Mathematical approach to identifying early detection of weight loss non-responders

Diana Thomas, Ph.D.
Can we quantify who responds to treatment early

- Introduction to quantifying weight change
- Background: Dynamic Models that Predict Weight Change
- Development of diagnostic: The Pounds Lost study
- Summary
THE RESPONSE TO LONG-TERM OVERFEEDING IN IDENTICAL TWINS

Claude Bouchard, Ph.D., Angelo Tremblay, Ph.D., Jean-Pierre Després, Ph.D., André Nadeau, M.D., Paul J. Lupien, M.D., Ph.D., Germain Thériault, M.D., Jean Dussault, M.D., Sital Moorjani, Ph.D., Sylvie Pinault, M.D., and Guy Fournier, B.Sc.
Background

Differential Weight Change

Weight gain ranged from 4.3-13.3 kg!
Based on the first law of thermodynamics (energy balance equation).

 Applies Differential Equations

 Dynamic models predict weight change over time in response to changes in intake and expenditure.

 **Dynamic models capture the continuous changes in energy expenditure during weight loss/weight gain**

 Dynamic models include the individual effects of age, gender, height, and baseline weight (*weight change is not the same for all*)
Background

The Antonetti Model

Background: Web Calculators


[Graphic of a BMI calculator with a sample input of a 50-year-old male weighing 140 lbs and 65 inches tall, with a baseline weight of 500 pounds and a calorie reduction input of 0, resulting in a BMI of 24.0.]
User inputs gender, age, height, baseline weight.

Differential equation model generates predicted weight loss curve and zone.

User inputs weekly target intake.
An Alternative to Food Records

User inputs weekly weights

Actual weight graph appears

Current intake is 2770 calories.
Your estimated baseline fat mass is 33.8 kg.
Your estimated baseline fat free mass is 51.2 kg.
Take Home Points

- Weight change is variable and dependent on individual age, height, gender, baseline weight, and baseline body composition.
- Dynamic models predict individual weight change resulting from changed energy intake with a high degree of accuracy.
- We can use the weight loss zone generated by dynamic models to develop a personalized diagnostic test that quantifies early response to weight loss.

Key Ingredients

- The Personalized Weight Loss Zone
- Pounds Lost Study
- ROC analysis (Personalized cut points for short term weight loss)
Development of Diagnostic

The Pounds Lost Study

The NEW ENGLAND JOURNAL of MEDICINE

Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates

Frank M. Sacks, M.D., George A. Bray, M.D., Vincent J. Carey, Ph.D., Steven R. Smith, M.D., Donna H. Ryan, M.D., Stephen D. Anton, Ph.D., Katherine McManus, M.S., R.D., Catherine M. Champagne, Ph.D., Louise M. Bishop, M.S., R.D., Nancy Laranjo, B.A., Meryl S. Leboff, M.D., Jennifer C. Rood, Ph.D., Lilian de Jonge, Ph.D., Frank L. Greenway, M.D., Catherine M. Loria, Ph.D., Eva Obarzanek, Ph.D., and Donald A. Williamson, Ph.D.
Four-Year Weight Losses in the Look AHEAD Study: Factors Associated With Long-Term Success

Thomas A. Wadden¹, Rebecca H. Neiberg², Rena R. Wing³, Jeanne M. Clark⁴, Linda M. Delahanty⁵, James O. Hill⁶, Jonathan Krakoff⁷, Amy Otto⁸, Donna H. Ryan⁹ and Mara Z. Vitolins¹⁰; The Look AHEAD Research Group


dietary intake and physical activity, and (2) dietary adherence—deviation from dietary prescriptions for total caloric intake and three macro-nutrients (fat, protein, and carbohydrates).¹
Development of Diagnostic

The Pounds Lost Study

<table>
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<th>Pounds Lost Study</th>
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<td>BMI (kg/m²)</td>
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Development of Diagnostic New Software
Females

Distance out of the zone Month 1 (kg)

% Weight Change

\[ y = 1.6493x - 11.571 \]

\[ R^2 = 0.1216 \]
Development of Diagnostic

ROC Analysis

- Can distance from the zone in Month 1 (or Month 2, 3) detect weight loss at one year?
- If so, what would be the cut point?
  - Is it in the zone?
  - 1 kg above the zone?
- Receiver operating characteristic (ROC) analysis provides us with a method to determine optimal cut points.
- ROC analysis provides the quality of your diagnostic test. Area under ROC curve gives our diagnostic a grade.
Area Under Curve = 0.61

Optimal Cut off Point: 3.5 kg above zone

Fair Diagnostic Test

AUC improves to 0.76 using Month 2
Area Under Curve = 0.8
Optimal Cut off Point: 2.5 kg above zone
Good Diagnostic Test
Development of Diagnostic Non-Responders

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Non-responders
Summary

What does this analysis add?

- **Known:** It is known that short term weight loss predicts long term weight loss.
- **Known:** Each individual’s magnitude of weight loss is dependent on age, height, gender, and baseline weight (Bouchard study, models)
- **New:** By analyzing the distance away from the zone versus raw magnitude of weight loss, we are analyzing actual weight loss versus the weight they should have lost.
- **New:** We now can diagnose long-term weight loss based on personalized cut points early in the intervention.
Take Home Points

- Using the results of the ROC analysis, we can identify non-responders in Month 1.
- This information can be applied to provide personalized weight loss treatment recommendations.
  - There are many weight loss treatment options (pharmacotherapy, surgery)
  - Identifying non-responders early will save time, money, reduces anxiety, and pair patients to optimal treatment strategies
  - High potential to reduce costs in pharmaceutical and research clinical trials
Thank you my collaborators


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Thank you!

Questions?