PHARMACODYNAMIC MODELS AS EARLY PREDICTORS OF WEIGHT LOSS EFFICACY IN EARLY-PHASE CLINICAL RESEARCH

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INTRODUCTION

In early clinical trials, the short duration and limited drug exposure make it difficult to see early signs of effectiveness, like weight loss, which take time to show. Finding pharmacodynamic (PD) models that can predict effectiveness as substitutes for weight loss could speed up drug development and decision making.

METHODS

- Narrative review of literature, informed by domain expertise, to identify PD models relevant to early-phase obesity trials.
- Identification of relevant biomarkers (circulating, behavioral, body composition).
- Selection criteria for biomarkers based on their ability to detect early signals before measurable weight loss occurs.

RESULTS

- Key early indicators of weight loss efficacy:
  - **Blood Ketones:** Elevated β-hydroxybutyrate correlates with enhanced fat oxidation.
  - **Indirect Calorimetry:** Metabolic shifts precede weight loss.
  - **Universal Eating Monitor (UEM):** Early appetite suppression correlates with long-term efficacy.
  - **Gut Hormones (GLP-1, PYY):** Predict reduced caloric intake and subsequent weight loss.
  - **Body Composition (DEXA, MRI):** Detects fat mass reduction before overall weight loss is significant.

Early metabolic shifts can forecast long-term weight loss success.

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A detailed supplement to this poster, including physiological rationale, implementation considerations, and references supporting the pharmacodynamic models presented.

CONCLUSION

- PD models provide early-phase indicators of weight-loss efficacy, allowing for faster decision-making in clinical research.
- Incorporating these early biomarkers could accelerate drug development by identifying effective therapies before traditional weight loss endpoints manifest.

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