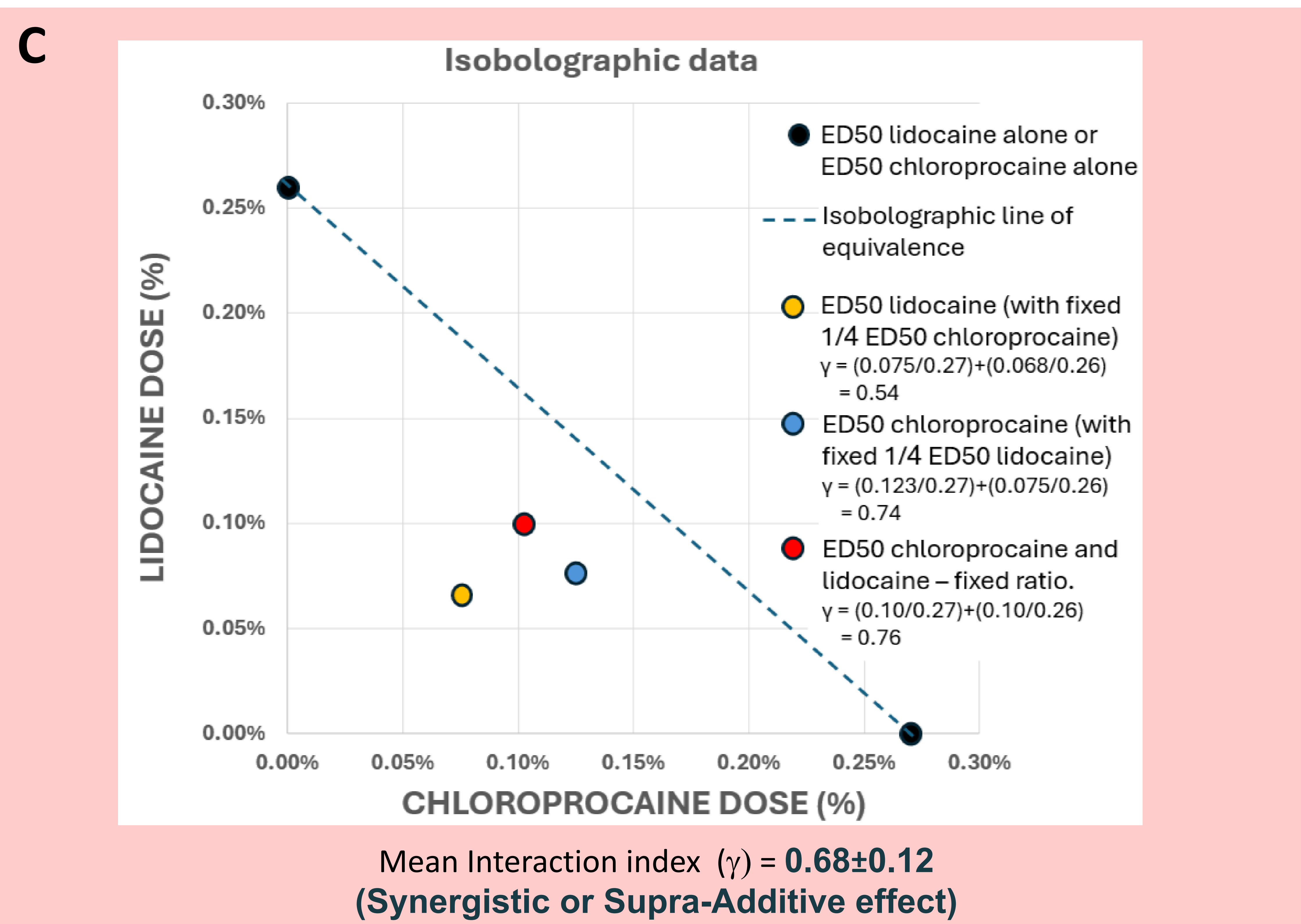
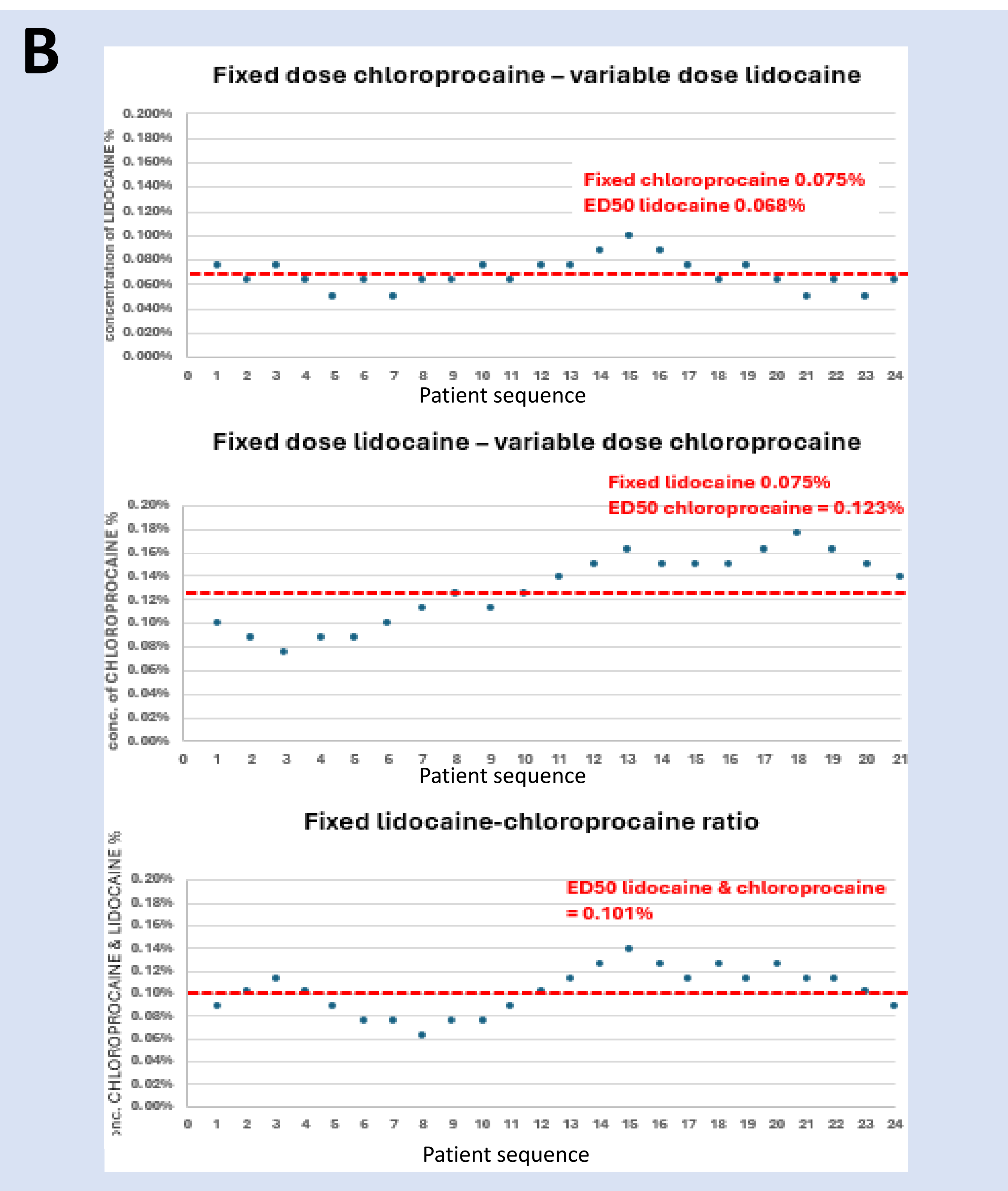
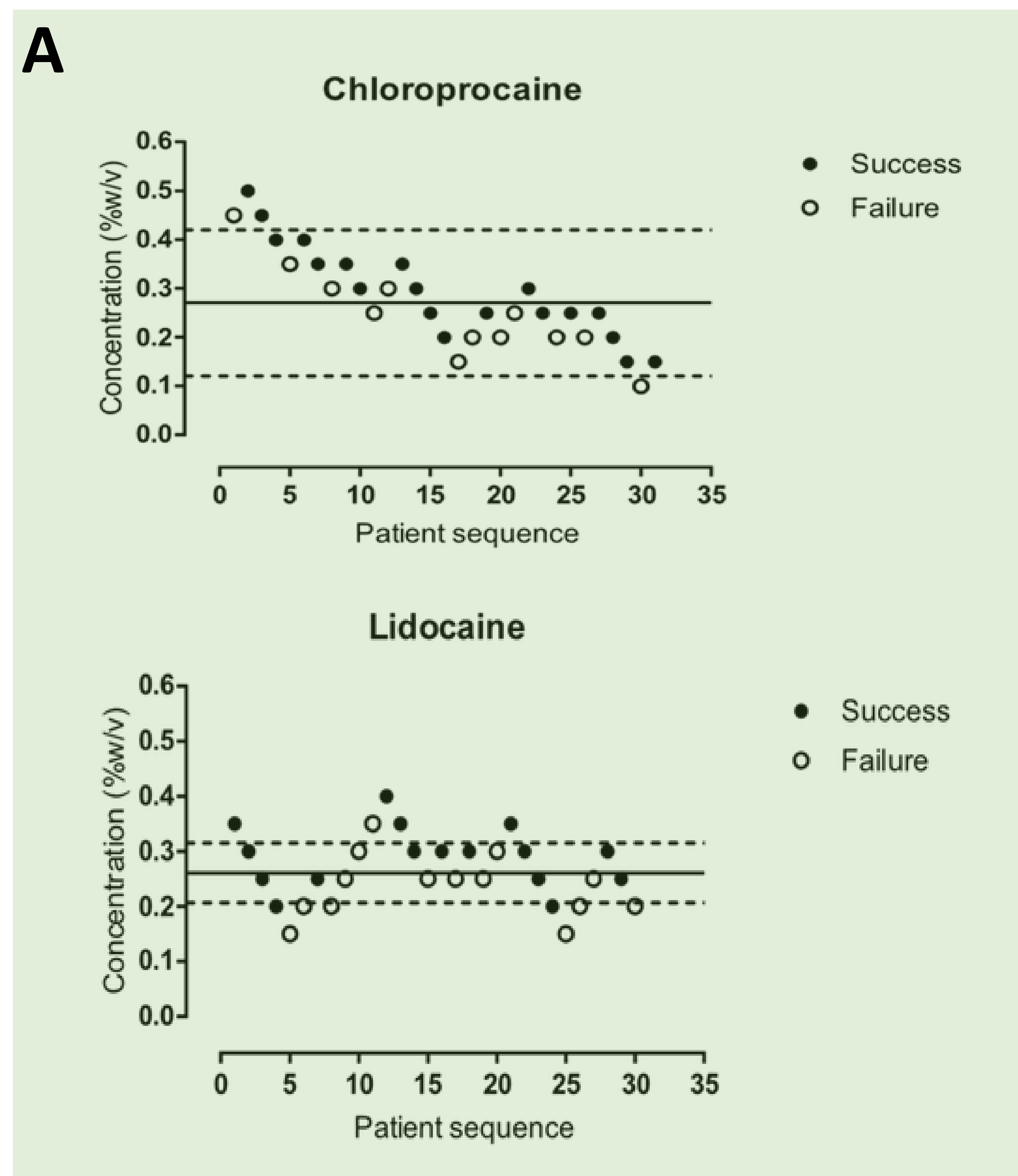
- Prospective **isobolographic** study to assess the interaction between epidural **lidocaine** and **chloroprocaine**
- 1) Measuring equipotential doses (stage 1) by determining ED50 using the up-down sequential method.
- 2) Quantitatively assess synergy (stage 2) through an **isobolographic** model
- 30 patients per group
- Success failure using the Likert scale! 😊



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Results

- A total of 142 patients were enrolled. The ED₅₀ of lidocaine was 0.26% (95% CI 0.20–0.31), and the ED₅₀ of chloroprocaine was 0.27% (95% CI 0.12–0.42).
- When co-administered with ¼ ED₅₀ of the other agent, the ED₅₀ values were 0.068% for lidocaine and 0.123% for chloroprocaine.
- Under a 1:1 fixed-ratio condition, the ED₅₀ for each drug was 0.101%
- The interaction index was **0.68±0.12 (synergistic effect)**



Conclusions

- 1st clinical evaluation of a TRPV1-based targeted strategy for pain-selective anesthesia
- The resulting interaction index following lidocaine and chloroprocaine co-application of 0.62 ± 0.12 suggests their synergistic effect
 - The results provide a basis for clinical application
- Nociceptive selective? Sympathectomy and motor effect?