Evaluation of Energy Metabolism, Weight Retention and Appetite in Postpartum Women

by

Leticia Cristina Radin Pereira

A thesis submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in

Nutrition and Metabolism

Department of Agricultural, Food and Nutritional Science
University of Alberta

Abstract

Postpartum weight retention (PPWR) is an important risk factor for long-term obesity. Accurate assessment and understanding of energy expenditure and other metabolic characteristics of postpartum women may improve weight management following childbirth. The overall aims of this research were to investigate the energy metabolism profile of postpartum women; and to explore key metabolic characteristics associated with weight retention during this life stage. Additionally, the validity of resting energy expenditure (REE) predictive equations was explored, as well as the accuracy of current recommendations in predicting total energy expenditure (TEE).

This was a longitudinal observational study involving women at three (3M-PP; n=52) and nine months postpartum (9M-PP; n=49); some measurements were only undertaken at 9M-PP. Women were stratified as high (>4.8 kg) or low (≤4.8 kg) weight retainers. Energy expenditure and macronutrient oxidation were measured by whole body calorimetry (WBC). Body composition was determined using dual-energy X-ray absorptiometry. Appetite sensations (i.e. hunger, prospective food consumption [PFC], fullness, satiety) were assessed using visual analogue scales, the results of which were then used to calculate a composite appetite score (CAS). Lactation pattern was measured using a 3-day breastfeeding diary including a 24-h infant test weighing protocol. Cardiorespiratory fitness was determined through a fitness test measuring the predicted maximal volume of oxygen consumption ($p\dot{V}O_2$ max). REE was compared to 17 commonly used predictive equations; measured TEE was compared to the Estimated Energy Requirements/DRI equation (EER_{DRI}).

This research showed that REE, TEE, and $p\dot{V}O_2$ max were lower in high-retainers than low-retainers. REE at 3M-PP was negatively associated with PPWR at 3M-PP (mean β ± SE: -0.570 ± 0.196, *P*=0.004) and 9M-PP (-0.688 ± 0.252, *P*=0.006). An increase in REE from early to late postpartum was observed in low-retainers, which was greater than predicted by changes in body composition. This was not observed in high-retainers. Daily duration of lactation episodes was associated with higher CAS (39.68 ± 15.56, *P*=0.015), hunger (3.56 ± 1.61, *P*=0.033), and PFC (4.22 ± 1.78, *P*=0.023), and with reduced sensations of fullness (-4.18 ± 1.94, *P*=0.038) and satiety (-3.83 ± 1.87, *P*=0.048). Women's perceptions of appetite were associated with PPWR (fullness: -2.97 ± 0.72, *P*<0.001; satiety: -2.75 ± 0.81, *P*=0.002; hunger: 2.19 ± 1.02, *P*=0.039, PFC: 2.19± 0.91, *P*=0.021, and CAS: 0.34 ± 0.09, *P*=0.001). Daily carbohydrate oxidation and physical activity level were also associated with appetite sensations. Several REE predictive equations performed well at a group level at both time points. At an individual level, high rates of inaccuracy and wide limits of agreement were observed. Compared to TEE, EER_{DRI} yielded inaccurate results for 33% of women, however accounting for individual lactation patterns improved accuracy.

In conclusion, lactation pattern, carbohydrate oxidation, and physical activity level were associated with appetite sensations. Along with appetite, energy expenditure and cardiorespiratory fitness were associated with body weight regulation. Additionally, commonly used predictive equations did not accurately estimate energy expenditure at an individual level. Collectively, these findings have the potential to contribute to 1) the development of future weight management strategies in postpartum women by targeting appetite and energy metabolism; and 2) the formation of energy recommendations tailored to the needs of individual postpartum women. These may also assist in promoting appropriate body weight and improving care during this life stage.

Preface

This thesis is an original work by Leticia Cristina Radin Pereira. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Health Research Ethics Board, “Calorimetry assessment in postpartum women”, No. Pro00042267, January 10, 2014. This preface is complemented by more detailed and extensive prefaces before each chapter.

Dedication

This thesis is dedicated to my loving and caring daughter, Helena.
You have taught me so much. Having you has changed me. In the best possible way.
I am so beyond lucky to have you in my life.
Helena means light, torch, bright, and that is exactly who you are!
You are my greatest blessing and my biggest achievement.
You light up my life with your brightness.
I pray to God to bless and protect you always.
I love you to the moon and back, my little girl!
With love, *sua mamãe*!

Acknowledgements

"No matter what accomplishments you make, somebody helped you." - Althea Gibson This was not different on accomplishing my Doctoral degree, and I am where I am today because of the numerous individuals who have supported me throughout my PhD program.

Thank you, my God, You provide me with strength daily, and you are the one who let me finish my degree. I will keep on trusting You for my future. Thank you, Lord.

I would like to express my sincere gratitude to my supervisors Drs. Carla Prado and Linda McCargar for your continuous commitment, support and guidance. Thank you for encouraging my research and for allowing me to grow as a research scientist.

I am also grateful to the members of my committee, Dr. Rhonda Bell and Dr. Paula Robson, for your patience, guidance, and support. Your assistance at some critical times during my data analysis is enormously appreciated, and your feedback throughout the analysis and writing process was greatly valued. Thank you to have shared your knowledge with me.

Thank you to Dr. Angelo Tremblay and Dr. Geoff Ball for participating in my thesis defense. Also thank you to Dr. Denise Hemmings and Dr. Steven Johnson for serving on my candidacy exam committee and helping me through the process.

Thank you to my colleagues that I have had the pleasure of working with: Dr. Aleida Song, Dr. Jingjie Xiao, Dr. Khanh Vu, Dr. Megan Mejer, Dr. Richard Oster, Dr. Sarah Elliott, Dr. Sarah Purcell, Camila Oliveira, Camila Orsso, Carlene Stoklossa, Edward Deehan, Grant Bruno, Isabella Carneiro, Jillian Morris, Katherine Ford, Laura Adam, Maha Alsaif, Maira Quintanilha, Mayra Viera, Ping Li, YuZhu Liang. In different ways, you all inspired me to aim higher in research.

Thank you to the Human Nutrition Research Unit staff, Adele Gagnon and Stephanie Ramage, and other staff members: Amanda Purkiss, Claire Trottier, Dragana Misita, Felicia Sim, Janis Cole, Jessica Thompson, Hara Nikolopoulos, Reena Duke, Sherin Fernandes, Taiwo Olobatuyi, Tracy Vetsch, for providing an excellent research environment and support.

In terms of the Postpartum Calorimetry study, I have multiple individuals I need to thank. Dr. Rhonda Bell, Dr. Paula Robson, Dr. Linda McCargar, and Dr. Carla Prado, thank you for the conceptual ideas and financial support for this research. Thank you to Dr. Sarah Elliott for your invaluable support in recruiting and collecting data for this study. Thank you also for sharing your knowledge on energy expenditure and for your continuous advice. Thank you to Emmanuel Guigard for your technical expertise with the whole body calorimetry unit and all the great moments we have shared during data collection. Thank you to Dr. Gordon Bell and Dr. Tasuku Terada for performing all the fitness tests for this project. Thank you to Dr. Aleida Song for conducting all biochemical analyses. I further would like to acknowledge the other individuals whose efforts contributed to the project such as calorimetry monitors, phlebotomists, babysitters, and cooks. I would also like to express my gratitude to the study participants who dedicated their time and efforts to this study. Without you, this project would not have been possible.

Thank you to the Canadian Institutes of Health Research through the Vanier CGS, and the University of Alberta for providing the funding for my graduate program. Your support for graduate students is so important and has made a huge difference for me.

Outside of university, I would like to start with an overwhelming thank you to my beloved husband, Estacio Pereira. Thank you for your love, patience, and faith. Thank you for being my best friend, for always supporting my dreams, and for encouraging me throughout this experience. Because you always understood me. *Te amo para sempre*! Thank you to Helena for just being who you are, you inspire me to be a better person every day. *Mamae te ama infinito*.

Words cannot express how grateful I am to my parents, who not just have provided emotional support throughout my life, but also for being incredible grandparents. I cannot thank you enough for your unconditional love, care, and support for me and Helena throughout my PhD. You are always there for me, and I am eternally grateful for this. *Amo voces*!

I am grateful to my amazing siblings Rafael Radin and Ana Carolina Radin, for always being by my side in good and bad moments. Thank you to my wonderful aunties Stella, Marcia, Regina and Rita Demarchi. You are my second mothers and I love you all forever.

Thank you *tia* Cristiane Gasperini, *tia* Ewa Makarewicz, and *tia* Priscilla Vanello for caring and loving Helena while I was working.

Thank you to my especial friends, the Avila-Pires's family, the Carneiro's family, the Dias's family, the Philippsen's family, the Quintanilha's family, the Zelyck's family, and father Glenn Mcdonald. Thank you for being my Canadian family. Thank you for your care and love. Thank you for all the happy and unforgettable moments together.

There are many, many others who have been with me through this journey. Although I cannot list all of your names you are all very special to me and I thank you all for your love and encouragement.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

ASM: Appendicular skeletal muscle

AUC: Area under the curve

BEE: Basal energy expenditure

BMI: Body mass index

BMR: Basal metabolic rate

CAS: Composite appetite score

DRI: Dietary reference intakes

EEE: Exercise energy expenditure

EER: Estimated energy requirements

EER_{DRI}: Estimated energy requirement/Dietary Reference Intake

ER_{WBC}: Energy requirement measured by whole body calorimetry

FAO/WHO/UNU: Food and Agriculture Organization/World Health Organization/United Nations University

FFM: Fat-free mass

FM: Fat mass

GEE: Generalized estimating equation

GWG: Gestational weight gain

HNRU: Human nutrition research unit

LOA: Limits of agreement

LST: Lean soft tissue

M-PP: Months postpartum

OLS: Regular linear regression

PA: Physical activity coefficient

PAL: Physical activity level

PFC: Prospective food consumption

PPWR: Postpartum weight retention

$\text{p}\dot{\text{V}}\text{O}_2$ max: Predicted maximal volume of oxygen consumption

REE: Resting energy expenditure

REE_{WBC}: Measured resting energy expenditure

RMR: Resting metabolic rate

RQ: Respiratory quotient

SEM: Structural equation modeling

SleepEE: Sleep energy expenditure

TEE: Total energy expenditure

TEE_{WBC}: Measured total energy expenditure

$\dot{V}CO_2$: Volume of carbon dioxide production

$\dot{V}O_2$: Volume of oxygen consumption

WBC: Whole body calorimetry

WBCU: Whole body calorimetry unit

Chapter 1: Introduction

1.1 Thesis Organization

This thesis has been prepared as a paper-format according to specifications provided by the Faculty of Graduate Studies and Research at the University of Alberta. Following the Introduction is a Literature Review (Chapter 2), three individual manuscripts (Chapters 3–5), and a Discussion and Conclusions section (Chapter 6). A preface precedes Chapters 3, 4, and 5 with a brief description of each study. A Case report is included as Appendix 1. Related figures and tables are provided at the end of each chapter.

1.2 Rationale

Obesity is a major public health problem. A recent report by Statistics Canada (1) showed the prevalence of overweight and obesity for women aged 18–34 years was 25% and 19%, respectively, and for women aged 35–49 years was 29% and 27%, respectively. In Canada, the economic impact of obesity, considering both direct costs to the health care system and indirect costs to productivity, is estimated to range from 4.6 to 7.1 billion dollars annually (2).

Postpartum weight retention (PPWR) is an important contributor to increased obesity rates in women (3). Weight gain during pregnancy and limited or lack of weight loss after pregnancy can increase the risk of longer-term weight retention (4, 5). In a follow-up study by Rooney and Schauberger (6), women who returned to their prepregnancy weight by six months postpartum were 2.4 kg heavier at 10 years postpartum, while women who retained any pregnancy weight were 8.3 kg heavier 10 years later. Weight retention following childbirth is estimated to be between 0.5 and 4 kg at one year postpartum with wide inter-individual variability (3-5, 7); for example, a gain of 27.5 kg to a loss of 19.09 kg from prepregnancy to one year postpartum have been reported in a prospective cohort study (8).

The multifactorial nature of PPWR may contributed to inter-individual variability in weight loss (3, 9). A better understanding of individual differences in factors that drive weight changes in the postpartum period is important to develop strategies to manage this issue. Prepregnancy body mass index (BMI), and gestational weight gain (GWG) are well-documented important risk factors for PPWR (10-12). Other changes that might affect maternal body weight, include hormonal fluctuations, psychological changes, altered sleep patterns (13), changes in dietary intake, physical activity, body composition, and lactation (14, 15). Energy metabolism is often overlooked, and yet it is re-emerging as a factor in body weight regulation (16). Previous studies (17-22) were primarily focused on metabolic adaptations related to the energy cost of lactation rather than the relationship between energy metabolism and PPWR. Using the energy balance concept to explore weight change provides an opportunity to integrate physiological and behavioral determinants of energy expenditure and food intake with dynamic changes in body composition (23). Numerous factors play a role in the regulation of food intake, including appetite control. Measures of appetite have been developed to evaluate its potential contribution to weight change, and although research in the postpartum period is limited, most studies in obesity research have shown that measures of appetite predict subsequent energy intake and indicate potential changes in body weight (24-26).

Therefore, all these factors may contribute to challenges for nutritional recommendations and weight management interventions after pregnancy. Energy requirements form the basis of all nutritional guidelines; excessive energy consumption over time leads to weight gain, i.e., a "positive" energy balance. Postpartum energy requirements are based on observations made decades ago (17, 19, 21, 27). As such, the current recommendation may not be appropriate for contemporary women. To determine accurate energy recommendations, total energy expenditure (TEE) must be characterized. As TEE is inherently costly to measure, resting energy expenditure (REE), the largest component of TEE, is most often used to understand energy expenditure in postpartum women. In clinical practice, energy expenditure is often estimated using predictive equations. Few studies have sought to describe the accuracy of TEE calculations or examine how REE (and the accuracy of predictive equations) might influence weight change throughout the postpartum period. Given the present state of the literature and existing gaps, additional research is required to understand components of energy expenditure, appetite, and other factors affecting PPWR in order to develop strategies to achieve adequate weight management following childbirth.

1.3 Purpose

The overall purpose of this research was to investigate the energy metabolism profile[1] of postpartum women and to explore key metabolic characteristics[2] associated with weight retention during this life stage. Additionally, this research aimed to examine the validity of predictive equations to assess REE, and to examine the accuracy of current recommendations in predicting TEE in postpartum women.

1.4 Research Questions

The research questions for this thesis were:

In women at three and nine months postpartum:

1. Is there a difference in energy metabolism between high and low weight retainers?
2. Is there a change in REE and fasting RQ from three to nine months postpartum in high retainers and low weight retainers, and in the entire sample?
3. What is the association between energy metabolism and PPWR?
4. Do commonly used prediction equations accurately estimate REE?

In women at nine months postpartum:

1. Does the current energy recommendation (Dietary Reference Intakes [DRI]) accurately estimate TEE?
2. What is the relationship between PPWR and appetite sensations (hunger, prospective food consumption [PFC], satiety, fullness) under conditions where energy intake and expenditure are precisely matched?

---

[1] **Energy metabolism profile (measured in a whole body calorimetry unit)**
At three months postpartum: resting energy expenditure (REE); fasting respiratory quotient (RQ)
At nine months postpartum: REE; exercise energy expenditure; sleep energy expenditure; total energy expenditure; predicted maximal volume of oxygen consumption ($p\dot{V}O_2max$), fasting RQ; Exercise RQ; Sleep RQ; 24-h RQ.

[2] **Metabolic characteristics**: Appetite sensations (hunger, prospective food consumption, satiety, fullness) and overall motivation to eat (i.e., composite appetite score); energy metabolism (energy expenditure, RQ, macronutrient oxidation, physical activity level, $p\dot{V}O_2max$); body composition (fat mass, fat-free mass); biochemical parameters (glucose, insulin, free-fatty acids, triglycerides); lactation (breast milk energy output, daily duration of lactation episodes).

3. Is there an association between appetite sensations and other metabolic variables[2] under conditions where energy intake and expenditure are precisely matched?

1.5 Objectives and Hypotheses

The objectives and hypotheses of this thesis were:

1.5.1 The influence of energy metabolism on postpartum weight retention (Chapter 3).

Women at three and nine months postpartum.

Objectives:

1a. To profile key components of energy metabolism[1] comparing high versus low weight retainers.

1b. To assess changes in REE and fasting RQ from three to nine months postpartum in high retainers and low weight retainers, and in the entire sample.

1c. To determine the association between energy metabolism and PPWR.

Hypotheses:

1a. Compared to low weight retainers, high weight retainers will present with a less favorable energy metabolism profile (i.e., lower energy expenditure rates and $p\dot{V}O_2max$, and higher RQ).

1b. From three to nine months postpartum: 1) REE will decrease in high weight retainers, and it will not change in low weight retainers, and in the entire sample; 2) Fasting RQ will not change in high weight retainers, and it will decrease in low weight retainers, and in the entire sample.

1c. Energy metabolism will be negatively associated with PPWR.

1.5.2 Associations of appetite sensations and metabolic characteristics with weight retention in postpartum women (Chapter 4).

Women at nine months postpartum whose energy intake and expenditure were precisely matched for 1 day in a whole body calorimetry unit.

Objectives:

2a. To examine differences in appetite sensations (hunger, PFC, satiety, fullness) and overall motivation to eat (i.e., composite appetite score [CAS]) between high and low weight retainers.

2b. To determine associations between appetite sensations and PPWR.

2c. To determine associations between appetite sensations and other metabolic variables^{2}.

Hypotheses:

2a. Compared to low weight retainers, hunger, PFC, and overall motivation to eat sensations will be greater, and satiety and fullness sensations will be lower in high weight retainers.

2b. PPWR will be positively associated with hunger, PFC, and overall motivation to eat sensations; and negatively associated with satiety and fullness sensations.

2c. Appetite sensations will be associated with energy metabolism, body composition, biochemical parameters, and lactation patterns.

1.5.3 The use of whole body calorimetry to compare measured versus predicted energy expenditure in postpartum women (Chapter 5).

Women at three and nine months postpartum:

Objectives:

3a. To assess the accuracy of commonly used REE predictive equations compared to measured REE.

3b. To assess differences in the accuracy of predictive equations commonly used in clinical practice among subgroups of women based on their current BMI classification, and lactation status.

Hypotheses:

3a. Compared to measured REE, most REE prediction equations will have an unacceptable group-level agreement (bias > ± 10%), and poor individual-level agreement (wide limits of agreement [LOA]–absolute LOA > 20%, and high rates of inaccuracy).

3b. REE equation bias and LOA will be poorer in women with obesity.

3c. REE equation bias and LOA will be poorer in lactating women.

Women at nine months postpartum:

Objectives:

4a. To assess accuracy of the current energy recommendation (DRI) compared to measured TEE.

4b. To compare measured TEE to energy recommendations among subgroups of women based on their current BMI classification and lactation status.

Hypotheses:

4a. The average energy recommendation will be significantly higher than the measured TEE (group-level agreement) and will have wide variation in individual-level agreement.

4b. TEE bias and LOA will be poorer in women with obesity.

4c. TEE bias and LOA will be poorer in lactating women.

1.6 References

1. Statistics Canada. Table 13-10-0096-20 Body mass index, overweight or obese, self-reported, adult, age groups (18 years and older). Available from: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009620 (acessed March 29, 2019).
2. Public Health Agency of Canada, Canadian Institute for Health Information. Obesity in Canada: A joint report from the Public Health Agency of Canada and the Canadian Institute for Health Information. Ottawa: Public Health Agency of Canada; 2011. Available from: https://www.canada.ca/en/public-health/services/health-promotion/healthy-living/obesity-canada.html (accessed March 13, 2019).
3. Endres LK, Straub H, McKinney C, Plunkett B, Minkovitz CS, Schetter CD, Ramey S, Wang C, Hobel C, Raju T, et al. Postpartum weight retention risk factors and relationship to obesity at 1 year. Obstet Gynecol 2015;125:144-152.
4. Schmitt NM, Nicholson WK, Schmitt J. The association of pregnancy and the development of obesity - results of a systematic review and meta-analysis on the natural history of postpartum weight retention. Int J Obes (Lond). 2007;31:1642-1651.
5. Lim S, O'Reilly S, Behrens H, Skinner T, Ellis I, Dunbar JA. Effective strategies for weight loss in post-partum women: a systematic review and meta-analysis. Obes Rev. 2015;16:972-987.
6. Rooney BL, Schauberger CW. Excess pregnancy weight gain and long-term obesity: one decade later. Obstet Gynecol 2002;100:245-252.
7. Begum F, Colman I, McCargar LJ, Bell RC. Gestational weight gain and early postpartum weight retention in a prospective cohort of Alberta women. J Obstet Gynaecol Can 2012;34:637-647.
8. Olson CM, Strawderman MS, Hinton PS, Pearson TA. Gestational weight gain and postpartum behaviors associated with weight change from early pregnancy to 1 y postpartum. Int J Obes Relat Metab Disord 2003;27:117-127.
9. Hollis JL, Crozier SR, Inskip HM, Cooper C, Godfrey KM, Harvey NC, Collins CE, Robinson SM. Modifiable risk factors of maternal postpartum weight retention: an analysis of their combined impact and potential opportunities for prevention. Int J Obes (Lond). 2017;41:1091-1098.

10. Nehring I, Schmoll S, Beyerlein A, Hauner H, von Kries R. Gestational weight gain and long-term postpartum weight retention: a meta-analysis. Am J Clin Nutr 2011;94:1225-1231.
11. Mannan M, Doi SA, Mamun AA. Association between weight gain during pregnancy and postpartum weight retention and obesity: a bias-adjusted meta-analysis. Nutr Rev 2013;71:343-352.
12. Rong K, Yu K, Han X, Szeto IM, Qin X, Wang J, Ning Y, Wang P, Ma D. Pre-pregnancy BMI, gestational weight gain and postpartum weight retention: a meta-analysis of observational studies. Public Health Nutr. 2015;18:2172-2182.
13. Dørheim SK, Bondevik GT, Eberhard-Gran M, Bjorvatn B. Sleep and depression in postpartum women: a population-based study. Sleep 2009;32:847-855.
14. Montgomery KS, Best M, Aniello TB, Phillips JD, Hatmaker-Flanigan E. Postpartum weight loss: weight struggles, eating, exercise, and breast-feeding. J Holist Nurs 2013;31:129-138.
15. Lopez-Olmedo N, Hernandez-Cordero S, Neufeld LM, Garcia-Guerra A, Mejia-Rodriguez F, Mendez Gomez-Humaran I. The associations of maternal weight change with breastfeeding, diet and physical activity during the postpartum period. Matern Child Health J 2016;20:270-280.
16. Muller MJ, Geisler C. From the past to future: from energy expenditure to energy intake to energy expenditure. Eur J Clin Nutr 2017;71:358-364.
17. Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Sawyer MB, Ashford J, Black AE. Longitudinal assessment of the components of energy balance in well-nourished lactating women. Am J Clin Nutr 1991;54:788-798.
18. Frigerio C, Schutz Y, Whitehead R, Jequier E. A new procedure to assess the energy requirements of lactation in Gambian women. Am J Clin Nutr. 1991;54:526-533.
19. Forsum E, Kabir N, Sadurskis A, Westerterp K. Total energy expenditure of healthy Swedish women during pregnancy and lactation. Am J Clin Nutr 1992;56:334-342.
20. Kopp-Hoolihan LE, van Loan MD, Wong WW, King JC. Longitudinal assessment of energy balance in well-nourished, pregnant women. Am J Clin Nutr 1999;69:697-704.
21. Butte NF, Wong WW, Hopkinson JM. Energy requirements of lactating women derived from doubly labeled water and milk energy output. J Nutr 2001;131:53-58.

22. Butte NF, Hopkinson JM, Mehta N, Moon JK, Smith EO. Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation. Am J Clin Nutr 1999;69:299-307.
23. Hopkins M, Finlayson G, Duarte C, Gibbons C, Johnstone AM, Whybrow S, Horgan GW, Blundell JE, Stubbs RJ. Biological and psychological mediators of the relationships between fat mass, fat-free mass and energy intake. Int J Obes (Lond) 2019;43:233-242.
24. Drapeau V, King N, Hetherington M, Doucet E, Blundell J, Tremblay A. Appetite sensations and satiety quotient: predictors of energy intake and weight loss. Appetite 2007;48:159-166.
25. Thomas EA, McNair B, Bechtell JL, Ferland A, Cornier MA, Eckel RH. Greater hunger and less restraint predict weight loss success with phentermine treatment. Obesity (Silver Spring) 2016;24:37-43.
26. Sayer RD, Peters JC, Pan Z, Wyatt HR, Hill JO. Hunger, food cravings, and diet satisfaction are related to changes in body weight during a 6-month behavioral weight loss intervention: The Beef WISE Study. Nutrients 2018;10:700.
27. Lovelady CA, Meredith CN, McCrory MA, Nommsen LA, Joseph LJ, Dewey KG. Energy expenditure in lactating women: a comparison of doubly labeled water and heart-rate-monitoring methods. Am J Clin Nutr. 1993;57:512-518.

Chapter 2: Literature Review

2.1 Preface

This chapter reviews the literature on weight change, energy expenditure, and appetite in women during the postpartum period. It begins by defining postpartum weight retention (PPWR) and identifying the variability in this outcome. The chapter then briefly describes the consequences of PPWR, including its place in the global obesity epidemic, and reviews the wide-ranging and complex factors that influence body weight trajectory after pregnancy. The chapter then provides a critical review of the literature on energy expenditure in the postpartum period and highlights landmark studies that assess total energy expenditure in this life stage. Finally, the chapter reviews and describes factors that influence appetite sensations, including lactation, and some methodological considerations for the assessment of appetite sensations.

2.2 Postpartum Body Weight

An increasing body of evidence consistently shows that maternal body weight status and suboptimal maternal nutrition prior to, during, and after pregnancy can impact the long-term health of the mother and offspring later in life (1). The "Developmental Origins of Health and Disease" hypothesis, pioneered by Dr. David Barker, provides evidence to suggest that weight management during a woman's reproductive years has benefits for both the mother and the next generations (2). This hypothesis suggests that the environment in utero, which is influenced by nutrition and weight gain, programs the fetus and can affect metabolism, organ structure, and physiological functions to permanently alter disease risk later in life (2); this process is known as developmental programming. Therefore, optimal nutrition and body weight status during the childbearing years are crucial to obtain best health outcomes for women and their offspring and future generations.

In 2009, the Institute of Medicine published revised guidelines for the amount of weight that a woman should gain throughout pregnancy (3). Health Canada adopted these guidelines in 2010 (4). The guidelines recommend ranges of weight gain based on a woman's prepregnancy body mass index (BMI). After childbirth, women are expected to lose the weight they gained during pregnancy. However, weight loss in the postpartum period is highly variable (5), and PPWR may have negative implications, including long-term obesity (6-10) and other adverse health outcomes for the mother and infant in future pregnancies and later in life (11-13). Therefore, public health researchers are recognizing excess weight gain specific to childbearing, including postpartum weight retention, as a new public health challenge among women (12) that deserves further investigation.

2.2.1 Definitions and variability.

The postpartum period is characterized by shifts in physiological processes and body shape as a woman's body moves from pregnancy to lactation to weaning of the child, and back to the nonpregnant, nonlactating state. Although the postpartum period is recognized as the time immediately following the birth of a baby, its duration is defined by the mother, and it often does not have a definitive end. Many of the morphological changes that occur during pregnancy, such as pregnancy-related fluid distribution, persist for up to six weeks postpartum (5, 14, 15). Given that other physiological and psychological changes, including breastfeeding, may extend beyond six weeks, the definition of the postpartum period can extend to one year after giving birth (16).

Changes in a woman's body weight are also characteristic of the postpartum period. Postpartum weight retention refers to weight change—loss or gain—from prepregnancy to postpartum (17-20). As such, the term *PPWR* will be used throughout this thesis to refer to the difference between postpartum weight (at three or nine months postpartum) and prepregnancy weight.

At one year postpartum, the average PPWR generally ranges from 0.5 kg to 4 kg (21-25), yet weight change in the postpartum period can vary widely, ranging from, for example, a gain of 27.5 kg to a loss of 19.09 kg from prepregnancy to one year postpartum (22). Several studies (5, 18, 22, 23, 26-28) that assessed maternal body weight trajectory after pregnancy have reported consistently that approximately 20% of women are 5 kg above their prepregnancy weight at one year postpartum. These findings highlight that a subset of women seems to be at increased risk of retaining significant amounts of weight following pregnancy. Despite variability in body weight change after pregnancy and the potential long-term health impact of PPWR, detailed guidelines have not been established to define cut-points for excess PPWR (17). There is, however, an average postpartum weight loss reported and used by the dietary reference intake (DRI) guidelines (29). These guidelines are based on a review by Butte and Hopkinson (30) of nine longitudinal studies conducted with affluent postpartum women that showed that well-nourished women experience an average weight loss of 0.8 kg/month in the first six months postpartum (total 4.8 kg weight loss). Weight stability is assumed after this period (29), and there is no consensus about the timelines for continued weight loss after the first six months postpartum. The present study defines women with excess PPWR (high retainers) based on the current DRI recommendations for postpartum weight loss over six months (4.8 kg weight loss) (29), and on the aforementioned literature (5, 18, 22, 23, 26-28) that reports that approximately 20% of women retain ~5 kg at one year postpartum compared to prepregnancy weight. Therefore, extrapolating the 4.8 kg value, this thesis defines those women who retained > 4.8 kg at nine months postpartum as high retainers.

2.2.2 Consequences of postpartum weight retention.

2.2.2.1 Obesity.

Gestational weight gain (GWG) and failing to lose weight in the postpartum period puts women at risk of obesity. Childbearing years, therefore, are an important life stage for weight management (18). The worldwide prevalence of obesity nearly tripled between 1975 and 2016 (31). As of 2016, global estimates from the World Health Organization (31) showed that approximately 40% of women aged 18 years and over were overweight, and of those, 15% were obese. In 2017, the prevalence of overweight and obesity among Canadian women aged 18 to 34 years was 25% and 19.3%, and for women aged 35 to 49 years old it was 28.9% and 27.4%, respectively (32). From an economic perspective, the burden of obesity in Canada is estimated to range from $4.6 to $7.1 billion annually, considering both direct costs to the healthcare system and indirect costs to productivity (33).

Concordant with the rates reported in women of childbearing age, rates of obesity in pregnancy are also increasing (34), and the cost and use of healthcare services is high for women who enter pregnancy overweight or obese (35). The findings that weight gain during pregnancy and the potential lack of, or limited, weight loss after pregnancy increases the risk of longer-term obesity are consistent across studies and worldwide. Longitudinal studies of women in the United States (36, 37), for example, have shown that women who have had a child were approximately 2 to 3 kg heavier in the follow-up period than those who have not. In a prospective cohort study of Canadian women (20), BMI increased by approximately 1.5 kg/m^2 from prepregnancy to 10 to 12 weeks postpartum across all prepregnancy BMI categories. A population-based study of 58,534 Canadians who experienced successive pregnancies (6) demonstrated that ~25% of women were ≥ 5 kg heavier at the beginning of a subsequent pregnancy, ~9% were heavier by 10 kg or more, and ~2% of women developed obesity after starting a previous pregnancy with a normal BMI. Similarly, a large cohort study of more than 56,000 Norwegian women (7) found that approximately 13% of women moved from a normal prepregnancy BMI to an overweight BMI classification by six months postpartum. Other prospective studies of women in the United States and Europe (8-10) demonstrated that lack of weight loss in the postpartum period was associated with higher body weight for up to 7 to 15 years following pregnancy. The effects of weight changes related to pregnancy may be cumulative over a woman's lifetime, as some studies suggest that higher parity is associated with a higher BMI among women in their forties and fifties (38). Weight gained during pregnancy that is not lost in the postpartum period may therefore contribute to a woman's lifelong risk of developing obesity.

2.2.2.2 Other adverse consequences of postpartum weight retention.

Retaining weight following pregnancy not only puts women at risk of developing long-term obesity, but it may also be associated with adverse pregnancy outcomes in future pregnancies and impact the long-term health of the mother later in life (11, 39). These adverse outcomes include pregnancy-related health issues (e.g., gestational diabetes mellitus, pregnancy-induced hypertension, preeclampsia), obstetrical or neonatal complications, and type 2 diabetes, cardiovascular diseases, depression, and certain types of cancer later in life (6, 11-13, 39-45). Thus, as the Barker hypothesis suggests, PPWR may be an important factor in the intergenerational cycle of obesity.

2.2.3 Determinants of postpartum weight retention.

A wide range of diverse and complex factors influence weight after pregnancy. The multifactorial nature of PPWR may explain inter-individual variability in weight loss after pregnancy (46, 47). A better understanding of individual differences in factors driving weight change in the postpartum period is important for developing targeted weight management strategies during this life stage. The following discussion reviews the key factors associated with PPWR as relevant to this thesis.

2.2.3.1 Prepregnancy BMI.

As described above, prepregnancy weight status is associated with pregnancy outcomes (6, 11-13, 39-45), and impacts developmental programming (1, 2). According to the Society of Obstetricians and Gynaecologists of Canada *Clinical Practice Guidelines for Obesity in Pregnancy* (48), women should be encouraged to enter pregnancy with a BMI < 30 kg/m^2, and ideally < 25 kg/m^2. The evidence is mixed with regard to the association between prepregnancy weight status and PPWR, as several (9, 10, 46, 49-51) but not all (47, 52) studies have demonstrated that having a higher prepregnacy BMI is associated with higher PPWR. A longitudinal study of 774 healthy women in the UK (46) showed that having a prepregnancy weight in the overweight BMI category was associated with a 3.2-fold higher risk of retaining 9.1 kg or more at one year postpartum, while those in the obese BMI category had a 3.8-fold increase in the odds of PPWR, relative to those who had a normal prepregnancy BMI. A recent population-based retrospective cohort study of over 49,000 American women (49) demonstrated that prepregnancy BMI in the overweight/obese categories was associated with a decreased likelihood of returning to prepregnancy BMI in the postpartum period. In contrast, a meta-analysis of 10 studies that analyzed PPWR of 116,735 women at different prepregnancy BMI categories, from one month to 15 years postpartum (52), demonstrated that women who had a prepregnancy BMI in the overweight and obese categories retained 0.81 kg (95% CI −1.23, −0.39) and 2.34 kg (95% CI −3.28, −1.40) less weight, respectively, compared to women who had a normal prepregnancy BMI.

2.2.3.2 Gestational weight gain.

GWG is an important global indicator of a healthy pregnancy, which includes maternal health as well as the healthy growth and development of the fetus. The increase in weight during pregnancy consists of amniotic fluid, formation of the placenta, and the growth of the fetus as well as the accretion of tissue in the uterus and breast, expansion of blood volume, and increase in maternal adipose tissue (3). Despite the fact that there are GWG guidelines (3) that aim to optimize outcomes for the woman and the infant, many studies report weight gain in excess of the guidelines (20, 53-55). A prospective cohort study of more than 1,500 Canadian women (54), for example, demonstrated that 49.4% of women exceeded the GWG guidelines.

GWG has been recognized as a major risk factor for PPWR, as several studies have demonstrated a positive correlation between excessive GWG and PPWR (9, 46, 50-52, 56-59). A recent meta-analysis of 11 observational studies that analyzed PPWR at different times with > 67,000 women (52) showed that women who exceeded GWG guidelines retained an additional 3.21 kg (95% CI 2.79, 3.62 kg) compared with women whose GWG was within the guidelines. These authors stratified the postpartum period into 1 to 3 months, 3 to 6 months, 6 to 12 months, 12 to 36 months, and ≥ 15 years, and the association between excessive GWG and PPWR exhibited a U-shaped trend—that is, from 4.33 kg at 3 months to 2.11 kg at 1 year, and from 2.11 kg at 1 year to 4.65 kg at ≥ 15 years (52).

2.2.3.3 Energy intake and physical activity.

Energy intake and physical activity are important regulators of body weight in the nonpregnant state (60) and are presumed to impact body weight in pregnancy and postpartum. Energy recommendations for lactating women suggest increased energy intake to satisfy the energetic demands required for breast milk synthesis and energy output (29). An additional 330 kilocalories per day (kcal/d; 500 [breast milk energy output] minus 170 [fat mobilization] kcal/d) is recommended during the first six months postpartum and 400 kcal/day (breast milk energy output) for the following months if women continue to breastfeed (29). For women who are not breastfeeding, the recommended energy intake is the same as the estimated energy requirements for adult nonpregnant nonlactating women (29).

Postpartum women are also encouraged to be physically active. In addition to having a positive impact on cardiovascular health (61), lipid profile (62), insulin sensitivity (61), and depression and anxiety symptoms (63), physical activity may help to facilitate weight loss after pregnancy. Current *Canadian Physical Activity Guidelines for Postpartum Women* (64, 65) recommend that "depending on the mode of delivery, most types of exercise can be continued or resumed in the postpartum period." The *Canadian Physical Activity Guidelines for Adults* (not pregnant) (66) recommend at least 150 minutes of moderate to vigorous intensity physical activity per week. Several prospective studies found increased energy intake (19, 50, 67), and lower amounts of physical activity (22, 46, 50, 68, 69) to be associated with PPWR. As a result, diet and physical activity are two common targets of interventions designed to reduce PPWR. A recent meta-analysis of 27 randomized trials including 4,610 postpartum women (70) demonstrated that combined dietary and physical activity interventions (ranging from 11 days to one year) resulted in greater mean weight loss than observed in controls after completion of the interventions (-2.49 kg; 95% CI -3.34 to -1.63; 12 studies with 1,156 women). The greater weight loss was maintained to one year postpartum in the intervention group compared to controls (-2.41 kg; 95% CI -3.89 to -0.93; 4 studies with 405 women).

2.2.3.4 Energy expenditure.

The basic components of energy balance include energy intake, energy expenditure, and energy storage (71). Therefore, body weight change is the result of an imbalance between dietary intake and energy expenditure to maintain life and to perform physical activity. The energy balance concept is complex in the postpartum period as women are expected to lose the weight they gained during pregnancy while maintaining sufficient energy to support lactation. Several studies have assessed energy expenditure in the postpartum period (72-81), mainly to determine the metabolic adaptations related to the energy cost of lactation. However, the impact of energy expenditure on body weight regulation has not been well documented during this life stage, and it is still controversial in the field of obesity (82). A cohort of more than 600 nonpregnant nonlactating subjects (83) demonstrated that lower-than-expected values of 24-h energy expenditure were predictive of both weight gain and fat mass (FM) increase. However, findings reported by different cohort studies (84, 85) demonstrated no association between energy expenditure and changes in body weight over time.

These conflicting findings about the relationship between energy expenditure and body weight may be related to differences in body composition. The main determinant of resting energy expenditure (REE) is fat-free mass (FFM), the most metabolically active compartment, which explains between approximately 50% and 70% of the variability in REE (86-88). Overall, increases in body weight occur alongside increases in both FM and FFM, wherein heavier individuals tend to have higher amounts of both FM and FFM. Therefore, adjustment for body composition is crucial in assessing differences in energy expenditure between individuals (82) (see 2.3.4 Adjustment for body composition and residual energy expenditure below for a detailed description).

Another important aspect to consider in the relationship between energy expenditure and body weight is the impact of lipid soluble persistent organic pollutants on adaptive thermogenesis. Accumulation of these compounds in the body seems to be related to fat mass, with individuals with obesity having a higher plasma organochlorine concentration than those without obesity. Indeed, some of these compounds (e.g. organochlorines) may be associated with altered immune and thyroid functions and with some types of cancer as well as with skeletal muscle oxidative potential (89). Tremblay and colleagues (90) demonstrated that after weight loss, the increased plasma organochlorine concentration was the factor explaining the greatest proportion of the residual sleep energy expenditure (SleepEE). Therefore, persistent organic pollutants might be a factor affecting the control of thermogenesis in some individuals experiencing body weight loss, deserving further investigation in postpartum women.

As previously mentioned, most of the knowledge on energy expenditure in the postpartum period is based on research focused on quantifying the metabolic adaptations to lactation. Investigations that examine energy expenditure in the postpartum period and its relationship to body weight regulation are needed.

2.2.3.5 Cardiorespiratory fitness.

Another benefit of regular physical activity in the postpartum period is that it can improve women's cardiorespiratory fitness (CRF) (91, 92), which in turn may be associated with less weight retention. CRF refers to the ability of the circulatory and respiratory systems to efficiently supply oxygen to the skeletal muscles during sustained physical activity (93). CRF is an important indicator of overall health status and is inversely associated with cardiovascular morbidity and mortality (93-97). CRF is usually expressed as maximum oxygen consumption ($\dot{V}O_2$ max) and is defined as the greatest rate at which a person is able to consume oxygen during sustained, exhaustive exercise (98). $\dot{V}O_2$ max is typically measured by indirect calorimetry while a person performs maximal, graded exercise tests on a treadmill, a cycle ergometer, or during a step test (93, 99). If a maximal exercise test is not possible due to physical or physiological limitations of the person being measured, a sub-maximal test such as the modified Bruce protocol is recommended (100). In this case, $\dot{V}O_2$ max is predicted rather than measured (i.e., $p\dot{V}O_2$ max).

A 20-year longitudinal study of 459 Canadian adults (236 women) (101) explored the association between body weight regulation and CRF, and found that CRF was an important predictor of weight gain, and low levels of CRF were associated with a higher future risk of obesity (OR 0.87; 95% CI 0.76, 0.99). Women with a higher $\dot{V}O_2$ max were less likely to experience a weight gain of $\geq$ 10kg over time (OR 0.82; 95% CI 0.72-0.93). Another study that assessed changes in physical activity, CRF, and strength in postpartum women of varying BMI (102) found that women at 27 weeks postpartum with a higher BMI had a lower $\dot{V}O_2$ max compared to women with a normal BMI.

2.2.3.6 Lactation.

Lactation has important health benefits both for the child and the mother (103). One potential benefit of lactation is its impact on body weight regulation after pregnancy. During pregnancy, physiological changes occur in the maternal metabolism to support the developing fetus and allow accumulation of energy stores for lactation (104). The premise of the reset hypothesis is that lactation plays an important role in mobilizing fat stores accumulated during pregnancy and reversing metabolic changes that promote fat accumulation, which in turn facilitates weight loss and reduces a woman's metabolic disease risk in the long term (104). These metabolic changes include, for example, re-establishing glucose homeostasis (75) and mobilizing lipids for milk synthesis (75, 104). Another potential explanation for the inverse association between lactation and PPWR is the high energetic demand process of lactation, since 400 to 500 kcal/d is expended for breast-milk-related energy output (29). Along with increased energetic demands of lactation, pregnancy-related hormones may also explain the effect of lactation on PPWR. The decreased levels of progesterone observed after childbirth and infant sucking stimulation can promote the release of prolactin, which decreases the level of estrogen and enhances the mobilization of adipose tissue stores (105).

A recent meta-analysis of 14 cohort studies (106) indicated that lactating women retained 0.38 kg (95% CI 0.64, 0.11 kg) less postpartum weight compared with women who bottle-fed their children. This meta-analysis also demonstrated that breastfeeding for 6 to 12 months is associated with decreased PPWR, but that breastfeeding for less than 6 or beyond 12 months was not associated with PPWR. Even though there are physiologic effects of lactation that may result in weight loss and studies confirming this association (22, 46, 50, 107-110), other studies did not report this effect (103, 111). These conflicting findings may be related to variations in study design, samples, group comparison, and time frame in the postpartum period. Hence, the role of lactation on postpartum weight change remains debatable.

2.2.3.7 Appetite.

Given that energy intake is one of the components of the energy balance equation, suboptimal regulation of food intake may facilitate the development of obesity (71). Many factors play a role in the regulation of food intake, including appetite control systems. In the most simplistic terms, energy homeostasis is the mechanism by which an organism reduces or induces energy intake when energy expenditure decreases or increases, respectively (112). For instance, an increase in energy expenditure is predicted to be followed by appetite stimulation and concomitant food intake initiation to maintain energy homeostasis (113-115). Appetite correlates with BMI and body composition (116-119), and can predict weight change (116, 120, 121). Most studies in obesity research suggest that appetite predicts subsequent energy intake, which further impacts body weight (120-122). Drapeau and colleagues (120) reported that reduced appetite sensations were associated with weight loss in 315 men and women (involved in six weight loss intervention studies), in which fasting, desire to eat, hunger, and prospective food consumption (PFC) were the best predictors of weight loss. The evidence linking appetite to body weight during the postpartum period is limited, and most research focuses on appetite-regulating or lactation-related hormones to assess the role of appetite in weight loss. For example, Larson-Meyer and colleagues (123) reported that circulating concentrations of appetite-regulating hormones were not predictive of PPWR and that higher postprandial ghrelin levels were observed in women who retained postpartum weight at the end of the first postpartum year. Since ghrelin is an orexigenic hormone, it may prevent weight loss by promoting increased appetite and/or reduced fat oxidation. Given the paucity of data that explores the association between maternal appetite control and body weight, further research is warranted.

2.2.3.8 Other factors.

Maternal characteristics including age, ethnicity, parity, socioeconomic status, and educational attainment have been found to be associated with PPWR (18, 22, 46, 50, 59, 124). Other factors such as sleep patterns (125) and psychological factors (e.g., depression, anxiety, and stress symptoms) (50, 126-128) have also been associated with PPWR. Some research suggests that obesity increases in parallel with decreased sleep; thus, this relationship could be a relevant component in postpartum weight regulation, given that sleep deprivation is a common characteristic in the postpartum period (129). Along with sleep patterns, psychological factors are also altered during the postpartum period. Phillips et al. (130) proposed a conceptual model of psychological predictors of PPWR that asserts that psychological factors are implicated in women’s ability to partake in healthful behaviours, which in turn impact PPWR. In conclusion, these findings represent the complex array of factors that influence PPWR, and understanding them may be helpful for targeting interventions.

2.3 Energy Metabolism of Postpartum Women

As previously discussed, energy intake and energy expenditure are the two main components of the energy balance equation (131). Understanding energy expenditure is therefore essential for accurate energy recommendations for weight management in the postpartum period. Thus, this section reviews the basic principles of each component of energy expenditure and measurement techniques used to assess them. The section then presents a detailed comparison of total energy expenditure (TEE) and its components in lactating and nonlactating women.

2.3.1 Methodological considerations for the assessment of energy expenditure.

TEE is comprised of three main components: resting (or basal) energy expenditure (REE or BEE), thermic effect of food (TEF), and activity energy expenditure (AEE) (132). REE can be further divided into energy expenditure during sleep (sleep energy expenditure; SleepEE) and energy used to maintain wakefulness without physical activity (i.e., REE = SleepEE + cost of arousal) (132). **Figure 2.1** describes important methodological considerations and key determinants of the three components of TEE.

2.3.1.1 Energy expenditure during resting conditions.

Basal metabolic rate (BMR) is the rate of energy expenditure of cellular and tissue metabolism needed to sustain physiological activity at complete rest (133). It accounts for approximately 50% to 75% of TEE and is usually expressed as kcal per minute (kcal/min) (134). Resting metabolic rate (RMR) represents BMR plus small amounts of additional energy expenditure, and it is usually 3% to 10% higher than BMR (134). Sleep metabolic rate (SMR) is another measure of energy expenditure assessed under resting conditions. It represents the energy expended during an overnight sleep, is 5% to 10% lower than BMR, and does not include the cost of arousal (135). Once BMR, RMR, and SMR are extrapolated to 24 h, they are defined as BEE, REE, and SleepEE, respectively, and expressed as kcal/d (29).

2.3.1.2 Thermic effect of food.

TEF refers to the increase in energy expenditure associated with the ingestion, digestion, absorption, and storage of food, constituting approximately 10% of TEE when consuming a mixed-nutrient diet (29, 134, 136). TEF is highly variable, with reported within-subject CV of greater than 20% (137, 138). Given the limited consensus about how TEF is mathematically defined and calculated, the long measurement durations that place a considerable burden on the participant, the variability in measuring BEE/REE and postprandial energy expenditure, as well as day-to-day biological variation in postprandial processing of nutrients, TEF is assumed to be 10% of TEE in most research studies (132).

2.3.1.3 Activity energy expenditure.

AEE accounts for energy expended in muscular work during spontaneous and voluntary exercise (132), and it refers to all energy consumed beyond REE and TEF (i.e., *AEE = TEE - REE - TEF*). AEE is the most variable component of energy expenditure, ranging from approximately 15% of TEE in very sedentary individuals to 50% or more in highly active people (139). It can be further divided into structured exercise (planned, repetitive, and purposive activities, such as sports, cycling, dancing) (140) and non-exercise activity thermogenesis (all occupation, leisure, sitting, standing, and ambulation activities) (139).

Two additional terminologies related to AEE are physical activity level (PAL) and physical activity coefficient (PA). PAL is the ratio of TEE to REE (i.e., *PAL = TEE/REE*), and it is the most common way to describe AEE (29). It is categorized into sedentary (PAL $\geq 1.0 < 1.4$), low active (PAL $\geq 1.4 < 1.6$), active (PAL $\geq 1.6 < 1.9$), and very active (PAL $\geq 1.9 < 2.5$) (29). PA is used in the estimated energy requirement equations and is based on the PAL categories (29), as follows: PA = 1.00 if PAL is estimated to be $\geq 1.0 < 1.4$ (sedentary); PA = 1.12 if PAL is estimated to be $\geq 1.4 < 1.6$ (low active); PA = 1.27 if PAL is estimated to be $\geq 1.6 < 1.9$ (active); PA = 1.45 if PAL is estimated to be $\geq 1.9 < 2.5$ (very active) (29).

2.3.1.4 Respiratory quotient and macronutrient oxidation.

The chemical composition of fats, carbohydrates, and proteins differ, and the amount of $\dot{V}O_2$ and $\dot{V}CO_2$ during the oxidation of these macronutrients vary. The ratio of $\dot{V}CO_2$ to $\dot{V}O_2$ can be used to provide a ratio of the fuel mixture being oxidized under different conditions (141). Carbohydrates are oxidized through aerobic respiration, resulting in an equal ratio of carbon dioxide release and oxygen consumption; therefore, a RQ of 1.0 reflects the exclusive oxidation of carbohydrates. It is generally accepted that a value of 0.7 indicates the exclusive metabolism of fat, and anywhere within this range indicates that a mixture of substrates is oxidized simultaneously (142). Thus, RQ indicates nutrient utilization such that a higher RQ corresponds to greater reliance on carbohydrates as the primary energy source, whereas a lower RQ indicates greater fat oxidation (143).

Protein is broken down into amino acids and deaminated before it can be oxidized. The amount of protein oxidized may be estimated from the amount of nitrogen excreted in a 24-h pooled urine sample. The classical value that has been used in the literature is 6.25 g of protein per gram of nitrogen; as such, the excretion of 1 g of nitrogen equates to the oxidation of approximately 6.25 g of protein (144, 145). Thus, when coupled with measures of 24-h urinary nitrogen excretion, indirect calorimetry derives protein oxidation data and informs on macronutrient utilization (132, 142). The measures of macronutrient oxidation have traditionally been calculated using stoichiometric equations (141). In this thesis, the equation by Brouwer (146) was used to calculated daily carbohydrate and fat oxidation **(Equations 1 and 2)**.

$$\textit{Carbohydrate oxidation (g/d)} = (4.170 \times \dot{V}CO_2) - (2.965 \times \dot{V}O_2) - (0.390 \times P)$$

Equation 1. Daily carbohydrate oxidation rates calculated according to Brouwer's equation (146). Where $\dot{V}O_2$ and $\dot{V}CO_2$ are in litres per day, and P is in grams per day. $\dot{V}O_2$: Volume of oxygen consumption; $\dot{V}CO_2$: Volume of carbon dioxide production; P: protein oxidation.

$$\textit{Fat oxidation (g/d)} = (1.718 \times \dot{V}O_2) - (1.718 \times \dot{V}CO_2) - (0.315 \times P)$$

Equation 2. Daily fat oxidation rates calculated according to Brouwer's equation (146). Where, $\dot{V}O_2$ and $\dot{V}CO_2$ are in litres per day, and P is in grams per day. $\dot{V}O_2$: Volume of oxygen consumption; $\dot{V}CO_2$: Volume of carbon dioxide production; P: protein oxidation.

2.3.1.5 Special considerations during lactation.

The energy cost of milk production is composed of the energy required for its synthesis and secretion and the energy content of milk (i.e., breast milk energy output) (80). TEE encompasses the synthetic cost of milk production; however, the actual energy content of the breast milk is not a component of TEE (76). In fact, in most research studies, breast milk energy output is estimated by the amount of milk that is produced and secreted, its energy content, and the efficiency with which dietary energy is converted to milk energy (72, 76, 80). The most widely accepted method for measuring the amount of milk that is produced and secreted is the infant test weighing, a procedure in which the infant is weighed before and after each breastfeeding episode, using a balance scale accurate to ±1 g (147). According to the Food and Agriculture Organization, World Health Organization, and United Nations University's (FAO/WHO/UNU) *Human Energy Requirements* report (136), to estimate breast milk energy output, breast milk volume should be corrected for insensible water losses (5%), assuming 1 g/mL breast milk, 0.67 kcal/g for energy content of breast milk, and an efficiency factor of 80%.

The current energy recommendation (29) states that breast milk energy output is estimated to be ~500 kcal/d for the first six months of lactation and ~400 kcal/d after this period. This energy output was estimated from the average milk production rates of 0.78 L/d from birth through 6 months of age (148, 149), and 0.6 L/d from 7 through 12 months of age (150). The energy density of human milk has been measured by bomb calorimetry or proximate macronutrient analysis of representative 24-h pooled milk samples (151-153), and the value of 0.67 kcal/g is used in the Institute of Medicine (29) and FAO/WHO/UNU *Human Energy Requirements* report (136).

2.3.1.6 Measuring total energy expenditure.

TEE can be measured using techniques that fall into three main categories: 1) direct calorimetry, which directly measures the rate of bodily heat production; 2) indirect calorimetry, which measures oxygen consumption and carbon dioxide production, which, in turn, are converted to energy expenditure using a formula; or 3) non-calorimetric techniques, which estimate energy expenditure by extrapolation from physiological measurements and observations (132, 154). Only the technique relevant to this thesis, indirect calorimetry by whole body calorimetry (WBC), is hereby discussed.

Whole body calorimetry

The indirect calorimetry method assesses energy expenditure by simultaneously measuring volume of oxygen consumption ($\dot{V}O_2$), and volume of CO_2 production ($\dot{V}CO_2$) (155), and it can be conducted for several days (156). Although there are different types of indirect calorimetry instruments, such as metabolic carts, portable indirect calorimeters, and live-in whole body calorimetry units (WBCU), only the WBC technique feasibly measures TEE. The use of this technique to measure TEE was pioneered in the late 1970s by Jéquier’s laboratory in Lausanne (157), and in the Dunn Clinical Nutrition Centre in Cambridge (158). In the late 1980s, Ravussin and colleagues (159) described a modified design of the WBCU, which has since been widely adopted in clinical research facilities. The TEE is calculated most often using Weir's equation (160), based on the measurements of $\dot{V}O_2$, $\dot{V}CO_2$, and urinary nitrogen excretion **(Equation 3)**.

$$TEE\ (kcal/d) = (3.941 \times \dot{V}O_2) + (1.106 \times \dot{V}CO_2) - (N \times 2.17)$$

Equation 3. Total energy expenditure calculated according to Weir's equation (160). Where, $\dot{V}O_2$ is the volume of oxygen consumption in litres/day; $\dot{V}CO_2$ is the volume of carbon dioxide production in litres/day; and N is the urinary nitrogen excretion in grams/day.

According to Dulloo and colleagues (161), the 24-h TEE measurements performed in a WBCU can reach a high-level accuracy (2–3%) and precision (1–2%). The within-subject CV for a WBCU assessing TEE is 2% to 3% (159, 161); the WBCU used in this thesis resulted in a within-subject CV of 2.2% for TEE (unpublished data). A unique feature of the WBCU is to provide real-time energy expenditure data that makes it ideal to distinguish and investigate TEE and its components integrated over 24 h while maintaining strict experimental protocol conditions (145, 161). It also measures RQ and macronutrient oxidation rates (133, 145) (see 2.3.1.4 Respiratory quotient and macronutrient oxidation above for a detailed description). Limitations of the WBCU method include the high cost and the need for highly qualified personnel (133). Since the participant must be confined to a live-in unit, the method may underestimate AEE compared to free-living conditions (161). Another disadvantage of the confinement method relevant for postpartum women is the separation of the lactating mother from her infant for a prolonged period of time.

2.3.2 Energy expenditure in the postpartum period.

This section of the literature review discusses energy metabolism in the postpartum period, and comprises studies that measured TEE using either doubly labeled water (DLW) (for details of methodological aspects refer to a recent review by Westerterp (162)) or WBC. These state-of-the-art tools were used to measure TEE, and compare lactating and nonlactating women. Given that studies measuring TEE usually do not measure TEF, studies comparing measurements of TEF between lactating and nonlactating women are also included here. Thus, this section summarizes findings about TEE and its components (BEE/REE and SleepEE, TEF, and AEE/PAL) among lactating and nonlactating women. Intervention studies (diet and/or exercise) are beyond the scope of this review.

A total of 10 studies were considered (72-81). Of the six studies that assessed TEE, four utilized DLW (72-74, 76) and two used WBC (75, 77). Five studies assessed TEF (74, 78-81), and one study assessed both TEE and TEF (74). Four studies were conducted in the United States (74-76, 80); two studies were conducted in the United Kingdom (72, 79), two in the Gambia (77, 78), one in Sweden (73), and one in the Netherlands (81). Studies were conducted between 1986 and 2001. Six (72-76, 81) were of longitudinal design, and four (77-80) were of cross-sectional design. The Gambian women did not present any clinical signs of malnutrition, and all other studies reported being conducted in well-nourished women. Lactating women were studied at various points during the postpartum period, ranging from four weeks to six months postpartum. The comparison groups of nonlactating women were defined differently among the studies, and included women either in the prepregnancy state (73, 74, 81), post-weaning state (72, 76, 79), formula-feeding women (75, 79, 80), or a control group of women who were not recently pregnant (77-80).

2.3.2.1 Energy expenditure during resting conditions.

Most studies (n= 9) (72-80) reported that the BMR/RMR values were not affected by lactation, as values were similar between lactating and nonlactating women. Only one study (81) reported a higher RMR value during lactation than during the nonlactating state. It is reasonable to assume that human milk synthesis is a continuous process that elevates BMR/RMR in lactating women due to the energy cost of milk synthesis (76). The fact that in most of the studies BMR/RMR was not higher during lactation, compared to women in other phases of life, may indicate that one or more components of metabolism were suppressed during this period; a finding that provides some evidence for energy-sparing adaptations to lactation (72). In summary, the majority of studies suggest no differences in energy expenditure at rest during lactation, which contradicts the belief that elevated BMR/RMR contributes to increased energy needs (80). Currently, there is little evidence of energy conservation, and it appears that BMR/RMR is constant or slightly elevated during lactation (76).

Only one (75) of the ten studies assessed the difference in SleepEE between lactating and nonlactating women. This was a longitudinal study investigating the energy expenditure and substrate utilization during late pregnancy (37 weeks gestation) and lactation (12 and 24 weeks postpartum) in North American women. SleepEE was assessed by indirect calorimetry using the

WBC method, and it was affected by the lactation process; higher values were observed in the lactating group versus the nonlactating group. This area is, therefore, important for future research as changes in sleep patterns are common in the postpartum period and the effect of lactation on SleepEE has not been adequately studied in postpartum women.

2.3.2.2 Thermic effect of food.

Five studies (74, 78-81) measured the difference in TEF responses during lactation and the nonlactation state. Of the five, three studies (74, 78, 81) reported no difference between groups; one study (79) reported lower TEF values in lactating women; and another (80) showed that TEF was higher over the course of lactation compared to a nonlactation state. Illingworth et al. (79) found that the response to a meal was lower in lactating women compared to the control group who had not been pregnant recently. When measurements were repeated post-weaning, TEF increased; it was higher than when these women were lactating and similar to that of the control group. In addition, TEF was similar among lactating women and women who bottle-fed their babies, which implies a reduced metabolic response to a meal in the postpartum state regardless of infant feeding type.

Conflicting findings between studies may be explained by differences in protocols, such as baseline measurement, duration of the post-meal measurement period, the timing of measurements (intermittent versus continuous), as well as the methods used to calculate TEF (163, 164). For example, the post-meal measurement period for the studies included in this review ranged from 120 minutes (80) to up to 240 minutes (74). Previous studies reported that TEF response may take as long as 8 to 10 h after consumption of large meals (i.e., 1,000 kcal), and longer than 3 to 6 h for smaller meals (i.e., between 400 and 1,000 kcal) (164). Therefore, it is likely that these studies have not assessed the full TEF response.

In summary, current evidence about the changes in TEF during lactation is inconclusive. However, when expressed over 24 h, the increases and/or decreases have a negligible effect on TEE. Therefore, available evidence does not support significant changes in TEF during lactation, and the assumption that TEF remains unchanged during lactation appears to be reasonable.

2.3.2.3 Activity energy expenditure and physical activity level.

Of the 10 studies, seven compared physical activity between lactating and nonlactating women (72-77, 81) using different approaches. Three studies (72-74) calculated AEE according to the equation ($AEE = TEE - BMR$). One study (76) used the equation [$AEE = TEE - (BMR + 0.1 \times TEE)$] and the seven-day recall method of physical activity, while one study (81) used indirect calorimetry. The remaining two studies (75, 77) used indirect calorimetry and the radar Doppler principle. When comparing AEE values between lactating and nonlactating women, one study (72) found the AEE value to be significantly lower in the lactating women, two studies (75, 77) reported higher AEE in lactating women, and four (73, 74, 76, 81) found similar results between the groups.

Of the seven studies (72-77, 81) that assessed physical activity, six (72-77) reported PAL values, four (72-74, 76) used DLW, and two (75, 77) used WBC methodologies. All four DLW studies (72-74, 76) reported PAL values that were consistently lower among lactating women than nonlactating women. Decreases in AEE and PAL values during lactation may be due to differences in activity patterns, as lactating women are more likely to spend more time doing sedentary and light activities due to required periods of rest associated with breastfeeding. In both WBC studies (75, 77), the PAL values were higher in lactating women than in nonlactating ones. It is important to emphasize that physical activity undertaken in a WBCU is not representative of activities encountered under free-living conditions. Overall, most research (5/7) found that the lactation process either did not alter AEE or tended to decrease energy expenditure associated with physical activity, especially in a free-living context.

2.3.2.4 Total energy expenditure.

Four studies (72-74, 76) used DLW to assess differences in TEE between lactating and nonlactating women. All four studies were conducted in healthy, well-nourished women aged 28 to 31.7 years. Comparing TEE values between lactating and nonlactating women, one study (72) found a difference between these two groups. In this study at 4, 8, and 12 weeks lactation, average TEE was lower than in nonlactating women, with the differences in TEE being 225, 164, and 197 kcal/d, respectively, ($P < 0.01$) (72). The other three studies (73, 74, 76) found similar TEE values between lactating and nonlactating states.

To date, only two studies (75, 77) have assessed the difference in TEE between lactating and nonlactating women using WBC. One study (75) was conducted longitudinally in the United States with 76 healthy women, including 40 lactating women and 36 nonlactating women (exclusively formula-feeding) at 12 and 24 weeks postpartum. The other was a cross-sectional study (77) carried out with 32 healthy Gambian women where 16 lactating women at 8 weeks postpartum were compared to 16 nonlactating women. The study in the Gambia (77) measured the combined energy expenditure of the mother and infant over 24 h in a WBCU and subtracted the infant's energy expenditure from the combined energy expenditure values to estimate the lactating mother's TEE. According to the authors (77), this approach allowed the calculation of the extra energy requirements for lactation using the energy retained by the infant for growth in conjunction with calorimetric measurements of the combined energy expenditure of mother and infant. However, the lactating mother's TEE was estimated—not necessarily measured—which may impact the accuracy of the value. Comparing the TEE of lactating versus nonlactating women, both studies (75, 77) found higher TEE in the lactating state. In the North American women, the TEE postpartum values were 4% to 5% higher in the lactating than in the nonlactating group (75). The TEE values of the Gambian lactating women (subtracting the infant's energy expenditure) were approximately 13% higher than in the nonlactating group (77).

In summary, findings related to the impact of lactation on TEE are conflicting. Most studies (73, 74, 76) did not find a difference in TEE values between lactating and nonlactating women. However, one study (72) reported lower TEE values, and two studies (75, 77) reported higher TEE values in the lactating state than in the nonlactating state. These conflicting findings may be driven by the variability in physical activity described in the previous section.

2.3.2.5 Respiratory quotient and macronutrient oxidation.

Four (75, 77, 78, 81) studies measured RQ values at different times of the day and compared RQ in lactating and nonlactating women. Only one study (81) assessed RQ in the same women before pregnancy and during lactation; other studies (75, 77, 78) assessed it in different women who were lactating and nonlactating. Two studies (75, 77) assessed RQ using WBC, and two (78, 81) using a metabolic cart. Fasting RQ did not differ between lactating and nonlactating women in three studies (75, 77, 78), and was lower during lactation (0.82 ± 0.03) compared to before pregnancy (0.85 ± 0.03; $P < 0.001$) in one study (81).

Postprandial RQ was compared between lactating and nonlactating women in two studies; Frigerio et al. (78) found similar values between groups, while Spaaij and colleagues (81) reported that postprandial RQ was lower during lactation (0.86 ± 0.02) than in the nonlactating state (0.89 ± 0.02; $P < 0.001$). Two other studies (75, 77) measured the 24-h RQ, and found that lactating women had a similar RQ (0.89 ± 0.01) compared to nonlactating women (0.88 ± 0.01, $P > 0.05$) (77), but a significantly higher RQ was observed in lactating (0.88 ± 0.02) compared to nonlactating women (0.86 ± 0.02, $P < 0.05$) in another study (75). Some authors have suggested that a higher RQ in lactation is the result of preferential use of glucose by the mammary gland (75), stimulating the lipogenic pathway, which would lead to an RQ > 1.0 (77), and could potentially explain the elevated 24-h RQ and carbohydrate utilization in lactating women (75).

2.3.2.6 Summary.

Overall, the available evidence suggests there is no difference in energy expenditure during the lactation process at rest and in the postprandial state. There were conflicting results on whether RQ values are affected by the lactation process, and no conclusions can be drawn about SleepEE, as only one study assessed this component and reported that lactation increased SleepEE. On the basis of the studies reviewed here, it is reasonable to conclude that differences in TEE are mostly explained by the variability in physical activity. However, most of our knowledge about TEE in the postpartum period using DLW and WBC methodologies dates back to research done at least 15 years ago. Thus, further research using controlled protocols to assess TEE in contemporary postpartum women is needed.

2.3.3 Predicting energy expenditure in postpartum women.

Predictive equations are useful for estimating energy expenditure in clinical practice and in research studies when it cannot be measured. A recent study (165) assessed the accuracy of 28 predictive equations in 1,726 outpatients with malnutrition, eating disorders, or obesity, and noted that the predicted energy expenditure using the Harris-Benedict equation was within 10% of measured energy expenditure in 72.9% of patients. To my knowledge, no study has assessed the accuracy of TEE estimations, and only one study (166) has examined the accuracy of REE prediction in postpartum women. De Sousa et al.'s (166) cross-sectional study measured REE in the immediate postpartum period and reported that, in most cases, predictive equations overestimated measured REE; all equations showed low agreement and accuracy compared to measured REE. It is important to investigate the accuracy of predictive equations to estimate REE and the current DRI recommendation for energy at different times in the postpartum period to identify the most suitable equation for this population.

2.3.4 Adjustment for body composition and residual energy expenditure.

Another relevant methodological consideration is the importance of adjustments for body composition when comparing energy expenditure longitudinally or between groups of individuals (167). There have been various approaches to mathematically adjusting for these changes in the ratio between REE and body composition, including log-log regression (168), generalized linear modeling, analysis of covariance (169), or residual energy expenditure from multiple linear regression (170). The use of the residual energy expenditure method (e.g., residual REE or residual SleepEE) for describing energy metabolism deviations is used increasingly (90, 171-178), and it is defined as the difference between measured and predicted energy expenditure. Leibel and colleagues (177) were pioneers in the use of this methodological approach; they demonstrated that measured energy expenditure after weight loss was lower than predicted by changes in body composition. This approach is calculated by applying a multiple linear regression model, with measured REE/SleepEE as the dependent variable, and FFM, FM, and other variables such as age and sex as independent variables.

In longitudinal studies, multiple linear regression analysis is used to generate an equation for REE/SleepEE for the entire cohort at baseline, and then this equation is used to predict REE/SleepEE values at follow-up points (90, 172, 174, 175, 177, 178). If changes in energy expenditure are proportional to changes in body composition, the predicted REE/SleepEE will be equal to the measured value. Significant differences in residual REE/SleepEE indicate that changes in energy expenditure are not explained by individual changes in FFM and FM.

Residual REE/SleepEE is also used in cross-sectional studies to evaluate abnormal metabolism (i.e., low or high metabolism) for a given individual relative to the whole cohort (171, 173, 176). Abnormal metabolism can be defined according to tertiles or by using a set distance from the regression line (e.g., 100 kcal) (171). When energy expenditure is proportional to body composition, predicted REE/SleepEE equals measured REE/SleepEE, and therefore, the higher the residual REE/SleepEE the higher the metabolism (high metabolism) relative to the entire cohort (171).

2.4 Appetite

Another crucial aspect of the study of energy balance is the role of food intake and other behavioural and metabolic influences on appetite (179). The physiology of appetite regulation comprises three main components: 1) a tonic drive for food arising from the physiological demand for energy (i.e., excitatory feature of appetite); 2) a tonic inhibition for food arising from signals of energy storage (i.e., inhibitory feature of appetite); and 3) episodic signals arising from the mouth and gastrointestinal tract in response to the periodic consumption of food (i.e., mainly inhibitory from satiety signals but also excitatory from food palatability signals) (180).

2.4.1 Determinants of appetite.

The control of appetite is complex and involves the coordination of inputs from physiological and behavioural determinants. Thus, different factors predict appetite. Classically, these factors were based on theoretical approaches that considered signals from glucose (glucostatic hypothesis (113)) and protein (aminostatic hypothesis (181)) metabolism, as well as adipose tissue (lipostatic hypothesis (182)). In the 1990s, there was an increased interest in the role of fuel utilization in the control of energy intake (183). Next, the focus was on pre-absorptive hormonal control of appetite, and on central nervous system models emphasizing other inputs from adipose tissue (i.e., leptin) and the gastrointestinal tract or associated organs (i.e., ghrelin, peptide YY, glucagon-like peptide 1, cholecystokinin, amylin and insulin) (112, 184). Along with all these factors, more recent studies have focused on body composition and energy expenditure and their contribution to regulating appetite (180, 185, 186). Thus, all of these factors might contribute to understanding the relative impact of biological and behavioural cues of appetite on body weight regulation (180). The following section focuses on factors that are relevant to this thesis—specifically body composition, energy expenditure, macronutrient oxidation, and lactation. Most current studies that assess the determinants of appetite do not involve postpartum women, and due to this paucity of data, studies conducted in other populations are reviewed in the following discussion. This gap in the research highlights the importance of the examination of these relationships in the postpartum period; a state of metabolic transition.

2.4.1.1 Body composition.

Since the discovery of leptin, the literature has focused on adipose tissue (or FM) as an important determinant of appetite. Several studies have demonstrated that the hypothalamic neuropeptide pathways regulating the stimulation and inhibition of food intake are influenced by leptin (184, 187-190). Although there is extensive literature on adipose tissue and leptin, a limited number of human studies have explored the effects that changes in adipose tissue exerts as a negative feedback signal on energy intake. More recent integrative models of energy balance regulation have used multiple regression models or mediation models with a path analysis approach to explore the relationships of FM, FFM, appetite, energy expenditure, and body weight (186, 191-193). These models have demonstrated that FFM is a strong predictor of energy intake. For example, Blundell et al. (191) investigated the relationship between body weight and composition with meal size and energy intake over a 12-week intervention period in 92 obese adults (BMI 31.6 ± 4.3 kg/m^2), and found that FFM, but not FM or BMI, was associated with meal size and daily energy intake. In a study that investigated the relationship of body composition with *ad libitum* food intake among 184 individuals with a wide range of adiposity (192), the researchers demonstrated that FFM index (i.e., FFM adjusted for height in meters squared; kg/m^2) was positively associated with mean daily energy intake, and mean daily intake of protein, carbohydrates, and fat. A recent study (185) found that FFM was a strong determinant of energy intake, but this effect was mediated by RMR, and FM was associated with energy intake via two opposing pathways: 1) a weak indirect positive association (mediated via RMR), and 2) a stronger direct negative association. The implication of this relationship is that the energy required to maintain the metabolically active tissue of the body (i.e., FFM) creates a physiological demand that acts as a signal to drive food intake (185).

2.4.1.2 Energy expenditure.

Energy expenditure may generate a tonic signal of energy demand that could act as a drive for food, with appetite control being a function of energy balance (180). This relationship is in accordance with the hypothesis proposed by Mayer (114, 115), which states that any increase in energy expenditure will be met with an equivalent increase in energy intake to maintain energy homeostasis. The relationships between body composition, energy intake, and expenditure were explored under controlled laboratory conditions in a study (186) with 59 subjects (BMI 26.1 ± 3.8; range 17.9–35.9 kg/m^2; 29 women) during a 14-day residential stay. The researchers found that RMR was a strong independent predictor of *ad libitum* energy intake (186). Similarly, Caudwell et al. (194) conducted a 12-week intervention with 41 adults with overweight and obesity (BMI 30.7 ± 3.9; 27 women) who were tested under conditions of varying physical activity (sedentary or active) and dietary energy density (17 or 10 kJ/g), and they confirmed that RMR was correlated with meal size, energy intake, and hunger ratings assessed by visual analogue scales (VAS). As discussed previously, it is plausible that energy expenditure mediates the impact of FFM on appetite control. This hypothesis was recently tested by Hopkins and colleagues (185), who confirmed that, although FFM was a strong determinant of energy intake, this effect was mediated by RMR, such that FFM did not statistically influence energy intake independent of its effect on RMR. These findings indicate that the energy needs of the body may play an important role in day-to-day energy intake.

2.4.1.3 Exercise.

Exercise acts as a stimulus that challenges energy balance, and it is expected that a compensatory response in energy intake follows an increase in energy expenditure. This assumption is based on the premise that reduction of energy availability is met with compensatory responses in energy intake to maintain homeostasis (114, 115). Edholm and colleagues (195) also proposed that differences between food intake among individuals originate from differences in energy expenditure. Additionally, the glycogenostatic theory proposed by Flatt (196, 197) suggests that the depletion of glycogen stores may act as a biological stimulus for energy intake in an attempt to restore glycogen levels to a predetermined set point (196, 197). Thus, given that exercise increases energy expenditure and alters substrate availability, compensatory eating may be induced to maintain energy and substrate balance. Exercise has other physiological effects that may influence appetite, including an overall increase in heart rate, changes in the distribution of blood flow, sympathetic nervous system, and gut hormone activities (198). Thus, exercise interacts with other biological and behavioural responses meaning that compensatory responses are highly variable (199, 200).

2.4.1.4 Macronutrient oxidation.

Metabolic fuel utilization confers properties on behaviour in the regulation of energy balance, in which physiological mediators act as drivers of behaviour. For example, metabolic disturbances that impair fat oxidation are commonly cited as causal factors in the susceptibility to weight gain. The glycogenostatic theory (196, 197) suggests that feeding is designed to maintain glycogen stores at a specific set point, and any disturbance to availability is strongly defended. Thus, as carbohydrate availability is tightly regulated and there is limited storage capacity (~400–

800g), carbohydrate restoration is a metabolic priority after depletion (201). Evidence suggests that carbohydrate balance is associated with energy intake and body weight regulation (202-204), in which a negative carbohydrate balance has been shown to predict greater *ad libitum* intake (203, 204) and weight gain (202).

2.4.1.5 Lactation as a special consideration for postpartum women.

Lactation is another important factor that leads to unique physiological changes that may impact appetite control by increasing energy expenditure resulting from breast milk synthesis and its energy output (29). Since glucose is the preferential source of energy used by the mammary gland, carbohydrate oxidation and possible glycogen depletion (75) may influence appetite (196, 197). Along with the increased energetic demands of lactation and the preferential source of glucose by the mammary gland, daily duration of lactation may also influence appetite. Physical suckling stimulates prolactin, and animal studies suggest that an increase in energy intake observed in lactating rats may reflect signals that are dependent on the physical stimulation of suckling. These signals involve prolactin secretion and are independent of milk delivery per se (205-207). The daily duration of lactation episodes may impact appetite independently of breast milk energy output through prolactin-mediated effects.

2.4.2 Methodological considerations for the assessment of appetite sensations.

2.4.2.1 Visual analogue scales.

Visual analogue scales (VAS) are commonly used by psychologists and clinicians to assess subjective feelings of bodily sensations such as pain (208, 209). VAS are also one of the most common tools used to ask participants structured questions relating to aspects of their appetite (179). In appetite-related research, VAS usually consist of a 100 mm straight and unmarked line anchored at each end by opposite descriptors of different appetite dimensions (e.g., for the sensation of hunger, the anchor statement on the left end is “not at all hungry,” and on the right end is “extremely hungry”). Subjects place a mark on the line corresponding to their appetite rating. The distance from the left end of the line to the mark is measured and recorded (179, 210).

The validity and reproducibility of VAS for the assessment of appetite sensations have been reported by Flint et al. (211). The questionnaire described by Flint and colleagues (211) asks four questions related to appetite sensations: “How hungry do you feel?” (I am not hungry at all/I have never been more hungry); “How satisfied do you feel?” (I am completely empty/I cannot eat another bite); “How full do you feel?” (Not at all full/Totally full); and “How much do you think you could eat now?” (Nothing at all/A lot). VAS are an easy and efficient tool to administer, and they are simple to interpret because the standardized format allows for results to be compared across different studies (179). Tracking changes in subjective appetite sensations over time provides important information about how appetite fluctuates throughout the day (179).

2.4.2.2 Composite appetite score.

The four dimensions of appetite (hunger, PFC, fullness, and satiety) may be combined to calculate a single composite appetite score (CAS) (212). This combined score is used as a general measure of appetite, which is a score that reflects an overall “motivation to eat” phenomenon. CAS has been used in the literature as it integrates appetite sensation ratings into one index (213-215). Given that appetite sensation ratings are strongly related to each other, Reid et al. (216) applied principal components analysis to identify distinct dimensions in the responses to the appetite questions described above. The first principal component explained at least 85% of the variation, whereas participants usually rated fullness and satiety as the opposite of hunger and PFC questions. Thus, to reflect a single score that represents an overall “motivation to eat” phenomenon, fullness and satiety were reverse scored (i.e., unfullness and lack of satiety, respectively): the maximum measurable value of the scale (i.e., 100) minus the recorded value for fullness (unfullness = 100 - fullness), and satiety (lack of satiety = 100 - satiety). Therefore, CAS may be calculated as the mean of hunger, PFC, and the inverse of fullness (i.e., 100 - fullness), and satiety (i.e., 100 - satiety) **Equation 4.** A higher CAS value is associated with a greater appetite sensations and a stronger motivation to eat.

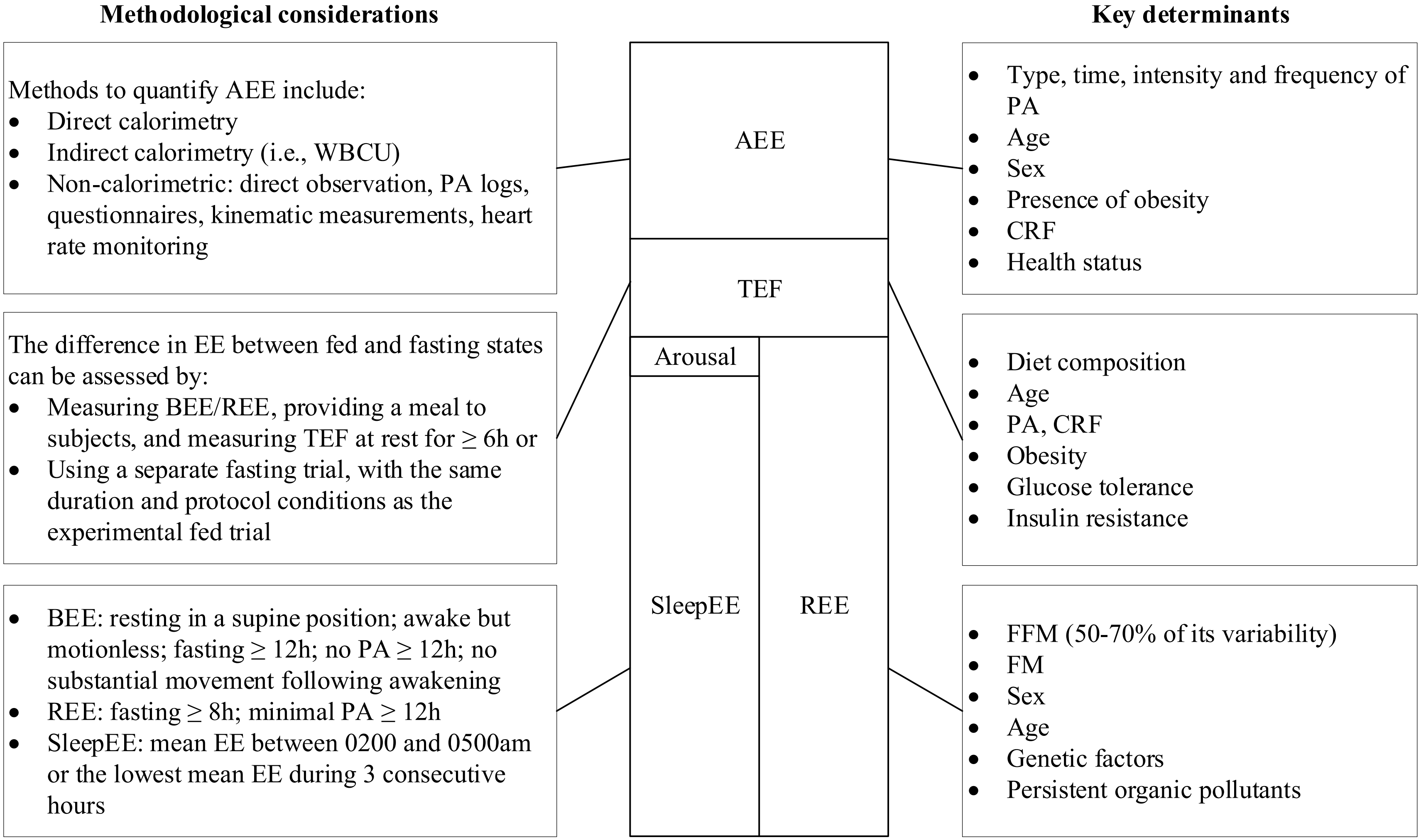
CAS (mm) = [hunger + prospective food consumption + unfullness (100 - fullness) + lack of satiety (100 - satiety)]/4.

Equation 4. Composite appetite score (CAS) (213-215).

2.5 Summary

The postpartum period includes several physiological changes, including changes in body weight. This period of transition is essential to reset women's physiology and metabolism. Although it is expected that, following childbirth, women will lose the weight gained during pregnancy, postpartum weight loss is highly variable. This high variability of PPWR may be explained by a multitude of factors that influence women's weight regulation during the postpartum period. This literature review has identified gaps in research about factors that may influence PPWR, such as energy expenditure, cardiorespiratory fitness, and appetite sensations, few of which have been well documented during this life stage. In addition, the potential impact of body composition, energy expenditure, macronutrient oxidation, and lactation on appetite sensations have also not been characterized in postpartum women. Understanding all these factors might be helpful for future targeted interventions and appropriate weight management strategies. More personalized and accurate energy recommendations are also essential for future strategies to promote appropriate postpartum weight management. This review demonstrates that there is minimal published information describing the accuracy of TEE and REE calculations. Overall, these oversights represent significant knowledge gaps in understanding energy expenditure in the postpartum period, and they need to be explored.

Thus, the research described in Chapters 3, 4, and 5 aims to investigate the energy metabolism profile of postpartum women, and to explore key metabolic variables associated with weight retention during this life stage. Additionally, the research examines the validity of predictive equations in the assessment of REE, and aims to assess the accuracy of current energy recommendations in predicting TEE in postpartum women.



Methodological considerations

Methods to quantify AEE include:
- Direct calorimetry
- Indirect calorimetry (i.e., WBCU)
- Non-calorimetric: direct observation, PA logs, questionnaires, kinematic measurements, heart rate monitoring

The difference in EE between fed and fasting states can be assessed by:
- Measuring BEE/REE, providing a meal to subjects, and measuring TEF at rest for ≥ 6h or
- Using a separate fasting trial, with the same duration and protocol conditions as the experimental fed trial

- BEE: resting in a supine position; awake but motionless; fasting ≥ 12h; no PA ≥ 12h; no substantial movement following awakening
- REE: fasting ≥ 8h; minimal PA ≥ 12h
- SleepEE: mean EE between 0200 and 0500am or the lowest mean EE during 3 consecutive hours

Key determinants

- Type, time, intensity and frequency of PA
- Age
- Sex
- Presence of obesity
- CRF
- Health status

- Diet composition
- Age
- PA, CRF
- Obesity
- Glucose tolerance
- Insulin resistance

- FFM (50-70% of its variability)
- FM
- Sex
- Age
- Genetic factors
- Persistent organic pollutants

Figure 2.1 Methodological considerations and key determinants of the three main components of total energy expenditure (TEE). TEE is comprised of resting (or basal) energy expenditure (REE or BEE), the thermic effect of food (TEF), and the activity energy expenditure (AEE). REE can be further divided into sleep energy expenditure (SleepEE) and the energy cost of arousal. Abbreviations: CRF, cardiorespiratory fitness; EE, energy expenditure; FFM, fat-free mass; FM, fat mass; PA, physical activity; WBCU, whole body calorimetry unit. Adapted from Lam and Ravussin (132).

2.6 References

1. de Boo HA, Harding JE. The developmental origins of adult disease (Barker) hypothesis. Aust N Z J Obstet Gynaecol 2006;46:4-14.
2. Barker DJ. The developmental origins of adult disease. J Am Coll Nutr 2004;23:588S-595S.
3. Institute of Medicine and National Research Council. Weight Gain During Pregnancy: Reexamining the Guidelines. Washington (DC): The National Academies Press, 2009. Available from: http://www.nap.edu/openbook.php?record_id=12584 (accessed March 13, 2019).
4. Health Canada. Prenatal nutrition guidelines for health professionals: gestational weight gain. Ottawa; 2010. Available from: http://publications.gc.ca/site/eng/378476/publication.html (accessed March 13, 2019).
5. Schmitt NM, Nicholson WK, Schmitt J. The association of pregnancy and the development of obesity - results of a systematic review and meta-analysis on the natural history of postpartum weight retention. Int J Obes (Lond) 2007;31:1642-1651.
6. Hutcheon JA, Chapinal N, Bodnar LM, Lee L. The INTERGROWTH-21st gestational weight gain standard and interpregnancy weight increase: A population-based study of successive pregnancies. Obesity (Silver Spring) 2017;25:1122-1127.
7. Haugen M, Brantsaeter AL, Winkvist A, Lissner L, Alexander J, Oftedal B, Magnus P, Meltzer HM. Associations of pre-pregnancy body mass index and gestational weight gain with pregnancy outcome and postpartum weight retention: a prospective observational cohort study. BMC Pregnancy Childbirth 2014;14:201.
8. Rooney BL, Schauberger CW. Excess pregnancy weight gain and long-term obesity: one decade later. Obstet Gynecol 2002;100:245-252.
9. Linne Y, Dye L, Barkeling B, Rossner S. Weight development over time in parous women--the SPAWN study--15 years follow-up. Int J Obes Relat Metab Disord 2003;27:1516-1522.
10. Kirkegaard H, Stovring H, Rasmussen KM, Abrams B, Sorensen TI, Nohr EA. How do pregnancy-related weight changes and breastfeeding relate to maternal weight and BMI-adjusted waist circumference 7 y after delivery? Results from a path analysis. Am J Clin Nutr 2014;99:312-319.

11. McBain RD, Dekker GA, Clifton VL, Mol BW, Grzeskowiak LE. Impact of inter-pregnancy BMI change on perinatal outcomes: a retrospective cohort study. Eur J Obstet Gynecol Reprod Biol 2016;205:98-104.
12. Poston L, Caleyachetty R, Cnattingius S, Corvalan C, Uauy R, Herring S, Gillman MW. Preconceptional and maternal obesity: epidemiology and health consequences. Lancet Diabetes Endocrinol 2016;4:1025-1036.
13. Athukorala C, Rumbold AR, Willson KJ, Crowther CA. The risk of adverse pregnancy outcomes in women who are overweight or obese. BMC Pregnancy Childbirth 2010:56.
14. Gunderson EP, Abrams B, Selvin S. Does the pattern of postpartum weight change differ according to pregravid body size? Int J Obes Relat Metab Disord 2001;25:853-862.
15. Ostbye T, Peterson BL, Krause KM, Swamy GK, Lovelady CA. Predictors of postpartum weight change among overweight and obese women: results from the Active Mothers Postpartum study. J Womens Health (Larchmt) 2012;21:215-222.
16. Walker LO, Wilging S. Rediscovering the "M" in "MCH": maternal health promotion after childbirth. J Obstet Gynecol Neonatal Nurs 2000;29:229-236.
17. Amorim Adegboye AR, Linne YM. Diet or exercise, or both, for weight reduction in women after childbirth. Cochrane Database Syst Rev 2013:Cd005627.
18. Gunderson EP. Childbearing and obesity in women: weight before, during, and after pregnancy. Obstet Gynecol Clin North Am 2009;36:317-ix.
19. Althuizen E, van Poppel MNM, de Vries JH, Seidell JC, van Mechelen W. Postpartum behaviour as predictor of weight change from before pregnancy to one year postpartum. BMC Public Health 2011;11:165.
20. Begum F, Colman I, McCargar LJ, Bell RC. Gestational weight gain and early postpartum weight retention in a prospective cohort of Alberta women. J Obstet Gynaecol Can 2012;34:637-647.
21. Linne Y, Barkeling B, Rossner S. Long-term weight development after pregnancy. Obes Rev 2002;3:75-83.
22. Olson CM, Strawderman MS, Hinton PS, Pearson TA. Gestational weight gain and postpartum behaviors associated with weight change from early pregnancy to 1 y postpartum. Int J Obes Relat Metab Disord 2003;27:117-127.

23. Lim S, O'Reilly S, Behrens H, Skinner T, Ellis I, Dunbar JA. Effective strategies for weight loss in post-partum women: a systematic review and meta-analysis. Obes Rev 2015;16:972-987.
24. Lipsky LM, Strawderman MS, Olson CM. Maternal weight change between 1 and 2 years postpartum: the importance of 1 year weight retention. Obesity (Silver Spring) 2012;20:1496-1502.
25. Martin JE, Hure AJ, Macdonald-Wicks L, Smith R, Collins CE. Predictors of post-partum weight retention in a prospective longitudinal study. Matern Child Nutr 2014;10:496-509.
26. Ohlin A, Rossner S. Maternal body weight development after pregnancy. Int J Obes 1990;14:159-173.
27. Rossner S, Ohlin A. Pregnancy as a risk factor for obesity: lessons from the Stockholm Pregnancy and Weight Development Study. Obes Res 1995;3:267s-275s.
28. Gunderson EP, Abrams B. Epidemiology of gestational weight gain and body weight changes after pregnancy. Epidemiol Rev 1999;21:261-275.
29. Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. Washington, DC: The National Academies Press, 2005.
30. Butte NF, Hopkinson JM. Body composition changes during lactation are highly variable among women. J Nutr 1998;128:381S-385S.
31. World Health Organization. Global health observatory data: overweight and obesity. Geneva (Switzerland): WHO; 2016.
32. Statistics Canada. Table 13-10-0096-20 Body mass index, overweight or obese, self-reported, adult, age groups (18 years and older). Available from: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009620 (accessed March 13, 2019).
33. Public Health Agency of Canada, Canadian Institute for Health Information. Obesity in Canada: A joint report from the Public Health Agency of Canada and the Canadian Institute for Health Information. Ottawa: Public Health Agency of Canada; 2011. Available from: https://www.canada.ca/en/public-health/services/health-promotion/healthy-living/obesity-canada.html (accessed March 13, 2019).

34. Lu GC, Rouse DJ, DuBard M, Cliver S, Kimberlin D, Hauth JC. The effect of the increasing prevalence of maternal obesity on perinatal morbidity. Am J Obstet Gynecol 2001;185:845-849.
35. Chu SY, Bachman DJ, Callaghan WM, Whitlock EP, Dietz PM, Berg CJ, O'Keeffe-Rosetti M, Bruce FC, Hornbrook MC. Association between obesity during pregnancy and increased use of health care. N Engl J Med 2008;358:1444-1453.
36. Williamson DF, Madans J, Pamuk E, Flegal KM, Kendrick JS, Serdula MK. A prospective study of childbearing and 10-year weight gain in US white women 25 to 45 years of age. Int J Obes Relat Metab Disord 1994;18:561-569.
37. Smith DE, Lewis CE, Caveny JL, Perkins LL, Burke GL, Bild DE. Longitudinal changes in adiposity associated with pregnancy. The CARDIA Study. Coronary Artery Risk Development in Young Adults Study. JAMA 1994;271:1747-1751.
38. Weng HH, Bastian LA, Taylor DHJ, Moser BK, Ostbye T. Number of children associated with obesity in middle-aged women and men: results from the health and retirement study. J Womens Health (Larchmt) 2004;13:85-91.
39. Sorbye LM, Skjaerven R, Klungsoyr K, Morken NH. Gestational diabetes mellitus and interpregnancy weight change: A population-based cohort study. PLoS Med 2017;14:e1002367-e1002367.
40. Ovesen P, Rasmussen S, Kesmodel U. Effect of prepregnancy maternal overweight and obesity on pregnancy outcome. Obstet Gynecol 2011;118:305-312.
41. Singh J, Huang CC, Driggers RW, Timofeev J, Amini D, Landy HJ, Miodovnik M, Umans JG. The impact of pre-pregnancy body mass index on the risk of gestational diabetes. J Matern Fetal Neonatal Med 2012;25:5-10.
42. Torloni MR, Betran AP, Horta BL, Nakamura MU, Atallah AN, Moron AF, Valente O. Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis. Obes Rev 2009;10:194-203.
43. Ertel KA, Huang T, Rifas-Shiman SL, Kleinman K, Rich-Edwards J, Oken E, James-Todd T. Perinatal weight and risk of prenatal and postpartum depressive symptoms. Ann Epidemiol 2017;27:695-700.e691.

44. Frederick IO, Rudra CB, Miller RS, Foster JC, Williams MA. Adult weight change, weight cycling, and prepregnancy obesity in relation to risk of preeclampsia. Epidemiology 2006;17:428-434.
45. Liu Y, Dai W, Dai X, Li Z. Prepregnancy body mass index and gestational weight gain with the outcome of pregnancy: a 13-year study of 292,568 cases in China. Arch Gynecol Obstet 2012;286:905-911.
46. Endres LK, Straub H, McKinney C, Plunkett B, Minkovitz CS, Schetter CD, Ramey S, Wang C, Hobel C, Raju T, et al. Postpartum weight retention risk factors and relationship to obesity at 1 year. Obstet Gynecol. 2015;125:144-152.
47. Hollis JL, Crozier SR, Inskip HM, Cooper C, Godfrey KM, Harvey NC, Collins CE, Robinson SM. Modifiable risk factors of maternal postpartum weight retention: an analysis of their combined impact and potential opportunities for prevention. Int J Obes (Lond) 2017;41:1091-1098.
48. Davies GAL, Maxwell C, McLeod L. No. 239-Obesity in Pregnancy. J Obstet Gynaecol Can 2018;40:e630-e639.
49. Ketterl TG, Dundas NJ, Roncaioli SA, Littman AJ, Phipps AI. Association of pre-pregnancy BMI and postpartum weight retention fefore second pregnancy, Washington State, 2003-2013. Matern Child Health J 2018;22:1339-1344.
50. Zanotti J, Capp E, Wender MC. Factors associated with postpartum weight retention in a Brazilian cohort. Rev Bras Ginecol Obstet 2015;37:164-171.
51. Nohr EA, Vaeth M, Baker JL, Sorensen TI, Olsen J, Rasmussen KM. Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy. Am J Clin Nutr 2008;87:1750-1759.
52. Rong K, Yu K, Han X, Szeto IM, Qin X, Wang J, Ning Y, Wang P, Ma D. Pre-pregnancy BMI, gestational weight gain and postpartum weight retention: a meta-analysis of observational studies. Public Health Nutr 2015;18:2172-2182.
53. Viswanathan M, Siega-Riz AM, Moos MK, Deierlein A, Mumford S, Knaack J, Thieda P, Lux LJ, Lohr KN. Outcomes of maternal weight gain. Evid Rep Technol Assess (Full Rep) 2008;168 1-223.

54. Jarman M, Yuan Y, Pakseresht M, Shi Q, Robson PJ, Bell RC, the Alberta Pregnancy O, Nutrition study t, the Et. Patterns and trajectories of gestational weight gain: a prospective cohort study. CMAJ Open 2016;4:E338-E345.
55. Lowell H, Miller DC. Weight gain during pregnancy: adherence to Health Canada's guidelines. Health Rep 2010;21:31-36.
56. Mannan M, Doi SA, Mamun AA. Association between weight gain during pregnancy and postpartum weight retention and obesity: a bias-adjusted meta-analysis. Nutr Rev 2013;71:343-352.
57. Nehring I, Schmoll S, Beyerlein A, Hauner H, von Kries R. Gestational weight gain and long-term postpartum weight retention: a meta-analysis. Am J Clin Nutr 2011;94:1225-1231.
58. Mamun AA, Kinarivala M, O'Callaghan MJ, Williams GM, Najman JM, Callaway LK. Associations of excess weight gain during pregnancy with long-term maternal overweight and obesity: evidence from 21 y postpartum follow-up. Am J Clin Nutr 2010;91:1336-1341.
59. Kac G, Benicio MH, Velasquez-Melendez G, Valente JG. Nine months postpartum weight retention predictors for Brazilian women. Public Health Nutr 2004;7:621-628.
60. Hall KD, Heymsfield SB, Kemnitz JW, Klein S, Schoeller DA, Speakman JR. Energy balance and its components: implications for body weight regulation. Am J Clin Nutr 2012;95:989-994.
61. Garnaes KK, Morkved S, Salvesen KA, Salvesen O, Moholdt T. Exercise training during pregnancy reduces circulating insulin levels in overweight/obese women postpartum: secondary analysis of a randomised controlled trial (the ETIP trial). BMC Pregnancy Childbirth 2018;18:18.
62. Lovelady CA, Nommsen-Rivers LA, McCrory MA, Dewey KG. Effects of exercise on plasma lipids and metabolism of lactating women. Med Sci Sports Exerc 1995;27:22-28.
63. Carter T, Bastounis A, Guo B, Jane Morrell C. The effectiveness of exercise-based interventions for preventing or treating postpartum depression: a systematic review and meta-analysis. Arch Womens Ment Health 2019;22:37-53.
64. Davies GA, Wolfe LA, Mottola MF, MacKinnon C, Arsenault MY, Bartellas E, Cargill Y, Gleason T, Iglesias S, Klein M, et al. Exercise in pregnancy and the postpartum period. J Obstet Gynaecol Can 2003;25:516-529.

65. Davies GAL, Wolfe LA, Mottola MF, MacKinnon C. No. 129-Exercise in Pregnancy and the Postpartum Period. J Obstet Gynaecol Can 2018;40:e58-e65.

66. CSEP. Canadian Society for Exercise Physiology. Canadian physical activity guidelines for adults; 2011. Available from: https://csepguidelines.ca/adults-18-64/ (accessed March 13, 2019).

67. Dujmovic M, Kresic G, Mandic ML, Kenjeric D, Cvijanovic O. Changes in dietary intake and body weight in lactating and non-lactating women: prospective study in northern coastal Croatia. Coll Antropol 2014;38:179-187.

68. Ohlin A, Rossner S. Trends in eating patterns, physical activity and socio-demographic factors in relation to postpartum body weight development. Br J Nutr 1994;71:457-470.

69. Kirkegaard H, Stovring H, Rasmussen KM, Abrams B, Sorensen TI, Nohr EA. Maternal weight change from prepregnancy to 7 years postpartum--the influence of behavioral factors. Obesity (Silver Spring) 2015;23:870-878.

70. Dodd JM, Deussen AR, O'Brien CM, Schoenaker D, Poprzeczny A, Gordon A, Phelan S. Targeting the postpartum period to promote weight loss: a systematic review and meta-analysis. Nutr Rev 2018;76:639-654.

71. Hill JO, Wyatt HR, Peters JC. Energy balance and obesity. Circulation 2012;126:126-132.

72. Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Sawyer MB, Ashford J, Black AE. Longitudinal assessment of the components of energy balance in well-nourished lactating women. Am J Clin Nutr 1991;54:788-798.

73. Forsum E, Kabir N, Sadurskis A, Westerterp K. Total energy expenditure of healthy Swedish women during pregnancy and lactation. Am J Clin Nutr 1992;56:334-342.

74. Kopp-Hoolihan LE, van Loan MD, Wong WW, King JC. Longitudinal assessment of energy balance in well-nourished, pregnant women. Am J Clin Nutr 1999;69:697-704.

75. Butte NF, Hopkinson JM, Mehta N, Moon JK, Smith EO. Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation. Am J Clin Nutr 1999;69:299-307.

76. Butte NF, Wong WW, Hopkinson JM. Energy requirements of lactating women derived from doubly labeled water and milk energy output. J Nutr 2001;131:53-58.

77. Frigerio C, Schutz Y, Whitehead R, Jequier E. A new procedure to assess the energy requirements of lactation in Gambian women. Am J Clin Nutr 1991;54:526-533.

78. Frigerio C, Schutz Y, Whitehead R, Jequier E. Postprandial thermogenesis in lactating and non-lactating women from The Gambia. Eur J Clin Nutr 1992;46:7-13.
79. Illingworth P, Jung R, Howie P, Leslie P, Isles T. Diminution in energy expenditure during lactation. Br Med J (Clin Res Ed) 1986;292:437-441.
80. Motil KJ, Montandon CM, Garza C. Basal and postprandial metabolic rates in lactating and nonlactating women. Am J Clin Nutr 1990;52:610-615.
81. Spaaij CJ, van Raaij JM, de Groot LC, van der Heijden LJ, Boekholt HA, Hautvast JG. Effect of lactation on resting metabolic rate and on diet- and work-induced thermogenesis. Am J Clin Nutr 1994;59:42-47.
82. Carneiro IP, Elliott SA, Siervo M, Padwal R, Bertoli S, Battezzati A, Prado CM. Is obesity associated with altered energy expenditure? Adv Nutr 2016;7:476-487.
83. Piaggi P, Thearle MS, Bogardus C, Krakoff J. Lower energy expenditure predicts long-term increases in weight and fat mass. J Clin Endocrinol Metab 2013;98:E703-707.
84. Katzmarzyk PT, Perusse L, Tremblay A, Bouchard C. No association between resting metabolic rate or respiratory exchange ratio and subsequent changes in body mass and fatness: 5-1/2 year follow-up of the Quebec family study. Eur J Clin Nutr 2000;54:610-614.
85. Marra M, Scalfi L, Covino A, Esposito-Del Puente A, Contaldo F. Fasting respiratory quotient as a predictor of weight changes in non-obese women. Int J Obes Relat Metab Disord 1998;22:601-603.
86. Nelson KM, Weinsier RL, Long CL, Schutz Y. Prediction of resting energy expenditure from fat-free mass and fat mass. Am J Clin Nutr 1992;56:848-856.
87. Johnstone AM, Murison SD, Duncan JS, Rance KA, Speakman JR. Factors influencing variation in basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex, circulating leptin, or triiodothyronine. Am J Clin Nutr 2005;82:941-948.
88. Speakman JR, Selman C. Physical activity and resting metabolic rate. Proc Nutr Soc 2003;62:621-634.
89. Pelletier C, Imbeault P, Tremblay A. Energy balance and pollution by organochlorines and polychlorinated biphenyls. Obes Rev 2003;4:17-24.

90. Tremblay A, Pelletier C, Doucet E, Imbeault P. Thermogenesis and weight loss in obese individuals: a primary association with organochlorine pollution. Int J Obes Relat Metab Disord 2004;28:936-939.
91. Sports Medicine Australia. SMA statement the benefits and risks of exercise during pregnancy. Sport Medicine Australia. J Sci Med Sport 2002;5.
92. U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans, 2nd edition. Washington, DC: U.S. Department of Health and Human Services; 2018. Available from: http://www.health.gov/paguidelines/ (accessed March 13, 2019).
93. Lee D, Artero EG, Sui X, Blair SN. Mortality trends in the general population: the importance of cardiorespiratory fitness. J Psychopharmacol 2010;24:27-35.
94. Blair SN, Kampert JB, Kohl HWr, Barlow CE, Macera CA, Paffenbarger RSJ, Gibbons LW. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. JAMA 1996;276:205-210.
95. Lee DC, Sui X, Artero EG, Lee IM, Church TS, McAuley PA, Stanford FC, Kohl HWr, Blair SN. Long-term effects of changes in cardiorespiratory fitness and body mass index on all-cause and cardiovascular disease mortality in men: the Aerobics Center Longitudinal Study. Circulation 2011;124:2483-2490.
96. Church TS, LaMonte MJ, Barlow CE, Blair SN. Cardiorespiratory fitness and body mass index as predictors of cardiovascular disease mortality among men with diabetes. Arch Intern Med 2005;165:2114-2120.
97. Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA 2009;301:2024-2035.
98. Institute of Medicine. Fitness measures and health outcomes in youth. Washington, DC; 2012.
99. Hung TH, Liao PA, Chang HH, Wang JH, Wu MC. Examining the relationship between cardiorespiratory fitness and body weight status: empirical evidence from a population-based survey of adults in Taiwan. ScientificWorldJournal 2014;2014:463736.
100. McInnis KJ, Balady GJ. Comparison of submaximal exercise responses using the Bruce vs modified Bruce protocols. Med Sci Sports Exerc 1994;26:103-107.

101. Brien SE, Katzmarzyk PT, Craig CL, Gauvin L. Physical activity, cardiorespiratory fitness and body mass index as predictors of substantial weight gain and obesity: the Canadian physical activity longitudinal study. Can J Public Health 2007;98:121-124.
102. Treuth MS, Butte NF, Puyau M. Pregnancy-related changes in physical activity, fitness, and strength. Med Sci Sports Exerc 2005;37:832-837.
103. Gunderson EP, Lewis CE, Wei GS, Whitmer RA, Quesenberry CP, Sidney S. Lactation and changes in maternal metabolic risk factors. Obstet Gynecol 2007;109:729-738.
104. Stuebe AM, Rich-Edwards JW. The reset hypothesis: lactation and maternal metabolism. Am J Perinatol 2009;26:81-88.
105. Pansini F, Bonaccorsi G, Genovesi F, Folegatti MR, Bagni B, Bergamini CM, Mollica G. Influence of estrogens on serum free fatty acid levels in women. J Clin Endocrinol Metab 1990;71:1387-1389.
106. Jiang M, Gao H, Vinyes-Pares G, Yu K, Ma D, Qin X, Wang P. Association between breastfeeding duration and postpartum weight retention of lactating mothers: A meta-analysis of cohort studies. Clin Nutr 2018;37:1224-1231.
107. Dewey KG, Heinig MJ, Nommsen LA. Maternal weight-loss patterns during prolonged lactation. Am J Clin Nutr 1993;58:162-166.
108. Baker JL, Gamborg M, Heitmann BL, Lissner L, Sorensen TI, Rasmussen KM. Breastfeeding reduces postpartum weight retention. Am J Clin Nutr 2008;88:1543-1551.
109. Lopez-Olmedo N, Hernandez-Cordero S, Neufeld LM, Garcia-Guerra A, Mejia-Rodriguez F, Mendez Gomez-Humaran I. The associations of maternal weight change with breastfeeding, diet and physical activity during the postpartum period. Matern Child Health J 2016;20:270-280.
110. Butte NF, M. HJ, Nicolson MA. Leptin in human reproduction: serum leptin levels in pregnant and lactating women. J Clin Endocrinol Metab 1997;82:585-589.
111. Sichieri R, Field AE, Rich-Edwards J, Willett WC. Prospective assessment of exclusive breastfeeding in relation to weight change in women. Int J Obes Relat Metab Disord 2003;27:815-820.
112. Keesey RE, Powley TL. Body energy homeostasis. Appetite 2008;51:442-445.
113. Mayer J. Glucostatic mechanism of regulation of food intake. N Engl J Med 1953;249:13-16.

114. Mayer J, Marshall NB, Vitale JJ, Christensen JH, Mashayekhi MB, Stare FJ. Exercise, food intake and body weight in normal rats and genetically obese adult mice. Am J Physiol 1954;177:544-548.
115. Mayer J, Roy P, Mitra KP. Relation between caloric intake, body weight, and physical work: studies in an industrial male population in West Bengal. Am J Clin Nutr 1956;4:169-175.
116. Hays NP, Bathalon GP, McCrory MA, Roubenoff R, Lipman R, Roberts SB. Eating behavior correlates of adult weight gain and obesity in healthy women aged 55-65 y. Am J Clin Nutr 2002;75:476-483.
117. Provencher V, Drapeau V, Tremblay A, Despres JP, Lemieux S. Eating behaviors and indexes of body composition in men and women from the Quebec family study. Obes Res 2003;11:783-792.
118. Dykes J, Brunner EJ, Martikainen PT, Wardle J. Socioeconomic gradient in body size and obesity among women: the role of dietary restraint, disinhibition and hunger in the Whitehall II study. Int J Obes Relat Metab Disord. 2004;28:262-268.
119. Drapeau V, Blundell J, Therrien F, Lawton C, Richard D, Tremblay A. Appetite sensations as a marker of overall intake. Br J Nutr 2005;93:273-280.
120. Drapeau V, King N, Hetherington M, Doucet E, Blundell JE, Tremblay A. Appetite sensations and satiety quotient: predictors of energy intake and weight loss. Appetite 2007;48:159-166.
121. Sayer RD, Peters JC, Pan Z, Wyatt HR, Hill JO. Hunger, food cravings, and diet satisfaction are related to changes in body weight during a 6-month behavioral weight loss intervention: The Beef WISE Study. Nutrients 2018;10:E700.
122. Thomas EA, McNair B, Bechtell JL, Ferland A, Cornier MA, Eckel RH. Greater hunger and less restraint predict weight loss success with phentermine treatment. Obesity (Silver Spring) 2016;24:37-43.
123. Larson-Meyer DE, Schueler J, Kyle E, Austin KJ, Hart AM, Alexander BM. Do lactation-induced changes in ghrelin, glucagon-like peptide-1, and peptide YY influence appetite and body weight regulation during the first postpartum year? J Obes. 2016;2016:ID 7532926.
124. Parker JD, Abrams B. Differences in postpartum weight retention between black and white mothers. Obstet Gynecol 1993;81:768-774.

125. Gunderson EP, Rifas-Shiman SL, Oken E, Rich-Edwards JW, Kleinman KP, Taveras EM, Gillman MW. Association of fewer hours of sleep at 6 months postpartum with substantial weight retention at 1 year postpartum. Am J Epidemiol 2008;167:178-187.
126. Herring SJ, Rich-Edwards JW, Oken E, Rifas-Shiman SL, Kleinman KP, Gillman MW. Association of postpartum depression with weight retention 1 year after childbirth. Obesity (Silver Spring) 2008;16:1296-1301.
127. Pedersen P, Baker JL, Henriksen TB, Lissner L, Heitmann BL, Sorensen TI, Nohr EA. Influence of psychosocial factors on postpartum weight retention. Obesity (Silver Spring) 2011;19:639-646.
128. Whitaker K, Young-Hyman D, Vernon M, Wilcox S. Maternal stress predicts postpartum weight retention. Matern Child Health J 2014;18:2209-2217.
129. Patel SR, Malhotra AF, White DP, Gottlieb DJ, Hu FB. Association between reduced sleep and weight gain in women. Am J Epidemiol 2006;164:947-954.
130. Phillips J, King R, Skouteris H. A conceptual model of psychological predictors of postpartum weight retention. J Reprod Infant Psychol 2012;30:278-288.
131. Hill JO, Wyatt HR, Peters JC. The importance of energy balance. Eur Endocrinol 2013;9:111-115.
132. Lam YY, Ravussin E. Analysis of energy metabolism in humans: A review of methodologies. Mol Metab 2016;5:1057-1071.
133. Pinheiro Volp AC, Esteves de Oliveira FC, Duarte Moreira Alves R, Esteves EA, Bressan J. Energy expenditure: components and evaluation methods. Nutr Hosp 2011;26:430-440.
134. Donahoo WT, Levine JA, Melanson EL. Variability in energy expenditure and its components. Curr Opin Clin Nutr Metab Care 2004;7:599-605.
135. Garby L, Kurzer MS, Lammert O, Nielsen E. Energy expenditure during sleep in men and women: evaporative and sensible heat losses. Hum Nutr Clin Nutr 1987;41:225-233.
136. FAO/WHO/UNU. Human energy requirements : report of a joint FAO/WHO/UNU Expert Consultation, Rome 17-24 October 2001. Rome: Food and Agriculture Organization of the United Nations, 2004.
137. Miles CW, Wong NP, Rumpler WV, Conway J. Effect of circadian variation in energy expenditure, within-subject variation and weight reduction on thermic effect of food. Eur J Clin Nutr 1993;47:274-284.

138. Piers LS, Soares MJ, Makan T, Shetty PS. Thermic effect of a meal. 1. Methodology and variation in normal young adults. Br J Nutr 1992;67:165-175.
139. Levine JA. Non-exercise activity thermogenesis (NEAT). Best Pract Res Clin Endocrinol Metab 2002;16:679-702.
140. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep 1985;100:126-131.
141. Jeukendrup AE, Wallis GA. Measurement of substrate oxidation during exercise by means of gas exchange measurements. Int J Sports Med 2005;26:S28-37.
142. Lam YY, Ravussin E. Indirect calorimetry: an indispensable tool to understand and predict obesity. Eur J Clin Nutr 2017;71:318-322.
143. Shechter A, Rising R, Wolfe S, Albu JB, St-Onge MP. Postprandial thermogenesis and substrate oxidation are unaffected by sleep restriction. Int J Obes (Lond) 2014;38:1153-1158.
144. McArdle WD, Katch FI, Katch VL. Sports and exercise nutrition. 3rd ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009.
145. Hibi M, Ando T, Tanaka S, Tokuyama K. Human calorimetry: Energy expenditure and substrate utilization easurements using a respiratory chamber. J Sports Med Phys Fitness 2013;2:93-99.
146. Brouwer E. On simple formulae for calculating the heat expenditure and the quantities of carbohydrate and fat oxidized in metabolism of men and animals, from gaseous exchange (Oxygen intake and carbonic acid output) and urine-N. Acta Physiol Pharmacol Neerl 1957;6:795-802.
147. Woolridge MW, Butte N, Dewey KG: Methods for the measurement of milk volume intake in the breast-fed infant. In: Jensen RG, Neville MC, eds. Human Lactation: Milk Components and Methodologies. New York: Plenum Press, 1985; 5-21.
148. Allen JC, Keller RP, Archer P, Neville MC. Studies in human lactation: milk composition and daily secretion rates of macronutrients in the first year of lactation. Am J Clin Nutr 1991;54:69-80.

149. Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: the DARLING Study. Am J Clin Nutr 1993;58:152-161.
150. Dewey KG, Finley DA, Lonnerdal B. Breast milk volume and composition during late lactation (7-20 months). J Pediatr Gastroenterol Nutr 1984;3:713-720.
151. Butte NF, Garza C, Johnson CA, Smith EO, Nichols BL. Longitudinal changes in milk composition of mothers delivering preterm and term infants. Early Hum Dev 1984;9:153-162.
152. Butte NF, Garza C, Smith EO, Nichols BL. Human milk intake and growth in exclusively breast-fed infants. J Pediatr 1984;104:187-195.
153. Neville MC: Determinants of milk volume and composition. In: Jensen RG, ed. Handbook of Milk Composition. San Diego, CA: Academic Press, 1995; 87-113.
154. Levine JA. Measurement of energy expenditure. Public Health Nutr 2005;8:1123-1132.
155. Jequier E, Schutz Y. Long-term measurements of energy expenditure in humans using a respiration chamber. Am J Clin Nutr 1983;38:989-998.
156. Smith SR, de Jonge L, Zachwieja JJ, Roy H, Nguyen T, Rood JC, Windhauser MM, Bray GA. Fat and carbohydrate balances during adaptation to a high-fat. Am J Clin Nutr 2000;71:450-457.
157. Ravussin E, Burnand B, Schutz Y, Jequier E. Twenty-four-hour energy expenditure and resting metabolic rate in obese, moderately obese, and control subjects. Am J Clin Nutr 1982;35:566-573.
158. Murgatroyd PR, Davies HL, Prentice AM. Intra-individual variability and measurement noise in estimates of energy expenditure by whole body indirect calorimetry. Br J Nutr 1987;58:347-356.
159. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. J Clin Invest 1986;78:1568-1578.
160. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1-9.
161. Dulloo AG, Jacquet J, Montani JP, Schutz Y. Adaptive thermogenesis in human body weight regulation: more of a concept than a measurable entity? Obes Rev 2012;13:105-121.

162. Westerterp KR. Doubly labelled water assessment of energy expenditure: principle, practice, and promise. Eur J Appl Physiol 2017;117:1277-1285.
163. Granata GP, Brandon LJ. The thermic effect of food and obesity: discrepant results and methodological variations. Nutr Rev 2002;60:223-233.
164. Ruddick-Collins L, King N, Byrne N, Wood R. Methodological considerations for meal-induced thermogenesis: measurement duration and reproducibility. Br J Nutr 2013;110:1978-1986.
165. Jesus P, Achamrah N, Grigioni S, Charles J, Rimbert A, Folope V, Petit A, Dechelotte P, Coeffier M. Validity of predictive equations for resting energy expenditure according to the body mass index in a population of 1726 patients followed in a Nutrition Unit. Clin Nutr 2015;34:529-535.
166. de Sousa TM, Maioli TU, Dos Santos ALS, Dos Santos LC. Energy expenditure in the immediate postpartum period: Indirect calorimetry versus predictive equations. Nutrition 2017;39-40:36-42.
167. Heymsfield SB, Gallagher D, Kotler DP, Wang Z, Allison DB, Heshka S. Body-size dependence of resting energy expenditure can be attributed to nonenergetic homogeneity of fat-free mass. Am J Physiol Endocrinol Metab 2002;282:E132-138.
168. Hill RJ, Cleghorn GJ, Withers GD, Lewindon PJ, Ee LC, Connor F, Davies PS. Resting energy expenditure in children with inflammatory bowel disease. J Pediatr Gastroenterol Nutr 2007;45:342-346.
169. Tschöp MH, Speakman JR, Arch JRS, Auwerx J, Brüning JC, Chan L, Eckel RH, Farese RVJ, Galgani JE, Hambly C, et al. A guide to analysis of mouse energy metabolism. Nat Methods 2011;9:57-63.
170. Ravussin E, Bogardus C. Relationship of genetics, age, and physical fitness to daily energy expenditure and fuel utilization. Am J Clin Nutr 1989;49:968-975.
171. Most J, Vallo PM, Gilmore LA, St Amant M, Hsia DS, Altazan AD, Beyl RA, Ravussin E, Redman LM. Energy expenditure in pregnant women with obesity does not support energy intake recommendations. Obesity (Silver Spring) 2018;26:992-999.
172. Redman LM, Smith SR, Burton JH, Martin CK, Il'yasova D, Ravussin E. Metabolic slowing and reduced oxidative damage with sustained caloric restriction support the rate of living and oxidative damage theories of aging. Cell Metab 2018;27:805-815.

173. Bosy-Westphal A, Braun W, Schautz B, Muller MJ. Issues in characterizing resting energy expenditure in obesity and after weight loss. Front Physiol 2013;4:1-9.

174. Siervo M, Faber P, Lara J, Gibney ER, Milne E, Ritz P, Lobley GE, Elia M, Stubbs RJ, Johnstone AM. Imposed rate and extent of weight loss in obese men and adaptive changes in resting and total energy expenditure. Metabolism 2015;64:896-904.

175. Muller MJ, Enderle J, Pourhassan M, Braun W, Eggeling B, Lagerpusch M, Gluer CC, Kehayias JJ, Kiosz D, Bosy-Westphal A. Metabolic adaptation to caloric restriction and subsequent refeeding: the Minnesota Starvation Experiment revisited. Am J Clin Nutr 2015;102:807-819.

176. Ostendorf DM, Melanson EL, Caldwell AE, Creasy SA, Pan Z, MacLean PS, Wyatt HR, Hill JO, Catenacci VA. No consistent evidence of a disproportionately low resting energy expenditure in long-term successful weight-loss maintainers. Am J Clin Nutr 2018;108:658-666.

177. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. N Engl J Med 1995;332:621-628.

178. Johannsen DL, Knuth ND, Huizenga R, Rood JC, Ravussin E, Hall KD. Metabolic slowing with massive weight loss despite preservation of fat-free mass. J Clin Endocrinol Metab 2012;97:2489-2496.

179. Stubbs RJ, Hughes DA, Johnstone AM, Rowley E, Reid C, Elia M, Stratton R, Delargy H, King N, Blundell JE. The use of visual analogue scales to assess motivation to eat in human subjects: a review of their reliability and validity with an evaluation of new hand-held computerized systems for temporal tracking of appetite ratings. Br J Nutr 2000;84:405-415.

180. Blundell JE, Caudwell P, Gibbons C, Hopkins M, Naslund E, King N, Finlayson G. Role of resting metabolic rate and energy expenditure in hunger and appetite control: a new formulation. Dis Model Mech 2012;5:608-613.

181. Mellinkoff SM, Frankland M, Boyle D, Greipel M. Relationship between serum amino acid concentration and fluctuations in appetite. J Appl Physiol 1956;8:535-538.

182. Kennedy GC. The role of depot fat in the hypothalamic control of food intake in the rat. Proc R Soc Lond B Biol Sci 1953;140:578-596.

183. Jequier E: Calorie balance versus nutrient balance. In: Kinney JM, Tucker HN, eds. Energy metabolism: tissue determinants and cellular corollaries. New York: Raven Press, 1992.

184. Schwartz MW, Woods SC, Porte DJ, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature 2000;404:661-671.
185. Hopkins M, Finlayson G, Duarte C, Gibbons C, Johnstone AM, Whybrow S, Horgan GW, Blundell JE, Stubbs RJ. Biological and psychological mediators of the relationships between fat mass, fat-free mass and energy intake. International Journal of Obesity 2019;43:233-242.
186. Hopkins M, Finlayson G, Duarte C, Whybrow S, Ritz P, Horgan GW, Blundell JE, Stubbs RJ. Modelling the associations between fat-free mass, resting metabolic rate and energy intake in the context of total energy balance. Int J Obes (Lond) 2016;40:312-318.
187. Morton GJ, Schwartz MW. The NPY/AgRP neuron and energy homeostasis. Int J Obes Relat Metab Disord 2001;25:S56-62.
188. Badman MK, Flier JS. The gut and energy balance: visceral allies in the obesity wars. Science 2005;307:1909-1914.
189. Morton GJ, Cummings DE, Baskin DG, Barsh GS, Schwartz MW. Central nervous system control of food intake and body weight. Nature 2006;443:289-295.
190. Woods SC, Ramsay DS. Food intake, metabolism and homeostasis. Physiol Behav 2011;104:4-7.
191. Blundell JE, Caudwell P, Gibbons C, Hopkins M, Naslund E, King NA, Finlayson G. Body composition and appetite: fat-free mass (but not fat mass or BMI) is positively associated with self-determined meal size and daily energy intake in humans. Br J Nutr 2012;107:445-449.
192. Weise CM, Hohenadel MG, Krakoff J, Votruba SB. Body composition and energy expenditure predict ad-libitum food and macronutrient intake in humans. Int J Obes (Lond) 2014;38:243-251.
193. Stubbs RJ, Hopkins M, Finlayson GS, Duarte C, Gibbons C, Blundell JE. Potential effects of fat mass and fat-free mass on energy intake in different states of energy balance. Eur J Clin Nutr 2018;72:698-709.
194. Caudwell P, Finlayson G, Gibbons C, Hopkins M, King N, Naslund E, Blundell JE. Resting metabolic rate is associated with hunger, self-determined meal size, and daily energy intake and may represent a marker for appetite. Am J Clin Nutr 2013;97:7-14.
195. Edholm OG, Fletcher JG, Widdowson EM, McCance RA. The energy expenditure and food intake of individual men. Br J Nutr 1955;9:286-300.

196.Flatt JP. The difference in the storage capacities for carbohydrate and for fat, and its implications in the regulation of body weight. Ann N Y Acad Sci 1987;499:104-123.

197.Flatt JP. Glycogen levels and obesity. Int J Obes Relat Metab Disord. 1996;20:S1-11.

198.Hopkins M, Jeukendrup A, King NA, Blundell JE. The relationship between substrate metabolism, exercise and appetite control: does glycogen availability influence the motivation to eat, energy intake or food choice? Sports Med 2011;41:507-521.

199.Barwell ND, Malkova D, Leggate M, Gill JM. Individual responsiveness to exercise-induced fat loss is associated with change in resting substrate utilization. Metabolism 2009;58:1320-1328.

200.King NA, Hopkins M, Caudwell P, Stubbs RJ, Blundell JE. Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss. Int J Obes (Lond) 2008;32:177-184.

201.Bessesen DH, Bull S, Cornier MA. Trafficking of dietary fat and resistance to obesity. Physiol Behav 2008;94:681-688.

202.Eckel RH, Hernandez TL, Bell ML, Weil KM, Shepard TY, Grunwald GK, Sharp TA, Francis CC, Hill JO. Carbohydrate balance predicts weight and fat gain in adults. Am J Clin Nutr 2006;83:803-808.

203.Pannacciulli N, Salbe AD, Ortega E, Venti CA, Bogardus C, Krakoff J. The 24-h carbohydrate oxidation rate in a human respiratory chamber predicts ad libitum food intake. Am J Clin Nutr 2007;86:625-632.

204.Galgani JE, de Jonge L, Most MM, Bray GA, Smith SR. Effect of a 3-dayhigh-fat feeding period on carbohydrate balance and adlibitum energy intake in humans. Int J Obes 2010;34:886-914.

205.Li C, Chen P, Smith MS. Neuropeptide Y and tuberoinfundibular dopamine activities are altered during lactation: role of prolactin. Endocrinology 1999;140:118-123.

206.Woodside B, Popeski N. The contribution of changes in milk delivery to the prolongation of lactational infertility induced by food restriction or increased litter size. Physiol Behav 1999;65:711-715.

207.Woodside B. Prolactin and the hyperphagia of lactation. Physiol Behav 2007;91:375-382.

208.Ohnhaus EE, Alder R. Methodological problems in the measurement of pain: a comparison between the verbal rating scale and the visual analogue scale. Pain 1975;1:379-384.

209. Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. Ann Rheum Dis 1978;37:378-381.
210. Bendinger T, Plunkett N. Measurement in pain medicine. BJA Education 2016;16:310-315.
211. Flint A, Raben A, Blundell JE, Astrup A. Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. Int J Obes Relat Metab Disord. 2000;24:38-48.
212. Blundell J, de Graaf C, Hulshof T, Jebb S, Livingstone B, Lluch A, Mela D, Salah S, Schuring E, van der Knaap H, et al. Appetite control: methodological aspects of the evaluation of foods. Obes Rev 2010;11:251-270.
213. Matu J, O'Hara J, Hill N, Clarke S, Boos C, Newman C, Holdsworth D, Ispoglou T, Duckworth L, Woods D, et al. Changes in appetite, energy intake, body composition, and circulating ghrelin constituents during an incremental trekking ascent to high altitude. European journal of applied physiology 2017;117:1917-1928.
214. Ravn AM, Gregersen NT, Christensen R, Rasmussen LG, Hels O, Belza A, Raben A, Larsen TM, Toubro S, Astrup A. Thermic effect of a meal and appetite in adults: an individual participant data meta-analysis of meal-test trials. Food & Nutrition Research 2013;57:10.3402/fnr.v3457i3400.19676.
215. Chaput JP, Gilbert JA, Gregersen NT, Pedersen SD, Sjodin AM. Comparison of 150-mm versus 100-mm visual analogue scales in free living adult subjects. Appetite 2010;54:583-586.
216. Reid CA, Harbron CG, Blundell JE, Stubbs RJ. What are psychometric assessments of appetite asking A preliminary multivariate analysis. International Journal of Obesity 1998;22:151A.

Chapter 3: The Influence of Energy Metabolism on Postpartum Weight Retention

3.1 Preface

The following chapter is based on data from the Postpartum Calorimetry Study of women at three ($n = 53$) and nine months postpartum ($n = 49$). This longitudinal study is the first to provide an in-depth profile of key components of energy metabolism (e.g. resting energy expenditure [REE], sleep energy expenditure [sleepEE], exercise energy expenditure [EEE], respiratory quotient [RQ], and 24-hour energy expenditure [TEE]) of contemporary women, comparing high vs. low weight retainers, using a state-of-the-art technique, the whole body calorimetry. Using different sophisticated statistical approaches, this study also explored associations between postpartum weight retention and energy metabolism.

These analyses built on our Case Report of a primigravid woman whose energy metabolism and body weight were assessed prepregnancy, during pregnancy, and at three and nine months postpartum (**Appendix 1**: *Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Prado CM. Changes in energy metabolism from prepregnancy to postpartum: A case report. Can J Diet Pract Res. 2018;79(4):191-195*). In that Case Report, we reported that 1) body weight returned to prepregnancy values at nine months postpartum, 2) REE was similar in prepregnancy, and at three and nine months postpartum, and 2) TEE returned to prepregnancy values by nine months postpartum, despite additional energy expended through breast milk synthesis.

A version of this chapter has been published. Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Vu K, Bell G, Robson PJ, Prado CM, the ENRICH Study Team. The influence of energy metabolism on postpartum weight retention. The American Journal of Clinical Nutrition 2019; 109:1588-1599, https://doi.org/10.1093/ajcn/nqy389.

LCRP, LJM, RCB, PJR, and CMP: designed the research; LCRP, SAE, and GB: conducted the research; LCRP and KV: analyzed the data and performed statistical analysis; LCRP and KV: wrote the manuscript; LCRP, LJM, RCB, PJR, and CMP: had primary responsibility for the final content; and all authors: read and approved the final manuscript.

3.2 Introduction

Obesity is a major public health problem. Globally, ~39% of women aged ≥18 years are overweight and 15% have obesity (1). Risks of developing obesity are increased among women of childbearing age, in part because of the expected weight gain during pregnancy and the potential lack of, or limited, weight loss after pregnancy, which increases the risk of longer-term weight retention (2, 3). Although, on average, postpartum weight retention (PPWR) may seem reasonable, often ranging from ~0.5 to 4 kg, it is highly variable at the individual level (2, 4). Several studies have demonstrated that ~20% of women retain >5 kg after pregnancy (5-7), and others have shown that lack of weight loss in the postpartum period may be associated with higher body weight for 10–15 years following pregnancy (8, 9). However, despite the potential long-term health impacts of PPWR, detailed guidelines describing timelines and evidence-based approaches to manage the issue do not exist (10).

Influences on PPWR are complex and multifactorial, and include prepregnancy body mass index (BMI), gestational weight gain (GWG), physical activity, dietary intake, sleep quality, mental health, and breastfeeding (11-13). Additionally, energy metabolism is often overlooked, yet it is re-emerging as a factor in PPWR regulation (14). Most of the knowledge on energy metabolism in the postpartum period is based on research completed a number of decades ago (15-20), when energy intake was lower and physical activity was higher in comparison with that observed in contemporary women (21). A longitudinal study from the early 1990s (15) reported that the basal metabolism of 10 well-nourished lactating women did not increase in accordance with the cost of milk production and there was no evidence of fat mobilization. Therefore, the energy cost of lactation was met through an increase in energy intake and a decrease in voluntary activities. In the early 2000s, another longitudinal study (20), conducted with 24 well-nourished women, suggested that energy needs during lactation were met primarily from energy intake and partially from fat mobilization, as there was limited evidence of adaptations in metabolism and physical activity. The main conclusion of these studies was that a large interindividual variation in adaptations to sustain energy balance occurred during lactation. Notably, most previous studies (15-20) were primarily focused on metabolic adaptations related to the energy cost of lactation vs. the relationship between energy metabolism and PPWR.

Herein, we conducted an in-depth analysis of key components of energy metabolism (i.e., total energy expenditure [TEE], REE, EEE, SleepEE, and RQ) of postpartum women comparing high vs. low weight retainers with the use of a state-of-the art methodology. Additionally, we examined the influence of energy metabolism on PPWR at two selected time points: three and nine months postpartum (3M-PP and 9M-PP, respectively).

3.3 Methods

3.3.1 Study design and participants.

The Postpartum Calorimetry Study was a cohort study, which used a convenience sample of 53 postpartum women recruited between February 2014 and December 2015. The number of eligible women who completed the study at 3M-PP and 9M-PP determined the final sample size. All measurements were performed at the Human Nutrition Research Unit (HNRU), University of Alberta. Participants were recruited with the use of newspaper advertisements, brochures, mailings to specific listserves, local events with maternity or baby themes, community health clinics, and by word of mouth. The postpartum women who enrolled in the study were ≥18 years of age, had a singleton term pregnancy (37–42 weeks) and were no more than 3M-PP at the time of enrollment. Participants had resting blood pressure and heart rate within normal ranges with no significant health issues, chronic diseases, or food allergies, and were not taking any medication that could affect their energy metabolism. The study was approved by the University of Alberta Health Research Ethics Board. All participants provided informed consent.

3.3.2 Study protocol.

Following recruitment, each participant completed demographic and pregnancy-related questionnaires. Next, participants visited the HNRU at ~3M-PP (3.2 ± 0.3 months) and 9M-PP (9.2 ± 0.3 months; follow-up time: 6.0 ± 0.4 months), chosen to reflect early vs. late postpartum periods, as well as a priori considerations of participant acceptability to the study protocol. At the 3M-PP time point, participants attended the HNRU, where anthropometrics, body composition, and REE were measured. These same measurements were repeated at the 9M-PP time point. Additionally, participants underwent a 24-hour total energy expenditure (TEE) test and a cardiorespiratory fitness assessment. The flowchart of the Postpartum Calorimetry Study is presented in **Figure 3.1**. A detailed description of the measurements is presented below.

3.3.2.1 Demographic and pregnancy-related characteristics.

Age (years), education level (high school or trade, or undergraduate or postgraduate), marital status (married or other), ethnicity (Caucasian or other), family income (<C$70,000 or ≥C$70,000), and parity (primiparous or multiparous) were collected by questionnaires. Information about smoking history (never smoked or ever smoked), birth and delivery (gestational length, mode of delivery, infant birth weight), and breastfeeding status (any breastfeeding yes or no) were also collected.

3.3.2.2 Anthropometrics and body composition.

Women were asked to report their prepregnancy weight as well as their highest weight in pregnancy. Current body weight was measured to the nearest 0.1 kg with the use of a Health o meter® Professional digital scale (752KL Pelstar-LLC; IL, USA); height was measured to the nearest 0.1 cm with the use of a 235 Heightronic digital stadiometer (Quick Medical; WA, USA); and waist circumference was measured in triplicate to the nearest 0.1 cm with the use of a nonelastic tape, with the average of the closest two values recorded.

Body composition was measured through the use of dual-energy X-ray absorptiometry (GE Medical Systems; WI, USA) and scans were analyzed with enCORE 9.20 software to generate estimates of fat mass (FM), lean soft tissue (LST), and bone mineral content. Fat-free mass (FFM) was calculated by summing the LST and bone mineral content. Appendicular skeletal muscle (ASM) was estimated by measuring the amount of LST in the arms and legs. Variables were also expressed adjusted for height in meters squared (index) (22).

BMI was calculated from self-reported body weight (prepregnancy), measured body weight (3M-PP and 9M-PP), and height measured at the 3M-PP visit. Participants were classified as underweight (<18.50 kg/m^2), normal weight (18.50–24.99 kg/m^2), overweight (25.00–29.99 kg/m^2), or obese (≥30.00 kg/m^2) (23), according to their BMI at the three time points (prepregnancy, 3M-PP, and 9M-PP). GWG was calculated as the difference between the highest weight in pregnancy and the prepregnancy weight. Participants were classified, according to adherence to GWG guidelines (24), as "below", "met", or "above" the recommended amount of GWG based on their prepregnancy BMI.

PPWR was calculated as the difference between body weight measured at the 3M-PP and 9M-PP visits and prepregnancy weight. In this study, high PPWR was defined based on the Dietary

Reference Intake guidelines (25). This criterion considers an average weight loss of 0.8 kg/month in the first six months postpartum (total 4.8 kg weight loss), with weight stability expected after this period (25). Therefore, high PPWR was defined as >4.8 kg weight retention at 9M-PP compared with prepregnancy weight. The sample was stratified into two groups according to the amount of weight retained at 9M-PP: high-retainers (>4.8 kg, *n* = 11) and low-retainers (≤4.8 kg, *n* = 38).

3.3.2.3 Energy metabolism profile.

Energy metabolism was measured by indirect calorimetry, by measuring the volume of oxygen consumption ($\dot{V}O_2$) and volume of carbon dioxide production ($\dot{V}CO_2$), with the use of a whole body calorimetry unit (WBCU), a technique explained in detail elsewhere (26). Participants completed a REE (1-hour) test at 3M-PP and 9M-PP, following the same protocol at both time points. TEE (24-hour) was measured only at 9M-PP, and participants adhered to a standardized schedule while in the WBCU (**Supplemental Table 3.1**).

Resting energy expenditure. REE was measured for 60 minutes, with the first 30 minutes excluded from analyses to account for acclimatization. Participants were instructed to rest in a supine position, being awake but motionless, after fasting for ≥8 hours and refraining from exercise for 24 hours prior to the test. Participants were requested to have only minimal physical activity on the morning of the test (e.g., get dressed; drive from home to the HNRU; and take the short walk from the parking lot to the HNRU). REE was expressed as kilocalories per day (measured REE), adjusted for kilograms of body weight (REE adjusted body weight) and for body composition (predicted REE). The latter is reported by applying a multiple linear regression model, with measured REE as the dependent variable and FFM and FM as independent variables. Age was not a significant predictor of REE and was therefore not included in the models. This linear regression analysis was used to generate equations for REE at baseline (3M-PP). Two different equations specifically for low and high-retainers were generated, as these two groups presented with different percentages of FM, and the impact of FM on the variance in REE depends on the grade of adiposity (27). These equations were used to predict REE values at 9M-PP from the measured FFM and FM values at 9M-PP. The difference between measured and predicted REE (i.e., residual REE) allows for a comparison of REE over time and between groups because it accounts for differences in REE owing to body composition. If changes in REE are proportional to changes in body composition, the predicted REE from the regression equation will be equal to the measured REE. Significant differences in residual REE indicate that REE is not explained by individual changes in FFM and FM. The importance of this approach to body composition adjustment is discussed elsewhere (28-30).

Total energy expenditure. TEE was measured for 24 hours, and components of TEE, including REE (described above), EEE, and SleepEE, and substrate oxidation were included in the measurements. During the other periods of the 24-hour test, participants performed leisure activities (e.g., watching TV, using their computer, reading). TEE was expressed as kilocalories per day, which was adjusted for total urinary nitrogen losses with the use of the complete Weir equation (31). A 24-hour pooled urine sample was collected during the test day and was used to measure concentrations of total urinary nitrogen, which was determined in triplicate by chemiluminescence (Shimadzu TOC-L CPH Model with ASI-L autosampler and TNM-L, Shimadzu Corporation; JS, China; coefficient of variation <1%). Additionally, TEE was adjusted for kilograms of body weight (TEE adjusted body weight).

Exercise energy expenditure. EEE was measured for 30 minutes, followed by a 5-minute cool down. The activity was a submaximal treadmill walk (BH T8 Sport North America; CA, USA), at an exercise intensity equivalent to the stage previous to the one that elicited the individual ventilatory threshold predetermined from the treadmill exercise test (detailed description below: cardiorespiratory fitness). This exercise was chosen as it represented a low to moderate intensity and would ensure that the individual RQ would be <1.0.

Sleep energy expenditure. SleepEE was measured for 8 hours and analyzed as 3-hour intervals, as it depicts constant plateau values (32). Participants were instructed to remain lying for the entire scheduled sleep time and requested not to sleep at any other time during the day.

Substrate oxidation. RQ was calculated as the ratio between $\dot{V}CO_2$ and $\dot{V}O_2$, allowing for the assessment of substrate oxidation during all activities performed while in the WBCU, including at rest.

3.3.2.4 Cardiorespiratory fitness.

To assess cardiorespiratory fitness and to standardize the intensity of the WBCU exercise session across the participants, a submaximal, graded treadmill exercise test was performed according to the modified Bruce protocol (33) a minimum of two days before the 24-hour test.

Prior to this testing session, participants completed the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) (34), and were instructed to avoid any strenuous exercise and alcohol the day before. Participants were also instructed to consume a light meal and hydrate with water, and to refrain from drinking caffeinated beverages, ≤2 hours before the test. Resting blood pressure and heart rate were checked after five minutes of sitting quietly. Prior to the beginning the test, all participants completed a 5-minute warm-up (2.5 minutes at 1.7 mph and 0% grade, followed by 2.5 minutes at 2.5 mph and 5% grade), followed by a 10-minute rest period. Gas exchange variables were measured with the use of a calibrated TrueMax metabolic measurement system (Parvo Medics; UT, USA). Heart rate was measured every minute (Polar Electro Heart Rate Monitor; Kempele, Finland). Systolic and diastolic blood pressure, with the use of a sphygmomanometer and stethoscope, and participant exercise intensity, according to a 20-point rating of perceived exertion (35), were measured during the last minute of every 3-minute exercise stage. The treadmill test was terminated once the individual exceeded their individual ventilatory threshold (see below), as observed by a trained exercise physiologist from the real-time graphical display of $\dot{V}O_2$ vs. $\dot{V}CO_2$ during the exercise test. All participants completed a 5-minute walking cool down at 1.7 mph and 0% grade after the treadmill test was terminated. The ventilatory threshold of each participant was determined with the use of the software provided with the metabolic measurement system, which uses the V-slope criteria (36), and was visually confirmed by an exercise physiologist. Predicted maximal volume of oxygen consumption (p$\dot{V}O_2$ max) was calculated based on the multistage model with the $\dot{V}O_2$ and heart rate from two different submaximal exercise stages according to the formulas reported by Heyward (37). Age-predicted maximum heart rate was calculated according to Tanaka et al. (38).

3.3.3 Food provided while inside the whole body calorimetry unit.

Food consumed by participants during the 24-hour WBCU stay was designed by a Registered Dietitian with the use of the Food Processor Nutrition Analysis Software (ESHA Research, Inc., version 10.6.0), with standardized macronutrient content (~50% carbohydrate, 30% fat, 20% protein) to maintain energy balance. The energy intake of each participant was initially estimated from the Mifflin-St Jeor prediction equation (39), and adjusted throughout the day on the basis of measured energy expenditure according to the WBCU data points. All food was weighed and prepared at the HNRU metabolic kitchen by trained staff. Participants received three meals (breakfast, lunch, and dinner) and two snacks (afternoon and evening snacks) throughout the 24-hour test day (Supplemental Table 3.1), and were instructed to eat all of the provided food within a 30-minute time period. Bottled water was provided *ad libitum*.

3.3.4 Statistical analysis.

A paired *t* test or Wilcoxon's signed-rank test was used, as appropriate, to determine differences in dependent variables from 3M-PP to 9M-PP in the entire cohort and within groups (high- and low-retainers). Differences in dependent variables between high- and low-retainers at 3M-PP and 9M-PP were evaluated by independent *t* test or Mann-Whitney *U* test, as appropriate. A 1-sample *t* test was used to determine whether residual REE (the difference between measured REE and predicted REE from a linear regression model) was significantly different from zero.

GEE analyses were used to investigate the relationship between PPWR (primary outcome) and REE (exposure variable and treated as a time-varying predictor) at 3M-PP and 9M-PP. Maternal age, prepregnancy BMI, GWG, FM at 3M-PP, and breastfeeding status (treated as a time-varying covariate) at 3M-PP and 9M-PP were included in the model to control for their potential confounding effects.

Ordinary least squares (OLS) analyses were fitted with PPWR at 9M-PP as the primary outcome, with the exposure variables being TEE, REE, SleepEE, and $p\dot{V}O_2$ max at 9M-PP. Maternal age, prepregnancy BMI, GWG, FM at 3M-PP, and breastfeeding status at 9M-PP were included as covariates owing to their potential biological impact on PPWR. Forward stepwise was employed as the approach to variable selection, and the backward approach was used as a sensitivity analysis. In the final models, owing to multicollinearity, each exposure variable was fitted in a separate model together with significant covariates identified in the stepwise stage.

SEM analyses were employed to understand the complex relations between PPWR (primary outcome), energy expenditure (exposure variables: REE at 3MPP and TEE at 9M-PP), and other covariates (maternal age, prepregnancy BMI, GWG, FM at 3M-PP, and breastfeeding status at 3M-PP and 9M-PP). A cross-lagged panel approach was used as part of the SEM analyses to investigate the potential bidirectional relation between PPWR and energy expenditure. Covariates were assessed for multicollinearity based on their variance inflation factor; only covariates with a variance inflation factor <10 were included in the GEE, OLS, and SEM analyses.

Change over time was analyzed with the use of 2-way mixed repeated-measures ANOVA. The basic model included a group factor (high- or low-retainers), a time factor (3M-PP or 9M-PP), and an interaction between group and time (PPWR × time). The main effects of group and time were explored for nonsignificant interactions. Significant interactions were examined further by the use of planned comparisons: 1) reanalyzing the simple main effect of group (comparing low- and high-retainer groups at both 3M-PP and 9M-PP) by independent *t* test or Mann-Whitney *U* test, as appropriate, and 2) reanalyzing the simple main effect of time (change from 3M-PP to 9M-PP in both low- and high-retainer groups) by paired *t* test or Wilcoxon's signed-rank test, as appropriate. No comparisons were performed between high-retainers at 3M-PP and low-retainers at 9M-PP, or between low-retainers at 3M-PP and high-retainers at 9M-PP.

Given that there is no definitive cutoff established in the literature to define a high postpartum weight retainer, we extrapolated the 4.8 kg value from the current recommendation for postpartum weight loss over six months. Therefore, as an exploratory analysis to compare our proposed 4.8 kg PPWR cutoff, we used a receiver operating characteristic curve to determine the ability of PPWR at 3M-PP to discriminate high-retainers from low-retainers at 9MPP.

Data were presented as either median and range (minimum, maximum) for continuous variables, or frequency with total number and percentage for categorical variables. Data were assessed with the use of Mplus version 7 (Muthén & Muthén; CA, USA) for SEM analyses, SAS version 9.4 (SAS Institute Inc.; NC, USA) for GEE and OLS analyses, and SPSS version 24 (IBM Corp.; NY, USA) for all other analyses. The threshold for significance was set at $P < 0.05$.

3.4 Results

Of the 53 participants enrolled in the study, four were lost to follow-up. One participant withdrew from the study prior to the 3M-PP time point assessment owing to time constraints, and three did not return for the 9M-PP follow-up test visit (two owing to subsequent pregnancies and one had moved away). Of the 49 participants included in the analyses, 43 completed the 24-hour test at the 9M-PP time point, and the other six completed the same measurements collected at the 3M-PP time point. Reasons for six women not completing the 24-hour test included anxiety over being away from infant for 24 hours ($n = 4$), feeling sick during the test ($n = 1$), and undergoing a minor surgical procedure ($n = 1$) (Figure 3.1). Women who did not complete the 24-hour test ($n =$

6) were no different from those who completed the test (*n* = 43) on the following measures: maternal age, body weight, BMI, FM, FFM, and measured REE (all $P > 0.05$).

3.4.1 Demographic and pregnancy-related characteristics.

Overall, the median (range) age of participants was 32.8 (25.5, 41.5) years. The majority were university educated (81.6%), married (87.8%), Caucasian (87.8%), with a high income (83.7%), and primiparous (53.1%). No participants were currently smokers. Before pregnancy, the median BMI was 24.3 (19.5, 41.7) kg/m^2, and just over half (57.1%, 28/49) of the participants being classified with normal weight, 24.5% (12/49) with overweight, and 18.4% (9/49) with obesity. From those in the obesity categories, five (10.2%) were classified with obesity class I, three (6.1%) with obesity class II, and one (2.1%) with obesity class III. The median GWG was 14.3 (3.5, 27.2) kg; 25 participants (51%) gained more weight than recommended during pregnancy, four (8.2%) participants gained less weight, and 20 (40.8%) met the GWG recommendation. Most women (77.6%, 38/49) had a vaginal delivery, and all women delivered a term infant [39.7 (37.0, 41.7) weeks gestation], with a median birth weight of 3487 (2272, 4734) grams. At 3M-PP, 79.6% (39/49) of women were breastfeeding, and 57.1% (28/49) continued to breastfeed at 9MPP.

3.4.2 Participant characteristics and change over time.

The changes in participants' characteristics from 3M-PP to 9M-PP are presented in Table 3.1. Although the median PPWR was not substantial at 3M-PP (3.1 kg) or 9M-PP (0.9 kg; $P < 0.001$), a high interindividual variability was observed at both time points, with an absolute difference between maximum and minimum values of 26.7 kg for 3M-PP and 33.2 kg for 9M-PP. Overall, participants decreased body weight and BMI from 3M-PP to 9MPP (both $P < 0.001$). However, a wide intraindividual variability was observed, with some participants losing ~10 kg and others gaining ~13 kg of body weight. In fact, 6 women (12.2%, 6/49) gained weight [2.6 (1.2, 12.7) kg], and 22.4% of participants (*n* = 11) retained >4.8 kg at the 9M-PP time point compared with prepregnancy weight. Reduction in body weight was mostly driven by an ~10% decrease in FM; the reduction was also observed for the FM index and the percentage of FM (all $P < 0.001$). There was also a decrease in waist circumference ($P < 0.001$), but no significant changes were observed in absolute or height-adjusted measurements of FFM, LST, and ASM from 3M-PP to 9M-PP (Table 3.1).

Even though body weight decreased from 3M-PP to 9M-PP, measured REE increased, on average, by 22 kcal/d over time ($P = 0.005$). There was a large interindividual variability at both time points, with an absolute difference between maximum and minimum values of 905 kcal/d and 1165 kcal/d at 3MPP and 9M-PP, respectively. Additionally, change in measured REE over time showed wide intraindividual variability, ranging from −14.7% to 18.9%. There was an overall 10% increase in REE adjusted body weight ($P < 0.001$); however, it decreased in 11 participants. Change in REE adjusted body weight was also highly variable within individuals, with the same percentage difference between maximum and minimum values (33.6%) as for measured REE. The residual REE at 9M-PP was significantly different from zero ($P = 0.001$); in other words, an increase of 51 kcal/d (−186, 451) in measured REE greater than predicted by changes in FM and FFM was observed. There was no change in fasting RQ between 3M-PP and 9M-PP ($P = 0.226$) (Table 3.1). During the 9-month 24-hour TEE test, median RQ values were 0.819 (0.754, 0.898) during fasting, 0.840 (0.790, 0.900) during sleeping, and 0.940 (0.894, 0.982) during exercise. The 24-hour RQ was 0.857 (0.791, 0.902). The median $p\dot{V}O_2$ max of cardiorespiratory fitness of participants at 9M-PP was 35 (21, 55) $mL \cdot kg^{-1} \cdot min^{-1}$.

3.4.3 Effects of energy metabolism on postpartum weight retention.

We also explored associations between PPWR and energy metabolism through the use of GEE, OLS, and SEM analyses. The GEE analyses showed that REE was negatively associated with PPWR; a 1 kcal/kg increase in REE was associated with a 0.74 kg decrease in body weight (95% CI: −1.29, −0.19 kg; $P = 0.0087$). Additionally, participants with a higher FM at 3M-PP had a higher PPWR at 3M-PP and 9M-PP. Each 1 kg increase in FM was associated with a 0.34 kg increase in body weight (95% CI: 0.13, 0.56 kg; $P = 0.0017$). PPWR was positively associated with GWG (β: 0.37; 95% CI: 0.19, 0.56; $P < 0.0001$), and negatively associated with prepregnancy BMI (β: −0.89; 95% CI: −1.30, −0.48; $P < 0.0001$) and breastfeeding (β: −2.05; 95% CI: −3.78, −0.33; $P = 0.0198$). Maternal age was nonsignificant in the GEE analyses (**Table 3.2**).

The OLS analyses showed that TEE (mean ± SE β: −0.08 ± 0.02; $P = 0.0009$), REE (β: −0.12 ± 0.02; $P < 0.0001$), SleepEE (β: −0.09 ± 0.03; $P = 0.0051$), and $p\dot{V}O_2$ max (β: −0.02 ± 0.01; $P = 0.047$) were negatively associated with PPWR at 9M-PP in the separate models.

Therefore, REE and other variables related to energy expenditure were significant predictors of PPWR. For TEE, REE, and SleepEE models, maternal age and prepregnancy BMI were included as potential confounders; GWG, FM at 3MPP, and breastfeeding status at 9M-PP were not included in the models owing to nonsignificance. For the model containing $p\dot{V}O_2$ max, maternal age, prepregnancy BMI, GWG, FM at 3MPP, and breastfeeding status at 9M-PP were not included into the model owing to nonsignificance. The same results (significant variables, size and sign of the β coefficients) were observed with forward and backward stepwise approaches. For the model containing REE, each increase of 1 kcal//kg was associated with a weight reduction of 0.12 ± 0.02 kg ($P < 0.0001$, data not shown).

In the SEM analyses, the total effect of the relations between energy expenditure and PPWR at 3M-PP and 9M-PP **(Table 3.3)** was estimated by the sum of the direct effect (direct arrows in **Figure 3.2**) and all the indirect effects of the pathways between exposure and outcome (total effect = direct effect + indirect effect). For example, the total effect of GWG on PPWR at 9MPP (β: 0.45 ± 0.15; $P = 0.003$, Table 3.3) is the sum of the direct effect between these (β: −0.47 ± 0.15; $P = 0.002$) and all the indirect effects through both REE at 3M-PP (β: −0.07 × β: −0.57 × β: 1.21, which is equal to β: 0.05) and PPWR at 3MPP (β: 0.72 × β: 1.21, which is equal to β: 0.87). Therefore, the total effect = −0.47 + (0.05 + 0.87) = 0.45. In general, the SEM analyses showed relations that were consistent with the GEE analyses. The SEM analyses supported the bidirectional relation between energy expenditure and PPWR. Each 1 kcal/kg increase in REE at 3M-PP was associated with a weight reduction of 0.57 ± 0.20 kg ($P = 0.004$) and 0.69 ± 0.25 kg ($P = 0.006$) at 3M-PP and 9M-PP, respectively. Conversely, each 1 kg increase in PPWR at 3M-PP was associated with a 0.26 ± 0.09 kcal/kg decrease in TEE at 9M-PP ($P = 0.005$). However, no association between PPWR at 9M-PP and TEE was observed. Additionally, FM at 3M-PP was positively associated with PPWR at 3M-PP (β: 0.09 ± 0.03; $P = 0.005$) and 9M-PP (β: 0.11 ± 0.04; $P = 0.008$), and negatively associated with REE (β: −0.16 ± 0.02; $P < 0.001$) and TEE (β: −0.15 ± 0.03; $P < 0.001$). GWG was positively associated with PPWR at 3M-PP and 9M-PP, but no association with energy metabolism was observed. Additionally, maternal age, prepregnancy BMI, and breastfeeding status were not significantly associated with body weight in the SEM analyses (Figure 3.2, Table 3.3).

3.4.4 Differences at three and nine months postpartum in high- and low-retainers.

High-retainers were older [35.3 (30.4, 40.9) years] than low-retainers [32.1 (25.5, 41.5) years] ($P = 0.032$), but did not differ in any other demographic or pregnancy-related characteristics. Breastfeeding status was not different between high- and low-retainers at either time point.

The 2-way mixed repeated-measures ANOVA revealed several significant interactions between PPWR and time (**Table 3.4**), including body weight, BMI, FM, FM index, FFM, FFM index, LST, ASM, ASM index, REE, and fasting RQ, requiring the additional analyses described below. Body weight did not differ significantly between groups at 3M-PP ($P = 0.067$), but it was lower ($P = 0.045$) in low-retainers than in high-retainers at 9MPP; it decreased by ~4% ($P < 0.001$) in low-retainers between time points, but did not change in high-retainers ($P = 0.878$).

Most low-retainers (57.9%, 22/38) and high-retainers (54.5%, 6/11) had a normal prepregnancy BMI; however, prepregnancy obesity was most prevalent in high- vs. low-retainers (27.3%, 3/11 vs. 15.8%, 6/38). At 3M-PP, BMI was lower ($P = 0.023$) in low-retainers, with 47.4% (18/38) having a normal BMI, than in high-retainers, where 27.3% (3/11) of women presented with overweight and over half (54.5%, 6/11) had a BMI ≥30 kg/m^2. Low-retainers changed BMI categories at 9M-PP ($P < 0.001$), with 57.9% (22/38) being in the normal category, whereas all high-retainers remained in the same BMI categories as 3M-PP ($P = 0.878$).

FM was 13.1 kg lower ($P = 0.013$) in low-retainers than in high-retainers at 3M-PP, and 11.3 kg lower ($P = 0.009$) at 9MPP. There was an ~12% decrease in FM in low-retainers between the two measurement times ($P < 0.001$), but there was no significant change over time in high-retainers ($P = 0.657$). In addition, FFM, FFM index, LST, ASM, and ASM index did not differ between groups for either time points (all $P > 0.05$), in spite of a significant increase in these variables over time in the high-retainer group (all $P < 0.05$, Table 3.4).

At 3M-PP, REE was 2 kcal/kg higher ($P = 0.014$) in low-retainers than in high-retainers, and it was 4 kcal/kg higher ($P = 0.001$) at 9M-PP. Low-retainers had an ~15% increase in REE between the two time points ($P < 0.001$), but REE did not differ in high-retainers at the two time points ($P = 0.328$). At 9M-PP, the residual REE was significantly different from zero ($P = 0.001$) in low-retainers, in which they presented with an increase of 60 kcal/d (−186, 451 kcal/d) in measured REE greater than predicted by changes in body composition. No difference between measured and predicted REE was observed in high-retainers ($P = 0.764$). Low-retainers had a lower fasting RQ [0.827 (0.763, 0.898)] than high-retainers [0.848 (0.795, 0.904), *P* = 0.031] at 3M-PP, but no difference between the two groups was observed at 9M-PP (*P* = 0.402, Table 3.4).

Table 3.5 shows a comparison between low- and high-retainers in cardiorespiratory fitness status and energy metabolism at 9MPP. Low-retainers presented with 7 mL · kg^{-1} · min^{-1} higher $\text{p}\dot{\text{V}}\text{O}_2$ max compared with high-retainers (*P* = 0.047). TEE was 4 kcal/kg higher in low-retainers than in high-retainers (*P* = 0.016). No differences between groups were observed in EEE, SleepEE, or substrate oxidation (Table 3.5).

3.4.5 Exploratory analysis with the receiver operating characteristic curve.

When defining high weight retention at 9M-PP as >4.8 kg, the probability of correct classification for high-retainers at 9MPP according to weight retention at 3M-PP was 77% (*P* = 0.007). The cutoff for PPWR at 3M-PP maximizing the sum of sensitivity and specificity was 3.5 kg. The sample was therefore restratified into two groups at 3M-PP based on the new cutoff for PPWR (high-retainers: >3.5 kg, low-retainers: ≤3.5 kg) and the analyses were repeated. Upon further analysis, the findings were similar with the lower cutoff for PPWR (data not shown).

3.5 Discussion

In this study, energy metabolism influenced the weight trajectory in postpartum women, whereby REE, TEE, and $\text{p}\dot{\text{V}}\text{O}_2$ max were negatively associated with PPWR, and were lower in the subset of women who retained substantial weight than in those who retained less weight. An increase in REE from early to late postpartum was observed in low-retainers, which was greater than predicted by changes in body composition. Additionally, FM was positively associated with PPWR and negatively associated with energy metabolism. To our knowledge, this study is the first to provide an in-depth profile analysis of key components of energy metabolism in early and late postpartum with the use of a WBCU, and investigating its influence on postpartum weight trajectory in contemporary women.

Our findings suggest that energy metabolism plays a pivotal role in PPWR, even after adjustments for potential biological confounding factors, such as body composition, maternal age, prepregnancy BMI, GWG, and breastfeeding status. Although a number of studies have assessed energy expenditure and lactation in the postpartum period, the impact of energy metabolism on weight regulation has not been well documented during this life stage. Indeed, the role of energy metabolism on changes in body weight and body fatness in any population is not entirely clear. For example, a 4-year follow-up landmark study with Pima Indians reported that low REE values were associated with weight gain (40). A more recent study with the same population showed that body weight was negatively associated with adjusted REE (41). Opposing findings were reported in a 5.5-year follow-up study that showed no association between REE and weight changes (42). Similarly, a cohort study of nonpregnant and nonlactating women found no correlation between REE and changes in body weight over a 3-year period (43). Disparate findings in studies examining the influence of energy metabolism on weight regulation may be explained by body composition. The main determinant of REE is FFM, the most metabolically active compartment, explaining between 53% and 88% of the variance (44). Overall, increases in body weight occur alongside increases in both FM and FFM; therefore, heavier individuals tend to have larger amounts of both FM and FFM. In our study, low- and high-retainers had similar amounts of FFM, but FM was higher in high- vs. low-retainers. These findings may account for the higher REE observed in low-retainers, as the relative impact of FM on REE variance decreases with a concomitant increase in the relative contribution of FFM. Pregnant women are expected to gain weight and FM for the development of maternal and fetal tissues. However, many of the pregnancy-related contributors to GWG, along with excess fluids gained during pregnancy, are lost in the first six weeks postpartum; after this period, PPWR is attributable mainly to increases in FM (3). The larger the amount of FM accrued during pregnancy, the longer it will take to return to prepregnancy weight (45). This is owing to the higher energy content per kilogram change of FM compared with FFM, so that an ~5-fold greater deficit in net energy is required to lose FM than is required for FFM (46). We demonstrated that FM was positively associated with PPWR, and that high-retainers did not lose FM between measurement time points. Additionally, FM was negatively associated with energy metabolism, and was different between low- and high-retainers, suggesting that FM may account for some of the differences in energy metabolism. Other studies have shown an independent contribution of FM to REE variance (27, 30, 44). In 1306 nonpregnant and nonlactating Caucasian women, the contribution of FM to REE variance increased with increasing adiposity but decreased at high levels of adiposity (>40% FM), suggesting that the metabolic rate of FM is reduced at >40% FM (27).

Importantly, evidence suggests that energy expenditure is under tight biological control, and occurs within a target range defined as energy expenditure set points (14, 47). The width between the lower and upper limits of these set points may vary between individuals, potentially explaining the variability in the propensity to gain weight (14). Additionally, human metabolism precludes an expansion of the energy expenditure set point beyond its upper limit with excess energy intake, showing an inefficient response to weight gain (14). This concept is an alternative explanation for our findings, in which a subset of postpartum women retained a substantial amount of weight accompanied by no changes in energy expenditure between 3M-PP and 9M-PP. Furthermore, low-retainers had an additional increase in REE that exceeded those explained by changes in body composition, which may lead to negative energy balance, allowing the body to dissipate excess calories in an attempt to return the body weight to prepregnancy values.

Another important finding of this study was the negative association between p$\dot{V}O_2$ max, as an indicator of cardiorespiratory fitness, and PPWR. A 20-year longitudinal study reported that women with a higher $\dot{V}O_2$ max were less likely to experience a weight gain of ≥10 kg over the follow-up period, and suggested that cardiorespiratory fitness was an important predictor of weight gain (48). A study on pregnancy-related changes in fitness levels noted that those with a high BMI had a lower $\dot{V}O_2$ max than the normal-BMI group at 0 and 27 weeks postpartum (49). It is likely that postpartum women who participate in certain physical activity programs present with a higher cardiorespiratory fitness, lower FM (50), and a more favorable energy expenditure profile, which would potentially assist in reducing body weight.

Our findings also indicated that lactation was negatively associated with PPWR. Anecdotally, lactation is thought to impact postpartum weight regulation, although this relation is controversial. A recent meta-analysis of 14 cohort studies demonstrated that breastfeeding for 6–12 months is associated with decreased PPWR; however, breastfeeding for <6 or >12 months may have little or no influence on weight change (13).

The findings of our current study should be assessed in light of its strengths and limitations. Our sample size was similar to or greater than others that have used comparable methods; however, it is possible that the number of participants may have led to failure to detect meaningful outcomes. One strength of the study was the rigorous and precise methodologies used to assess energy expenditure, body composition, and cardiorespiratory fitness. Ideally, we would have preferred to assess 24-hour TEE at 3M-PP; however, it was not feasible to separate mothers and infants for a prolonged time when many of them were exclusively breastfeeding. Furthermore, the inclusion of additional time points for data collection would have improved our understanding of postpartum weight trajectory (e.g., prepregnancy and 6-month time points), but it is likely that the loss to follow-up would have increased because of the extensive time commitment required for each study visit. Importantly, the drop-out rate for our study was low, with only 4 women lost to follow-up. The use of self-reported information may have introduced some bias, especially for prepregnancy weight. However, several cohort studies indicate that utilization of self-reported and measured prepregnancy weight resulted in identical categories of BMI classification for most women (51, 52), suggesting that self-reported prepregnancy weights are reasonably accurate. Also, our participants were primarily a group of Caucasian women, with a high income and high educational level, and results may not be generalizable to all postpartum women.

Finally, these findings suggest that energy expenditure, body fatness, and cardiorespiratory fitness are associated with weight trajectory during the postpartum period. Less favorable energy metabolism profile, body composition, and cardiorespiratory fitness were observed in the subset of women who retained a substantial amount of weight compared with those retaining small amounts in early and late postpartum. Therefore, postpartum women are individuals with different weight management needs, which may be driven by complexities of energy metabolism that are not yet fully understood. This provides the foundation for the development of future strategies to promote appropriate postpartum weight management.

Table 3.1 Participants' anthropometric, body composition and metabolic characteristics at three and nine months postpartum (n = 49)[1]

Characteristics	3M-PP	9M-PP	*P* value
Anthropometrics and body composition	–	–	
Postpartum weight retention,[2] kg	3.1 (-5.0, 21.7)	0.9 (-9.3, 23.9)	<0.001[3]
Body weight, kg	71.0 (53.7, 127.9)	68.0 (52.7, 125.7)	<0.001[3]
Waist circumference, cm	87.4 (69.0, 118.4)	84.1 (67.7, 122.3)	<0.001[3]
Fat mass, kg	25.7 (10.0, 63.1)	22.9 (9.7, 66.7)	<0.001[3]
Fat mass index, kg/m^2	9.5 (3.6, 21.7)	8.4 (3.6, 21.3)	<0.001
Fat mass, %	38.0 (20.3, 55.4)	35.1 (17.8, 55.5)	<0.001
Fat-free mass, kg	44.6 (34.0, 60.4)	45.0 (34.8, 59.0)	0.109
Fat-free mass index, kg/m^2	15.9 (11.8, 20.8)	16.2 (12.1, 21.0)	0.136
Lean soft tissue, kg	42.0 (31.7, 57.4)	42.4 (32.8, 55.9)	0.083
Lean soft tissue index, kg/m^2	14.9 (11.0, 19.7)	15.3 (11.4, 19.9)	0.105
Appendicular skeletal muscle, kg	18.7 (14.1, 24.5)	18.9 (14.0, 25.3)	0.106
Appendicular skeletal muscle index, kg/m^2	6.8 (4.9, 8.4)	6.7 (4.9, 8.6)	0.116
BMI categories, kg/m^2	–	–	
Normal weight (18.50–24.99)	20 (40.8)	24 (49.0)	
Overweight (25.00–29.99)	16 (32.7)	13 (26.5)	
Obese (≥30.00)	13 (26.5)	12 (24.5)	
Energy metabolism	–	–	
Measured REE, kcal/day	1435 (1193, 2098)	1457 (1152, 2317)	0.005[3]
REE adjusted body weight, kcal/kg	20 (15, 24)	22 (14, 26)	<0.001
Residual REE (measured *minus* predicted REE),[4] kcal/day	–	51 (-186, 451)	0.001
Fasting respiratory quotient	0.830 (0.763, 0.904)	0.819 (0.754, 0.898)	0.226

[1] Values are median (range) or frequency (%), as appropriate. *P* values were calculated from paired *t* tests. BMI, body mass index; REE, resting energy expenditure; M-PP, months postpartum.

[2] Postpartum weight retention was calculated as the difference between current weight (measured at 3M-PP and 9M-PP visits) and self-reported prepregnancy weight.

[3] A nonparametric test was used: the Wilcoxon's signed-rank test.

[4] Resting energy expenditure was adjusted for fat-free mass and fat mass based on regression analyzes performed at baseline (3M-PP), and predictive equations specifically for low-retainers and high-retainers were derived. *P* values were calculated from a 1-sample *t* test.

Table 3.2 Generalized estimating equation analyses examining the effect of resting energy expenditure on postpartum weight retention at three and nine months postpartum (*n* = 49)[1]

Explanatory variables	***β***	**SE**	**95% CI**	***P* value**
Intercept	27.62	8.26	11.44, 43.81	0.0008
Time (9M-PP vs. 3M-PP)	-1.59	0.78	-3.13, -0.06	0.042
Resting energy expenditure, kcal/kg	-0.74	0.28	-1.29, -0.19	0.0087
Fat mass 3M-PP, kg	0.34	0.11	0.13, 0.56	0.0017
Gestational weight gain, kg	0.37	0.10	0.19, 0.56	<0.0001
Prepregnancy BMI, kg/m^2	-0.89	0.21	-1.30, -0.48	<0.0001
Breastfeeding status	-2.05	0.88	-3.78, -0.33	0.0198

[1] Maternal age was nonsignificant in the generalized estimating equation analyses. 95% CI, 95% confidence interval; *β*, regression coefficient; BMI, body mass index; M-PP, months postpartum; SE, standard error of *β*.

Table 3.3 Total effects of the relationships explored in the structural equation modeling analyses (*n* = 49)[1]. *Related to Figure 3.2.*

Relationships	***β***	**SE**	***P* value**
REE 3M-PP --> PPWR 3M-PP	-0.57	0.20	0.004
REE 3M-PP --> PPWR 9M-PP	-0.69	0.25	0.006
REE 3M-PP --> TEE 9M-PP	0.89	0.17	< 0.001
PPWR 3M-PP --> PPWR 9M-PP	1.21	0.15	< 0.001
PPWR 3M-PP --> TEE 9M-PP	-0.26	0.09	0.005
FM 3M-PP --> PPWR 3M-PP	0.09	0.03	0.005
FM 3M PP --> PPWR 9M-PP	0.11	0.04	0.008
FM 3M-PP --> REE 3M-PP	-0.16	0.02	<0.001
FM 3M-PP --> TEE 9M-PP	-0.15	0.03	<0.001
Prepregnancy BMI --> TEE 9M-PP	-0.20	0.07	0.005
GWG --> PPWR 3M-PP	0.76	0.09	<0.001
GWG --> PPWR 9M-PP	0.45	0.15	0.003
GWG --> REE 3M-PP	-0.07	0.04	0.052
GWG --> TEE 9M-PP	-0.00	0.01	0.980

[1] The total effect of a relationship is estimated by the sum of the direct effect and all the indirect effects of the pathways between the exposure (energy expenditure) and the outcome (PPWR). Total effect = direct effect + indirect effect. For example, the total effect of GWG on PPWR at 9M-PP (mean ± SE *β*: 0.45 ± 0.15; *P* = 0.003) is the sum of the direct effect between these (*β*: -0.47 ± 0.15; *P* = 0.002) and all the indirect effects through both REE at 3M-PP (*β*: -0.07 × *β*: -0.57 × *β*: 1.21, which is equal to *β*: 0.05) and PPWR at 3M-PP (*β*: 0.72 × *β*: 1.21, which is equal to *β*: 0.87). Therefore, total effect = -0.47 + (0.05 + 0.87) = 0.45. All the direct effects of the relations between variables are presented in Figure 3.2. Maternal age, prepregnancy BMI, and breastfeeding status were not significant associated with body weight in the structural equation modeling (SEM) analyses. SEM analyses goodness of fit: Comparative Fit Index: 0.937, Standardized Root Mean Square Residual: 0.037. *β*, regression coefficient; BMI, body mass index; FM, fat mass; GWG, gestational weight gain; M-PP, months postpartum; PPWR, postpartum weight retention; REE, resting energy expenditure; SE, standard error of *β*; SEM, structural equation modeling; TEE, total energy expenditure.

Table 3.4 Anthropometrics, body composition, and energy metabolism characteristics of participants classified as high-retainers and low-retainers at three and nine months postpartum (n = 49)[1]

	High-retainers (n = 11)		Low-retainers (n = 38)		P value		
Characteristics	**3M-PP**	**9M-PP**	**3M-PP**	**9M-PP**	**PPWR**	**Time**	**PPWR × Time**
Anthropometrics and body composition	–	–	–	–			
Body weight,[2] kg	81.5^{ax} (57.8, 113.0)	78.0^{ax} (55.2, 125.7)	69.7^{ax} (53.7, 127.9)	67.2^{by} (52.7, 125.2)	0.035	0.153	0.002
Body mass index,[2] kg/m^2	31.6^{ax} (24.2, 36.3)	30.2^{ax} (23.1, 40.2)	25.6^{bx} (19.3, 43.9)	24.5^{by} (18.9, 43.0)	0.023	0.079	0.003
Waist circumference,[2] cm	98.5^{ax} (74.8, 118.4)	92.5^{ax} (74.1, 122.3)	86.1^{ax} (69.0, 118.1)	82.5^{ay} (67.6, 115.7)	0.058	<0.001	0.187
Fat mass,[2] kg	37.6^{ax} (22.6, 58.3)	32.9^{ax} (19.7, 66.7)	24.5^{bx} (10.0, 63.1)	21.6^{by} (9.7, 61.3)	0.008	0.015	0.016
Fat mass index, kg/m^2	12.5^{ax} (8.9, 18.6)	12.0^{ax} (8.2, 21.3)	8.9^{bx} (3.6, 21.7)	7.7^{by} (3.6, 21.1)	0.009	0.008	0.022
Fat mass, %	45.8^{ax} (35.3, 53.4)	43.5^{ax} (33.1, 55.5)	36.4^{bx} (20.3, 55.4)	32.4^{by} (17.8, 53.6)	0.002	<0.001	0.138
Fat-free mass, kg	43.7^{ax} (34.2, 53.0)	45.3^{ay} (35.1, 53.8)	44.8^{ax} (34.0, 60.4)	44.9^{ax} (34.8, 59.0)	0.973	0.011	0.031
Fat-free mass index, kg/m^2	15.8^{ax} (13.6, 20.6)	16.3^{ay} (13.8, 21.0)	15.9^{ax} (11.8, 20.8)	15.7^{ax} (12.2, 20.3)	0.907	0.016	0.037
Lean soft tissue, kg	41.2^{ax} (32.0, 50.3)	42.9^{ay} (33.0, 51.0)	42.4^{ax} (31.7, 57.4)	42.3^{ax} (32.7, 55.9)	0.952	0.011	0.049
Lean soft tissue index, kg/m^2	14.8^{ax} (12.8, 19.6)	15.4^{ay} (12.8, 19.9)	15.0^{ax} (11.0, 19.7)	14.8^{ax} (11.4, 19.2)	0.926	0.016	0.058
Appendicular skeletal muscle, kg	18.6^{ax} (14.2, 24.4)	18.9^{ay} (14.4, 25.3)	18.8^{ax} (14.1, 24.5)	18.8^{ax} (14.0, 24.1)	0.851	0.007	0.015
Appendicular skeletal muscle index, kg/m^2	6.8^{ax} (5.8, 8.0)	7.2^{ay} (5.9, 8.4)	6.8^{ax} (4.9, 8.4)	6.7^{ax} (4.9, 8.6)	0.770	0.007	0.015
Energy metabolism	–	–	–	–			
Measured REE,[2] kcal/day	1456^{ax}	1536^{ax}	1432^{ax}	1454^{ay}	0.619	0.022	0.811

	(1229, 1944)	(1241, 1950)	(1193, 2098)	(1152, 2317)			
REE adjusted body weight, kcal/kg	18^{ax} (15, 23)	19^{ax} (14, 22)	20^{bx} (16, 24)	23^{by} (16, 26)	0.002	<0.001	0.015
Residual REE (measured *minus* predicted REE),[3] kcal/day	–	30 (-149, 149)	–	60 (-186, 451)	0.764[4]	0.001[5]	0.308[6]
Fasting respiratory quotient	0.848^{ax} (0.795, 0.904)	0.810^{ay} (0.786, 0.855)	0.827^{bx} (0.763, 0.898)	0.822^{ax} (0.754, 0.898)	0.321	0.021	0.021

[1] Values are median (range). *P* values for PPWR, time, and PPWR × time columns are from the 2-way mixed repeated-measures ANOVA. Results of an independent *t* test or Mann-Whitney *U* test (as appropriate) for between-subject analysis are represented by the letters a and b. Median values not sharing a common superscript letter are significantly different at $P < 0.05$. No comparisons were performed between high-retainers at 3M-PP and low-retainers at 9M-PP; or between low-retainers at 3M-PP and high-retainers at 9M-PP. Results of the paired *t* test or Wilcoxon's signed-rank test (as appropriate) for within-subject analysis are represented by the letters x and y. Median values not sharing a common superscript letter are significantly different at $P < 0.05$. M-PP, months postpartum; PPWR, postpartum weight retention; REE, resting energy expenditure.

[2] Nonparametric tests were used: the Mann-Whitney *U* test or Wilcoxon's signed-rank test, as appropriate.

[3] Resting energy expenditure was adjusted for fat-free mass and fat mass based on regression analyzes performed at baseline (3M-PP), and predictive equations specifically for low-retainers and high-retainers were derived.

[4] 1-sample *t* test performed for high-retainers.

[5] 1-sample *t* test performed for low-retainers.

[6] Independent *t* test between low- and high-retainers.

Table 3.5 Comparison of cardiorespiratory fitness status and energy metabolism between participants classified as high- and low-retainers at nine months postpartum [1]

Characteristics	High-retainers	Low-retainers	*P* value
Cardiorespiratory fitness status	–	–	
$\mathrm{p\dot{V}O_2}$ max,[2] mL/kg/min	29 (25, 43)	36 (21, 55)	0.047
Energy expenditure	–	–	
Exercise energy expenditure,[2] (kcal/min)	5.44 (3.98, 9.09)	5.11 (3.34, 8.87)	0.228[4]
Sleep energy expenditure (2:00am to 5:00am),[3] kcal/min	1.00 (0.80, 1.20)	1.01 (0.76, 1.44)	0.698[4]
Total energy expenditure,[3] kcal/day	2020 (1550, 2620)	1940 (1495, 2879)	0.811[4]
Total energy expenditure,[3] kcal/kg	26 (21, 33)	30 (22, 34)	0.016
Substrate oxidation	–	–	
Exercise respiratory quotient[2]	0.943 (-0.900, 0.982)	0.939 (0.894, 0.982)	0.559
Sleep respiratory quotient (2:00am to 5:00am)[3]	0.842 (0.799, 0.876)	0.838 (0.790, 0.900)	0.876
24-hour respiratory quotient[3]	0.862 (0.827, 0.885)	0.854 (0.791, 0.902)	0.483[4]

[1] Values are median (range). *P* values were calculated from an independent *t* test. $\mathrm{p\dot{V}O_2}$ max, predicted maximal volume of oxygen consumption.

[2] $\mathrm{p\dot{V}O_2}$ max and exercise metabolism: high-retainers ($n = 11$) and low-retainers ($n = 36$).

[3] Sleep and total metabolism: high-retainers ($n = 9$) and low-retainers ($n = 34$).

[4] A nonparametric test was used: the Mann-Whitney *U* test.

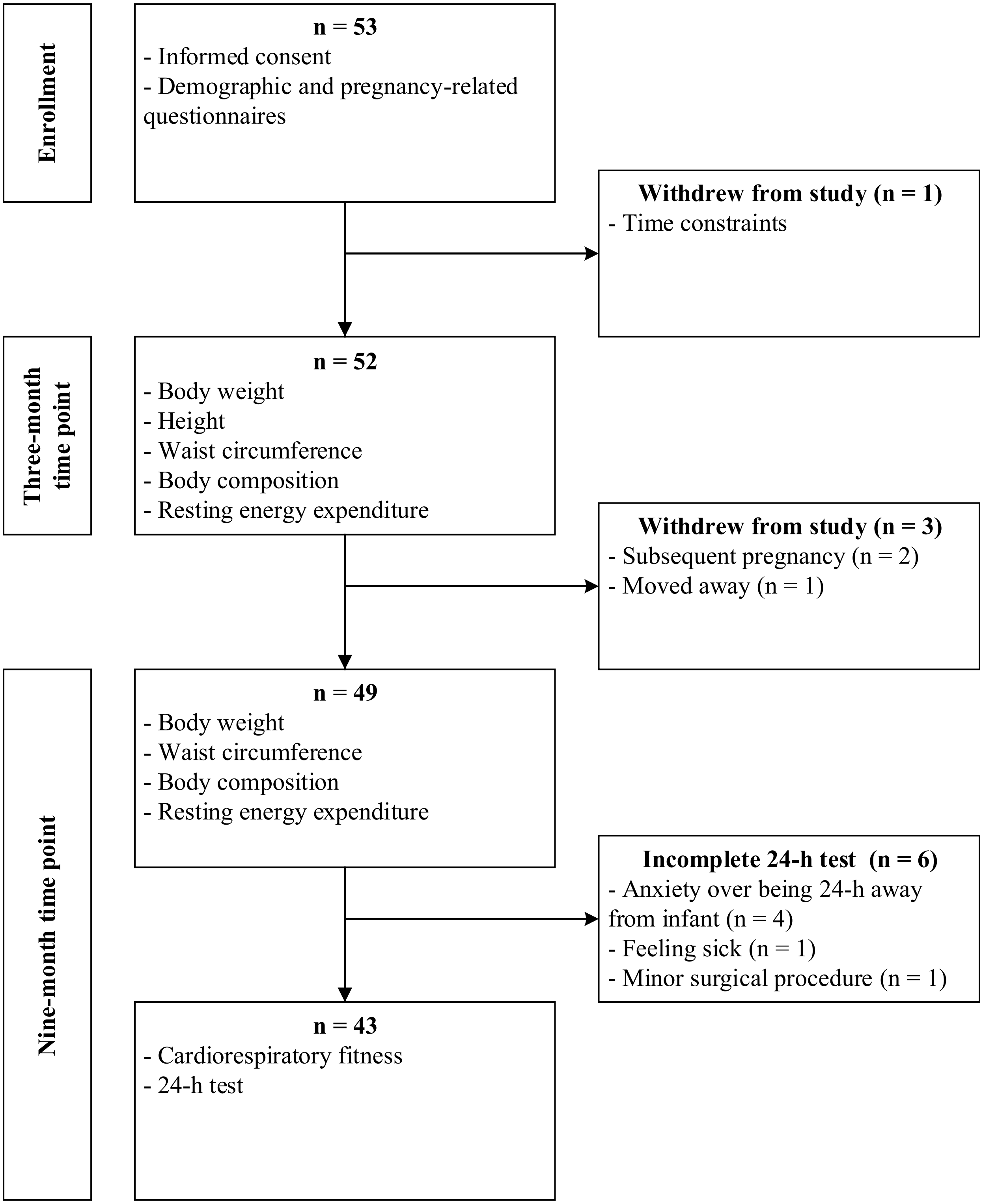


Figure 3.1 Flowchart of the Postpartum Calorimetry study

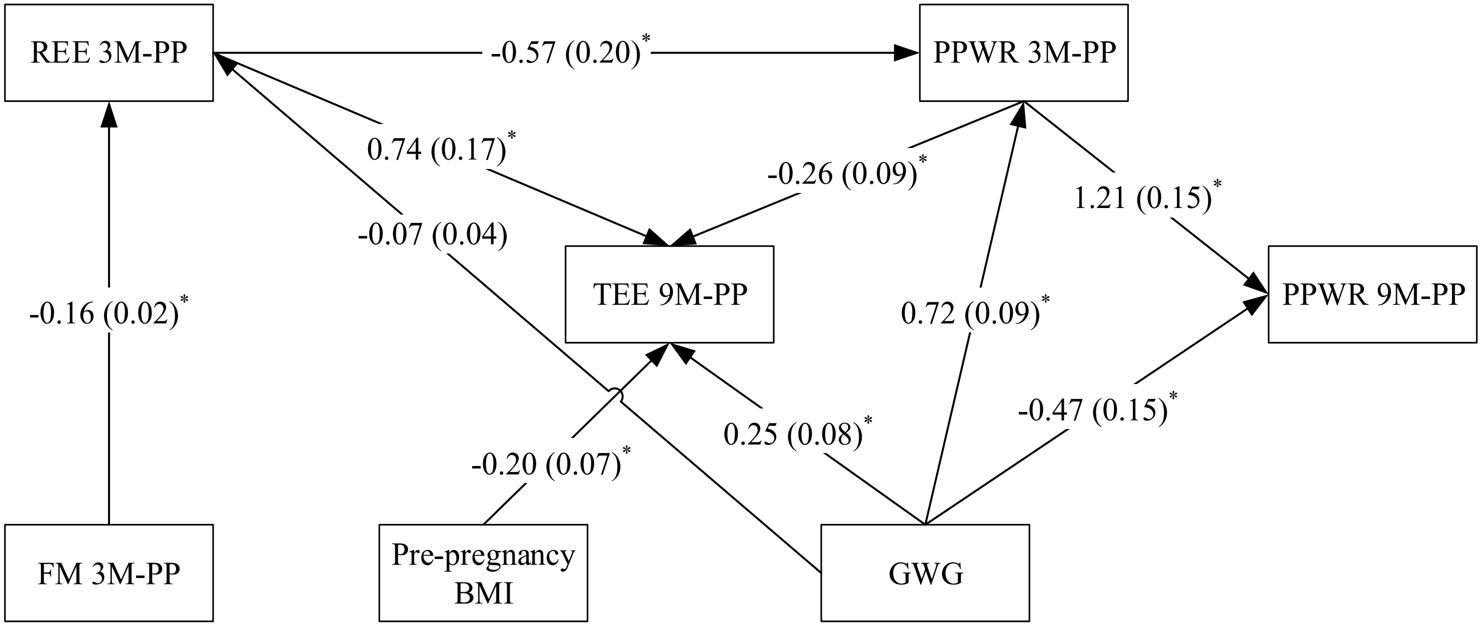


Figure 3.2 Structural equation modeling analyses examining the relations between energy expenditure (REE at 3M-PP and TEE at 9M-PP), postpartum weight retention (PPWR at 3M-PP and 9M-PP), and other covariates (maternal age, prepregnancy BMI, GWG, FM at 3M-PP, and breastfeeding at 3M-PP and 9M-PP). This figure depicts all the direct effects of the relations between variables; the total effect of these relations is presented in Table 3.3. Numbers in the diagram represent regression coefficients (standard error of β). Significant beta terms are indicated using an asterisk. Maternal age, prepregnancy BMI, and breastfeeding status were not significantly associated with body weight in the SEM analyses. SEM analyses goodness of fit: Comparative Fit Index: 0.937, Standardized Root Mean Square Residual: 0.037. SEM analyses investigate the directional relations of all relevant variables by solving a system of related equations, allowing for more complex modeling where the outcomes, exposures, and covariates are interrelated. The total effect of a relation is estimated by the sum of the direct effect (the direct arrows in Figure 3.2) and all the indirect effects of the pathways between the exposure (energy expenditure) and the outcome (PPWR). Total effect = direct effect + indirect effect. For example, the total effect of GWG on PPWR at 9M-PP (mean ± SE β: 0.45 ± 0.15; $P = 0.003$; Table 3.3) is the sum of the direct effect between them (β: -0.47 ± 0.15; $P = 0.002$) and all the indirect effects through both REE at 3M-PP (β: -0.07 × β: -0.57 × β: 1.21, which is equal to β: 0.05), and PPWR at 3M-PP (β: 0.72 × β: 1.21, which is equal to β: 0.87). Therefore, total effect = -0.47 + (0.05 + 0.87) = 0.45. The SEM model supports the bidirectional relations between energy metabolism and PPWR; REE at 3M-PP was negatively associated with PPWR at 3M-PP (β: -0.57 ± 0.20; $P = 0.004$) and 9M-PP (β: -0.69 ± 0.25; $P = 0.006$). Additionally, PPWR at 3M-PP was negatively associated TEE at 9M-PP (β: -0.26 ± 0.09; $P = 0.005$); however, no association between PPWR at 9M-PP and TEE at

9M-PP was observed. See also Table 3.3. BMI, body mass index; FM, fat mass; GWG, gestational weight gain; M-PP, months postpartum; PPWR, postpartum weight retention; REE, resting energy expenditure; SEM, structural equation modeling; TEE, total energy expenditure.

Supplemental Table 3.1 Whole body calorimetry unit schedule

Time	Task
07:00am	Arrival Anthropometric measurements 1st energy expenditure prediction using Mifflin-St Jeor equation
08:00am	24-hour test begins
08:00 – 09:00am	**Resting energy expenditure** (measured for 60 minutes)
08:45am	2nd energy expenditure prediction using WBCU data points
09:00 – 09:30am	Breakfast (all food must be eaten within 30 minutes)
09:30 – 12:00pm	Participants leisure/work time (TV, computer, reading)
11:15am	3rd energy expenditure prediction using WBCU data points
12:00 – 12:30pm	Lunch (all food must be eaten within 30 minutes)
12:30 – 02:00pm	Participants leisure/work time (TV, computer, reading)
02:00 – 02:35pm	**Exercise energy expenditure** (exercise session on treadmill – measured for 30 minutes followed by five-minute cool down)
02:35 – 03:00pm	Participants leisure/work time (TV, computer, reading)
03:00 – 03:30pm	Afternoon snack (all food must be eaten within 30 minutes)
03:15pm	4th energy expenditure prediction using WBCU data points
03:30 – 06:00pm	Participants leisure/work time (TV, computer, reading)
06:00 – 06:30pm	Dinner (all food must be eaten within 30 minutes)
06:30 – 09:00pm	Participants leisure/work time (TV, computer, reading)
09:00 – 09:30pm	Evening snack (all food must be eaten within 30 minutes)
09:30 – 10:30pm	Participants leisure/work time (TV, computer, reading) and get ready for bed
10:30 – 06:30am	Sleep scheduled time
02:00 – 05:00am	**Sleep energy expenditure**
06:30am	Wake-up call
07:15am	Out of unit

WBCU, whole body calorimetry unit.

3.6 Reference

1. World Health Organization. Global Health Observatory data: overweight and obesity. Geneva (Switzerland): WHO; 2014.
2. Lim S, O'Reilly S, Behrens H, Skinner T, Ellis I, Dunbar JA. Effective strategies for weight loss in post-partum women: a systematic review and meta-analysis. Obes Rev 2015;16:972-987.
3. Schmitt NM, Nicholson WK, Schmitt J. The association of pregnancy and the development of obesity - results of a systematic review and meta-analysis on the natural history of postpartum weight retention. Int J Obes (Lond) 2007;31:1642-1651.
4. Begum F, Colman I, McCargar LJ, Bell RC. Gestational weight gain and early postpartum weight retention in a prospective cohort of Alberta women. J Obstet Gynaecol Can 2012;34:637-647.
5. Gunderson EP, Abrams B. Epidemiology of gestational weight gain and body weight changes after pregnancy. Epidemiol Rev 1999;21:261-275.
6. Ma D, Szeto IM, Yu K, Ning Y, Li W, Wang J, Zheng Y, Zhang Y, Wang P. Association between gestational weight gain according to prepregnancy body mass index and short postpartum weight retention in postpartum women. Clin Nutr 2015;34:291-295.
7. Hutcheon JA, Chapinal N, Bodnar LM, Lee L. The INTERGROWTH-21st gestational weight gain standard and interpregnancy weight increase: A population-based study of successive pregnancies. Obesity (Silver Spring) 2017;25:1122-1127.
8. Rooney BL, Schauberger CW. Excess pregnancy weight gain and long-term obesity: one decade later. Obstet Gynecol 2002;100:245-252.
9. Linne Y, Dye L, Barkeling B, Rossner S. Weight development over time in parous women--the SPAWN study--15 years follow-up. Int J Obes Relat Metab Disord 2003;27:1516-1522.
10. Amorim Adegboye AR, Linne YM. Diet or exercise, or both, for weight reduction in women after childbirth. Cochrane Database Syst Rev 2013:Cd005627.
11. Nehring I, Schmoll S, Beyerlein A, Hauner H, von Kries R. Gestational weight gain and long-term postpartum weight retention: a meta-analysis. Am J Clin Nutr 2011;94:1225-1231.
12. Martin JE, Hure AJ, Macdonald-Wicks L, Smith R, Collins CE. Predictors of post-partum weight retention in a prospective longitudinal study. Matern Child Nutr 2014;10:496-509.

13. Jiang M, Gao H, Vinyes-Pares G, Yu K, Ma D, Qin X, Wang P. Association between breastfeeding duration and postpartum weight retention of lactating mothers: A meta-analysis of cohort studies. Clin Nutr 2018;37:1224-1231.
14. Muller MJ, Geisler C. From the past to future: from energy expenditure to energy intake to energy expenditure. Eur J Clin Nutr 2017;71:358-364.
15. Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Sawyer MB, Ashford J, Black AE. Longitudinal assessment of the components of energy balance in well-nourished lactating women. Am J Clin Nutr 1991;54:788-798.
16. Frigerio C, Schutz Y, Whitehead R, Jequier E. A new procedure to assess the energy requirements of lactation in Gambian women. Am J Clin Nutr 1991;54:526-533.
17. Forsum E, Kabir N, Sadurskis A, Westerterp K. Total energy expenditure of healthy Swedish women during pregnancy and lactation. Am J Clin Nutr 1992;56:334-342.
18. Kopp-Hoolihan LE, van Loan MD, Wong WW, King JC. Longitudinal assessment of energy balance in well-nourished, pregnant women. Am J Clin Nutr 1999;69:697-704.
19. Butte NF, Hopkinson JM, Mehta N, Moon JK, Smith EO. Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation. Am J Clin Nutr 1999;69:299-307.
20. Butte NF, Wong WW, Hopkinson JM. Energy requirements of lactating women derived from doubly labeled water and milk energy output. J Nutr 2001;131:53-58.
21. Ng SW, Popkin BM. Time use and physical activity: a shift away from movement across the globe. Obes Rev 2012;13:659-680.
22. Heymsfield SB, Heo M, Thomas D, Pietrobelli A. Scaling of body composition to height: relevance to height-normalized indexes. Am J Clin Nutr 2011;93:736-740.
23. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:i-xii, 1-253.
24. Institute of Medicine and National Research Council. Weight gain during pregnancy: reexamining the guidelines. Washington, DC: The National Academies Press, 2009. Available from: http://www.nap.edu/openbook.php?record_id=12584.
25. Institute of Medicine. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: The National Academies Press, 2005.

26. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. J Clin Invest 1986;78:1568-1578.
27. Bosy-Westphal A, Muller MJ, Boschmann M, Klaus S, Kreymann G, Luhrmann PM, Neuhauser-Berthold M, Noack R, Pirke KM, Platte P, et al. Grade of adiposity affects the impact of fat mass on resting energy expenditure in women. Br J Nutr 2009;101:474-477.
28. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. N Engl J Med 1995;332:621-628.
29. Johannsen DL, Knuth ND, Huizenga R, Rood JC, Ravussin E, Hall KD. Metabolic slowing with massive weight loss despite preservation of fat-free mass. J Clin Endocrinol Metab 2012;97:2489-2496.
30. Bosy-Westphal A, Braun W, Schautz B, Muller MJ. Issues in characterizing resting energy expenditure in obesity and after weight loss. Front Physiol 2013;4:47.
31. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1-9.
32. Schoffelen PF, Westerterp KR. Intra-individual variability and adaptation of overnight- and sleeping metabolic rate. Physiol Behav 2008;94:158-163.
33. McInnis KJ, Balady GJ. Comparison of submaximal exercise responses using the Bruce vs modified Bruce protocols. Med Sci Sports Exerc 1994;26:103-107.
34. Warburton DER, Jamnik VK, Bredin SSD, Gledhill N. The Physical Activity Readiness Questionnaire (PAR-Q+) and electronic Physical Activity Readiness Medical Examination (ePARmed-X+) Health Fitness J Can 2011;4:3-17.
35. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14:377-381.
36. Beaver WL, Wasserman K, Whipp BJ. Improved detection of lactate threshold during exercise using a log-log transformation. J Appl Physiol (1985) 1985;59:1936-1940.
37. Heyward VH. Advanced fitness assessment and exercise prescription. 6th ed. Champaign, IL: Human Kinetics, 2010.
38. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. J Am Coll Cardiol 2001;37:153-156.

39. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr 1990;51:241-247.
40. Ravussin E, Lillioja S, Knowler WC, Christin L, Freymond D, Abbott WG, Boyce V, Howard BV, Bogardus C. Reduced rate of energy expenditure as a risk factor for body-weight gain. N Engl J Med 1988;318:467-472.
41. Tataranni PA, Harper IT, Snitker S, Del Parigi A, Vozarova B, Bunt J, Bogardus C, Ravussin E. Body weight gain in free-living Pima Indians: effect of energy intake vs expenditure. Int J Obes Relat Metab Disord 2003;27:1578-1583.
42. Katzmarzyk PT, Perusse L, Tremblay A, Bouchard C. No association between resting metabolic rate or respiratory exchange ratio and subsequent changes in body mass and fatness: 5-1/2 year follow-up of the Quebec family study. Eur J Clin Nutr 2000;54:610-614.
43. Marra M, Scalfi L, Covino A, Esposito-Del Puente A, Contaldo F. Fasting respiratory quotient as a predictor of weight changes in non-obese women. Int J Obes Relat Metab Disord 1998;22:601-603.
44. Nelson KM, Weinsier RL, Long CL, Schutz Y. Prediction of resting energy expenditure from fat-free mass and fat mass. Am J Clin Nutr 1992;56:848-856.
45. Krummel DA. Postpartum weight control: a vicious cycle. J Am Diet Assoc 2007;107:37-40.
46. Hall KD, Sacks G, Chandramohan D, Chow CC, Wang YC, Gortmaker SL, Swinburn BA. Quantification of the effect of energy imbalance on bodyweight. Lancet 2011;378:826-837.
47. Pontzer H. Energy expenditure in humans and other Primates: a new synthesis. Ann Rev Anthropol 2015;44:169-187.
48. Brien SE, Katzmarzyk PT, Craig CL, Gauvin L. Physical activity, cardiorespiratory fitness and body mass index as predictors of substantial weight gain and obesity: the Canadian physical activity longitudinal study. Can J Public Health 2007;98:121-124.
49. Treuth MS, Butte NF, Puyau M. Pregnancy-related changes in physical activity, fitness, and strength. Med Sci Sports Exerc 2005;37:832-837.
50. Zourladani A, Zafrakas M, Chatzigiannis B, Papasozomenou P, Vavilis D, Matziari C. The effect of physical exercise on postpartum fitness, hormone and lipid levels: a randomized controlled trial in primiparous, lactating women. Arch Gynecol Obstet 2015;291:525-530.

51. Bannon AL, Waring ME, Leung K, Masiero JV, Stone JM, Scannell EC, Moore Simas TA. Comparison of Self-reported and Measured Pre-pregnancy Weight: Implications for Gestational Weight Gain Counseling. Matern Child Health J 2017;21:1469-1478.
52. Jarman M, Yuan Y, Pakseresht M, Shi Q, Robson PJ, Bell RC, the Alberta Pregnancy Outcomes and Nutrition study team, the ENRICH team. Patterns and trajectories of gestational weight gain: a prospective cohort study. CMAJ Open 2016;4:E338-E345.

Chapter 4: Associations of Appetite Sensations and Metabolic Characteristics with Weight Retention in Postpartum Women

4.1 Preface

Findings from Chapter 3 led us to explore other potential determinants of postpartum weight retention (PPWR). Given that energy expenditure may generate a drive for food, appetite control may potentially affect body weight regulation in the postpartum period. To our knowledge, this is the first study to comprehensively evaluate differences in appetite sensations throughout the day under conditions in which energy intake and energy expenditure (measured by whole body calorimetry) were precisely matched; along with measurements of daily duration of lactation episodes, and PPWR in contemporary women at nine months postpartum (n = 49).

A version of this chapter has been submitted for publication: Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Robson PJ, Prado CM, the ENRICH Study Team. Submitted to British Journal of Nutrition on May 2019.

LCRP, LJM, RCB, PJR and CMP: Conception and/or design of the study; LCRP, SAE: acquisition of data; LCRP, LJM, RCB, PJR and CMP: analysis and interpretation of data; All authors: drafting the article or revising it critically. All authors read and approved the final manuscript.

4.2 Introduction

Postpartum weight retention (PPWR) is estimated to be between 0.5 and 4 kg with approximately 20% of women retaining >5 kg body weight at one year postpartum (1-3). Inter-individual variability (2-5) in weight gain or loss may be associated with a variety of exposures and behaviours (e.g., gestational weight gain [GWG], dietary intake) (5, 6), and a better understanding of individual differences in factors driving weight change in the postpartum period is needed.

Using the energy balance concept to investigate weight change allows for an integration of physiological and behavioral determinants of energy expenditure and food intake with dynamic changes in body composition (7). Numerous factors play a role in the regulation of food intake, including appetite control. Energy expenditure, for example, may generate a drive for food, with appetite control being a function of energy balance (8). This hypothesis is based on the premise that an increase in energy expenditure is followed by a concomitant increase in energy intake to maintain energy homeostasis (9, 10). As body composition is a major determinant of energy expenditure, fat-free mass (FFM) and fat mass (FM) may also play important roles in appetite control (7, 8).

Assessment of appetite sensations is a valid method of measuring subjective states of motivation to eat before and in response to meals (11). Measures of appetite have been developed to evaluate potential contributors to weight change, and studies with individuals with obesity show that subjective measures of appetite predict subsequent energy intake, further impacting body weight (12, 13). In the postpartum period, lactation leads to unique physiological changes that may impact appetite control by altering energetic demands resulting from breast milk synthesis and its energy output (14). Along with the energetic demands of lactation, daily lactation duration may also be a contributing factor. Although research in humans is limited, animal studies suggest that prolactin drives increased food intake in response to physical suckling stimulation, independent of milk delivery (15, 16). Thus, the effect of lactation on appetite may differ for women with similar breast milk energy output but different daily duration of lactation episodes. Lactation has also been associated with differences in glucose and lipid homeostasis, with lower levels of glucose, insulin (17, 18) and triglycerides observed in lactating vs. nonlactating women (19).

To date, most research has focused on investigating the impact of a fixed or *ad libitum* test meal intervention on appetite sensations. However, little is known regarding how appetite sensations may change throughout the day in women whose energy intake and expenditure is precisely matched. To the best of our knowledge, these relationships have not been investigated in postpartum women. Therefore, the objectives of this study were to: 1) determine the association between PPWR and appetite sensations (hunger, prospective food consumption [PFC], satiety, fullness) throughout the day, under conditions in which energy intake and energy expenditure were precisely matched; and 2) examine the association between appetite sensations, lactation, metabolic characteristics including body composition, energy metabolism, and biochemical parameters in women at nine months postpartum.

4.3 Subjects and Methods

4.3.1 Study design.

This study was a cross-sectional analysis of data collected as part of a longitudinal observational study (Postpartum Calorimetry study) designed to assess energy expenditure in women at three and nine months postpartum (9M-PP). The present analysis assessed anthropometrics, body composition, lactation patterns, energy metabolism, appetite sensations, and biochemical parameters at 9M-PP (9.2 ± 0.3 months) in a convenience sample of 49 postpartum women at the Human Nutrition Research Unit, University of Alberta (Edmonton, Alberta, Canada). This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and the study was approved by the University of Alberta Health Research Ethics Board. All participants provided written informed consent prior to participation.

4.3.2 Participants and recruitment.

Details of this study protocol have been published elsewhere (20, 21). Briefly, study participants were recruited via newspaper advertisements, community health clinics, and word of mouth. Inclusion criteria were singleton term pregnancy (37-42 weeks), age ≥18 years, resting blood pressure and heart rate within normal ranges, no significant health issues, chronic diseases, and/or food allergies. Exclusion criteria included medications that might affect energy intake or expenditure.

4.3.3 Study protocol in the whole body calorimetry unit.

The protocol began at 0730 of Day 1, after participants had fasted for >8 hours and had refrained from exercise for 24 hours prior to the test. Body weight and appetite sensations were measured, and a basal blood sample was taken for assessment of glucose, insulin, free-fatty acids, and triglycerides. Participants entered the whole body calorimetry unit (WBCU) at 0800 of Day 1 and stayed until 0715 of Day 2 (23h 15 min). Total energy expenditure (TEE) measured in the WBCU was extrapolated to a 24-h period (kcal/d).

Participants completed a standardized schedule while in the WBCU, **Figure 4.1** Meals were served at 0900, 1200, and 1800, with snacks at 1500 and 2100 and participants were fed enough food to meet their individual energy expenditure. Energy intake for each participant was initially estimated using the Mifflin-St Jeor prediction equation (22), and adjusted throughout the day based on actual measured energy expenditure obtained in the WBCU. If energy intake was not within 100 kcal compared to the WBCU energy expenditure prediction, the quantity of calories provided to each woman was adjusted in ± 100 kcal increments. Menus were designed by a Registered Dietitian to contain 50% carbohydrate, 20% protein, and 30% fat (Food Processor Nutrition Analysis Software [ESHA Research, Inc., version 10.6.0]). The proportion of energy was as follows: 25% from each meal (i.e., breakfast, lunch, and dinner), and 12.5% from each snack (i.e., afternoon and evening snack). Participants were instructed to eat all the food provided within 30 minutes, and they were not allowed to eat any non-study foods. Bottled water was provided *ad libitum*. All food was prepared by research staff in the adjacent metabolic kitchen.

Participants rated their appetite sensations (described below) immediately before and after each meal and snack as well as at one and two hours after each meal for a total of 17 assessments throughout the day. Resting energy expenditure (REE; kcal/d) and respiratory quotient (Fasting RQ) were measured for 60 minutes from 0800 to 0900 and the last 30 minutes were averaged and used for analysis. An additional blood sample was taken two hours after breakfast.

Participants exercised for 30 minutes in the afternoon from 1400 to 1430 followed by a five-minute cool down by walking on a treadmill (BH T8 Sport North America; CA, USA). The exercise intensity was predetermined from a treadmill exercise cardiorespiratory fitness test (21), in which predicted maximal volume of oxygen consumption (p$\dot{V}O_2$max) was evaluated. For the remainder of the day, participants chose a variety of leisure activities (e.g., watching television, using computer or phone, reading, writing). Lights were turned off at 2230 and participants were awakened at 0630. Sleep energy expenditure (SleepEE) and RQ (Sleep RQ) were analyzed from 0200 to 0500. Participants exited the WBCU at 0715.

4.3.4 Anthropometric assessments.

Prepregnancy weight and highest weight in pregnancy was self-reported. Body weight at 9M-PP was measured to the nearest 0.1 kg (Health o meter® Professional, 752KL Pelstar-LLC; IL, USA). Height was measured twice to the nearest 0.1 cm at an earlier study visit using a wall-mounted digital stadiometer (235 Heightronic, Quick Medical; WA, USA). Participants were classified as underweight (<18.50 kg/m^2), normal weight (18.50-24.99 kg/m^2), overweight (25.00-29.99 kg/m^2) or obese (≥30.00 kg/m^2), according to their BMI during prepregnancy and postpartum periods (23).

GWG was calculated as the difference between highest weight in pregnancy and prepregnancy weight. PPWR was calculated as the difference between body weight measured at 9M-PP visit and prepregnancy weight. In this study, high PPWR was defined based on the Dietary Reference Intake guidelines (14). This criterion considers an average weight loss of 0.8 kg/month in the first six months postpartum (total 4.8kg weight loss), with weight stability expected after this period. High PPWR was defined as >4.8kg weight retention at 9M-PP compared to prepregnancy weight, and the sample was stratified into two groups: high-retainers (>4.8kg, n = 11), and low-retainers (≤4.8kg, n = 38).

4.3.5 Body composition.

Body composition was measured by dual-energy X-ray absorptiometry (GE Medical Systems; WI, USA) and scans were analyzed by a single individual using enCORE software version 9.20. Scans were used to generate estimates of FM, lean soft tissue, and bone mineral content; FFM was calculated by adding lean soft tissue and bone mineral content. Variables were also expressed adjusted for height in meters squared (index) (24).

4.3.6 Lactation pattern.

Lactating women completed a prospective 3-day breastfeeding diary which collected information on the number of lactation episodes and the duration of each episode for each day. This diary also included a 24-h infant test weighing protocol (25) as women recorded infants' weights on an electronic digital baby scale (BabyWeigh™ II Scale, Medela; IL, USA) before and after each lactation episode. This information was used to estimate breast milk volume (g/d), and breast milk energy output (kcal/d). The latter was calculated according to the Food and Agriculture Organization/World Health Organization/United Nations University (FAO/WHO/UNU) Human Energy requirements report (26), with breast milk volume corrected for insensible water losses (5%), assuming 1 g/mL breast milk, 0.67 kcal/g for energy content of breast milk, and an efficiency of 80%.

4.3.7 Energy metabolism.

Energy metabolism was assessed by indirect calorimetry, by continuously measuring the volume of oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) in the WBCU (27). Total urinary nitrogen excretion was determined in triplicate from a 24-h pooled urine collection (chemiluminescence, TOC-L CPH Model with ASI-L autosampler and TNM-L, Shimadzu Corporation; JS, China; coefficient of variation < 1%). The RQ was calculated as the ratio $\dot{V}CO_2/\dot{V}O_2$. Physical activity level (PAL) was defined as TEE divided by REE.

4.3.7.1 Energy and macronutrient oxidation rates.

TEE was calculated using the complete Weir equation, **Equation 1**, including the urinary nitrogen data (g/d) (28). Carbohydrate and fat oxidation were calculated using the formulas derived by Brouwer (1957) (29), **Equation 2**. Protein oxidation was calculated by multiplying the total urinary nitrogen (g/d) by 6.25.

Equation 1 (28)

$$\text{Total energy expenditure (kcal/d)} = (3.941\times\dot{V}O_2) + (1.106\times\dot{V}CO_2) - (2.17\times N)$$

$\dot{V}O_2$: Volume of oxygen consumption; $\dot{V}CO_2$: Volume of carbon dioxide production; N: Nitrogen, where, $\dot{V}O_2$ and $\dot{V}CO_2$ are in liters per day, and N is in grams per day.

Equation 2 (29)

$$\text{Carbohydrate oxidation (g/d)} = (4.170\times\dot{V}CO_2) - (2.965\times\dot{V}O_2) - (0.390\times P)$$

$$\text{Fat oxidation (g/d)} = (1.718\times\dot{V}O_2) - (1.718\times\dot{V}CO_2) - (0.315\times P)$$

$\dot{V}O_2$: Volume of oxygen consumption; $\dot{V}CO_2$: Volume of carbon dioxide production; P: protein oxidation, where, $\dot{V}O_2$ and $\dot{V}CO_2$ are in liters per day, and P is in grams per day.

4.3.7.2 Residual energy expenditure.

The difference between measured and predicted SleepEE is called residual SleepEE, and when energy expenditure is proportional to body composition, predicted SleepEE equals measured SleepEE. Therefore, the higher the residual SleepEE the higher the metabolism (high metabolism) (30). Thus, to determine if participants in the current study presented with low or high metabolism relative to the whole cohort, predicted SleepEE was examined as a function of FFM and FM in a linear regression model. Age was not a significant predictor of SleepEE and was therefore not included in the model.

4.3.8 Appetite sensations.

Participants rated their appetite sensations 17 times (Figure 4.1) across four dimensions: hunger, PFC, satiety, and fullness, using a 0-100 mm visual analogue scale (11). Questions were worded as follows: “How hungry do you feel?”, “How much do you think you can eat?”, “How satisfied do you feel?”, “How full do you feel?”, and answers were anchored as “not at all” to “extremely”. Using these ratings, a composite appetite score (CAS) was calculated at each time of measurement as the average of hunger, PFC, and the inverse of fullness (i.e., 100 - fullness), and satiety (i.e., 100 - satiety), as reported by others (31-33), **Equation 3**. For this study, the CAS combined the four dimensions of appetite to derive a general measure of appetite that reflects a single "motivation to eat” phenomenon. The CAS is increasingly used in research because it integrates appetite sensations into one index (31-33). A higher CAS value is associated with a greater appetite sensation and a subsequent stronger motivation to eat.

Equation 3 (31-33)

Composite appetite score (mm) = [hunger + prospective food consumption + unfullness (100 - fullness) + lack of satiety (100 - satiety)]/4.

Each of the four perceived appetite sensations and the CAS responses were compared between low- and high-retainers. Total daily responses to perceived appetite sensations and CAS (hereafter overall motivation to eat) were assessed over 14 hours using the area under the curve (14h-AUC) analyses, which was calculated from the fasting time point at 0730 to the postprandial evening snack at 2130. We further divided the 24-h WBCU stay into four key time periods to represent morning from 0900 to 1200, early afternoon from 1200 to 1500, late afternoon from 1500 to 1800, and evening from 1800 to 2100, and AUC were calculated for each time period (3h-AUC). The trapezoidal method was used to calculate AUC (34).

4.3.9 Biochemical parameters.

Fasting and 2-h postprandial (following breakfast) venous blood samples were collected (BD Vacutainer® Fluoride Tubes containing Sodium Fluoride 10 mg, Potassium Oxalate 8 mg, or serum separator tubes; NJ, USA). Plasma and serum samples were separated from whole blood following centrifugation (2500 rpm for 10 min; Jouan CR 4.22 centrifuge) and stored at -80°C until analyzed. Plasma glucose and serum triglycerides (Sekisui Diagnotics PEI Inc., PE, Canada), and free-fatty acids concentrations (Zen-Bio Inc.; NC, USA) were measured using colorimetric assays. Serum insulin was determined by ELISA (Insulin Ultrasensitive Enzyme-Linked Immunosorbent Immunoassay kit; ALPCO Diagnostics; NH, USA). All metabolites were analyzed in duplicate with a coefficient of variation <5%. The homeostasis model assessment of insulin resistance was calculated using the equation described by Matthews et al (1985) (35).

4.3.10 Statistical analysis.

All statistical analyses were performed using SPSS version 24 (IBM Corp.; NY, USA); data are presented as mean ± standard deviation (SD) and the threshold for significance was set at $P<0.05$. Normal distribution was evaluated using the Shapiro-Wilk test. Differences between low- and high-retainers were determined via independent *t* test or Mann-Whitney *U* test, as appropriate.

Five multiple linear regression models were conducted with PPWR (kg) as a continuous dependent variable. Independent variables included in the models were appetite-related variables (all expressed as 14h-AUC): model 1 included overall motivation to eat, model 2 included fullness, model 3 included satiety, model 4 included hunger, model 5 included PFC. GWG (kg), $p\dot{V}O_2max$ (ml/min/kg), lactation (daily duration of lactation episodes, min/d), fasting glucose (mg/dL), and residual SleepEE (kcal/d) were included as covariates in all five models due to their potential biological impact on PPWR.

Multiple linear regression models were also used to describe associations between appetite sensations (all expressed as 14h-AUC) and other metabolic characteristics. The dependent variable for model 1 was the overall motivation to eat, for model 2 was fullness, for model 3 was satiety, for model 4 was hunger, and for model 5 was PFC. Lactation (daily duration of lactation episodes, min/d) was the independent variable; and FM (kg), FFM (kg), residual SleepEE (kcal/d), PAL, and carbohydrate oxidation (g/d) were included as covariates in all five models, to control for their potential biological effects on appetite.

Results from regression models are presented as β-coefficients (B) and standard error of the coefficient (SE). All models were tested for statistical assumptions, including: 1) Independence of residuals; 2) Linear relationship between the dependent variable and each of the independent variables, and between the dependent variable and independent variables collectively; 3) Homoscedasticity of residuals; 4) Co-linearity among independent variables; 5) Normal distribution of the residuals; 6) Unusual data points (i.e., outliers, high leverage points, highly influential points).

4.4 Results

4.4.1 Subject characteristics.

A total of 49 postpartum women were included in the analysis. Of these, 43 completed the 24-h test and six completed at least the pre-breakfast measurements (i.e., anthropometrics, fasting blood sample, REE, three appetite sensations ratings), Figure 4.1. Five women did not complete the 24-h test due to a recent minor surgery (*n* = 1), and anxiety over being away from their infant (*n* = 4); however, they did complete a shortened version of the test including at least the pre-breakfast measurements. One participant was unable to complete the 24-h test due to a migraine. These six women did not differ from those who completed the 24-h test for the following measures: maternal age, body weight, BMI, FM, FFM, measured REE (all $p > 0.05$).

Characteristics of study participants are shown in **Table 4.1**, with a more extensive description previously reported (20, 21). Briefly, participants were primarily a group of Caucasian women in their early 30s, with a high income, high educational level, and 53% were primiparous. Average GWG was 15.09 ± 5.12 kg, and the weight retained at 9M-PP was 2.14 ± 6.10 kg. When classified according to BMI, 24 women (49.0%) were normal weight, 13 (26.5%) were overweight, and 12 (24.5%) were obese. Twenty-eight women (57.1%) were lactating, and they nursed their infants 7 ± 3 times/d for 12 ± 5 min/feed, with an average estimated breast milk energy output of 465 ± 198 kcal/d. Average measured SleepEE was 1475 ± 204 kcal/d, and residual SleepEE was 1 ± 83 kcal/d, with a wide variability (range: -170 to 188 kcal/d). Average measured TEE was 2028 ± 286 kcal/d, with 227 ± 52 grams of carbohydrate being oxidized per 24h. All participants had normal fasting glucose and no evidence of abnormal insulin resistance.

4.4.2 Postpartum weight retention and appetite.

Figure 4.2 depicts appetite sensations throughout the 24-h WBCU stay. Compared to low-retainers, high-retainers were hungrier immediately after and one hour after breakfast (*P*=0.004, and *P* =0.033, respectively), and immediately after dinner (*P*=0.016, Figure 4.2A). High-retainers reported reduced PFC while fasting (1.5 hours before breakfast, *P*=0.048; and immediately before breakfast, *P*=0.021), but greater immediately after breakfast (*P*=0.018, Figure 4.2B). High-retainers also reported lower satiety sensations immediately after the evening snack (*P*=0.031, Figure 4.2C); and lower sensations of fullness immediately after and one hour after breakfast (*P*=0.011, and *P*=0.038, respectively), and immediately after lunch (*P*=0.036), and the evening snack (*P*=0.029, Figure 4.2D), compared to low-retainers. Overall, high-retainers reported greater overall motivation to eat than low-retainers immediately after and one hour after breakfast (*P*=0.001, and *P*=0.027, respectively), and immediately after dinner (*P*=0.029, Figure 4.2E). The 3h-AUC for subjective appetite sensations for key periods of the day are shown in **Figure 4.3**. In the morning, high-retainers were hungrier than low-retainers (Figure 4.3A), and reported reduced sensations of fullness (Figure 4.3D) and greater motivation to eat (Figure 4.3E). No differences in appetite sensations between low- and high-retainers were observed in other periods of the day, and in the total daily response assessed over 14 hours (Figure 4.3, and **Figure 4.4).**

Results of univariate and multiple linear regression analyses for factors associated with PPWR are shown in **Table 4.2.** In univariate analysis, GWG (R^2=0.135), p$\dot{V}O_2$max (R^2=0.116), fasting glucose (R^2=0.221), overall motivation to eat (R^2=0.099), and fullness (R^2=0.094) were associated with PPWR. In all five multiple linear regression models, appetite sensations were associated with PPWR, after adjusting for covariates. Overall motivation to eat, hunger, and PFC were positively associated with PPWR, and the overall models explained 63.4%, 54.3%, and 55.8% of variance in PPWR, respectively. Fullness and satiety sensations were negatively associated with PPWR, explaining 65.8%, and 61.1%, of variance in PPWR, respectively. PPWR was positively associated with GWG and fasting glucose, and negatively associated with $p\dot{V}O_2max$ and residual SleepEE in all five models. Daily duration of lactation episodes was not associated with PPWR in any model (Table 4.2).

4.4.3 Appetite sensations and other metabolic characteristics.

In univariate analysis, daily duration of lactation episodes (R^2=0.114; R^2=0.095; R^2=0.105, respectively), and PAL (R^2=0.148; R^2=0.168; R^2=0.127, respectively) were associated with overall motivation to eat, hunger, and PFC assessed over 14 hours. PAL was also associated with fullness (R^2=0.122), and carbohydrate oxidation was associated with fullness (R^2=0.129), and satiety (R^2=0.122), **Supplemental Table 4.1**.

Table 4.3 shows results of multiple linear regression analyses for metabolic characteristics associated with appetite sensations. Lactation was associated with all five appetite sensations assessed over 14 hours, after adjusting for covariates. Daily duration of lactation episodes was positively associated with overall motivation to eat, hunger, and PFC, and negatively associated with fullness and satiety. PAL was positively associated with overall motivation to eat, hunger, and PFC, and negatively associated with fullness. Carbohydrate oxidation over 24 hours was negatively associated fullness and satiety sensations, and positively associated with overall motivation to eat. FM, FFM, and residual SleepEE were not significant predictors of any appetite sensations.

4.5 Discussion

To our knowledge, this is the first study to comprehensively evaluate maternal differences in appetite sensations throughout the day under conditions in which energy intake and energy expenditure were precisely matched, along with measurements of daily duration of lactation episodes and PPWR. The present data indicated that appetite sensations were associated with PPWR, lactation, carbohydrate oxidation and PAL.

Variation in appetite sensations during the postpartum period may reflect possible underlying biological factors influencing PPWR, which might contribute to the high variability in body weight and composition after childbirth (3, 36). We determined that PPWR was negatively associated with fullness and satiety, and positively associated with overall motivation to eat, hunger, and PFC. Similarly, in other populations, appetite has been shown to correlate with BMI and body composition (37-39), and to predict weight change (12, 13, 37). In our study, high-retainers were hungrier and had a greater overall motivation to eat after breakfast and dinner compared to low-retainers. Similar results were observed in 315 men and women with obesity, in which lower weight loss was associated with higher postprandial 1-h AUC for desire to eat and lower postprandial 1-h AUC for fullness (12). Snoek and colleagues (40) also reported that after an *ad libitum* lunch, individuals with obesity had a greater appetite for a meal or snack than normal-weight individuals, suggesting a greater "wanting" for more food among individuals with obesity. In free-living conditions, this could promote shorter frequency of food intake initiation between meals.

The present study also demonstrated that PFC sensations were lower in high-retainers than low-retainers during fasting conditions. Although further research is needed, one explanation might be related to the downregulation of ghrelin in the postpartum period (41), as observed in other populations (42, 43). Fasting ghrelin concentrations are inversely correlated with body weight (41), and adiposity (44) in women at 4-5 weeks postpartum. This suggests ghrelin may change with increased adiposity and may potentially impact body weight (41). In the postpartum period, the evidence is limited on how and if appetite affects body weight regulation, as studies have mainly focused on appetite-regulating or lactation-related hormones. Larson-Meyer and colleagues (44) reported that although circulating concentrations of appetite-regulating hormones were not predictive of PPWR, higher postprandial ghrelin was observed in women who retained weight at one year postpartum.

Additionally, the present study determined that PPWR was positively correlated with GWG and fasting glucose concentrations. GWG is a major risk factor for PPWR, with several studies (45) demonstrating its direct association with the amount of weight retained after pregnancy. The relationship between glucose regulation to changes in body weight was explored by Ehrlich and colleagues (46) and found that women who lost weight from 6 weeks to 12 months postpartum had lower fasting glucose and insulin at 12 months postpartum compared with those who maintained or gained weight over time.

The present study also found an inverse correlation between PPWR and p$\dot{V}O_2$max, similar to other studies (21, 47), suggesting an association between cardiorespiratory fitness and weight status in the postpartum period. A negative association between PPWR and residual SleepEE was also observed in this study, which is consistent with a recent study by Ostendorf and colleagues (48) that found residual REE to be positively correlated with weight loss, but not with duration of weight loss maintenance, suggesting that sustained weight loss may not always result in disproportionately lower-than-predicted energy expenditure.

In addition to identifying a relationship between appetite and PPWR, we demonstrated that lactation was associated with women's perceptions of appetite throughout the day. Greater duration of lactation episodes over 24 hours was associated with higher motivation to eat, hunger, and PFC, and reduced sensations of fullness and satiety. Larson-Meyer and colleagues (44) also used visual analogue scales to assess hunger, desire to eat, fullness and satiety sensations at baseline and at 30, 60, 90, 120, and 150 minutes after a test meal, and at 20 and 60 minutes following an *ad libitum* meal. They reported (44) appetite ratings and AUC for the four appetite sensations were not different between lactating women and never-pregnant controls.

Several physiological mechanisms may explain the reported relationship between appetite and lactation; however, future investigations are warranted. One mechanism is the glucostatic theory proposed by Mayer (49), in which hunger is initiated by decline of blood glucose level. Lactose is the most abundant carbohydrate in human milk and plasma glucose is the primary precursor (50), increasing the glucose production rates by ~30% during lactation (51). Higher glucose production rates may stimulate appetite to increase energy intake and thereafter blood glucose levels. Another mechanism could lie in increasing glycogenolysis rates during lactation (51). According to the glycogenostatic theory proposed by Flatt (52, 53), low glycogen stores stimulate food intake to maintain or replenish glycogen stores. More recently, several studies have included assessments of the appetite-regulating hormones, ghrelin, PYY and leptin and demonstrated that lactation may be associated with higher ghrelin (54) and PYY (54, 55), and lower leptin (56), although these results are inconsistent (41, 44). This association may suggest that lactation-induced neuroendocrine signals increased energy intake to offset increased needs to meet the energetic demands of lactation.

It is also possible that lactation-related hormones are directly involved in the regulation of appetite control. Prolactin controls milk production in which physical suckling is the main stimulus for its secretion (57). Although mechanisms are not clearly understood, prolactin might suppress leptin during lactation (58), which in turn may reduce satiety signals, facilitating energy intake (59). Animal studies have documented that changes in energy intake observed in lactating rats are driven not only by signals of increased energetic demands but also by physical suckling stimulation, independent of milk delivery *per se* (15, 16). In this way, daily duration of lactation episodes may impact appetite independently of breast milk energy output.

Other interesting findings of our study were the associations between appetite and carbohydrate oxidation, and appetite and PAL. These relationships were not influenced by body composition, and are consistent with the glycogenostatic theory of feeding (52, 53). Higher daily carbohydrate oxidation and PAL may lead to a greater depletion of glycogen stores, thereby stimulating appetite and prompting energy intake. In support of this concept, Pannacciulli and colleagues (60), found that 24-h carbohydrate oxidation in a respiratory chamber predicted *ad libitum* food intake over three days, explaining 15% of its variance. Additionally, our study found that body composition and low/high metabolism do not appear to be associated with appetite in postpartum women, unlike at other periods across the life course (7, 8).

The present study was well controlled and used rigorous and precise methodologies to assess energy expenditure, body composition, cardiorespiratory fitness, and lactation patterns. However, it is not without limitations. Given recruitment feasibility and the extensive time commitment required for each study visit, the current study has a limited sample size, and a larger group of women may have increased our ability to detect differences in other metabolic characteristics. Additionally, our analysis had only one-time point for the 24-h test, and data are incomplete for six participants. Finally, our study focused on subjective appetite sensations ratings and did not measure appetite-regulating hormones (e.g., total and acylated ghrelin, PYY, GLP-1), and lactation-related hormones (e.g., prolactin).

The results of this study support the hypothesis that daily duration of lactation, daily carbohydrate oxidation and PAL are associated with appetite, which in turn is associated with body weight during the postpartum period. Further well-controlled longitudinal studies, including information on appetite-regulating and lactation-related hormones, would be of interest to understand the causal relationships between changes in appetite, lactation patterns, and body weight associated with child bearing.

Table 4.1 Characteristics of women at nine months postpartum[1].

Variables	Mean ± SD
General (n = 49)	
Age (y)	33 ± 4
Prepregnancy BMI (kg/m^2)	25.7 ± 5.3
Gestational weight gain (kg)[2]	15.1 ± 5.1
Anthropometrics and body composition (n = 49)	
Body weight (kg)	73.6 ± 18.0
BMI (kg/m^2)	26.5 ± 5.8
Postpartum weight retention (kg)[3]	2.1 ± 6.1
Fat mass (kg)	27.5 ± 13.5
Fat mass index (kg/m^2)	9.9 ± 4.7
Fat-free mass (kg)	45.2 ± 5.3
Fat-free mass index (kg/m^2)	16.3 ± 1.9
Breastfeeding pattern (n = 28)	
Number of breastfeeding episodes (times/d)	7 ± 3
Duration of each episode (min/feed)	12 ± 5
Average daily duration of breastfeeding (min/d)	88 ± 63
Breast milk volume (g/d)	530 ± 225
Breast milk energy output (kcal/d)	465 ± 198
Energy metabolism (n = 43)	
Fasting RQ (*n* = 49)	0.822 ± 0.028
Sleep RQ	0.842 ± 0.024
24h RQ	0.856 ± 0.020
Measured resting energy expenditure (kcal/d) (*n* = 49)	1531 ± 224
Measured SleepEE (kcal/d)	1475 ± 204
Residual SleepEE (kcal/d)[4]	1 ± 83
Physical activity level	1.32 ± 0.07
p$\dot{V}O_2$max (ml/kg/min) (*n* = 47)	35.1 ± 7.3
Total energy expenditure (kcal/d)	2028 ± 286
Protein oxidation (g/d)	77 ± 29
Carbohydrate oxidation (g/d)	227 ± 52
Fat oxidation (g/d)	76 ± 24
Biochemical parameters (n = 47)	
Glucose (mg/dL)	
Fasting	79.1 ± 12.7
2h-Postprandial	73.4 ± 12.4
Insulin (µIU/ml)	
Fasting	4.4 ± 2.4
2h-Postprandial	10.6 ± 10.2
Triglycerides (mg/dL)	
Fasting	57.5 ± 24.8
2h-Postprandial	67.4 ± 32.9
Free-fatty acids (µmol/L)	
Fasting	506.3 ± 223.7
2h-Postprandial	290.8 ± 186.6

HOMA-IR	0.85 ± 0.56

[1] BMI, body mass index; HOMA-IR, homeostasis model assessment of insulin resistance; p$\dot{V}O_2$max, predicted maximal volume of oxygen consumption; RQ, respiratory quotient; SleepEE, sleep energy expenditure.

[2] Gestational weight gain was calculated as the difference between self-reported highest weight in pregnancy and prepregnancy weight.

[3] Postpartum weight retention was calculated as the difference between current weight (measured at the study visit) and self-reported prepregnancy weight.

[4] Residual SleepEE was calculated as the difference between measured and predicted SleepEE, where predicted SleepEE was calculated from a linear regression-derived equation using fat mass and fat-free mass as independent variables.

Table 4.2 Multiple linear regression of factors associated with weight retention in postpartum women (*n* = 49)[1].

	Univariate analysis		Model 1		Model 2		Model 3		Model 4		Model 5	
Variable	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***
Intercept			-20.69 ± 6.77	**0.004**	3.19 ± 6.28	0.614	3.66 ± 6.95	0.601	-13.41 ± 6.91	0.061	-16.66 ± 7.25	**0.028**
GWG (kg)	0.44 ± 0.16	**0.009**	0.36 ± 0.14	**0.011**	0.33 ± 0.13	**0.015**	0.37 ± 0.14	**0.011**	0.37 ± 0.15	**0.018**	0.37 ± 0.15	**0.018**
$p\dot{V}O_2max$ (ml/min/kg)	-0.28 ± 0.12	**0.019**	-0.31 ± 0.09	**0.002**	-0.29 ± 0.09	**0.003**	-0.30 ± 0.10	**0.004**	-0.30 ± 0.11	**0.008**	-0.29 ± 0.10	**0.008**
Lactation duration (min/d x 10^{-2})	1.62 ± 1.37	0.241	0.52 ± 1.06	0.626	0.66 ± 1.00	0.512	0.81 ± 1.06	0.450	1.01 ± 1.17	0.393	0.91 ± 1.15	0.434
Fasting glucose (mg/dL)	0.23 ± 0.06	**0.001**	0.18 ± 0.06	**0.003**	0.20 ± 0.05	**0.001**	0.18 ± 0.06	**0.003**	0.16 ± 0.06	**0.016**	0.18 ± 0.06	**0.006**
Residual SleepEE (kcal/d x 10^{-2})	-1.90 ± 1.10	0.093	-2.25 ± 0.78	**0.007**	-2.68 ± 0.76	**0.001**	-2.44 ± 0.80	**0.005**	-1.89 ± 0.86	**0.036**	-1.91 ± 0.85	**0.031**
CAS (14h-AUC x 10^{-3})	0.25 ± 0.12	**0.039**	0.34 ± 0.09	**0.001**								
Fullness (14h-AUC x 10^{-3})	-1.99 ± 0.97	**0.046**			-2.97 ± 0.72	**<0.001**						
Satiety (14h-AUC x 10^{-3})	-1.92 ± 1.06	0.078					-2.75 ± 0.81	**0.002**				
Hunger (14h-AUC x 10^{-3})	2.22 ± 1.22	0.077							2.19 ± 1.02	**0.039**		
PFC (14h-AUC x 10^{-3})	1.82 ± 1.11	0.109									2.19± 0.91	**0.021**

[1] AUC, area under the curve; B, coefficient; CAS, composite appetite score; GWG, gestational weight gain; PFC, prospective food consumption; $p\dot{V}O_2max$, predicted maximal volume of oxygen consumption; SE, standard error; SEE, standard error of the estimate; SleepEE, sleep energy expenditure.

Model 1: F(6, 33) = 9.450, $P < 0.001$; $R^2 = 0.632$; SEE = 4.024.
Model 2: F(6, 33) = 10.710, $P < 0.001$; $R^2 = 0.661$; SEE = 3.865.
Model 3: F(6, 33) = 8.872, $P < 0.001$; $R^2 = 0.617$; SEE = 4.105.
Model 4: F(6, 33) = 6.660, $P < 0.001$; $R^2 = 0.548$; SEE = 4.462.
Model 5: F(6, 33) = 7.064, $P < 0.001$; $R^2 = 0.562$; SEE = 4.390.

Table 4.3 Multiple linear regression of factors associated with appetite sensations in postpartum women (*n* = 49)[1].

	Model 1		**Model 2**		**Model 3**		**Model 4**		**Model 5**	
	CAS, 14h-AUC		**Fullness, 14h-AUC**		**Satiety, 14h-AUC**		**Hunger, 14h-AUC**		**PFC, 14h-AUC**	
Variable	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***
Intercept	-11603.57 ± 20060.48	0.567	9926.11 ± 2497.56	**<0.001**	8723.23 ± 2413.71	**0.001**	-2162.32 ± 2076.48	0.305	-701.41 ± 2292.90	0.761
Lactation duration (min/d)	39.68 ± 15.56	**0.015**	-4.18 ± 1.94	**0.038**	-3.83 ± 1.87	**0.048**	3.56 ± 1.61	**0.033**	4.22 ± 1.78	**0.023**
Fat mass (kg)	-114.74 ± 89.72	0.209	10.36 ± 11.17	0.360	9.48 ± 10.80	0.386	-12.07 ± 9.29	0.202	-13.73 ± 10.26	0.189
Fat-free mass (kg)	-81.57 ± 246.06	0.742	8.69 ± 30.63	0.778	0.80 ± 29.61	0.979	-2.97 ± 25.47	0.908	-20.84 ± 28.12	0.463
Residual SleepEE (kcal/d)	6.61 ± 12.08	0.588	-2.10 ± 1.50	0.172	-1.51 ± 1.45	0.307	-0.51 ± 1.25	0.686	-0.48 ± 1.38	0.730
Physical activity level	34772.52 ± 13973.51	**0.018**	-3650.70 ± 1739.72	**0.043**	-2537.04 ± 1681.31	0.140	4040.46 ± 1446.41	**0.008**	3790.53 ± 1597.16	**0.023**
Carbohydrate oxidation (g/d)	51.82 ± 23.38	**0.033**	-7.23 ± 2.91	**0.018**	-6.35 ± 2.81	**0.030**	2.60 ± 2.42	0.291	4.39 ± 2.67	0.109

[1] AUC, area under the curve; B, coefficient; CAS, composite appetite score; PFC, prospective food consumption; SE, standard error; SEE, standard error of the estimate; SleepEE, sleep energy expenditure.

Model 1: F(6, 36) = 3.445, $P = 0.009$; $R^2 = 0.365$; SEE = 6523.454.

Model 2: F(6, 36) = 3.345, $P = 0.010$; $R^2 = 0.358$; SEE = 812.178.

Model 3: F(6, 36) = 2.508, $P = 0.039$; $R^2 = 0.295$; SEE = 784.911.

Model 4: F(6, 36) = 2.677, $P = 0.030$; $R^2 = 0.308$; SEE = 675.250.

Model 5: F(6, 36) = 2.749, $P = 0.027$; $R^2 = 0.314$; SEE = 745.626.

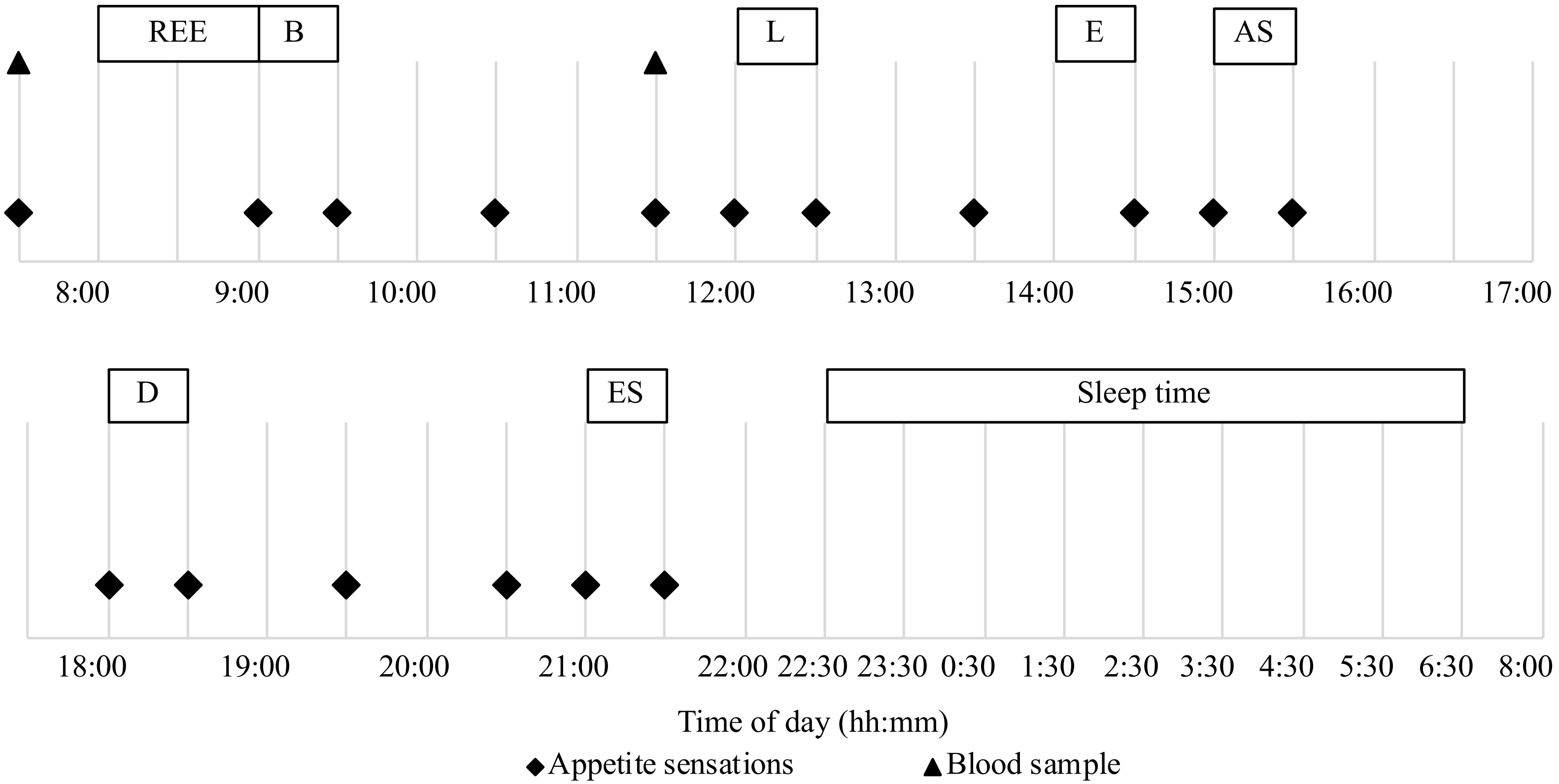
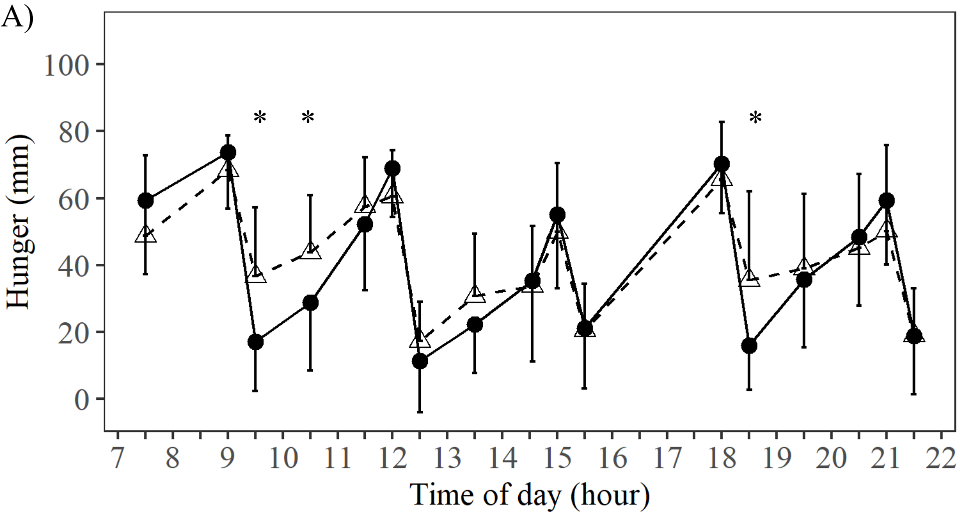


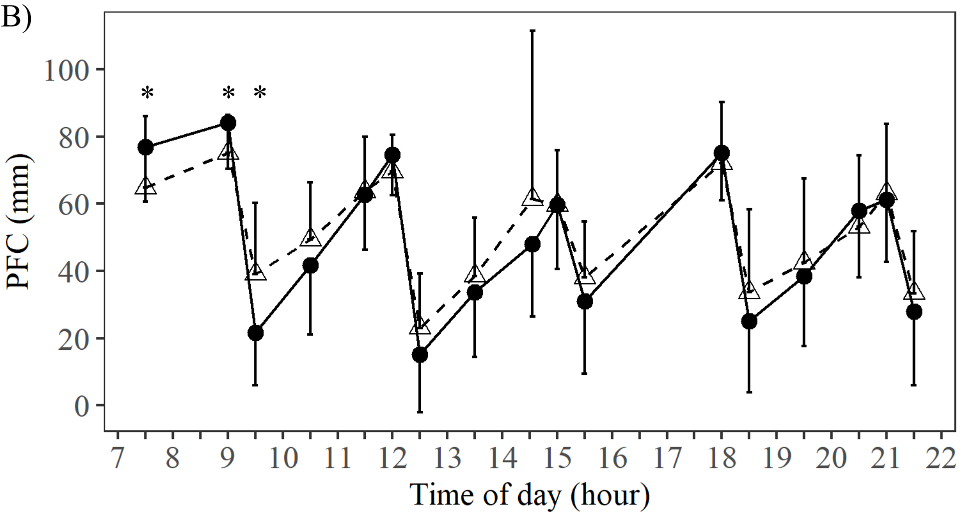
Figure 4.1 Study design. Forty-three women at approximately nine months postpartum (9.2 ± 0.3 months) were studied during 24 hours of whole body calorimetry at the Human Nutrition Research Unit, University of Alberta (Edmonton, Canada); and six women were studied until at least after breakfast. Abbreviations: AS, afternoon snack; B, breakfast; D, dinner; ES, evening snack; E, exercise; L, lunch; REE, resting energy expenditure.

(A)



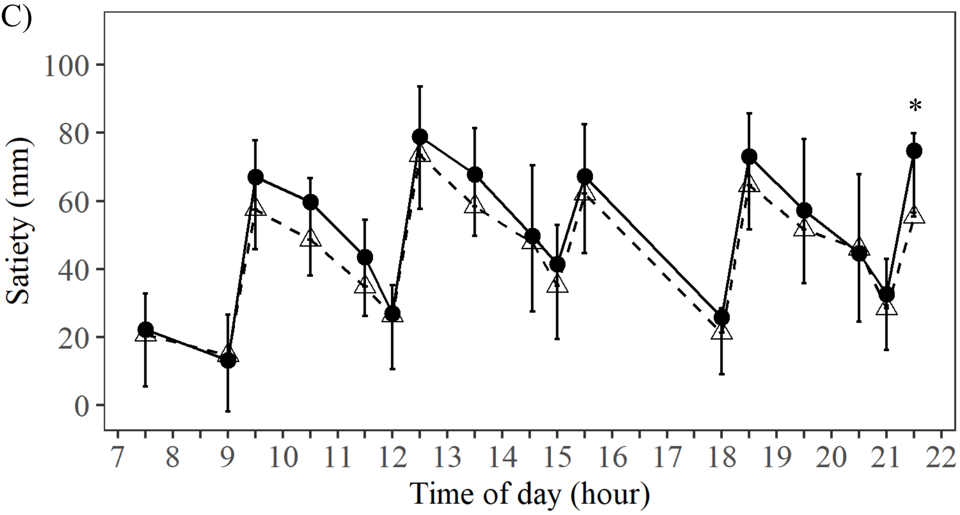
Hunger (mm)
0
20
40
60
80
100
*
*
*
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Time of day (hour)

(B)



PFC (mm)
0
20
40
60
80
100
*
*
*
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Time of day (hour)

(C)



Satiety (mm)
0
20
40
60
80
100
*
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Time of day (hour)

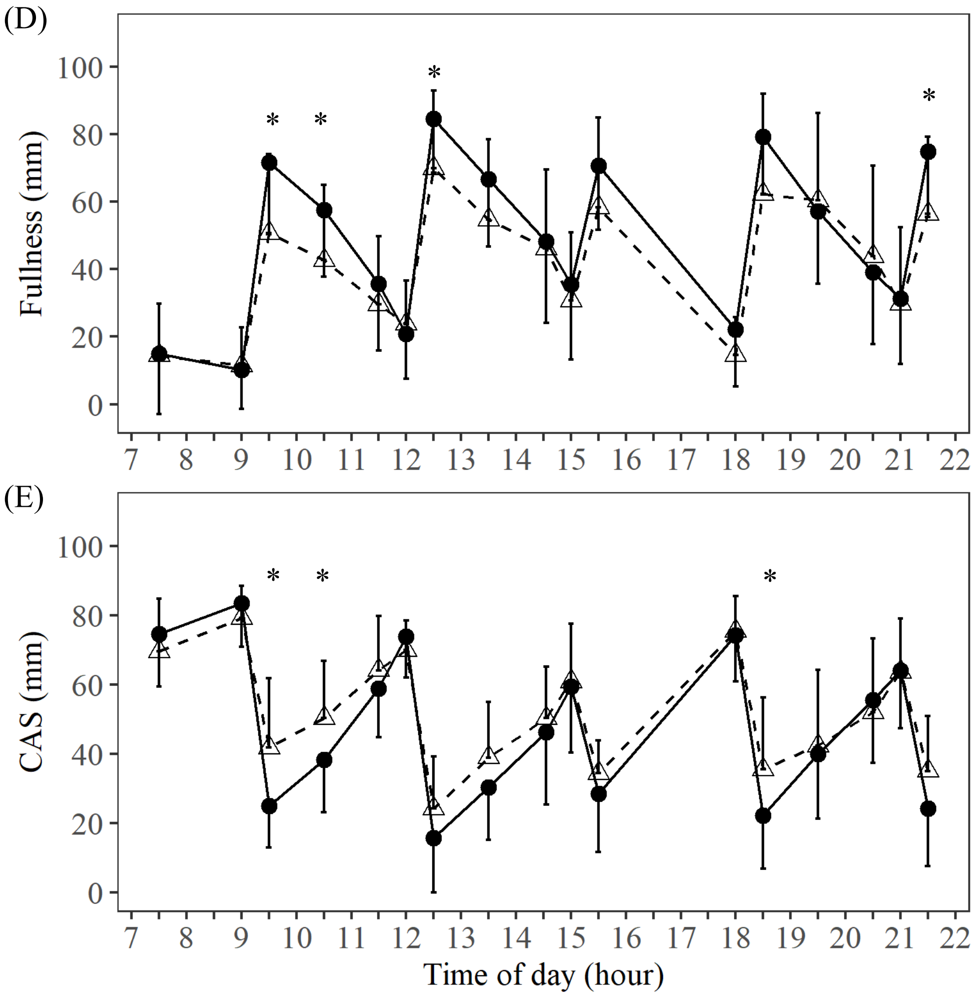
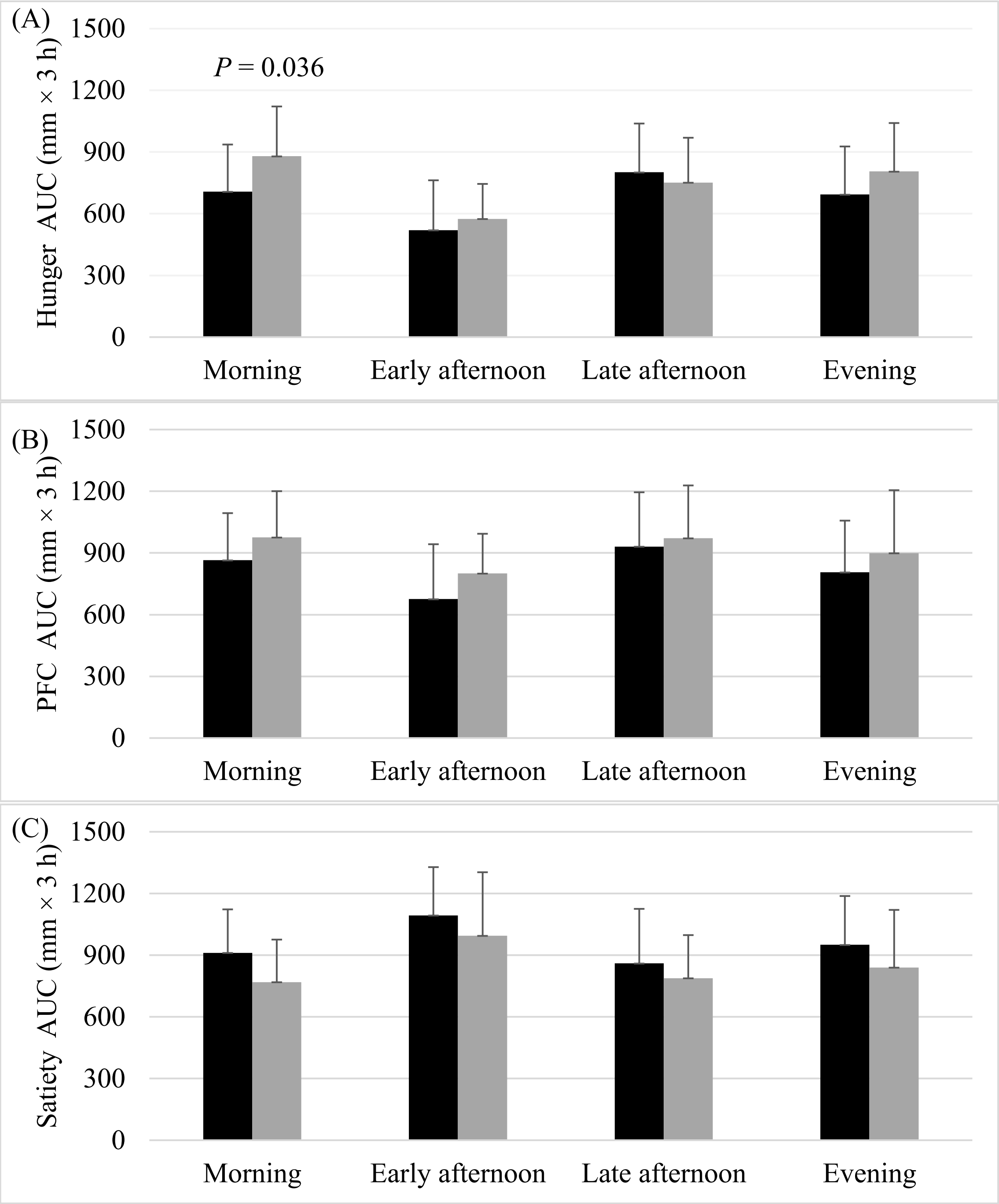


Figure 4.2 Appetite sensations over 14 hours of whole body calorimetry unit stay. (A) hunger, (B) PFC, (C) satiety, (D) fullness, and (E) CAS in low-retainers (*n* = 38, solid circles, solid lines), and high-retainers (*n* = 11, blank triangle, dashed lines) postpartum women. Data are expressed as mean ± SD. *P* values between low- and high-retainers were calculated from independent samples *t* test or Mann-Whitney *U* test, as appropriate. Breakfast, lunch, afternoon snack, dinner, and evening snack were provided at 0900h, 1200h, 1500h, 1800h, and 2100h, respectively. Abbreviations: CAS, composite appetite score; PFC, prospective food consumption. *$P < 0.05$.


(A)
P = 0.036
Hunger AUC (mm × 3 h)
1500
1200
900
600
300
0
Morning
Early afternoon
Late afternoon
Evening
(B)
PFC AUC (mm × 3 h)
1500
1200
900
600
300
0
Morning
Early afternoon
Late afternoon
Evening
(C)
Satiety AUC (mm × 3 h)
1500
1200
900
600
300
0
Morning
Early afternoon
Late afternoon
Evening

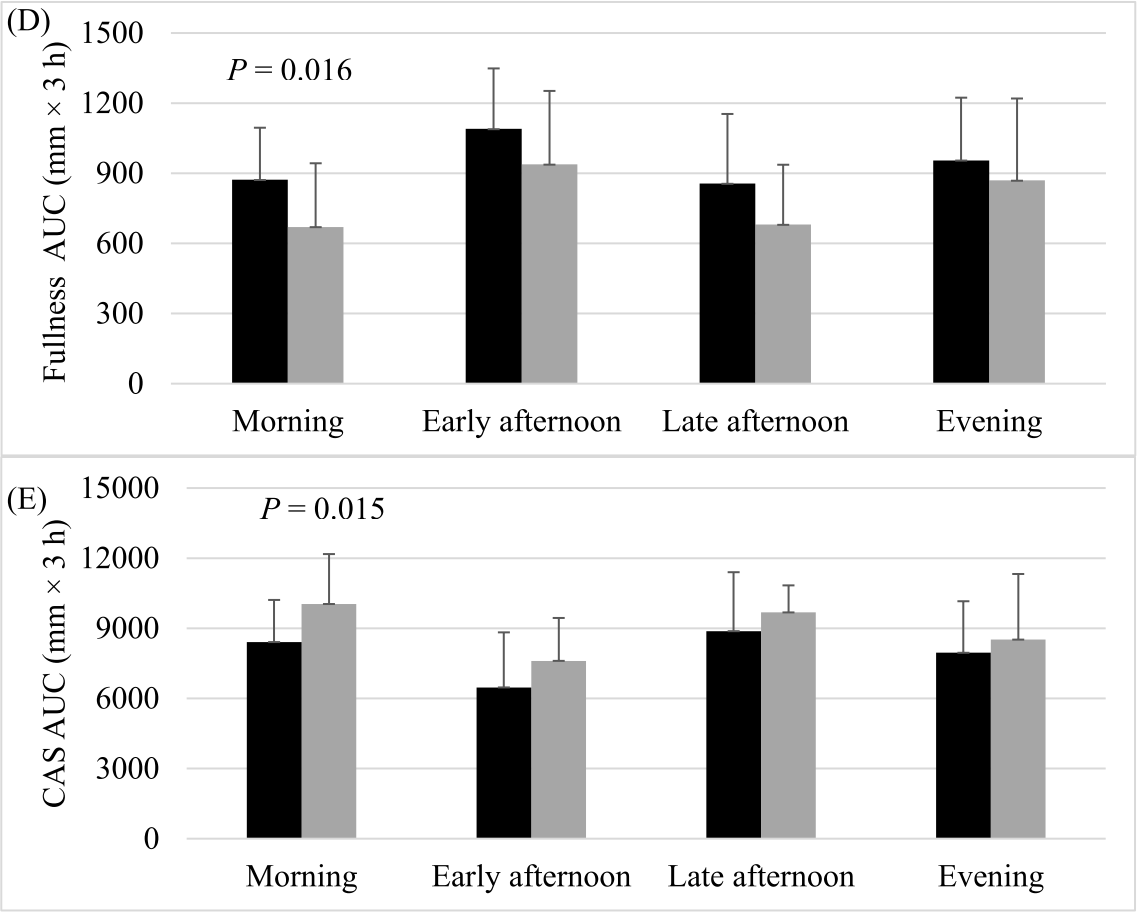


Figure 4.3 Appetite sensations in key periods of the day comparing low-retainers (n = 38, black bars) and high-retainers (*n* = 11, grey bars). (A) hunger, (B) PFC, (C) satiety, (D) fullness, and (E) CAS. Key periods of the day (morning, early afternoon, late afternoon, and evening) were calculated as 3h-AUC. Data are expressed as mean ± SD. *P* values between low- and high-retainers were calculated from independent samples *t* test or Mann-Whitney *U* test (i.e., PFC, morning; and Fullness, early afternoon), as appropriate. Significant *P* values are shown in the figure. Abbreviations: AUC, area under the curve; CAS, composite appetite score; PFC, prospective food consumption.

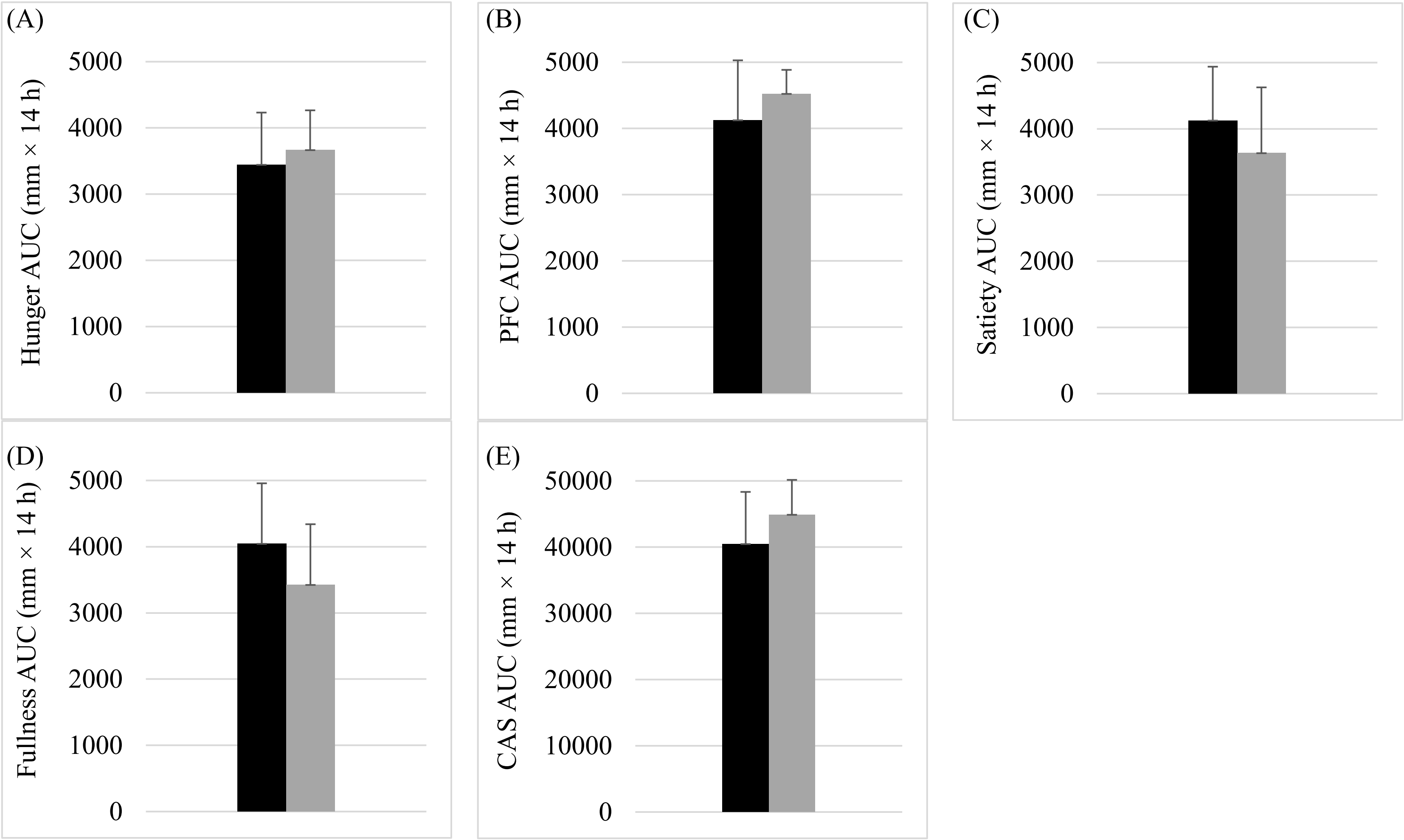


Figure 4.4 Total daily response of appetite sensations assessed over 14 hours comparing low-retainers (n = 38, black bars) and high-retainers (n = 11, grey bars). (A) hunger, (B) PFC, (C) satiety, (D) fullness, and (E) CAS. Total daily response was calculated as 14h-AUC. Data are expressed as mean ± SD. P values between low- and high-retainers were calculated from independent samples t test or Mann-Whitney U test (i.e., PFC), as appropriate. There are no significant P values. Abbreviations: AUC, are under the curve; CAS, composite appetite score; PFC, prospective food consumption.

Supplemental Table 4.1. Univariate analysis of factors associated with appetite sensations in postpartum women (n = 49)[1].

	CAS 14h-AUC		**Fullness 14h-AUC**		**Satiety 14h-AUC**		**Hunger 14h-AUC**		**PFC 14h-AUC**	
Variable	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***	**B ± SE**	***P***
Fat mass (kg)	-32.84 ± 87.75	0.710	-0.83 ± 10.88	0.939	-1.42 ± 10.04	0.888	-6.31 ± 8.66	0.471	-9.14 ± 9.56	0.345
Fat-free mass (kg)	72.26 ± 223.42	0.748	-18.87 ± 27.55	0.497	-22.07 ± 25.31	0.388	-0.90 ± 22.19	0.968	-12.14 ± 24.53	0.623
Residual SleepEE (kcal/d)	8.85 ± 14.12	0.534	-2.34 ± 1.72	0.181	-1.72 ± 1.60	0.289	-0.31 ± 1.41	0.828	-0.24 ± 1.56	0.877
Lactation (duration, min/d)	39.43 ± 17.17	**0.027**	-4.18 ± 2.16	0.061	-3.79 ± 2.00	0.065	3.57 ± 1.72	**0.045**	4.16 ± 1.90	**0.034**
Physical activity level	39769.58 ± 14879.52	**0.011**	-4460.88 ± 1871.32	**0.022**	-3284.04 ± 1768.41	0.070	4200.00 ± 1458.98	**0.006**	4049.91 ± 1657.08	**0.019**
Carbohydrate oxidation (g/d)	43.01 ± 21.83	0.056	-6.50 ± 2.64	**0.018**	-5.84 ± 2.44	**0.021**	2.08 ± 2.24	0.360	2.65 ± 2.48	0.291

[1] AUC, area under the curve; B, coefficient; CAS, composite appetite score; PFC, prospective food consumption; SE, standard error; SleepEE, sleep energy expenditure.

4.6 References

1. Gunderson EP, Abrams B. Epidemiology of gestational weight gain and body weight changes after pregnancy. Epidemiol Rev 1999;21:261-275.
2. Lim S, O'Reilly S, Behrens H, Skinner T, Ellis I, Dunbar JA. Effective strategies for weight loss in post-partum women: a systematic review and meta-analysis. Obes Rev. 2015;16:972-987.
3. Schmitt NM, Nicholson WK, Schmitt J. The association of pregnancy and the development of obesity - results of a systematic review and meta-analysis on the natural history of postpartum weight retention. Int J Obes (Lond) 2007;31:1642-1651.
4. Begum F, Colman I, McCargar LJ, Bell RC. Gestational weight gain and early postpartum weight retention in a prospective cohort of Alberta women. J Obstet Gynaecol Can 2012;34:637-647.
5. Endres LK, Straub H, McKinney C, Plunkett B, Minkovitz CS, Schetter CD, Ramey S, Wang C, Hobel C, Raju T, et al. Postpartum weight retention risk factors and relationship to obesity at 1 year. Obstet Gynecol 2015;125:144-152.
6. Hollis JL, Crozier SR, Inskip HM, Cooper C, Godfrey KM, Harvey NC, Collins CE, Robinson SM. Modifiable risk factors of maternal postpartum weight retention: an analysis of their combined impact and potential opportunities for prevention. Int J Obes (Lond) 2017;41:1091-1098.
7. Hopkins M, Finlayson G, Duarte C, Gibbons C, Johnstone AM, Whybrow S, Horgan GW, Blundell JE, Stubbs RJ. Biological and psychological mediators of the relationships between fat mass, fat-free mass and energy intake. Int J Obes (Lond) 2019;43:233-242.
8. Blundell JE, Caudwell P, Gibbons C, Hopkins M, Naslund E, King N, Finlayson G. Role of resting metabolic rate and energy expenditure in hunger and appetite control: a new formulation. Dis Model Mech 2012;5:608-613.
9. Mayer J, Marshall NB, Vitale JJ, Christensen JH, Mashayekhi MB, Stare FJ. Exercise, food intake and body weight in normal rats and genetically obese adult mice. Am J Physiol 1954;177:544-548.
10. Mayer J, Roy P, Mitra KP. Relation between caloric intake, body weight, and physical work: studies in an industrial male population in West Bengal. Am J Clin Nutr 1956;4:169-175.

11. Flint A, Raben A, Blundell JE, Astrup A. Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. Int J Obes Relat Metab Disord. 2000;24:38-48.
12. Drapeau V, King N, Hetherington M, Doucet E, Blundell JE, Tremblay A. Appetite sensations and satiety quotient: predictors of energy intake and weight loss. Appetite 2007;48:159-166.
13. Sayer RD, Peters JC, Pan Z, Wyatt HR, Hill JO. Hunger, food cravings, and diet satisfaction are related to changes in body weight during a 6-month behavioral weight loss intervention: The Beef WISE Study. Nutrients 2018;10:700.
14. Institute of Medicine. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: The National Academies Press; 2005.
15. Li C, Chen P, Smith MS. Neuropeptide Y and tuberoinfundibular dopamine activities are altered during lactation: role of prolactin. Endocrinology 1999;140:118-123.
16. Woodside B. Prolactin and the hyperphagia of lactation. Physiol Behav 2007;91:375-382.
17. Gunderson EP, Y. C, Chiang V, Walton D, Azevedo RA, Fox G, Elmasian C, Young S, Salvador N, Lum M, et al. Influence of breastfeeding during the postpartum oral glucose tolerance test on plasma glucose and insulin. Obstet Gynecol 2012;120:136-143.
18. Chouinard-Castonguay S, J. WS, Tchernof A, Robitaille J. Relationship between lactation duration and insulin and glucose response among women with prior gestational diabetes. Eur J Endocrinol 2013;168:515-523.
19. Butte NF, M. HJ, Mehta N, K. MJ, Smith EO. Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation. Am J Clin Nutr 1999;69:299-307.
20. Pereira LCR, Purcell SA, Elliott SA, McCargar LJ, Bell RC, Robson PJ, Prado CM. The use of whole body calorimetry to compare measured versus predicted energy expenditure in postpartum women. Am J Clin Nutr 2019;109:554-565.
21. Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Khanh V, Bell G, Robson PJ, ENRICH Study Team. The influence of energy metabolism on postpartum weight retention. Am J Clin Nutr 2019;https://doi.org/10.1093/ajcn/nqy389.

22. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr 1990;51:241-247.
23. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:i-xii, 1-253.
24. Heymsfield SB, Heo M, Thomas D, Pietrobelli A. Scaling of body composition to height: relevance to height-normalized indexes. Am J Clin Nutr 2011;93:736-740.
25. Woolridge MW, Butte N, Dewey KG: Methods for the measurement of milk volume intake in the breast-fed infant. In: Jensen RG, Neville MC, eds. Human Lactation: Milk Components and Methodologies. New York: Plenum Press, 1985;5-21.
26. FAO/WHO/UNU. Human energy requirements: report of a joint FAO/WHO/UNU Expert Consultation, Rome 17–24 October 2001. Rome: Food and Agriculture Organization of the United Nations, 2004.
27. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. J Clin Invest 1986;78:1568-1578.
28. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1-9.
29. Brouwer E. On simple formulae for calculating the heat expenditure and the quantities of carbohydrate and fat oxidized in metabolism of men and animals, from gaseous exchange (Oxygen intake and carbonic acid output) and urine-N. Acta Physiol Pharmacol Neerl 1957;6:795-802.
30. Most J, Vallo PM, Gilmore LA, St Amant M, Hsia DS, Altazan AD, Beyl RA, Ravussin E, Redman LM. Energy expenditure in pregnant women with obesity does not support energy intake recommendations. Obesity (Silver Spring) 2018;26:992-999.
31. Chaput JP, Gilbert JA, Gregersen NT, Pedersen SD, Sjodin AM. Comparison of 150-mm versus 100-mm visual analogue scales in free living adult subjects. Appetite 2010;54:583-586.
32. Ravn AM, Gregersen NT, Christensen R, Rasmussen LG, Hels O, Belza A, Raben A, Larsen TM, Toubro S, Astrup A. Thermic effect of a meal and appetite in adults: an individual

participant data meta-analysis of meal-test trials. Food Nutr Res 2013;57:10.3402/fnr.v3457i3400.19676.

33. Matu J, O'Hara J, Hill N, Clarke S, Boos C, Newman C, Holdsworth D, Ispoglou T, Duckworth L, Woods D, et al. Changes in appetite, energy intake, body composition, and circulating ghrelin constituents during an incremental trekking ascent to high altitude. Eur J Appl Physiol 2017;117:1917-1928.
34. Matthews JN, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. BMJ 1990;300:230-235.
35. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-419.
36. Elliott SA, Pereira LCR, McCargar LJ, Prado CM, Bell RC. Trajectory and determinants of change in lean soft tissue over the postpartum period. Br J Nutr 2018;4:1-9.
37. Hays NP, Bathalon GP, McCrory MA, Roubenoff R, Lipman R, Roberts SB. Eating behavior correlates of adult weight gain and obesity in healthy women aged 55-65 y. Am J Clin Nutr 2002;75:476-483.
38. Provencher V, Drapeau V, Tremblay A, Despres JP, Lemieux S. Eating behaviors and indexes of body composition in men and women from the Quebec family study. Obes Res 2003;11:783-792.
39. Drapeau V, Blundell J, Therrien F, Lawton C, Richard D, Tremblay A. Appetite sensations as a marker of overall intake. Br J Nutr 2005;93:273-280.
40. Snoek HM, L. H, Van Gemert LJ, De Graaf C, Weenen H. Sensory-specific satiety in obese and normal-weight women. Am J Clin Nutr 2004;80:823-831.
41. Larson-Meyer DE, Ravussin E, Heilbronn L, DeJonge L. Ghrelin and peptide YY in postpartum lactating and nonlactating women. Am J Clin Nutr 2010;91:366-372.
42. Tschöp M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. Diabetes 2001;50:707-709.
43. Cummings DE, Weigle DS, Frayo RS, Breen PA, Ma MK, Dellinger EP, Purnell JQ. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. N Engl J Med 2002;346:1623-1630.

44. Larson-Meyer DE, Schueler J, Kyle E, Austin KJ, Hart AM, Alexander BM. Do lactation-induced changes in ghrelin, glucagon-like peptide-1, and peptide YY influence appetite and body weight regulation during the first postpartum year? J Obes. 2016;2016:ID 7532926.
45. Rong K, Yu K, Han X, Szeto IM, Qin X, Wang J, Ning Y, Wang P, Ma D. Pre-pregnancy BMI, gestational weight gain and postpartum weight retention: a meta-analysis of observational studies. Public Health Nutr 2015;18:2172-2182.
46. Ehrlich SF, Hedderson MM, Quesenberry CP, Jr., Feng J, Brown SD, Crites Y, Ferrara A. Post-partum weight loss and glucose metabolism in women with gestational diabetes: the DEBI Study. Diabet Med 2014;31:862-867.
47. Zourladani A, Zafrakas M, Chatzigiannis B, Papasozomenou P, Vavilis D, Matziari C. The effect of physical exercise on postpartum fitness, hormone and lipid levels: a randomized controlled trial in primiparous, lactating women. Arch Gynecol Obstet 2015;291:525-530.
48. Ostendorf DM, Melanson EL, Caldwell AE, Creasy SA, Pan Z, MacLean PS, Wyatt HR, Hill JO, Catenacci VA. No consistent evidence of a disproportionately low resting energy expenditure in long-term successful weight-loss maintainers. Am J Clin Nutr 2018;108:658-666.
49. Mayer J. Glucostatic mechanism of regulation of food intake. N Engl J Med 1953;249:13-16.
50. Sunehag AL, Louie K, Bier JL, Tigas S, Haymond MW. Hexoneogenesis in the human breast during lactation. J Clin Endocrinol Metab 2002;87:297-301.
51. Tigas S, Sunehag A, Haymond MW. Metabolic adaptation to feeding and fasting during lactation in humans. J Clin Endocrinol Metab 2002:302-307.
52. Flatt JP. The difference in the storage capacities for carbohydrate and for fat, and its implications in the regulation of body weight. Ann N Y Acad Sci 1987;499:104-123.
53. Flatt JP. Glycogen levels and obesity. Int J Obes Relat Metab Disord. 1996;20:S1-11.
54. Stuebe AM, Mantzoros C, Kleinman K, Gillman MW, Rifas-Shiman S, Gunderson EP, Rich-Edwards J. Duration of lactation and maternal adipokines at 3 years postpartum. Diabetes 2011;60:1277-1285.
55. Vila G, Hopfgartner J, Grimm G, Baumgartner-Parzer SM, Kautzky-Willer A, Clodi M, Luger A. Lactation and appetite-regulating hormones: increased maternal plasma peptide YY concentrations 3-6 months postpartum. Br J Nutr 2015;114:1203-1208.

56. Gunderson EP, Kim C, Quesenberry CP, Jr., Marcovina S, Walton D, Azevedo RA, Fox G, Elmasian C, Young S, Salvador N, et al. Lactation intensity and fasting plasma lipids, lipoproteins, non-esterified free fatty acids, leptin and adiponectin in postpartum women with recent gestational diabetes mellitus: the SWIFT cohort. Metabolism 2014;63:941-950.
57. Norman AW, Henry HL: III. Structure, synthesis, secretion, and target cells of the hypothalamic releasing hormones: E. Hypothalamic control of prolactin secretion. In: Hormones: Academic Press, 2014; p. 66.
58. Ben-Jonathan N, Hugo ER, Brandebourg TD, LaPensee CR. Focus on prolactin as a metabolic hormone. Trends Endocrinol Metab 2006;17:110-116.
59. Smith MS, True C, Grove KL. The neuroendocrine basis of lactation-induced suppression of GnRH: role of kisspeptin and leptin. Brain Res 2010;1364:139-152.
60. Pannacciulli N, Salbe AD, Ortega E, Venti CA, Bogardus C, Krakoff J. The 24-h carbohydrate oxidation rate in a human respiratory chamber predicts *ad libitum* food intake. Am J Clin Nutr 2007;86:625-632.

Chapter 5: The Use of Whole Body Calorimetry to Compare Measured versus Predicted Energy Expenditure in Postpartum Women

5.1 Preface

Findings from previous chapters demonstrated that postpartum weight retention was highly variable among the women enrolled in the PCAL study (Chapter 3), and multiple factors were associated with postpartum body weight regulation (Chapters 3 and 4). These, collectively, suggest that the postpartum period is a critical time for weight-management interventions, and that targeted weight management strategies during this life period are needed. The development of personalized recommendations to support appropriate weight management relies on accurate assessment of energy needs. The study described in this chapter is the first to determine the accuracy of several resting energy expenditure (REE) equations in women at three (n = 53) and nine (n = 49) months postpartum, and to determine the accuracy of the current energy recommendation for women at nine (n = 43) months postpartum. This chapter also investigates potential differences in equation accuracy among postpartum women grouped by BMI-specific categories (normal weight, overweight, or obese), or by lactation status (lactating, or nonlactating).

A version of this chapter has been published. Pereira LCR, Purcell SA, Elliott SA, McCargar LJ, Bell RC, Robson PJ, Prado CM, the ENRICH Study Team. The use of whole body calorimetry to compare measured versus predicted energy expenditure in postpartum women. The American Journal of Clinical Nutrition 2019;109:554-565, https://doi.org/10.1093/ajcn/nqy312.

LCRP, LJM, RCB, PJR, and CMP: designed the research; LCRP and SAE: conducted the research; LCRP and SAP: analyzed the data and performed the statistical analysis; LCRP and SAP: wrote the article; LCRP, LJM, and CMP: had primary responsibility for the final content; and all authors read and approved the final manuscript.

5.2 Introduction

Pregnancy and postpartum periods are characterized by major physiological changes, including body weight alterations to support the developing fetus and accumulation of energy stores in preparation for lactation (1, 2). Previous longitudinal studies have reported that up to 12 months postpartum, 50–80% of women retained between 1.3 and 5 kg of body weight gained during pregnancy (3-5). Previous population-based research has shown that ~25% of women were heavier by ≥ 5 kg at the beginning of a subsequent pregnancy, and ~2% of women developed obesity after starting a previous pregnancy with a normal body mass index (BMI) (6). Therefore, postpartum weight retention can have adverse health outcomes including prepregnancy obesity in subsequent pregnancies and future long-term obesity (7-9).

Given the potential impact of excessive weight retention after pregnancy, the childbearing years are a critical time for weight-management interventions (10-12). The development of personalized dietary recommendations relies on accurate assessment of energy expenditure in this population. Predictive energy equations may be used for individualized nutritional counseling, to assist women to achieve an optimal weight status through behaviour change (13).

Energy expenditure can be measured or predicted through the use of a variety of methods. Indirect calorimetry measures oxygen consumption and carbon dioxide production and provides an accurate determination of energy expenditure under controlled conditions (14). However, it is expensive, time consuming, and requires trained personnel and rigorous adherence to standardized testing conditions (15). As such, estimation of energy expenditure in clinical practice is often done with the use of predictive equations.

Several predictive equations have been developed for distinct populations and physiological conditions. However, to the best of our knowledge, only one cross-sectional study (16) has investigated the accuracy of predictive equations for postpartum women and reported that equations frequently overestimated resting energy expenditure (REE). Furthermore, there is little published information describing the accuracy of total energy expenditure (TEE) calculations or how REE (and the subsequent equation accuracy) might change throughout the postpartum period.

Given the current state of the literature and the importance of postpartum healthcare, it is important to investigate the accuracy of predictive equations for this population. Thus, the present study had the following objectives: 1) to compare REE measured by a state-of-the-art technique, whole body calorimetry (WBC), with REE estimated from the use of 17 predictive equations at two postpartum time points (three and nine months); and 2) to compare TEE measured by WBC with the estimated energy requirements (EER) through the use of the Dietary Reference Intakes (DRI) equation (17) at nine months postpartum.

5.3 Methods

5.3.1 Study design and participants.

The Postpartum Calorimetry study was a longitudinal study assessing energy expenditure in women at three and nine months postpartum. Participants were recruited between February 2014 and December 2015, and all measurements (REE and TEE [**primary outcomes**], anthropometry and body composition) were performed at the Human Nutrition Research Unit, University of Alberta. Women were ≥ 18 years of age, had a singleton term pregnancy (37–42 weeks), and were no more than three months postpartum at the time of enrollment. Inclusion criteria included no significant health issues, chronic diseases, or food allergies, and absence of any treatment/medication impacting energy metabolism. As this was an observational study, the number of eligible women who completed the study at three and nine months postpartum determined the sample size. A post-hoc power analysis is included in the Results Section. This study was approved by the University of Alberta Health Research Ethics Board. All participants provided informed consent prior to beginning any measurements. Age, ethnicity (Caucasian or other), and lactation status (any breastfeeding yes/no) were reported.

5.3.2 Anthropometric and body composition measurements.

Anthropometrics and body composition were measured at three and nine months postpartum. Body weight was measured to the nearest 0.1 kg (Health o meter® Professional digital scale 752KL; Pelstar LLC; IL, USA), and height was measured to the nearest 0.1 cm (235 Heightronic digital stadiometer; Quick Medical; WA, USA). BMI was calculated as measured weight (kg) divided by height (m^2) and stratified as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (≥30 kg/m^2) (18).

Body composition was measured using whole body dual-energy X-ray absorptiometry (GE Medical Systems; WI, USA) and scans were analyzed with enCORE 9.20 software to generate estimates of fat mass (FM), lean soft tissue, and bone mineral content. Fat-free mass (FFM) was calculated by adding lean soft tissue and bone mineral content values.

5.3.3 Breastfeeding patterns.

All participants were asked detailed questions about their past and current breastfeeding practices at three and nine months postpartum. Nonlactating women were asked to report if they had breastfed at all, and if so, when they had stopped. Lactating women were asked whether they were exclusively breastfeeding, providing their infant with complementary milks or foods, or actively weaning. They also completed a prospective 3-day breastfeeding diary that included a 24-hour infant test weighing protocol (described below). In this diary, women recorded the number of breastfeeding episodes and the duration of each episode for each day. This information was used to calculate the average daily number of breastfeeding episodes (times/day), the average duration of each episode (minutes/feed), and average daily total duration of breastfeeding (minutes/day). Breast milk energy output (kcal/day) was estimated from breast milk volume production (grams/day) using the 24-hour infant test weighing technique (19). This method involved recording infants' weights on an electronic baby scale (digital display; accuracy within 0.1 g and precision of ± 2.0 g; BabyWeigh II Scale, Medela; IL, USA) before and after each breastfeeding episode for 24 hours. Breast milk energy output was calculated according to the Food and Agriculture Organization/World Health Organization/United Nations University (FAO/WHO/UNU) Human Energy requirements report (20), with breast milk volume corrected for insensible water losses (5%), assuming 1 g/mL breast milk, 0.67 kcal/g for energy content of breast milk, and an efficiency of 80%.

5.3.4 Indirect calorimetry.

REE and TEE were measured by indirect calorimetry through the use of WBC, a technique explained in detail elsewhere (21). The reliability of our WBC and its analytical systems was tested in a previous study and has an average coefficient of variation of 2.2% for TEE (n = 10 healthy participants assessed on two different occasions one day apart, unpublished data).

5.3.4.1 Resting energy expenditure

REE was measured for 60 minutes at three and nine months postpartum (REE_{WBC}), and participants followed the same standardized protocol at both time points. The first 30 minutes were considered an acclimatization period and were excluded from the analysis. Participants were instructed to rest in a supine position, being awake but motionless, after fasting for ≥ eight hours, having refrained from exercise for 24 hours prior to the test, and avoided unnecessary activity on the morning of testing. REE was expressed as kcal per 24-hour (kcal/day).

5.3.4.2 Total energy expenditure.

TEE was measured once for 24 hours at nine months postpartum (TEE_{WBC}). All participants followed the same standardized protocol within the WBC unit, which includes 60 minutes of REE, 35 minutes of exercise, eight hours of sleep, and the remaining time spent on sedentary activities. TEE was adjusted for total urinary nitrogen losses (described below) through the use of the complete Weir equation (22), and was expressed as kcal/day. A 24-hour pooled urine sample was collected during the test day and total urinary nitrogen was measured in triplicate by chemiluminescence (Shimadzu TOC-L CPH with ASI-L autosampler and TNM-L; Shimadzu Corporation; JS, China; coefficient of variation <1%). For lactating women, TEE_{WBC} and breast milk energy output were summed to provide an overall estimate of energy requirements (ER_{WBC}). For nonlactating women, energy requirements were measured as TEE_{WBC}. To simplify the reporting of results, measured energy requirements for nonlactating women were also identified as ER_{WBC}, and in this case, breast milk energy output was zero.

5.3.5 Predictive equations.

5.3.5.1 Resting energy expenditure

REE_{WBC} was compared with 17 REE predictive equations commonly used in clinical practice or obtained by screening previous literature (17, 23-33). Three equations (24, 28, 31) were based on body composition (FFM and FM) measured by dual-energy X-ray absorptiometry (**Table 5.1**).

5.3.5.2 Total energy expenditure.

ER_{WBC} was compared with the current recommendation for energy requirements for postpartum women (EER_{DRI}) (17). EER_{DRI} was calculated based on the EER for adult women and used current age, weight, and physical activity coefficient with an addition of 400 kcal/day if lactating. The latter is recommended for lactating women after six months postpartum as an estimate of breast milk energy output (17). Physical activity level (PAL) was estimated by dividing TEE_{WBC} by REE_{WBC}. The average PAL for the entire cohort was 1.3, considered a sedentary category ($PAL \geq 1.0 < 1.4$) and a physical activity coefficient of 1.0 was therefore used in the EER_{DRI} (17). To explore the accuracy of the 400-kcal/day DRI recommendation for lactation, we compared ER_{WBC} to EER_{DRI} by replacing the 400 kcal/day with the women's breast milk energy output estimated from the 24-hour infant test weighing.

5.3.6 Statistical analysis.

Data were assessed with SPSS version 24 (IBM Corp.; NY, USA) and presented as mean ± SDs where appropriate. The threshold for significance was set at $p<0.05$. Data were assessed in the entire sample and subanalyses were completed by BMI-specific categories (normal weight, overweight, or obese) or according to lactation status (lactating [any breastfeeding] or nonlactating). Proportional bias was assessed with the use of Pearson correlation coefficients (Pearson's *r*) between bias and the mean of measured and predicted REE or TEE, to assess for trends in the magnitude of bias with increasing REE or TEE. A Bonferroni correction was applied to all analyses to account for multiple comparisons.

Group-level agreement between predicted and measured energy expenditure values was assessed by Pearson's *r*, paired *t* test, and bias (average difference between predicted and measured energy expenditure values) from Bland-Altman analyses (34). The mean percentage bias was calculated by dividing bias by measured REE or TEE and multiplied by 100.

Bland-Altman analyses were also used to assess accuracy at an individual level, based on the limits of agreement (LOA). These values were calculated as bias ± 2 SDs and were expressed as a percentage of measured energy expenditure. Values that were closer together indicated that two measurements agree better for each individual. The percentage of women with predicted energy expenditure within 10% of measured was also used to describe individual-level accuracy. A prediction between 90% and 110% of measured REE or TEE was considered accurate. A prediction <90% of measured REE or TEE was classified as an underprediction, and a prediction >110% of measured REE or TEE was classified as an overprediction (35). Differences in the proportion of individual accuracy with either EER_{DRI} (400 kcal/day for breast milk energy output) or EER_{DRI} (replacing the 400 kcal/day with breast milk energy output estimated for each lactating woman from the 24-hour infant test weighing) were tested with McNemar test. The Pitman test was used to compare difference in variance between the residual of measured and predicted EER_{DRI} based on 400 kcal/day for breast milk energy output and the residual of measured and predicted EER_{DRI} calculated from the breast milk energy output estimated for each lactating woman from the 24-hour infant test weighing.

5.4 Results

Fifty-three postpartum women were enrolled in the study and 52 completed the three-month postpartum assessment; one participant withdrew from the study due to time constraints. Three were lost to follow-up (two due to subsequent pregnancy, and one moved away), with 49 women completing the nine-month postpartum assessment (follow-up time: 6.0 ± 0.4 months). Of these, 43 completed the 24-hour test at the nine-month time point, and the other six completed the same measurements as collected at three months postpartum. The reasons for the six women not completing the 24-hour test included anxiety over being away from their infant for > 24 hours ($n = 4$), feeling sick during the test ($n = 1$), or having had a minor surgical procedure ($n = 1$), **Supplemental Figure 5.1**. Women who did not complete the 24-hour test ($n = 6$) were not different from those who completed ($n = 43$) in terms of the following measures: REE_{WBC}, age, weight, BMI, FM, and FFM (all $P > 0.05$). The sample size for TEE measures ($n = 43$) yielded a post-hoc power of 0.89 with the use of a two-tailed paired t test (effect size = 0.5, $\alpha = 0.05$) to assess the difference between ER_{WBC} and EER_{DRI}.

Participant characteristics are presented in **Table 5.2**. Almost 90% ($n = 46$) of participants were Caucasian. At the group level, a decrease of 0.8 ± 1.4 kg/m^2 in BMI from three to nine months postpartum was observed ($P = 0.002$), which included an ~7% decrease in FM ($P < 0.001$). At three months postpartum, 21 (40.4%) women were classified with normal weight according to their BMI, 17 (32.7%) with overweight, and 14 (26.9%) with obesity. At nine months postpartum, 24 (49%) women were normal weight, 13 (26.5%) women were with overweight, and 12 (24.5%) women were with obesity. Most women (41/52, 78.8%) were lactating at three months postpartum, whereas this number was lower at nine months postpartum (28/49, 57.1%). Of the 41 lactating women at three months postpartum, 31 were exclusively breastfeeding and 10 were complementing breastfeeding with other milk or infant formula. Overall, lactating women at three months postpartum nursed their infants 9 ± 3 times/day (range: 3–15 times/day) for 16 ± 6 minutes/feed (range: 7–30 minutes/feed), which equated to 149 ± 71 minutes/day (range: 58–334 minutes/day). Mean breast milk volume produced was 771 ± 261 g/day (range: 227–1417 grams/day), resulting in an estimated breast milk energy output of 678 ± 230 kcal/day (range: 200–1246 kcal/day). At nine months postpartum, all lactating women were complementing breastfeeding with solid foods, and of these, one was actively weaning her infant. They nursed their infants 7 ± 3 times/day (range: 2–15 times/day) for 12 ± 5 minutes/feed (range: 5–21 minutes/feed), which equated to 88 ± 63 minutes/day (range: 13–309 minutes/day). Mean breast milk volume produced was 530 ± 225 g/day (range: 61–860 g/day), for a mean estimated breast milk energy output of 465 ± 198 kcal/day (range: 54–756 kcal/day). Women who were not breastfeeding at three months postpartum had stopped a mean of 58 ± 21 days (range: 30–92 days) prior to the test day, and those who were not breastfeeding at nine months postpartum had stopped 157 ± 88 days (range: 24–271 days) prior to the nine-month time point.

5.4.1 Resting energy expenditure.

REE_{WBC} increased 48 ± 108 kcal/day between three and nine months postpartum ($P = 0.020$, paired *t* test; Table 5.2). All predicted REE values from equations were strongly correlated to REE_{WBC} at both time points (all Pearson's $r \geq 0.751$, $P < 0.001$) (data not shown). **Tables 5.3** and **5.4** show results of paired *t* tests, Bland-Altman analyses, and the proportion of participants with REE predicted within 10% of REE_{WBC} at three and nine months postpartum, respectively. At three months postpartum, six equations yielded REEs that were significantly different than REE_{WBC}, meaning that group-level agreement was inaccurate. At nine months postpartum, 10 equations were different than REE_{WBC}, which included six equations that were different from those identified at three months postpartum. Many equations performed well at a group-level (i.e. low bias) at both time points. The best equation was the DRI at three months postpartum (-7 kcal, -0.1%; absolute and percentage bias, respectively), and the Harris-Benedict at nine months postpartum (-17 kcal, -0.5%). At an individual level, the FAO/WHO/UNU height and weight equation performed the best at both time points. In fact, 100% of the REE predictions at three months and 98% at nine months postpartum were within 10% of REE_{WBC}. The FAO/WHO/UNU height and weight equation also had the smallest LOA values at both time points. At three months postpartum, six equations had negative proportional bias. At nine months postpartum, five equations had negative and three had positive proportional bias (**Supplemental Table 5.1**).

Overall patterns at a group level at three and nine months postpartum were similar when participants were assessed by BMI-specific categories (**Figures 5.1** and **5.2)**, or lactation status. That is, equations that under or overpredicted REE at a group level for the entire cohort did so for all BMI categories. However, increasing LOA were observed with increasing BMI categories. In other words, the largest individual variation was observed in participants with obesity at both time points. Additionally, in most cases, LOA were larger in nonlactating women than in lactating women at both time points (data not shown). The FAO/WHO/UNU height and weight equation was also the most accurate with the smallest individual variation for all BMI-specific categories and lactation status at both time points. Equations that used body composition were not more accurate at group or individual levels than equations that used anthropometric measurements.

5.4.2 Total energy expenditure.

The mean TEE_{WBC} was 2028 ± 286 kcal/day, and was not different between lactating and nonlactating women (2000 ± 223 compared with 2063 ± 354 kcal/day, $P = 0.480$). The mean ER_{WBC} was 2281 ± 371 kcal/day (range: 1550–2963 kcal/day). There was a significant correlation between EER_{DRI} and ER_{WBC} (Pearson's $r = 0.77$, $P < 0.0001$). EER_{DRI} was lower than ER_{WBC} by 36 kcal/day (percentage bias of -0.4%) on average for the entire cohort, although this was not significant ($P = 0.651$). Mean bias (absolute and percentage, respectively) was larger in women with overweight (-60 kcal/day, -2.2%) or obese (-60 kcal/day, -1.6%) compared with normal weight (-9 kcal/day, 1.3%). For lactating women, the EER_{DRI} mean bias was -58 kcal/day (percentage bias of -1.3%, $P > 0.05$) compared to ER_{WBC}; for nonlactating women, the mean bias was -9 kcal/day (percentage bias of 0.8%, $P > 0.05$). For lactating women, a positive proportional bias was present (Pearson's $r = 0.885$, $P < 0.001$) but was not present for nonlactating women (Pearson's $r = 0.385$, $P = 0.207$).

At an individual level, EER_{DRI} predicted TEE within 10% of ER_{WBC} in 29 women and over- or underpredicted ER_{WBC} outside 10% in 33% of women (*n* = 5, 12%, overpredicted; *n*=9, 21% underpredicted). Substantial individual variability in the entire cohort and within each BMI category was observed (**Supplemental Figure 5.2**). EER_{DRI} inaccurately predicted ER_{WBC} outside 10% in 42% of lactating women, whereas EER_{DRI} was similar (values within 10%) to ER_{WBC} in 79% of nonlactating women. Individual variability was higher with larger LOA, in lactating women compared with nonlactating women (**Figure 5.3)**.

Of the 43 women who completed the 24-hour test at nine months postpartum, 24 were still breastfeeding but complementing it with solid food, and one of those was actively weaning her infant. Overall, the breast milk volume produced was 516 ± 238 g/day (range: 61–860 grams/day) and breast milk energy output was 453 ± 210 kcal/day (range: 54–756 kcal/day). When the DRI-recommended 400 kcal/day for lactation was replaced by the breast milk energy output estimated for each lactating woman from the 24-hour infant test weighing, the mean bias at a group level did not improve (bias changed from -58 kcal/day [-1.3%] to -4 kcal/day [0.3%], $P = 0.899$). However, the percentage of lactating women with predicted energy expenditure within 10% of measured increased by almost 35% ($n = 8$; from 14/24 [58% of accurate predictions] to 22/24, [92% of accurate predictions]; $P = 0.008$), and the LOA were smaller (LOA changed from -593 to 477 to -324 to 316). The Pitman test for difference in variance also showed higher variance for EER_{DRI} based on 400 kcal/day for breast milk energy output compared with EER_{DRI} based on breast milk energy output estimated for each lactating woman from the 24-hour infant test weighing ($P < 0.001$). Proportional bias was not present when breast milk energy output estimated for each lactating woman from the 24-hour infant test weighing replaced the DRI-recommended 400 kcal/day for lactating women (Pearson's $r = -0.224$, $P > 0.05$).

5.5 Discussion

This study identified considerable variability in agreement between measured and predicted energy expenditure, comparing group with individual assessments, postpartum period time points, presence of obesity, and the addition of calories for lactation. To our knowledge, this study is the first to assess measured, compared with predicted, energy expenditure in early and late postpartum through the use of WBC and to assess the accuracy of the current energy recommendations for contemporary women.

At a group level, the most accurate equation predicting REE in this group of women was the DRI equation at three months postpartum and the Harris-Benedict equation at nine months postpartum, although many equations performed well. A study by de Sousa et al (16) assessed the accuracy of REE predictive equations in 79 women who were 1–10 days postpartum and demonstrated that, overall, equations significantly overpredicted REE. In that study (16), the Harris-Benedict equation best predicted REE at a group level but only ~18% of estimates accurately predicted REE at an individual level; the DRI equation had the highest mean bias.

Differences between these observations and our own may be related to physiological changes in the immediate postpartum period, including fluid shifts, labor, delivery, and breastfeeding initiation. In our study, the FAO/WHO/UNU height and weight equation had the highest level of accuracy at an individual level at both time points, and therefore this may be the best equation for predicting REE of postpartum women in clinical practice. Other studies (16, 36) also described this equation as one of the best performing for estimating REE at an individual level.

REE prediction error and individual accuracy were not improved with the inclusion of body composition variables, contrary to expected patterns, because FFM is a major determinant of REE (37). FFM is comprised of tissues and organs with different metabolic rates, ranging from 13 kcal/kg for skeletal muscle to 440 kcal/kg for heart and kidneys (38). Thus, small differences in organ size can significantly affect REE, which might not be captured when FFM and FM are used in predictive equations.

Regarding our analysis stratified by BMI categories, at an individual level, equations were generally more accurate in women who were normal weight compared with those with overweight or obesity. Most equations were developed from populations predominantly without obesity (17, 24-27, 29, 30, 32, 33). However, a similar pattern was observed for equations derived from individuals with obesity or with BMI-specific equations (23, 28, 31). The etiology of obesity is complex and multifactorial (39), and as such, different factors may alter energy expenditure and contribute to high individual variability. The Academy of Nutrition and Dietetics (40) recommends the use of the Mifflin-St. Jeor equation for estimating REE in adults with overweight or obesity when indirect calorimetry is not available. However, our findings suggested that this equation produces high individual variability and was not more accurate than the FAO/WHO/UNU height and weight equation for estimating REE in postpartum women with overweight or obesity.

It is noteworthy that nonlactating women presented with larger individual variability in REE compared with lactating women. Stuebe and Rich-Edwards (41) explored the role of lactation in resetting maternal metabolism and suggested that lactation is associated with favorable changes that persist after weaning. The wide range in time elapsed after weaning may contribute to larger REE LOA in nonlactating women in this study, as lactation may still be affecting women's metabolism.

This study also examined the accuracy of the current DRI recommendation for total energy requirements (17) compared with ER_{WBC} as the reference method. It is important to note that the

WBC technique is not entirely representative of free-living conditions due to the confined space of the chamber and therefore the physical activity coefficient may not be representative of daily life. Additionally, the milk supply-demand cycle of infant feeding may differ compared with the pumping of breast milk inside the WBC unit. However, in clinical practice, the physical activity coefficient used in the EER_{DRI} can be adjusted according to the level of physical activity reported by each woman. An important strength of the WBC is that it is an accurate technique conducted within a strictly controlled environment and therefore is the true energy expenditure for a sedentary, structured day (42).

The EER_{DRI} for lactating women after six months postpartum recommends adding 400 kcal/day to account for breast milk energy output (17). Our findings suggested that including this amount of additional calories to all women leads to inaccurate predictions in approximately one-third of women. In fact, EER_{DRI} overpredicted ER_{WBC} by up to almost 450 kcal and underpredicted ER_{WBC} by more than 500 kcal in some individuals. Replacing the single 400-kcal/day recommendation with the amount of breast milk energy output estimated for each woman through the use of the infant weighing technique improved individual level accuracy of the EER_{DRI} by ~35%. The LOA were smaller, and an accurate prediction was observed in 92% of lactating women. This suggests that including information about a woman's individual breast milk energy output improves the estimation of energy requirements. Individual breast milk output is not routinely assessed for estimating energy requirements but could have important implications for promoting appropriate weights in postpartum women. Future studies could work toward easier ways to capture this information, such as through the use of breastfeeding diaries at different times in the postpartum period or as weaning progresses. Another approach could be to operationalize definitions of full and partial breastfeeding as proposed by the WHO (43) and the Interagency Group for Action on Breastfeeding (44) and to link these categories to estimates of breast milk energy output, and subsequently to energy requirements.

Our findings also indicated that lactating women at nine months postpartum have a TEE that is similar to that of nonlactating women. Our recent case report (45) highlighted that energy expenditure returned to prepregnancy values by nine months postpartum despite additional energy costs of breast milk synthesis, suggesting that adaptations in energy metabolism may occur throughout the postpartum period. Other studies have shown that REE was not affected by lactation (46-48).

Overall, data presented here suggested that the DRI energy recommendations, especially for lactating women, may lead to inaccurate prediction of energy requirements. This may be explained by the highly variable contribution of lactation to energy requirements at nine months postpartum. Adding the standard 400 kcal/day for breast milk energy output after six months postpartum increased inaccuracy rates, highlighting the need for more specific recommendations.

There are important limitations to this study that should be considered when interpreting the results. Although our study had a sample size that was similar to or greater than others that use comparable methods, it is still relatively restricted. This is somewhat offset by the fact that the WBC is a very precise method. Participants in this study were also mainly Caucasian, free of any underlying metabolic disorder, and in their early 30s. This could limit the generalizability of our findings.

In conclusion, many predictive equations were accurate for group assessment of REE in this group of postpartum women. The FAO/WHO/UNU height and weight equation had the highest individual level of accuracy for REE. EER_{DRI} performed well at a group level; however, it was not an accurate predictor of ER_{WBC} at an individual level, with wide individual variability, and high rates of inaccuracy. Additional studies are needed to understand the physiology driving energy expenditure, and the contribution of lactation to total energy requirements in the postpartum period, both short and long term. Understanding these physiological changes will assist in better predicting energy expenditure, ultimately supporting appropriate diet- and weight-management interventions in this population.

Table 5.1 Equations used to predict resting and total energy expenditure[1]

Equation (number and name)	Formula	**Original population**: number of subjects, sex, age range or mean, weight status or BMI range or mean; body composition method when applicable
Resting energy expenditure		
(1) Bernstein (23)	7.48 × W – 0.042 × H – 3 × A + 844	*n* = 202 (48 M, 154 F); age 39.4 ± 12.0 years; BMI ± 37 kg/m^2 (obese subjects); mean body weight (entire sample) 103.4 ± 26.0 kg (60–2014 kg)
(2) Cunningham, BC (24)	(21.6 × FFM) + 370	*n* = 223 (120M, 103 F); body weight not reported; BIA
(3) DRI (17)	247 – 2.67 × A + 401.5 × H + 8.6 × W	*n* = 407 (169 M, 238 F), age 20–96 years; BMI 18.5 to ≥ 25 kg/m^2
(4) FAO/WHO/UNU, weight (25)	Age 18–30: 14.7 × W + 496 Age 30–60: 8.7 × W + 829	*n* ~ 11,000 (M, F, and children); age variable; equations based on Schofield but extended to greater number of subjects from several countries (large number of Italian participants)
(5) FAO/WHO/UNU, height and weight (25)	Age 18–30: 13.3 × W + 334 × H +35 Age 30–60: 8.7 × W – 25 × H + 865	
(6) Harris-Benedict (26)	655 + (9.563 × W) + (1.85 × H) – (4.676 × A)	*n* = 239 (136 M, 103 F); age 29 ± 14 years; body weight not reported but predominantly normal weight
(7) Henry, weight (27)	Age 18–30: 13.1 × W + 558 Age 31–60: 9.7 × W + 694	*n* = 10,552 (5974 M, 4702 F) from 166 separate investigations – excluding all Italians and included more from tropical regions
(8) Henry, height and weight (27)	Age 18–30: 10.4 × W + 615 × H – 282 Age 31–60: 8.18 × W + 502 × H – 11.6	
(9) Lazzer, height and weight[2] (28)	0.042 × W + 3.619 × H – 2.678	*n* = 182 F; age 19–60 years; BMI 45.6 kg/m^2; BIA
(10) Lazzer, BC[2] (28)	0.067 × FFM + 0.046 × FM + 1.568	
(11) Livingston (29)	248 × $W^{0.4356}$ – (5.9 × A)	*n* = 655 (299 M, 356 F), age 18–95 years; body weight 33–278 kg
(12) Mifflin-St Jeor (30)	(10 × W) + (6.25 × H) – (5 × A) – 161	*n* = 498 (251 M, 248 F); age 19–78 years; 264 normal weight and 234 obese; BMI 17–42 kg/m^2

(13) Muller, weight[2] (31)	BMI >18.5 to 25 kg/m^2: $0.02219 \times W + 0.02118 \times H + 0.884 \times S - 0.01191 \times A + 1.233$ BMI >25 to <30 kg/m^2: $0.04507 \times W + 1.006 \times S - 0.01553 \times A + 3.407$ BMI ≥30 kg/m^2: $0.05 \times W + 1.103 \times S - 0.01586 \times A + 2.924$	*n* = 2528, high prevalence of overweight and obesity; *n* = 1046 (388 M, 658 F) for equation creation; age 44.2 ± 17.3 years; BMI 27.1 ± 7.7 kg/m^2; BIA or skinfolds
(14) Muller, BC[2] (31)	BMI >18.5 to 25 kg/m^2: $0.0455 \times FFM + 0.0278 \times FM + 0.879 \times S - 0.01291 \times A + 3.634$ BMI >25 to <30 kg/m^2: $0.03776 \times FFM + 0.03013 \times FM + 0.93 \times S - 0.01196 \times A + 3.928$ BMI ≥30 kg/m^2: $0.05685 \times FFM + 0.04022 \times FM + 0.808 \times S - 0.01402 \times A + 2.818$	
(15) Owen (32)	$795 + (7.18 \times W)$	*n* = 44 healthy lean and obese F, age 18–82 years; BMI 27.8 ± 8.6 kg/m^2; underwater weighing
(16) Schofield, weight[2] (33)	Age 18–30: $0.062 \times W + 2.036$ Age 30–60: $0.034 \times W + 3.538$	*n* = 4814; >18 years; BMI 21–24 kg/m^2; European, North American, and tropical countries
(17) Schofield, height and weight[2] (33)	Age 18–30: $0.057 \times W + 1.184 \times H + 0.411$ Age 30–60: $0.034 \times W + 0.006 \times H + 3.530$	
Total energy expenditure		
Estimated energy requirements DRIs[3] (17)	$354 - (6.91 \times A) + PA \times (9.36 \times W) + (726 \times H)$	*n* = 407 (169 M, 238 F), mostly Caucasian, healthy *n* = 12 lactating F, age 21–36 years to derive + 400 kcal after 6 months

[1] A, age (years); BC, body composition; BIA, bioelectrical impedance analysis; BMI, body mass index; DRI, Dietary Reference Intake; F, female; FAO/WHO/UNU, Food and Agricultural Organization/World Health Organization/United Nations University; FM, fat mass (kg); FFM, fat-free mass (kg); H, height (cm or m where appropriate); M, male; PA, physical activity coefficient, set at 1.0; REE, resting energy expenditure; S, sex, female = 0; TEE, total energy expenditure; W, weight (kg).

[2] Resting energy expenditure was calculated as MJ/day and then converted to kcal/day.

[3] EER_{DRI} was calculated with 400kcal/day added to lactating women.

Table 5.2 Participant characteristics at three and nine months postpartum[1]

	Three months **(n = 52)**	**Nine months** **(n = 49 with REE; n = 43 with TEE)**	**p-value**
Age, years	32 ± 4	33 ± 4	<0.001
BMI, kg/m^2	27.3 ± 5.6	26.5 ± 5.8	0.002
Fat mass, kg	29.5 ± 12.2	27.5 ± 13.5	<0.001
Fat-free mass, kg	44.8 ± 5.1	45.2 ± 5.3	0.545
REE_{WBC},[2] kcal/day	1483 ± 194	1531 ± 222	0.020
TEE_{WBC},[2] kcal/day	–	2028 ± 286	–
ER_{WBC},[3] kcal/day	–	2281 ± 371	–
EER_{DRI},[4] kcal/day	–	2245 ± 256	–

[1] Values are means ± SDs. *P* values were calculated from paired *t* tests (n = 49), and Bonferroni corrections were applied to account for multiple comparisons. BMI, body mass index; EER_{DRI}, estimated energy requirement/Dietary Reference Intake; ER_{WBC}, energy requirement measured by whole body calorimetry; REE, resting energy expenditure; REE_{WBC}, measured REE; TEE, total energy expenditure; TEE_{WBC}, measured TEE; WBC, whole body calorimetry.

[2] Measured by WBC.

[3] Defined as the sum of TEE_{WBC} and breast milk energy output estimated from the 24-hour infant test weighing for lactating women and as TEE_{WBC} for nonlactating women.

[4] Estimated by the DRI equation for adult women (≥ 19 years older) based on current age, weight, and physical activity coefficient plus 400 kcal/day for milk energy output if lactating (17).

Table 5.3 Agreement between measured and predicted resting energy expenditure at three months postpartum (n = 52)[1]

Equation number and name (ref.)	Predicted REE (mean ± SD)	Predicted vs measured[2]	Bias[3]	Limits of agreement[4]	Accurate predictions[5]	Underpredictions[6]	Overpredictions[7]
	kcal/day	*P value*	%	%	%	%	%
REE$_{\mathrm{WBC}}$[8]	1483 ± 194	–	–	–	–	–	–
1. Bernstein (23)	1241 ± 122	<0.001	-15.9	-27.1, -4.7	13	87	0
2. Cunningham, BC (24)	1339 ± 111	<0.001	-9.0	-23.9, 5.9	54	46	0
3. DRI (17)	1476 ± 151	>0.05	0.1	-13.9, 14.0	85	9	6
4. FAO/WHO/UNU, weight (25)	1515 ± 196	0.509	2.4	-10.7, 15.6	83	4	13
5. FAO/WHO/UNU, height and weight (25)	1507 ± 185	>0.05	1.0	-5.6, 7.5	100	0	0
6. Harris-Benedict (26)	1533 ± 160	0.023	3.8	-10.2, 17.7	73	4	23
7. Henry, weight (27)	1461 ± 191	>0.05	-1.3	-14.3, 11.8	87	9	4
8. Henry, height and weight (27)	1463 ± 166	>0.05	-0.9	-14.5, 12.7	87	9	4
9. Lazzer, height and weight[9] (28)	1555 ± 191	0.002	5.2	-11.3, 21.8	67	2	31
10. Lazzer, BC[9] (28)	1417 ± 190	<0.001	-4.3	-17.2, 8.6	77	23	0
11. Livingston (29)	1457 ± 147	>0.05	-1.3	-14.6, 11.9	85	11	4
12. Mifflin-St Jeor (30)	1471 ± 180	>0.05	-0.6	-15.4, 14.3	81	12	8
13. Muller, weight[9] (31)	1507 ± 178	>0.05	1.9	-11.9, 15.7	85	11	4

14. Muller, BC[9] (31)	1473 ± 148	>0.05	-0.2	-13.1, 12.6	87	9	4
15. Owen (32)	1336 ± 118	<0.001	-9.3	-21.7, 3.0	58	42	0
16. Schofield, weight[9] (33)	1498 ± 196	>0.05	1.3	-12.2, 14.8	81	8	11
17. Schofield, height and weight[9] (33)	1495 ± 187	>0.05	1.1	-12.2, 14.5	83	8	9

[1] BC, body composition; DRI, Dietary Reference Intake; FAO/WHO/UNU, Food and Agricultural Organization/World Health Organization/United Nations University; REE, resting energy expenditure; $\mathrm{REE}_{\mathrm{WBC}}$, measured REE; WBC, whole body calorimetry.

[2] Paired *t* tests. Bonferroni corrections were applied to account for multiple comparisons.

[3] Mean percent error between predicted and measured REE from Bland-Altman analyses.

[4] Bland-Altman analyses.

[5] Percentage of women with REE predicted between 90% and 110% of $\mathrm{REE}_{\mathrm{WBC}}$.

[6] Percentage of women with REE predicted by <90% of $\mathrm{REE}_{\mathrm{WBC}}$.

[7] Percentage of women with REE predicted by >110% of $\mathrm{REE}_{\mathrm{WBC}}$.

[8] Measured by WBC.

[9] REE was calculated as MJ/day and then converted to kcal/day.

Table 5.4 Agreement between measured and predicted resting energy expenditure at nine months postpartum (*n* = 49)[1]

Equation number and name (ref.)	Predicted REE (mean ± SD)	Predicted vs measured[2]	Bias[3]	Limits of agreement[4]	Accurate predictions[5]	Underpredictions[6]	Overpredictions[7]
	kcal/day	*P value*	*%*	*%*	*%*	*%*	*%*
REE_{WBC}[8]	1531 ± 222	–	–	–	–	–	–
1. Bernstein (23)	1226 ± 134	<0.001	-19.3	-32.6, -6.0	8	92	0
2. Cunningham, BC (24)	1346 ± 114	<0.001	-11.2	-26.9, 4.4	45	55	0
3. DRI (17)	1462 ± 165	0.015	-3.8	-19.6, 11.9	71	25	4
4. FAO/WHO/UNU, weight (25)	1496 ± 207	>0.05	-1.8	-18.7, 15.1	74	16	10
5. FAO/WHO/UNU, height and weight (25)	1489 ± 197	0.812	-1.1	-9.5, 7.3	98	2	0
6. Harris-Benedict (26)	1514 ± 176	>0.05	-0.5	-16.8, 15.9	76	14	10
7. Henry, weight (27)	1430 ± 199	<0.001	-6.1	-22.9, 10.6	63	35	2
8. Henry, height and weight (27)	1441 ±176	0.001	-5.3	-21.5, 11.0	71	27	2
9. Lazzer, height and weight[9] (28)	1541 ± 206	>0.05	1.2	-16.5, 18.8	80	10	10
10. Lazzer, BC[9] (28)	1400 ± 206	<0.001	-8.2	-23.3, 6.8	53	45	2
11. Livingston (29)	1436 ± 161	<0.001	-5.6	-21.0, 9.9	67	29	4
12. Mifflin-St Jeor (30)	1452 ± 197	0.005	-4.7	-21.2, 11.9	65	27	8
13. Muller, weight[9] (31)	1493 ± 193	>0.05	-1.9	-18.5, 14.6	76	16	8

14. Muller, BC[9] (31)	1459 ± 163	0.008	-4.0	-19.1, 11.2	69	27	4
15. Owen (32)	1324 ± 129	<0.001	-12.8	-27.1, 1.5	35	65	0
16. Schofield, weight[9] (33)	1467 ± 194	0.098	-3.6	-21.1, 13.9	67	25	8
17. Schofield, height and weight[9] (33)	1474 ± 197	0.186	-3.1	-20.1, 13.9	72	20	8

---

[1] BC, body composition; DRI, Dietary Reference Intake; FAO/WHO/UNU, Food and Agricultural Organization/World Health Organization/United Nations University; REE, resting energy expenditure; REE_{WBC}, measured REE; WBC, whole body calorimetry.

[2] Paired *t* tests. Bonferroni corrections were applied to account for multiple comparisons.

[3] Mean percent error between predicted and measured REE from Bland-Altman analyses.

[4] Bland-Altman analyses.

[5] Percentage of women with REE predicted between 90% and 110% of REE_{WBC}.

[6] Percentage of women with REE predicted by <90% of REE_{WBC}.

[7] Percentage of women with REE predicted by >110% of REE_{WBC}.

[8] Measured by WBC.

[9] REE was calculated as MJ/day and then converted to kcal/day.

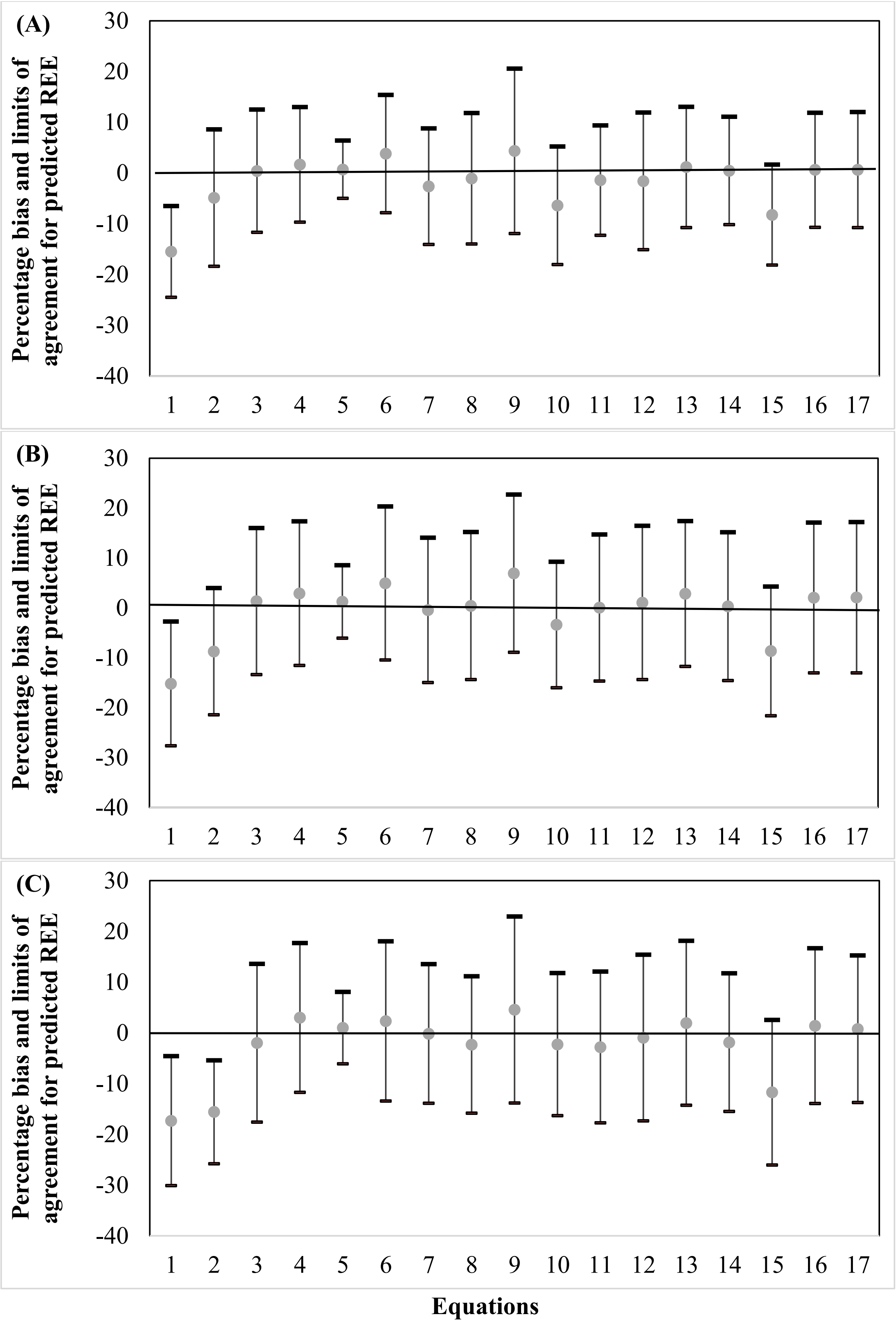

(A)
(B)
(C)
Percentage bias and limits of agreement for predicted REE
30
20
10
0
-10
-20
-30
-40
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
Equations

Figure 5.1 Percentage bias and limits of agreement for predicted resting energy expenditure at three months postpartum in normal-weight postpartum women (*n* = 21) (A), postpartum women with overweight (*n* = 17) (B), and postpartum women with obesity (*n* = 14) (C). Each grey dot represents the equation percentage bias (mean percentage difference between predicted and measured), whiskers are the percentage limits of agreement for each equation, and the black line represents the measured REE value (percentage bias and limits of agreement are from Bland-Altman analyses). Numbers represent the following equations: *1)* Bernstein; *2)* Cunningham (body composition); *3)* DRI; *4)* FAO/WHO/UNU (weight); *5)* FAO/WHO/UNU (height and weight); *6)* Harris-Benedict; *7)* Henry (weight); *8)* Henry (height and weight); *9)* Lazzer (height and weight); *10)* Lazzer (body composition); *11)* Livingston; *12)* Mifflin-St Jeor; *13)* Muller (weight); *14)* Muller (body composition); *15)* Owen (weight); *16)* Schofield (weight); *17)* Schofield (height and height). DRI, Dietary Reference Intake; FAO/WHO/UNU, Food and Agriculture Organization/World Health Organization/United Nations University; REE, resting energy expenditure.

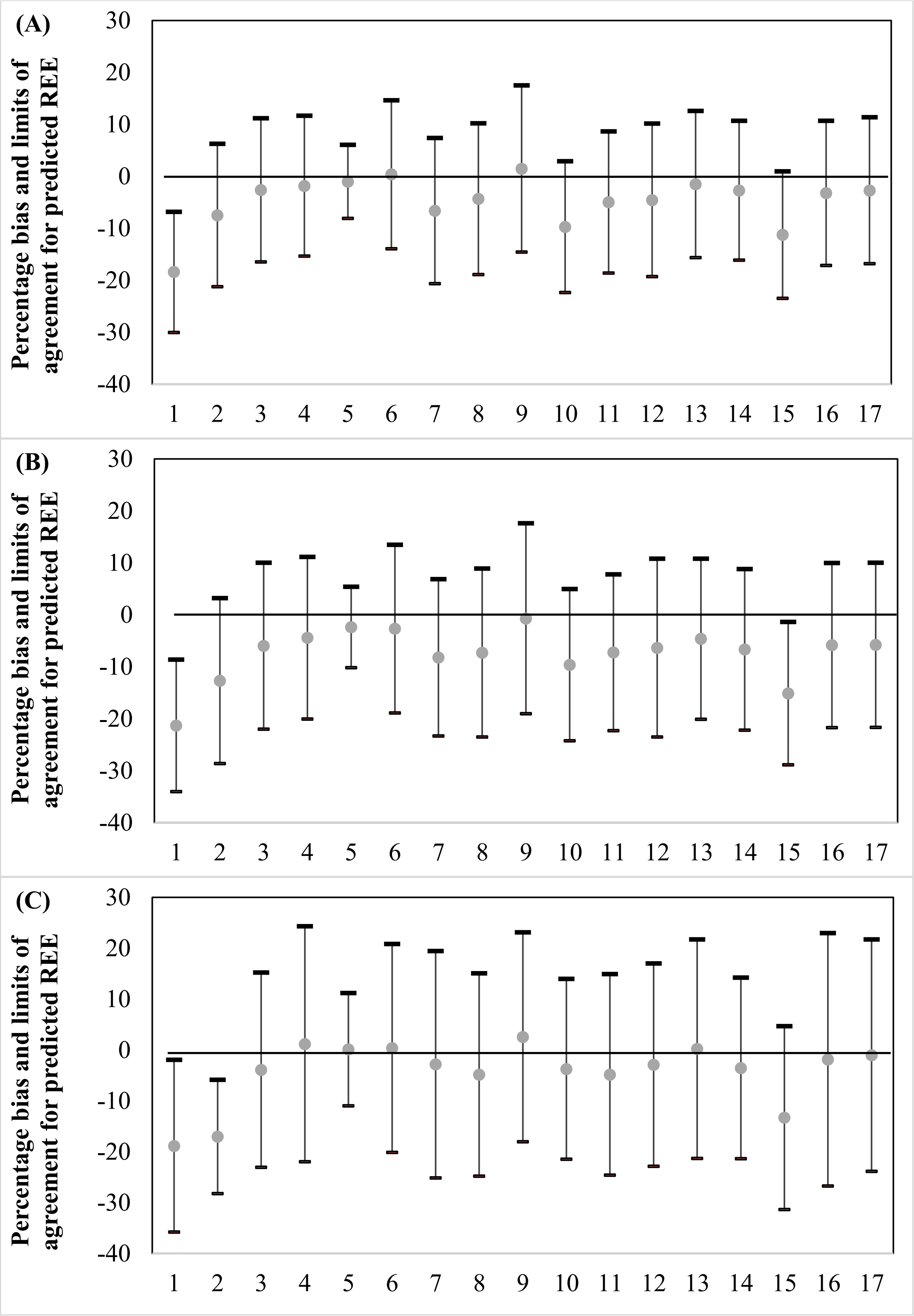

(A)
(B)
(C)
Percentage bias and limits of agreement for predicted REE
30
20
10
0
-10
-20
-30
-40
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
Equations

Figure 5.2 Percentage bias and limits of agreement for predicted resting energy expenditure at nine months postpartum in normal-weight postpartum women (*n* = 24) (A), postpartum women with overweight (*n* = 13) (B), and postpartum women with obesity (*n* = 12) (C). Each grey dot represents the equation percentage bias (mean percentage difference between predicted and measured), whiskers are the percentage limits of agreement for each equation, and the black line represents the measured REE value (percentage bias and limits of agreement are from Bland-Altman analyses). Numbers represent the following equations: *1)* Bernstein; *2)* Cunningham (body composition); *3)* DRI; *4)* FAO/WHO/UNU (weight); *5)* FAO/WHO/UNU (height and weight); *6)* Harris-Benedict; *7)* Henry (weight); *8)* Henry (height and weight); *9)* Lazzer (height and weight); *10)* Lazzer (body composition); *11)* Livingston; *12)* Mifflin-St Jeor; *13)* Muller (weight); *14)* Muller (body composition); *15)* Owen (weight); *16)* Schofield (weight); *17)* Schofield (height and height). DRI, Dietary Reference Intake; FAO/WHO/UNU, Food and Agriculture Organization/World Health Organization/United Nations University; REE, resting energy expenditure.

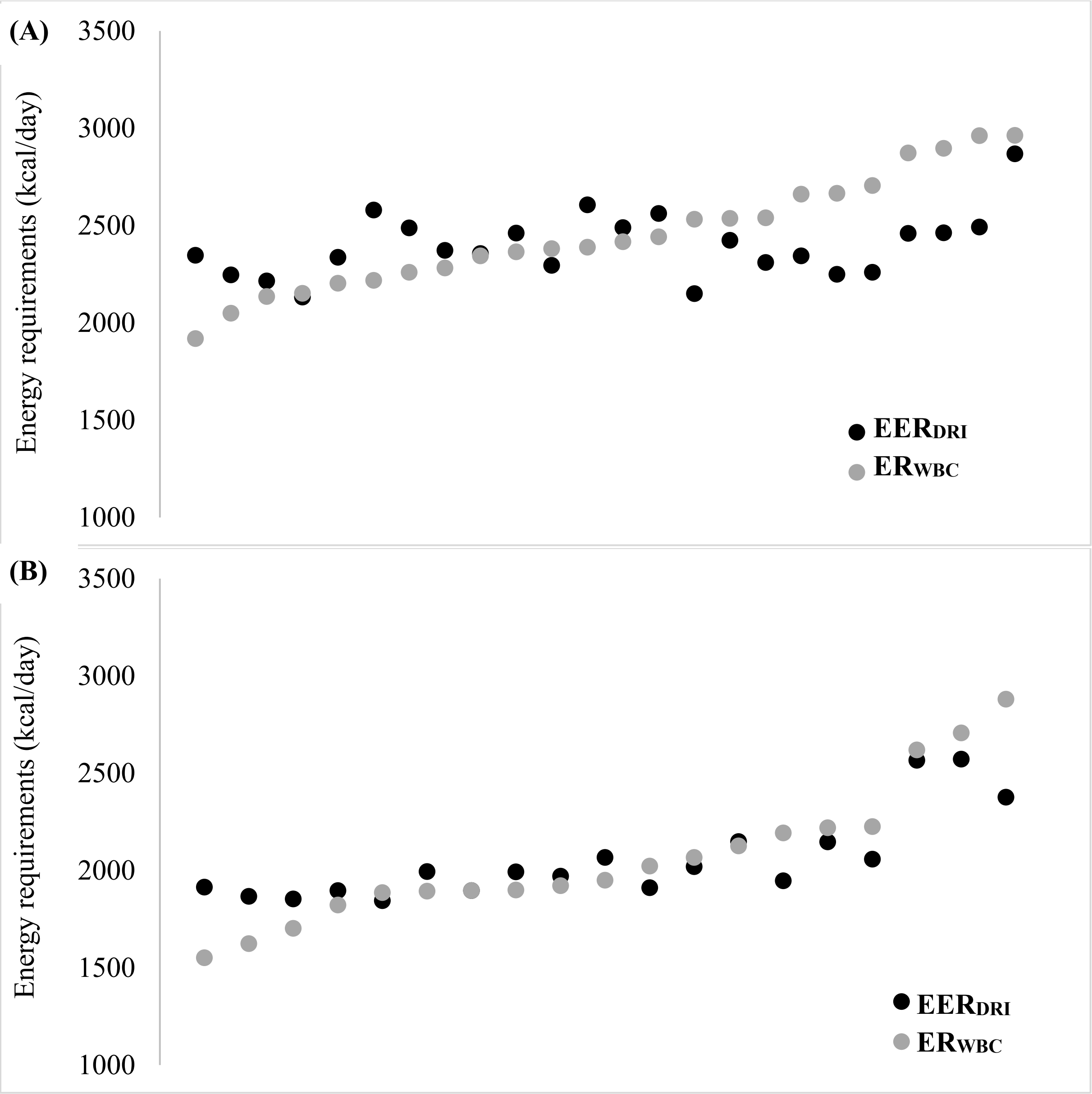
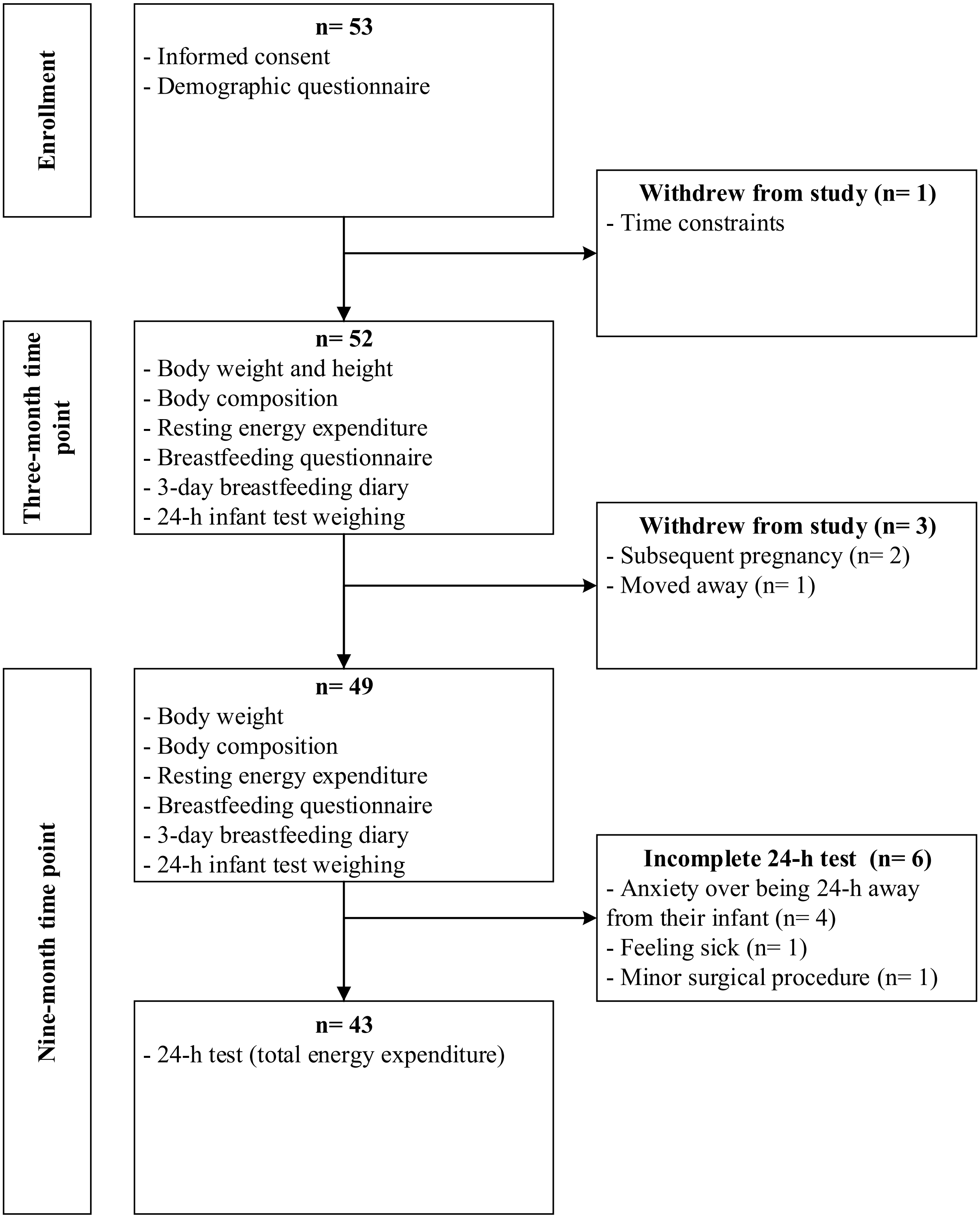


Figure 5.3 Energy requirements measured by whole body calorimetry ($\mathrm{ER}_{\mathrm{WBC}}$) compared with estimated energy requirements ($\mathrm{EER}_{\mathrm{DRI}}$) in lactating (*n* = 24) (A) and nonlactating (*n* = 19) (B) women. Each point is an individual subject. All subjects have two values; some values overlap. DRI, Dietary Reference Intake; WBC, whole body calorimetry.

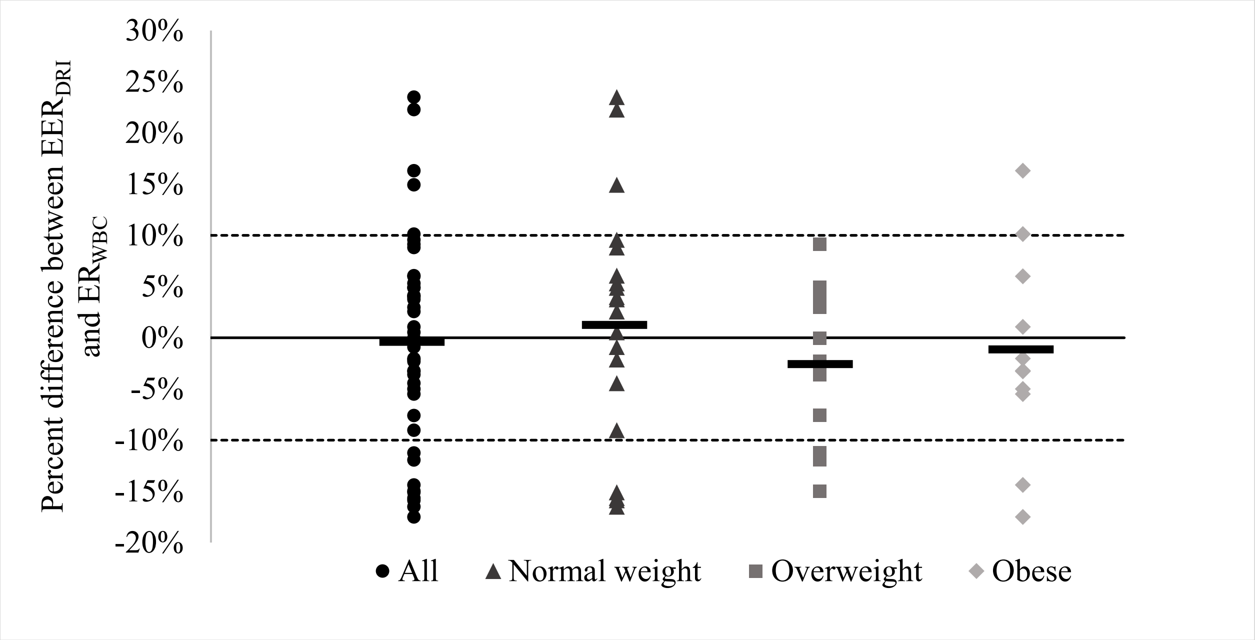
Supplemental Table 5.1 Proportional bias for resting energy expenditure at three and nine months postpartum[1]

	Three months postpartum (n=52)		Nine months postpartum (n=49)	
Equation, number and name (ref.)	r	p	r	p
1. Bernstein (23)	-0.669	**<0.001**	-0.646	**<0.001**
2. Cunningham, BC (24)	-0.669	**<0.001**	-0.748	**<0.001**
3. DRI (17)	-0.410	**0.043**	-0.438	**0.028**
4. FAO/WHO/UNU, weight (25)	0.020	>0.05	-0.103	>0.05
5. FAO/WHO/UNU, height and weight (25)	-0.088	>0.05	-0.178	>0.05
6. Harris-Benedict (26)	-0.330	0.284	-0.350	0.232
7. Henry, weight (27)	-0.030	>0.05	-0.165	>0.05
8. Henry, height and weight (27)	-0.272	0.874	-0.340	0.286
9. Lazzer, height and weight[9] (28)	-0.026	>0.05	-0.113	>0.05
10. Lazzer, BC[9] (28)	-0.036	>0.05	-0.125	>0.05
11. Livingston (29)	-0.455	**0.012**	-0.464	**0.013**
12. Mifflin-St Jeor (30)	-0.125	>0.05	-0.184	>0.05
13. Muller, weight[9] (31)	-0.152	>0.05	-0.219	>0.05
14. Muller, BC[9] (31)	-0.469	**0.008**	-0.469	**0.012**
15. Owen (32)	-0.691	**<0.001**	0.914	**<0.001**
16. Schofield, weight[9] (33)	0.024	>0.05	0.920	**<0.001**
17. Schofield, height and weight[9] (33)	-0.070	>0.05	0.928	**<0.001**

[1] P-values were calculated from Pearson correlation coefficients. Bonferroni corrections were applied to account for multiple comparisons. Proportional bias was assessed using correlation between the mean of measured and predicted resting energy expenditure and bias. Bolded values are significant. BC: body composition; FAO/WHO/UNU: Food and Agricultural Organization/World Health Organization/United Nations University.



Supplemental Figure 5.1 Flowchart of the Postpartum Calorimetry study.



Supplemental Figure 5.2 Percent difference between estimated energy requirements from the DRI (EER$_{DRI}$) and energy requirements measured by whole body calorimetry (ER$_{WBC}$) by BMI category. Each point is a participant and the short black line is the mean percent difference (bias) in each category. All (*n* = 43), normal weight (*n* = 20), overweight (*n*=12), and obese (*n* = 11). BMI, body mass index; DRI, Dietary Reference Intake; WBC, whole body calorimetry.

5.6 References

1. Picciano MF. Pregnancy and lactation: physiological adjustments, nutritional requirements and the role of dietary supplements. J Nutr 2003;133:1997s-2002s.
2. Kominiarek MA, Rajan P. Nutrition Recommendations in Pregnancy and Lactation. Med Clin North Am 2016;100:1199-1215.
3. Olson CM, Strawderman MS, Hinton PS, Pearson TA. Gestational weight gain and postpartum behaviors associated with weight change from early pregnancy to 1 y postpartum. Int J Obes Relat Metab Disord 2003;27:117-127.
4. Lipsky LM, Strawderman MS, Olson CM. Maternal weight change between 1 and 2 years postpartum: the importance of 1 year weight retention. Obesity (Silver Spring) 2012;20:1496-1502.
5. Martin JE, Hure AJ, Macdonald-Wicks L, Smith R, Collins CE. Predictors of post-partum weight retention in a prospective longitudinal study. Matern Child Nutr 2014;10:496-509.
6. Hutcheon JA, Chapinal N, Bodnar LM, Lee L. The INTERGROWTH-21st gestational weight gain standard and interpregnancy weight increase: A population-based study of successive pregnancies. Obesity (Silver Spring) 2017;25:1122-1127.
7. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. Lancet 2006;368:1164-1170.
8. Schmitt NM, Nicholson WK, Schmitt J. The association of pregnancy and the development of obesity - results of a systematic review and meta-analysis on the natural history of postpartum weight retention. Int J Obes (Lond) 2007;31:1642-1651.
9. Mannan M, Doi SA, Mamun AA. Association between weight gain during pregnancy and postpartum weight retention and obesity: a bias-adjusted meta-analysis. Nutr Rev 2013;71:343-352.
10. Krummel DA, Semmens E, Boury J, Gordon PM, Larkin KT. Stages of change for weight management in postpartum women. J Am Diet Assoc 2004;104:1102-1108.
11. Kuhlmann AK, Dietz PM, Galavotti C, England LJ. Weight-management interventions for pregnant or postpartum women. Am J Prev Med 2008;34:523-528.
12. Barker M, Dombrowski SU, Colbourn T, Fall CHD, Kriznik NM, Lawrence WT, Norris SA, Ngaiza G, Patel D, Skordis-Worrall J, et al. Intervention strategies to improve nutrition and health behaviours before conception. Lancet 2018;391:1853-1864.

13. Imanaka M, Ando M, Kitamura T, Kawamura T. Impact of registered dietitian expertise in health guidance for weight loss. PLoS One 2016;11:e0151456.
14. Hills AP, Mokhtar N, Byrne NM. Assessment of physical activity and energy expenditure: an overview of objective measures. Front Nutr 2014;1:5.
15. Ndahimana D, Kim E-K. Measurement methods for physical activity and energy expenditure: a review. Clin Nutr Res 2017;6:68-80.
16. de Sousa TM, Maioli TU, Dos Santos ALS, Dos Santos LC. Energy expenditure in the immediate postpartum period: Indirect calorimetry versus predictive equations. Nutrition 2017;39-40:36-42.
17. Institute of Medicine. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: The National Academies Press, 2005.
18. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:i-xii, 1-253.
19. Woolridge MW, Butte N, Dewey KG ea: Methods for the measurement of milk volume intake in the breast-fed infant. In: Jensen RG, Neville MC, eds. Human Lactation: Milk Components and Methodologies. New York: Plenum Press, 1985;5–21.
20. FAO/WHO/UNU. Human energy requirements: report of a joint FAO/WHO/UNU Expert Consultation, Rome 17-24 October 2001. Rome: Food and Agriculture Organization of the United Nations, 2004.
21. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. J Clin Invest 1986;78:1568-1578.
22. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1-9.
23. Bernstein RS, Thornton JC, Yang MU, Wang J, Redmond AM, Pierson RN, Jr., Pi-Sunyer FX, Van Itallie TB. Prediction of the resting metabolic rate in obese patients. Am J Clin Nutr 1983;37:595-602.
24. Cunningham JJ. Body composition as a determinant of energy expenditure: a synthetic review and a proposed general prediction equation. Am J Clin Nutr 1991;54:963-969.

25. FAO/WHO/UNU. Energy and protein requirements. Report of a joint FAO/WHO/UNU Expert Consultation. World Health Organ Tech Rep Ser 1985;724:1-206.
26. Harris JA, Benedict FG. A Biometric Study of Human Basal Metabolism. Proc Natl Acad Sci U S A 1918;4:370-373.
27. Henry CJ. Basal metabolic rate studies in humans: measurement and development of new equations. Public Health Nutr 2005;8:1133-1152.
28. Lazzer S, Agosti F, Resnik M, Marazzi N, Mornati D, Sartorio A. Prediction of resting energy expenditure in severely obese Italian males. J Endocrinol Invest 2007;30:754-761.
29. Livingston EH, Kohlstadt I. Simplified resting metabolic rate-predicting formulas for normal-sized and obese individuals. Obes Res 2005;13:1255-1262.
30. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr 1990;51:241-247.
31. Muller MJ, Bosy-Westphal A, Klaus S, Kreymann G, Luhrmann PM, Neuhauser-Berthold M, Noack R, Pirke KM, Platte P, Selberg O, et al. World Health Organization equations have shortcomings for predicting resting energy expenditure in persons from a modern, affluent population: generation of a new reference standard from a retrospective analysis of a German database of resting energy expenditure. Am J Clin Nutr 2004;80:1379-1390.
32. Owen OE, Kavle E, Owen RS, Polansky M, Caprio S, Mozzoli MA, Kendrick ZV, Bushman MC, Boden G. A reappraisal of caloric requirements in healthy women. Am J Clin Nutr 1986;44:1-19.
33. Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. Hum Nutr Clin Nutr 1985;39 Suppl 1:5-41.
34. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-310.
35. Frankenfield D, Roth-Yousey L, Compher C. Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review. J Am Diet Assoc 2005;105:775-789.
36. Weijs PJ, Kruizenga HM, van Dijk AE, van der Meij BS, Langius JA, Knol DL, Strack van Schijndel RJ, van Bokhorst-de van der Schueren MA. Validation of predictive equations for resting energy expenditure in adult outpatients and inpatients. Clin Nutr 2008;27:150-157.

37. Lam YY, Ravussin E. Analysis of energy metabolism in humans: A review of methodologies. Mol Metab 2016;5:1057-1071.

38. Elia M: Organ and tissue contribution to metabolic rate. In: JM K, HN T, eds. Energy metabolism: tissue determinants and cellular corollaries. New York, NY: Raven Press, 1992; 61–80.

39. Ravussin E, Ryan Donna H. Three New Perspectives on the Perfect Storm: What's Behind the Obesity Epidemic? Obesity 2017;26:9-10.

40. Academy of Nutrition and Dietetics Evidence Analysis Library. 2014 Adult Weight Management Evidence-Based Nutrition Practice Guideline. In; 2014. Available from: https://www.andeal.org/topic.cfm?menu=5276&cat=4688 (accessed Oct 8, 2018).

41. Stuebe AM, Rich-Edwards JW. The reset hypothesis: lactation and maternal metabolism. Am J Perinatol 2009;26:81-88.

42. Schoffelen PFM, Plasqui GA-Ohoo. Classical experiments in whole-body metabolism: open-circuit respirometry-diluted flow chamber, hood, or facemask systems. Eur J Appl Physiol. 2018;118:33-49.

43. World Health Organization. Indicators for assessing infant and young child feeding practices: conclusion of a consensus meeting held 6–8 November 2007. Geneva: WHO; 2008.

44. Labbok M, Krasovec K. Toward consistency in breastfeeding definitions. Stud Fam Plann 1990;21:226-230.

45. Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Prado CM. Changes in Energy metabolism from prepregnancy to postpartum: a case report. Can J Diet Pract Res 2018;79:191-195.

46. Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Sawyer MB, Ashford J, Black AE. Longitudinal assessment of the components of energy balance in well-nourished lactating women. Am J Clin Nutr 1991;54:788-798.

47. Forsum E, Kabir N, Sadurskis A, Westerterp K. Total energy expenditure of healthy Swedish women during pregnancy and lactation. Am J Clin Nutr 1992;56:334-342.

48. Butte NF, Wong WW, Hopkinson JM. Energy requirements of lactating women derived from doubly labeled water and milk energy output. J Nutr 2001;131:53-58.

Chapter 6: General Discussion and Conclusion

6.1 Introduction

The postpartum period is characterized by important physiological changes that may affect weight regulation and consequently impact the risk of future long-term obesity in women. This thesis evaluated a cohort of women in Edmonton, Alberta, Canada at three (n = 53) and nine months postpartum (n = 49) who participated in a comprehensive suite of measurements related to body weight, energy metabolism, and appetite.

In **Chapter 3**, the cohort was stratified based on the amount of weight retained at nine months postpartum compared to prepregnancy weight to test the hypothesis that high-retainers (those retaining > 4.8 kg; n = 11) would present with a less favorable energy metabolism profile (i.e., lower rates of energy expenditure) compared to low-retainers (those retaining ≤ 4.8 kg, n = 38). Using a longitudinal design, it was also hypothesized that resting energy expenditure (REE) would decrease over time in high-retainers, and it would not change in low-retainers. We demonstrated that REE, total energy expenditure (TEE), and predicted maximum oxygen consumption ($p\dot{V}O_2$ max) were lower in high-retainers than low-retainers, and that these variables were negatively associated with postpartum weight retention (PPWR). An increase in REE from early (three months) to late (nine months) postpartum was observed in low-retainers, which was greater than predicted by changes in body composition. No difference between measured and predicted REE was observed in high-retainers.

In **Chapter 4**, it was hypothesized that metabolic variables such as energy metabolism, body composition, and lactation patterns would be associated with appetite sensations (i.e., hunger, prospective food consumption [PFC], fullness, satiety, and overall motivation to eat [i.e., composite appetite score, CAS]) at nine months postpartum. Appetite sensations, in turn, would be associated with PPWR. Daily carbohydrate oxidation, physical activity level (PAL), and daily duration of lactation episodes, but not body composition or low or high metabolism, were associated with appetite in the postpartum women enrolled in our study. Women's perceptions of appetite were associated with postpartum body weight.

In **Chapter 5**, it was hypothesized that 1) REE and TEE prediction equations would not be accurate at both group and individual levels, and 2) REE and TEE equations bias and limits of agreement would be poorer in women with obesity and in lactating women. In the cohort of women enrolled in our study, we demonstrated that several REE predictive equations had bias within ± 10% error, contrary to the hypotheses, whereas limits of agreement were wider for women with obesity and nonlactating women. TEE prediction equations performed well at a group level, but we observed wide individual variability and high rates of inaccuracy, especially for lactating women. Taking into account individual lactation patterns improved the accuracy of these equations.

Altogether, these findings contribute to the body of literature pertaining to energy metabolism in the postpartum period, and they collectively demonstrate that postpartum women have individual weight management needs. Little is understood about the complex interactions among energy metabolism, appetite, lactation pattern, and body weight and composition. The studies presented in this thesis aid in identifying needs, gaps, and opportunities in the current postpartum research field. Addressing these limitations can advance the care that women receive in weight management support during this life stage. The following sections discuss the implications and limitations of key findings in Chapters 3, 4, and 5. Furthermore, suggestions for future research are provided.

6.2 Postpartum Body Weight Variability and Retention

Chapter 3 explored body weight during early and late postpartum in a cohort of women. Although the median PPWR was not substantial at three and nine months postpartum, a high inter-individual variability was observed at both time points. For example, approximately 22% of women retained more than 4.8 kg at nine months postpartum compared to prepregnancy weight. A wide intra-individual variability was also observed with some participants losing ~10 kg and others gaining ~13 kg of body weight between three and nine months postpartum.

The variability in body weight changes during the postpartum period observed in our study is consistent with previous studies (1-7), and it highlights that some women may be at increased risk of retaining substantial amounts of weight following childbirth. Thus, pregnancy-related weight gain and weight retention after childbirth, along with any additional gain of weight in the postpartum period, may put some women at risk of obesity over the long term (1, 8, 9). Often after pregnancy, women are in the pre-conception period for the next gestation, suggesting that the postpartum period may be an opportune time of transition to reset metabolism. This reset is important because excessive PPWR negatively impacts maternal and child outcomes in a future pregnancy (10, 11). Since maternal body weight is an important indicator of maternal health and a predictor of offspring body weight (12), maternal body weight has the potential to influence the risk of obesity in future generations (i.e., Barker hypothesis) (13). Given the high variability in body weight after childbirth and the adverse risk of substantial amounts of weight retained in the postpartum period, it is imperative to assess and anticipate factors that may influence body weight regulation during early and late postpartum periods.

6.3 Determinants of Postpartum Weight Retention

According to the energy balance concept, changes in body weight are the result of imbalances between energy intake and energy expenditure as the body maintains life and performs physical activity. Thus, understanding energy expenditure is essential for investigating potential factors influencing the regulation of body weight (14, 15). Studies assessing the impact of energy expenditure on body weight regulation are limited; most postpartum research has focused on metabolic adaptations to lactation (16-25).

Chapter 3 provided an in-depth profile of key components of energy expenditure (e.g. REE, sleep energy expenditure [SleepEE], exercise energy expenditure [EEE], TEE, and respiratory quotient [RQ]) in a cohort of women at three and nine months postpartum using a whole body calorimetry. We observed a negative association between PPWR and energy expenditure (REE, TEE, SleepEE) after adjusting for body composition, as well as other potentially confounding biological factors (maternal age, prepregnancy BMI, gestational weight gain [GWG], and lactation status). Longitudinal studies involving men or nonpregnant, nonlactating women (26-28) have suggested a metabolic adaptation with weight loss, specifically a decrease in REE after weight loss that is greater than expected based on changes in body composition. The research presented in Chapter 3 adds that low-retainers (80% of our cohort) had an increase in REE over time that was greater than predicted by changes in body composition. This postpartum increase in REE may contribute to negative energy balance, allowing the body to dissipate excess calories and return body weight to prepregnancy values.

Adjustment of energy expenditure for body composition using the residual energy expenditure technique (29-31) was also explored in Chapter 4. We reported a negative association between PPWR and residual SleepEE; the lower residual SleepEE (low metabolism) the higher the PPWR. A recent study by Ostendorf and colleagues (32) found residual REE to be positively correlated with weight loss, but not with duration of weight loss maintenance, suggesting that successful weight loss maintenance may not always result in disproportionately lower-than-predicted energy expenditure. Other behavioral changes may be involved. Given the importance of metabolic adaptation with weight loss, especially in postpartum women, investigating factors influencing residual energy expenditure in this population warrants further research.

It was also demonstrated that cardiorespiratory fitness (CRF) was negatively associated with PPWR (Chapters 3 and 4), and it was higher in low-retainers compared to high-retainers (Chapter 3). Regular physical activity is one of the most important modifiable determinants of CRF (33). Therefore, encouraging postpartum women to be physically active following childbirth may contribute to improvements in CRF (34, 35) and body weight regulation. Another metabolic alteration that may occur in postpartum women is change in appetite. We determined that PPWR was negatively associated with fullness and satiety, and positively associated with overall motivation to eat, hunger, and PFC. Appetite is associated with BMI and body composition (36-38), and has been demonstrated to predict weight change (36, 39, 40) in other populations. Appetite may impact PPWR through alterations in energy intake. Although not consistent across studies (41), results from six weight loss studies that were analyzed retrospectively (39), indicated that appetite sensations were potential predictors of individual energy intake and weight loss. In a clinical context, assessment of appetite sensations could be a useful tool to assist in providing recommendations for weight management.

Our findings indicated that energy metabolism and appetite are all important factors regulating body weight after childbirth. Despite the fact that more remains to be learned and understood about energy metabolism and appetite in the postpartum context, future strategies to promote appropriate weight in the postpartum period could target these different factors.

6.4 Determinants of Appetite Sensations

Given that appetite sensations were associated with PPWR in the cohort of women enrolled in our study, we further explored some potential determinants of appetite. Daily duration of lactation episodes was associated with women's perceptions of appetite sensations. To our knowledge, only one other study (42) has assessed the impact of lactation on appetite sensations and they reported that appetite ratings and the area under the curve (AUC) for the four appetite sensations (i.e., hunger, desire to eat, fullness, and satiety) were not different between 24 lactating women at 4-5 weeks postpartum and 20 never-pregnant controls. Possible mechanisms that could explain the relationship between appetite and lactation include: 1) the glucostatic theory proposed by Mayer (43), in which hunger is initiated by decline of blood glucose level; 2) the glycogenostatic theory proposed by Flatt (44, 45), in which low glycogen stores stimulate food intake to maintain or replenish glycogen stores; 3) appetite-regulating hormones (e.g ghrelin, peptide YY, and leptin) may be affected by lactation; 4) lactation-related hormones (e.g. prolactin) may be involved in the regulation of appetite. Given that there is a paucity of studies examining these relationships in postpartum women, further research is needed.

This thesis provides an in-depth assessment of lactation patterns using a 3-day breast milk diary including a 24-h infant test weighing protocol (46). These two methodologies allowed us to explore not only breast milk energy output but also the duration of lactation episodes for each day. In animal studies involving lactating rats, changes in energy intake were driven by signals of increased energetic demands as well as by the stimulation resulting from physical suckling, independent of milk delivery *per se* (47-49). Thus, it is possible that daily duration of lactation episodes may impact appetite independently of breast milk energy output in humans.

Other metabolic responses affecting appetite that may occur in postpartum women, were related to increased carbohydrate oxidation and PAL. A longitudinal study comparing lactating and nonlactating women (19) found higher carbohydrate oxidation during lactation at six months postpartum, which is consistent with the preferential use of glucose by the mammary gland (50). Higher daily carbohydrate oxidation and PAL may lead to a greater depletion of glycogen stores, thereby stimulating appetite to initiate energy intake in order to replenish glycogen stores; this is consistent with the glycogenostatic theory (44, 45). This thesis provides critical data and insights on appetite control during the postpartum period, in which daily duration of lactation episodes, daily carbohydrate oxidation, and PAL are some of the important metabolic characteristics that deserve further investigation.

6.5 Knowledge Translation: Estimation of Energy Expenditure in the Postpartum Period

The development of personalized recommendations to support appropriate weight management relies on accurate assessment of energy needs. Several equations have been designed to estimate energy expenditure when indirect calorimetry is not available or when measurements are unfeasible to attain in clinical or research settings. To our knowledge, this research is the first to assess measured versus predicted REE in early and late postpartum, and to assess the accuracy of the current DRI energy recommendation for postpartum women (51) using whole body calorimetry (Chapter 5).

Although several equations for REE were accurate at a group level, individual prediction of REE, using different equations, showed high rates of inaccuracy. Therefore, such equations should be used with caution when predicting individuals' energy needs in the postpartum period. The highest level of REE accuracy at an individual level at both time points was estimated by the FAO/WHO/UNU height and weight equation. Inaccuracy in either direction (i.e., under or over-estimation) might lead to inappropriate lifestyle recommendations that could compromise women's health. Inaccuracy of estimating energy expenditure could also negatively impact clinical trials assessing the effectiveness of nutrition and exercise interventions on postpartum body weight.

Average measured TEE was accurately predicted by the DRI recommendation (51); however, it was not an accurate predictor at an individual level. Our findings suggested that the addition of the DRI-recommended 400 kcal/day for lactation to all women led to inaccurate predictions in approximately one-third of women. For example, predicted energy expenditure overestimated the measured energy expenditure by up to 450 kcal and underestimated the measured energy expenditure by more than 500 kcal in some individuals. Such recommendations should be used cautiously for individual energy intake recommendations. The results of our study highlight the need for refining recommendations when using them to predict individual's energy needs. The primary factor contributing to the inaccuracy is lactation (i.e., breast milk energy output), because it is highly variable among women, ranging from ~50 kcal to 750 kcal at nine months postpartum. Thus, including information about a woman's individual breast milk energy output improved the estimation of energy requirements by ~35%, which could have important implications for promoting appropriate weights in postpartum women. Future studies could therefore work toward alternative ways to capture this information, as the infant test weighing protocol is not always feasible in clinical settings.

To conclude, a better estimation of energy expenditure for postpartum women is needed to support appropriate diet and weight management interventions in this population. Future investigations are warranted to understand the physiology driving energy expenditure and the contribution of lactation to total energy requirements in the postpartum period, both short and long term.

6.6 Limitations

The findings of this thesis should be assessed considering its strengths and limitations. First, the results from this thesis were based on observation of postpartum women who were predominantly Caucasian, free of major underlying metabolic disorders, in their early thirties, highly educated, and with a high income. This cohort of women represents a subset of postpartum women in comparison to the general population. In addition, selection bias should also be considered as a limitation; participants who volunteer for health research studies are likely to have higher interest in healthy living compared with those participants who decline participation. Even though this thesis had a sample size that was similar to or greater than other studies in this research area (16-21), it was still relatively restricted.

Although our sample size may have limited our ability to detect significant interactions among some variables, we have used rigorous and precise methodologies to assess research variables and to ensure well-controlled accurate measurements. The advantages and limitations of the whole body calorimetry method were outlined in Chapter 2. The use of self-reported information for some of our data may have also introduced some bias, especially for prepregnancy weight, which was used in the calculation of GWG and PPWR. However, a retrospective cohort study (52) with 7,483 women, showed that utilization of self-reported or measured prepregnancy weight for BMI classification resulted in identical categorization for the majority of women. Sensitivity analyses, from another cohort study (53), also suggested that using self-reported prepregnancy weight for prepregnancy BMI classification was reasonably accurate. We used a previously validated tool to assess appetite sensations (54) (Chapter 4). However, measurements of hormones that control appetite (e.g., total and acylated ghrelin, PYY, GLP-1) and lactation (e.g., prolactin and oxytocin) were beyond the scope of this research. These hormones could be an important focus of future studies.

Measurements were obtained at three and nine months postpartum which allowed for analysis of both cross-sectional and longitudinal comparisons; these time points were chosen to reflect early versus late postpartum periods. The 24-h TEE measurement was assessed once at nine months postpartum. Ideally, we would have assessed it at three months postpartum, but it was not feasible to separate mothers and infants for a prolonged time when many of them were exclusively breastfeeding. Furthermore, the inclusion of additional time points for data collection (e.g., six and twelve months postpartum) would have improved our understanding of the trajectory of variables that change throughout the postpartum period. However, it is likely that recruitment would have been more difficult and/or loss to follow-up would have increased because of the extensive time commitment required for each study visit. Therefore, the study was designed to consider participant acceptability to the study protocol and to collect as much information as possible to answer the research questions while minimizing patient burden. Only four women were lost to follow-up in this study, suggesting that an appropriate balance was achieved.

An important statistical phenomenon to consider in future longitudinal studies is regression to the mean, in which subjects' average values on an outcome variable (e.g., BMI) may change in a systematic direction over time despite there being no treatment effect. Without a proper control group, changes thought to be associated with an intervention may be due to regression to the mean. Obesity research is particularly vulnerable, because the typical outcome (obesity) is defined based on a deviation from the mean (55). Therefore, to avoid making incorrect inferences, regression to the mean may be considered when designing studies and interpreting data.

6.7 Future Research

Several considerations should be discussed to move the field of postpartum energy metabolism forward. The following are suggested research areas that may be explored in future analyses and/or studies:

Assessing Metabolic Adaptation in the Postpartum Period

Since residual energy expenditure is associated with PPWR (Chapter 4), future research investigating the determinants of residual SleepEE in postpartum women is warranted. Our findings also indicated that lactating women at nine months postpartum have a similar TEE to nonlactating women (Chapter 5). In addition, findings from our case study (56) reported that TEE returned to prepregnancy values by nine months postpartum despite additional energy costs of breast milk synthesis (Appendix 1). These results suggest that adaptations in energy metabolism might occur throughout the postpartum period. Thus, future longitudinal studies with repeated measures of energy metabolism are warranted to better identify and describe adaptive changes in thermogenesis in women during the postpartum period. Such studies could compare energy expenditure measured before pregnancy and energy expenditure predicted by body weight or composition at different postpartum time points. Another approach could be to use a control sample of matched nonpregnant women as a reference group and predict energy expenditure at different postpartum time points (Tremblay 2018, personal communication (57)).

Building a Framework to Capture the Variability in Breast Milk Energy Output

Including information about a woman's individual breast milk energy output improves the estimation of energy requirements for lactating women (Chapter 5), but it is not always feasible to measure breast milk energy output directly. Larger studies are warranted to identify alternative ways to capture this information. One suggestion would be to operationalize definitions of full and partial breastfeeding as proposed by the WHO (58) and the Interagency Group for Action on Breastfeeding (59) and to link these categories to estimates of breast milk energy output.

Exploring the Relationship between Appetite and Postpartum Body Weight

In this research, we studied the relationship between appetite sensations and body weight, as well as appetite sensations and other metabolic characteristics (e.g. energy metabolism, lactation) (Chapter 4). Other longitudinal studies should be performed to explore the relationship between these variables and changes in different appetite-regulating hormones and lactation-related hormones. Future studies assessing these relationships would build on the knowledge gained from the findings presented in Chapter 4.

Improving the Estimation of Postpartum Energy Expenditure

This research highlighted the variability of postpartum body weight and the complexity of factors influencing its trajectory (Chapters 3 and 4). Additionally, high rates of inaccuracy in measuring energy expenditure in the postpartum period was demonstrated (Chapter 5). A better estimation of energy expenditure in clinical settings for weight management in the postpartum period is warranted. The following are different research directions that could improve care for postpartum women who aim to achieve a healthy body weight: 1) Future studies using mathematical modeling techniques are needed to frame, understand, and discuss the variability and complexities of body weight regulation in the postpartum period. This model, which is similar to the foresight obesity system map (60), would assist in understanding how different interconnected factors influence postpartum body weight; 2) Future larger studies using data from indirect calorimetry would allow sophisticated mathematical modeling to simulate changes in energy expenditure during the postpartum period to predict weight loss, as previously described in other populations (61, 62) including pregnant women (63). Examples of online calculators to predict weight loss (64, 65) or GWG (66), obtained from large samples of individuals, have been developed by the Pennington Biomedical Research Center (64, 66) and the National Institutes of Health (65). The database of this thesis, combined with larger databases, could potentially be used to develop this type of mathematical energy balance modeling for postpartum women.

6.8 Conclusion

This thesis captured some of the complexity of interconnected factors associated with body weight trajectories in the postpartum period such as energy metabolism, cardiorespiratory fitness, and appetite. Furthermore, this research indicated that lactation patterns, carbohydrate oxidation, and PAL are associated with appetite sensations, which in turn were also associated with body weight regulation in the postpartum period. All these factors may contribute to the high variability of body weight observed, while highlighting that postpartum women are individuals with different weight management needs. This thesis also adds much needed evidence to the body of literature on energy metabolism in the postpartum period, showing that REE, TEE, and breast milk energy output are highly variable at the individual level. Furthermore, current predictive equations, or energy recommendations should be used cautiously by postpartum women and healthcare providers, especially for those women who are lactating. Collectively, findings from this research have great importance in identifying weight management strategies, and they also have the potential to contribute to the formation of more individualized energy recommendations for postpartum women, with the ultimate goal of promoting appropriate body weight and improving care in the postpartum period.

6.9 References

1. Schmitt NM, Nicholson WK, Schmitt J. The association of pregnancy and the development of obesity - results of a systematic review and meta-analysis on the natural history of postpartum weight retention. Int J Obes (Lond) 2007;31:1642-1651.
2. Ohlin A, Rossner S. Maternal body weight development after pregnancy. Int J Obes 1990;14:159-173.
3. Rossner S, Ohlin A. Pregnancy as a risk factor for obesity: lessons from the Stockholm Pregnancy and Weight Development Study. Obes Res 1995;3:267s-275s.
4. Olson CM, Strawderman MS, Hinton PS, Pearson TA. Gestational weight gain and postpartum behaviors associated with weight change from early pregnancy to 1 y postpartum. Int J Obes Relat Metab Disord 2003;27:117-127.
5. Lim S, O'Reilly S, Behrens H, Skinner T, Ellis I, Dunbar JA. Effective strategies for weight loss in post-partum women: a systematic review and meta-analysis. Obes Rev 2015;16:972-987.
6. Gunderson EP, Abrams B. Epidemiology of gestational weight gain and body weight changes after pregnancy. Epidemiol Rev 1999;21:261-275.
7. Gunderson EP. Childbearing and obesity in women: weight before, during, and after pregnancy. Obstet Gynecol Clin North Am 2009;36:317-ix.
8. Endres LK, Straub H, McKinney C, Plunkett B, Minkovitz CS, Schetter CD, Ramey S, Wang C, Hobel C, Raju T, et al. Postpartum weight retention risk factors and relationship to obesity at 1 year. Obstet Gynecol 2015;125:144-152.
9. Linne Y, Dye L, Barkeling B, Rossner S. Weight development over time in parous women--the SPAWN study--15 years follow-up. Int J Obes Relat Metab Disord. 2003;27:1516-1522.
10. McBain RD, Dekker GA, Clifton VL, Mol BW, Grzeskowiak LE. Impact of inter-pregnancy BMI change on perinatal outcomes: a retrospective cohort study. Eur J Obstet Gynecol Reprod Biol 2016;205:98-104.
11. Sorbye LM, Skjaerven R, Klungsoyr K, Morken NH. Gestational diabetes mellitus and interpregnancy weight change: A population-based cohort study. PLoS Med 2017;14:e1002367-e1002367.

12. Yu Z, Han S, Zhu J, Sun X, Ji C, Guo X. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: a systematic review and meta-analysis. PLoS One 2013;8:e61627.
13. Barker DJ. The developmental origins of adult disease. J Am Coll Nutr 2004;23:588S-595S.
14. Hill JO, Wyatt HR, Peters JC. Energy balance and obesity. Circulation 2012;126:126-132.
15. Hall KD, Heymsfield SB, Kemnitz JW, Klein S, Schoeller DA, Speakman JR. Energy balance and its components: implications for body weight regulation. Am J Clin Nutr 2012;95:989-994.
16. Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Sawyer MB, Ashford J, Black AE. Longitudinal assessment of the components of energy balance in well-nourished lactating women. Am J Clin Nutr 1991;54:788-798.
17. Forsum E, Kabir N, Sadurskis A, Westerterp K. Total energy expenditure of healthy Swedish women during pregnancy and lactation. Am J Clin Nutr 1992;56:334-342.
18. Kopp-Hoolihan LE, van Loan MD, Wong WW, King JC. Longitudinal assessment of energy balance in well-nourished, pregnant women. Am J Clin Nutr 1999;69:697-704.
19. Butte NF, Hopkinson JM, Mehta N, Moon JK, Smith EO. Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation. Am J Clin Nutr 1999;69:299-307.
20. Butte NF, Wong WW, Hopkinson JM. Energy requirements of lactating women derived from doubly labeled water and milk energy output. J Nutr 2001;131:53-58.
21. Frigerio C, Schutz Y, Whitehead R, Jequier E. A new procedure to assess the energy requirements of lactation in Gambian women. Am J Clin Nutr 1991;54:526-533.
22. Frigerio C, Schutz Y, Whitehead R, Jequier E. Postprandial thermogenesis in lactating and non-lactating women from The Gambia. Eur J Clin Nutr 1992;46:7-13.
23. Illingworth PJ, Jung RT, Howie PW, Leslie P, Isles TE. Diminution in energy expenditure during lactation. Br Med J (Clin Res Ed) 1986;292:437–441.
24. Motil KJ, Montandon CM, Garza C. Basal and postprandial metabolic rates in lactating and nonlactating women. Am J Clin Nutr 1990;52:610-615.
25. Spaaij CJ, van Raaij JM, de Groot LC, van der Heijden LJ, Boekholt HA, Hautvast JG. Effect of lactation on resting metabolic rate and on diet- and work-induced thermogenesis. Am J Clin Nutr 1994;59:42-47.

26. Rosenbaum M, Hirsch J, Gallagher DA, Leibel RL. Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. Am J Clin Nutr 2008;88:906-912.
27. Westerterp KR. Metabolic adaptations to over--and underfeeding--still a matter of debate? Eur J Clin Nutr 2013;67:443-445.
28. Wing RR, Phelan S. Long-term weight loss maintenance. Am J Clin Nutr 2005;82:222S-225S.
29. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. N Engl J Med 1995;332:621-628.
30. Bosy-Westphal A, Braun W, Schautz B, Muller MJ. Issues in characterizing resting energy expenditure in obesity and after weight loss. Front Physiol 2013;4:47.
31. Most J, Vallo PM, Gilmore LA, St Amant M, Hsia DS, Altazan AD, Beyl RA, Ravussin E, Redman LM. Energy expenditure in pregnant women with obesity does not support energy intake recommendations. Obesity (Silver Spring) 2018;26:992-999.
32. Ostendorf DM, Melanson EL, Caldwell AE, Creasy SA, Pan Z, MacLean PS, Wyatt HR, Hill JO, Catenacci VA. No consistent evidence of a disproportionately low resting energy expenditure in long-term successful weight-loss maintainers. Am J Clin Nutr 2018;108:658-666.
33. Lakoski SG, Barlow CE, Farrell SW, Berry JD, Morrow JR, Jr., Haskell WL. Impact of body mass index, physical activity, and other clinical factors on cardiorespiratory fitness (from the Cooper Center longitudinal study). Am J Cardiol 2011;108:34-39.
34. Sports Medicine Australia. SMA statement the benefits and risks of exercise during pregnancy. Sport Medicine Australia. J Sci Med Sport 2002;5.
35. U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans, 2nd edition. Washington, DC: U.S. Department of Health and Human Services; 2018. Available from: http://www.health.gov/paguidelines/ (accessed March 13, 2019).
36. Hays NP, Bathalon GP, McCrory MA, Roubenoff R, Lipman R, Roberts SB. Eating behavior correlates of adult weight gain and obesity in healthy women aged 55-65 y. Am J Clin Nutr 2002;75:476-483.

37. Provencher V, Drapeau V, Tremblay A, Despres JP, Lemieux S. Eating behaviors and indexes of body composition in men and women from the Quebec family study. Obes Res 2003;11:783-792.
38. Drapeau V, Blundell J, Therrien F, Lawton C, Richard D, Tremblay A. Appetite sensations as a marker of overall intake. Br J Nutr 2005;93:273-280.
39. Drapeau V, King N, Hetherington M, Doucet E, Blundell JE, Tremblay A. Appetite sensations and satiety quotient: predictors of energy intake and weight loss. Appetite 2007;48:159-166.
40. Sayer RD, Peters JC, Pan Z, Wyatt HR, Hill JO. Hunger, food cravings, and diet satisfaction are related to changes in body weight during a 6-month behavioral weight loss intervention: The Beef WISE Study. Nutrients 2018;10:700.
41. Doucet E, St-Pierre S, Almeras N, Tremblay A. Relation between appetite ratings before and after a standard meal and estimates of daily energy intake in obese and reduced obese individuals. Appetite 2003;40:137-143.
42. Larson-Meyer DE, Schueler J, Kyle E, Austin KJ, Hart AM, Alexander BM. Do lactation-induced changes in ghrelin, glucagon-like peptide-1, and peptide YY influence appetite and body weight regulation during the first postpartum year? J Obes. 2016;2016:ID 7532926.
43. Mayer J. Glucostatic mechanism of regulation of food intake. N Engl J Med 1953;249:13-16.
44. Flatt JP. The difference in the storage capacities for carbohydrate and for fat, and its implications in the regulation of body weight. Ann N Y Acad Sci 1987;499:104-123.
45. Flatt JP. Glycogen levels and obesity. Int J Obes Relat Metab Disord. 1996;20:S1-11.
46. Woolridge MW, Butte N, Dewey KG: Methods for the measurement of milk volume intake in the breast-fed infant. In: Jensen RG, Neville MC, eds. Human Lactation: Milk Components and Methodologies. New York: Plenum Press, 1985;5-21.
47. Li C, Chen P, Smith MS. Neuropeptide Y and tuberoinfundibular dopamine activities are altered during lactation: role of prolactin. Endocrinology 1999;140:118-123.
48. Woodside B, Popeski N. The contribution of changes in milk delivery to the prolongation of lactational infertility induced by food restriction or increased litter size. Physiol Behav 1999;65:711-715.
49. Woodside B. Prolactin and the hyperphagia of lactation. Physiol Behav 2007;91:375-382.

50. Tigas S, Sunehag A, Haymond MW. Metabolic adaptation to feeding and fasting during lactation in humans. J Clin Endocrinol Metab 2002:302-307.
51. Institute of Medicine. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: The National Academies Press, 2005.
52. Bannon AL, Waring ME, Leung K, Masiero JV, Stone JM, Scannell EC, Moore Simas TA. Comparison of self-reported and measured pre-pregnancy weight: implications for gestational weight gain counseling. Matern Child Health J 2017;21:1469-1478.
53. Jarman M, Yuan Y, Pakseresht M, Shi Q, Robson PJ, Bell RC, the Alberta Pregnancy Outcomes and Nutrition study team, the ENRICH team. Patterns and trajectories of gestational weight gain: a prospective cohort study. CMAJ Open 2016;4:E338-E345.
54. Flint A, Raben A, Blundell JE, Astrup A. Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. Int J Obes Relat Metab Disord. 2000;24:38-48.
55. Cockrell Skinner A, Goldsby TU, Allison DB. Regression to the mean: A commonly overlooked and misunderstood factor leading to unjustified conclusions in pediatric obesity research. Child Obes. 2016;12:155-158.
56. Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Prado CM. Changes in energy metabolism from prepregnancy to postpartum: a case report. Can J Diet Pract Res 2018;79:191-195.
57. Tremblay, A. Personal communication. Canadian Nutrition Society 2018 Annual Conference. May 5, 2018.
58. World Health Organization. Indicators for assessing infant and young child feeding practices: conclusion of a consensus meeting held 6–8 November 2007. Geneva: WHO; 2008.
59. Labbok M, Krasovec K. Toward consistency in breastfeeding definitions. Stud Fam Plann 1990;21:226-230.
60. Vandenbroeck P, Goossens J, Clemens M. Foresight Tackling Obesities: Future Choices—Building the Obesity System Map. Government Office for Science, UK Government's Foresight Programme 2007. Available from: http://www.foresight.gov.uk/Obesity/12.pdf (acessed April 30, 2019).

61. Thomas DM, Martin CK, Heymsfield S, Redman LM, Schoeller DA, Levine JA. A simple model predicting individual weight change in humans. J Biol Dyn 2011;5:579-599.
62. Hall KD, Sacks G, Chandramohan D, Chow CC, Wang YC, Gortmaker SL, Swinburn BA. Quantification of the effect of energy imbalance on bodyweight. Lancet 2011;378:826-837.
63. Thomas DM, Navarro-Barrientos JE, Rivera DE, Heymsfield SB, Bredlau C, Redman LM, Martin CK, Lederman SA, M Collins L, Butte NF. Dynamic energy-balance model predicting gestational weight gain. Am J Clin Nutr 2012;95:115-122.
64. Pennington Biomedical Research Center. Weight loss predictor. Available from: https://www.pbrc.edu/research-and-faculty/calculators/weight-loss-predictor/ (acessed March 29, 2019).
65. National Institutes of Health. Body weight planner.Available from: https://www.niddk.nih.gov/bwp (acessed March 29, 2019).
66. Pennington Biomedical Research Center. Gestational weight gain calculator. Available from: https://www.pbrc.edu/research-and-faculty/calculators/gestational-weight-gain/ (acessed March 29, 2019).

Alphabetical Bibliography

Academy of Nutrition and Dietetics Evidence Analysis Library. 2014 Adult Weight Management Evidence-Based Nutrition Practice Guideline. In; 2014. Available from: https://www.andeal.org/topic.cfm?menu=5276&cat=4688 (accessed Oct 8, 2018).

Allen JC, Keller RP, Archer P, Neville MC. Studies in human lactation: milk composition and daily secretion rates of macronutrients in the first year of lactation. Am J Clin Nutr 1991;54:69-80.

Althuizen E, van Poppel MNM, de Vries JH, Seidell JC, van Mechelen W. Postpartum behaviour as predictor of weight change from before pregnancy to one year postpartum. BMC Public Health 2011;11:165.

Amorim Adegboye AR, Linne YM. Diet or exercise, or both, for weight reduction in women after childbirth. Cochrane Database Syst Rev 2013:Cd005627.

Athukorala C, Rumbold AR, Willson KJ, Crowther CA. The risk of adverse pregnancy outcomes in women who are overweight or obese. BMC Pregnancy Childbirth 2010:56.

Badman MK, Flier JS. The gut and energy balance: visceral allies in the obesity wars. Science 2005;307:1909-1914.

Baker JL, Gamborg M, Heitmann BL, Lissner L, Sorensen TI, Rasmussen KM. Breastfeeding reduces postpartum weight retention. Am J Clin Nutr 2008;88:1543-1551.

Bannon AL, Waring ME, Leung K, Masiero JV, Stone JM, Scannell EC, Moore Simas TA. Comparison of self-reported and measured pre-pregnancy weight: implications for gestational weight gain counseling. Matern Child Health J 2017;21:1469-1478.

Barker DJ. The developmental origins of adult disease. J Am Coll Nutr 2004;23:588S-595S.

Barker M, Dombrowski SU, Colbourn T, Fall CHD, Kriznik NM, Lawrence WT, Norris SA, Ngaiza G, Patel D, Skordis-Worrall J, et al. Intervention strategies to improve nutrition and health behaviours before conception. Lancet 2018;391:1853-1864.

Barwell ND, Malkova D, Leggate M, Gill JM. Individual responsiveness to exercise-induced fat loss is associated with change in resting substrate utilization. Metabolism 2009;58:1320-1328.

Beaver WL, Wasserman K, Whipp BJ. Improved detection of lactate threshold during exercise using a log-log transformation. J Appl Physiol (1985) 1985;59:1936-1940.

Begum F, Colman I, McCargar LJ, Bell RC. Gestational weight gain and early postpartum weight retention in a prospective cohort of Alberta women. J Obstet Gynaecol Can 2012;34:637-647.

Ben-Jonathan N, Hugo ER, Brandebourg TD, LaPensee CR. Focus on prolactin as a metabolic hormone. Trends Endocrinol Metab 2006;17:110-116.

Bendinger T, Plunkett N. Measurement in pain medicine. BJA Education 2016;16:310-315.

Bernstein RS, Thornton JC, Yang MU, Wang J, Redmond AM, Pierson RN, Jr., Pi-Sunyer FX, Van Itallie TB. Prediction of the resting metabolic rate in obese patients. Am J Clin Nutr 1983;37:595-602.

Bessesen DH, Bull S, Cornier MA. Trafficking of dietary fat and resistance to obesity. Physiol Behav 2008;94:681-688.

Blair SN, Kampert JB, Kohl HWr, Barlow CE, Macera CA, Paffenbarger RSJ, Gibbons LW. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. JAMA 1996;276:205-210.

Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-310.

Blundell J, de Graaf C, Hulshof T, Jebb S, Livingstone B, Lluch A, Mela D, Salah S, Schuring E, van der Knaap H, et al. Appetite control: methodological aspects of the evaluation of foods. Obes Rev 2010;11:251-270.

Blundell JE, Caudwell P, Gibbons C, Hopkins M, Naslund E, King N, Finlayson G. Role of resting metabolic rate and energy expenditure in hunger and appetite control: a new formulation. Dis Model Mech 2012;5:608-613.

Blundell JE, Caudwell P, Gibbons C, Hopkins M, Naslund E, King NA, Finlayson G. Body composition and appetite: fat-free mass (but not fat mass or BMI) is positively associated with self-determined meal size and daily energy intake in humans. Br J Nutr 2012;107:445-449.

Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14:377-381.

Bosy-Westphal A, Braun W, Schautz B, Muller MJ. Issues in characterizing resting energy expenditure in obesity and after weight loss. Front Physiol 2013;4:47.

Bosy-Westphal A, Muller MJ, Boschmann M, Klaus S, Kreymann G, Luhrmann PM, Neuhauser-Berthold M, Noack R, Pirke KM, Platte P, et al. Grade of adiposity affects the impact of fat mass on resting energy expenditure in women. Br J Nutr 2009;101:474-477.

Brien SE, Katzmarzyk PT, Craig CL, Gauvin L. Physical activity, cardiorespiratory fitness and body mass index as predictors of substantial weight gain and obesity: the Canadian physical activity longitudinal study. Can J Public Health 2007;98:121-124.

Brouwer E. On simple formulae for calculating the heat expenditure and the quantities of carbohydrate and fat oxidized in metabolism of men and animals, from gaseous exchange (Oxygen intake and carbonic acid output) and urine-N. Acta Physiol Pharmacol Neerl 1957;6:795-802.

Butte NF, Garza C, Johnson CA, Smith EO, Nichols BL. Longitudinal changes in milk composition of mothers delivering preterm and term infants. Early Hum Dev 1984;9:153-162.

Butte NF, Garza C, Smith EO, Nichols BL. Human milk intake and growth in exclusively breast-fed infants. J Pediatr 1984;104:187-195.

Butte NF, Hopkinson JM, Mehta N, Moon JK, Smith EO. Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation. Am J Clin Nutr 1999;69:299-307.

Butte NF, Hopkinson JM. Body composition changes during lactation are highly variable among women. J Nutr 1998;128:381S-385S.

Butte NF, M. HJ, Nicolson MA. Leptin in human reproduction: serum leptin levels in pregnant and lactating women. J Clin Endocrinol Metab 1997;82:585-589.

Butte NF, Wong WW, Hopkinson JM. Energy requirements of lactating women derived from doubly labeled water and milk energy output. J Nutr 2001;131:53-58.

Carneiro IP, Elliott SA, Siervo M, Padwal R, Bertoli S, Battezzati A, Prado CM. Is obesity associated with altered energy expenditure? Adv Nutr 2016;7:476-487.

Carter T, Bastounis A, Guo B, Jane Morrell C. The effectiveness of exercise-based interventions for preventing or treating postpartum depression: a systematic review and meta-analysis. Arch Womens Ment Health 2019;22:37-53.

Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep 1985;100:126-131.

Caudwell P, Finlayson G, Gibbons C, Hopkins M, King N, Naslund E, Blundell JE. Resting metabolic rate is associated with hunger, self-determined meal size, and daily energy intake and may represent a marker for appetite. Am J Clin Nutr 2013;97:7-14.

Chaput JP, Gilbert JA, Gregersen NT, Pedersen SD, Sjodin AM. Comparison of 150-mm versus 100-mm visual analogue scales in free living adult subjects. Appetite 2010;54:583-586.

Chouinard-Castonguay S, J. WS, Tchernof A, Robitaille J. Relationship between lactation duration and insulin and glucose response among women with prior gestational diabetes. Eur J Endocrinol 2013;168:515-523.

Chu SY, Bachman DJ, Callaghan WM, Whitlock EP, Dietz PM, Berg CJ, O'Keeffe-Rosetti M, Bruce FC, Hornbrook MC. Association between obesity during pregnancy and increased use of health care. N Engl J Med 2008;358:1444-1453.

Church TS, LaMonte MJ, Barlow CE, Blair SN. Cardiorespiratory fitness and body mass index as predictors of cardiovascular disease mortality among men with diabetes. Arch Intern Med 2005;165:2114-2120.

Cockrell Skinner A, Goldsby TU, Allison DB. Regression to the mean: A commonly overlooked and misunderstood factor leading to unjustified conclusions in pediatric obesity research. Child Obes. 2016;12:155-158.

CSEP. Canadian Society for Exercise Physiology. Canadian physical activity guidelines for adults; 2011. Available from: https://csepguidelines.ca/adults-18-64/ (accessed March 13, 2019).

Cummings DE, Weigle DS, Frayo RS, Breen PA, Ma MK, Dellinger EP, Purnell JQ. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. N Engl J Med 2002;346:1623-1630.

Cunningham JJ. Body composition as a determinant of energy expenditure: a synthetic review and a proposed general prediction equation. Am J Clin Nutr 1991;54:963-969.

Davies GA, Wolfe LA, Mottola MF, MacKinnon C, Arsenault MY, Bartellas E, Cargill Y, Gleason T, Iglesias S, Klein M, et al. Exercise in pregnancy and the postpartum period. J Obstet Gynaecol Can 2003;25:516-529.

Davies GA, Wolfe LA, Mottola MF, MacKinnon C. No. 129-Exercise in Pregnancy and the Postpartum Period. J Obstet Gynaecol Can 2018;40:e58-e65.

Davies GA, Maxwell C, McLeod L. No. 239-Obesity in Pregnancy. J Obstet Gynaecol Can 2018;40:e630-e639.

de Boo HA, Harding JE. The developmental origins of adult disease (Barker) hypothesis. Aust N Z J Obstet Gynaecol 2006;46:4-14.

de Sousa TM, Maioli TU, Dos Santos ALS, Dos Santos LC. Energy expenditure in the immediate postpartum period: Indirect calorimetry versus predictive equations. Nutrition 2017;39-40:36-42.

Dewey KG, Finley DA, Lonnerdal B. Breast milk volume and composition during late lactation (7-20 months). J Pediatr Gastroenterol Nutr 1984;3:713-720.

Dewey KG, Heinig MJ, Nommsen LA. Maternal weight-loss patterns during prolonged lactation. Am J Clin Nutr 1993;58:162-166.

Dodd JM, Deussen AR, O'Brien CM, Schoenaker D, Poprzeczny A, Gordon A, Phelan S. Targeting the postpartum period to promote weight loss: a systematic review and meta-analysis. Nutr Rev 2018;76:639-654.

Donahoo WT, Levine JA, Melanson EL. Variability in energy expenditure and its components. Curr Opin Clin Nutr Metab Care 2004;7:599-605.

Dørheim SK, Bondevik GT, Eberhard-Gran M, Bjorvatn B. Sleep and depression in postpartum women: a population-based study. Sleep 2009;32:847-855.

Doucet E, St-Pierre S, Almeras N, Tremblay A. Relation between appetite ratings before and after a standard meal and estimates of daily energy intake in obese and reduced obese individuals. Appetite 2003;40:137-143.

Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. Ann Rheum Dis 1978;37:378-381.

Drapeau V, Blundell J, Therrien F, Lawton C, Richard D, Tremblay A. Appetite sensations as a marker of overall intake. Br J Nutr 2005;93:273-280.

Drapeau V, King N, Hetherington M, Doucet E, Blundell JE, Tremblay A. Appetite sensations and satiety quotient: predictors of energy intake and weight loss. Appetite 2007;48:159-166.

Dujmovic M, Kresic G, Mandic ML, Kenjeric D, Cvijanovic O. Changes in dietary intake and body weight in lactating and non-lactating women: prospective study in northern coastal Croatia. Coll Antropol 2014;38:179-187.

Dulloo AG, Jacquet J, Montani JP, Schutz Y. Adaptive thermogenesis in human body weight regulation: more of a concept than a measurable entity? Obes Rev 2012;13:105-121.

Dykes J, Brunner EJ, Martikainen PT, Wardle J. Socioeconomic gradient in body size and obesity among women: the role of dietary restraint, disinhibition and hunger in the Whitehall II study. Int J Obes Relat Metab Disord. 2004;28:262-268.

Eckel RH, Hernandez TL, Bell ML, Weil KM, Shepard TY, Grunwald GK, Sharp TA, Francis CC, Hill JO. Carbohydrate balance predicts weight and fat gain in adults. Am J Clin Nutr 2006;83:803-808.

Edholm OG, Fletcher JG, Widdowson EM, McCance RA. The energy expenditure and food intake of individual men. Br J Nutr 1955;9:286-300.

Ehrlich SF, Hedderson MM, Quesenberry CP, Jr., Feng J, Brown SD, Crites Y, Ferrara A. Post-partum weight loss and glucose metabolism in women with gestational diabetes: the DEBI Study. Diabet Med 2014;31:862-867.

Elia M: Organ and tissue contribution to metabolic rate. In: JM K, HN T, eds. Energy metabolism: tissue determinants and cellular corollaries. New York, NY: Raven Press, 1992; 61–80.

Elliott SA, Pereira LCR, McCargar LJ, Prado CM, Bell RC. Trajectory and determinants of change in lean soft tissue over the postpartum period. Br J Nutr 2018;4:1-9.

Endres LK, Straub H, McKinney C, Plunkett B, Minkovitz CS, Schetter CD, Ramey S, Wang C, Hobel C, Raju T, et al. Postpartum weight retention risk factors and relationship to obesity at 1 year. Obstet Gynecol 2015;125:144-152.

Ertel KA, Huang T, Rifas-Shiman SL, Kleinman K, Rich-Edwards J, Oken E, James-Todd T. Perinatal weight and risk of prenatal and postpartum depressive symptoms. Ann Epidemiol 2017;27:695-700.e691.

FAO/WHO/UNU. Energy and protein requirements. Report of a joint FAO/WHO/UNU Expert Consultation. World Health Organ Tech Rep Ser 1985;724:1-206.

FAO/WHO/UNU. Human energy requirements : report of a joint FAO/WHO/UNU Expert Consultation, Rome 17-24 October 2001. Rome: Food and Agriculture Organization of the United Nations, 2004.

Flatt JP. Glycogen levels and obesity. Int J Obes Relat Metab Disord. 1996;20:S1-11.

Flatt JP. The difference in the storage capacities for carbohydrate and for fat, and its implications in the regulation of body weight. Ann N Y Acad Sci 1987;499:104-123.

Flint A, Raben A, Blundell JE, Astrup A. Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. Int J Obes Relat Metab Disord. 2000;24:38-48.

Forsum E, Kabir N, Sadurskis A, Westerterp K. Total energy expenditure of healthy Swedish women during pregnancy and lactation. Am J Clin Nutr 1992;56:334-342.

Frankenfield D, Roth-Yousey L, Compher C. Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review. J Am Diet Assoc 2005;105:775-789.

Frederick IO, Rudra CB, Miller RS, Foster JC, Williams MA. Adult weight change, weight cycling, and prepregnancy obesity in relation to risk of preeclampsia. Epidemiology 2006;17:428-434.

Frigerio C, Schutz Y, Whitehead R, Jequier E. A new procedure to assess the energy requirements of lactation in Gambian women. Am J Clin Nutr. 1991;54:526-533.

Frigerio C, Schutz Y, Whitehead R, Jequier E. Postprandial thermogenesis in lactating and non-lactating women from The Gambia. Eur J Clin Nutr 1992;46:7-13.

Galgani JE, de Jonge L, Most MM, Bray GA, Smith SR. Effect of a 3-dayhigh-fat feeding period on carbohydrate balance and *ad libitum* energy intake in humans. Int J Obes 2010;34:886-914.

Garby L, Kurzer MS, Lammert O, Nielsen E. Energy expenditure during sleep in men and women: evaporative and sensible heat losses. Hum Nutr Clin Nutr 1987;41:225-233.

Garnaes KK, Morkved S, Salvesen KA, Salvesen O, Moholdt T. Exercise training during pregnancy reduces circulating insulin levels in overweight/obese women postpartum: secondary analysis of a randomised controlled trial (the ETIP trial). BMC Pregnancy Childbirth 2018;18:18.

Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Sawyer MB, Ashford J, Black AE. Longitudinal assessment of the components of energy balance in well-nourished lactating women. Am J Clin Nutr 1991;54:788-798.

Granata GP, Brandon LJ. The thermic effect of food and obesity: discrepant results and methodological variations. Nutr Rev 2002;60:223-233.

Gunderson EP, Abrams B, Selvin S. Does the pattern of postpartum weight change differ according to pregravid body size? Int J Obes Relat Metab Disord 2001;25:853-862.

Gunderson EP, Abrams B. Epidemiology of gestational weight gain and body weight changes after pregnancy. Epidemiol Rev 1999;21:261-275.

Gunderson EP, Kim C, Quesenberry CP, Jr., Marcovina S, Walton D, Azevedo RA, Fox G, Elmasian C, Young S, Salvador N, et al. Lactation intensity and fasting plasma lipids, lipoproteins, non-esterified free fatty acids, leptin and adiponectin in postpartum women with recent gestational diabetes mellitus: the SWIFT cohort. Metabolism 2014;63:941-950.

Gunderson EP, Lewis CE, Wei GS, Whitmer RA, Quesenberry CP, Sidney S. Lactation and changes in maternal metabolic risk factors. Obstet Gynecol 2007;109:729-738.

Gunderson EP, Rifas-Shiman SL, Oken E, Rich-Edwards JW, Kleinman KP, Taveras EM, Gillman MW. Association of fewer hours of sleep at 6 months postpartum with substantial weight retention at 1 year postpartum. Am J Epidemiol 2008;167:178-187.

Gunderson EP, Y. C, Chiang V, Walton D, Azevedo RA, Fox G, Elmasian C, Young S, Salvador N, Lum M, et al. Influence of breastfeeding during the postpartum oral glucose tolerance test on plasma glucose and insulin. Obstet Gynecol 2012;120:136-143.

Gunderson EP. Childbearing and obesity in women: weight before, during, and after pregnancy. Obstet Gynecol Clin North Am 2009;36:317-ix.

Hall KD, Heymsfield SB, Kemnitz JW, Klein S, Schoeller DA, Speakman JR. Energy balance and its components: implications for body weight regulation. Am J Clin Nutr 2012;95:989-994.

Hall KD, Sacks G, Chandramohan D, Chow CC, Wang YC, Gortmaker SL, Swinburn BA. Quantification of the effect of energy imbalance on bodyweight. Lancet 2011;378:826-837.

Harris JA, Benedict FG. A Biometric Study of Human Basal Metabolism. Proc Natl Acad Sci U S A 1918;4:370-373.

Haugen M, Brantsaeter AL, Winkvist A, Lissner L, Alexander J, Oftedal B, Magnus P, Meltzer HM. Associations of pre-pregnancy body mass index and gestational weight gain with pregnancy outcome and postpartum weight retention: a prospective observational cohort study. BMC Pregnancy Childbirth 2014;14:201.

Hays NP, Bathalon GP, McCrory MA, Roubenoff R, Lipman R, Roberts SB. Eating behavior correlates of adult weight gain and obesity in healthy women aged 55-65 y. Am J Clin Nutr 2002;75:476-483.

Health Canada. Prenatal nutrition guidelines for health professionals: gestational weight gain. Ottawa; 2010. Available from: http://publications.gc.ca/site/eng/378476/publication.html (accessed March 13, 2019).

Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: the DARLING Study. Am J Clin Nutr 1993;58:152-161.

Henry CJ. Basal metabolic rate studies in humans: measurement and development of new equations. Public Health Nutr 2005;8:1133-1152.

Herring SJ, Rich-Edwards JW, Oken E, Rifas-Shiman SL, Kleinman KP, Gillman MW. Association of postpartum depression with weight retention 1 year after childbirth. Obesity (Silver Spring) 2008;16:1296-1301.

Heymsfield SB, Gallagher D, Kotler DP, Wang Z, Allison DB, Heshka S. Body-size dependence of resting energy expenditure can be attributed to nonenergetic homogeneity of fat-free mass. Am J Physiol Endocrinol Metab 2002;282:E132-138.

Heymsfield SB, Heo M, Thomas D, Pietrobelli A. Scaling of body composition to height: relevance to height-normalized indexes. Am J Clin Nutr 2011;93:736-740.

Heyward VH. Advanced fitness assessment and exercise prescription. 6th ed. Champaign, IL: Human Kinetics, 2010.

Hibi M, Ando T, Tanaka S, Tokuyama K. Human calorimetry: Energy expenditure and substrate utilization easurements using a respiratory chamber. J Sports Med Phys Fitness 2013;2:93-99.

Hill JO, Wyatt HR, Peters JC. Energy balance and obesity. Circulation 2012;126:126-132.

Hill JO, Wyatt HR, Peters JC. The importance of energy balance. Eur Endocrinol 2013;9:111-115.

Hill RJ, Cleghorn GJ, Withers GD, Lewindon PJ, Ee LC, Connor F, Davies PS. Resting energy expenditure in children with inflammatory bowel disease. J Pediatr Gastroenterol Nutr 2007;45:342-346.

Hills AP, Mokhtar N, Byrne NM. Assessment of physical activity and energy expenditure: an overview of objective measures. Front Nutr 2014;1:5.

Hollis JL, Crozier SR, Inskip HM, Cooper C, Godfrey KM, Harvey NC, Collins CE, Robinson SM. Modifiable risk factors of maternal postpartum weight retention: an analysis of their combined impact and potential opportunities for prevention. Int J Obes (Lond). 2017;41:1091-1098.

Hopkins M, Finlayson G, Duarte C, Gibbons C, Johnstone AM, Whybrow S, Horgan GW, Blundell JE, Stubbs RJ. Biological and psychological mediators of the relationships between fat mass, fat-free mass and energy intake. Int J Obes (Lond) 2019;43:233-242.

Hopkins M, Finlayson G, Duarte C, Whybrow S, Ritz P, Horgan GW, Blundell JE, Stubbs RJ. Modelling the associations between fat-free mass, resting metabolic rate and energy intake in the context of total energy balance. Int J Obes (Lond) 2016;40:312-318.

Hopkins M, Jeukendrup A, King NA, Blundell JE. The relationship between substrate metabolism, exercise and appetite control: does glycogen availability influence the motivation to eat, energy intake or food choice? Sports Med 2011;41:507-521.

Hung TH, Liao PA, Chang HH, Wang JH, Wu MC. Examining the relationship between cardiorespiratory fitness and body weight status: empirical evidence from a population-based survey of adults in Taiwan. ScientificWorldJournal 2014;2014:463736.

Hutcheon JA, Chapinal N, Bodnar LM, Lee L. The INTERGROWTH-21st gestational weight gain standard and interpregnancy weight increase: A population-based study of successive pregnancies. Obesity (Silver Spring) 2017;25:1122-1127.

Illingworth PJ, Jung RT, Howie PW, Leslie P, Isles TE. Diminution in energy expenditure during lactation. Br Med J (Clin Res Ed)1986;292:437-441.

Imanaka M, Ando M, Kitamura T, Kawamura T. Impact of Registered Dietitian Expertise in Health Guidance for Weight Loss. PLoS One 2016;11:e0151456.

Institute of Medicine and National Research Council. Weight gain during pregnancy: reexamining the guidelines. Washington, DC: The National Academies Press, 2009. Available from: http://www.nap.edu/openbook.php?record_id=12584.

Institute of Medicine. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: The National Academies Press, 2005.

Institute of Medicine. Fitness measures and health outcomes in youth. Washington, DC; 2012.

Jarman M, Yuan Y, Pakseresht M, Shi Q, Robson PJ, Bell RC, the Alberta Pregnancy Outcomes and Nutrition study team, the ENRICH team. Patterns and trajectories of gestational weight gain: a prospective cohort study. CMAJ Open 2016;4:E338-E345.

Jequier E, Schutz Y. Long-term measurements of energy expenditure in humans using a respiration chamber. Am J Clin Nutr 1983;38:989-998.

Jequier E: Calorie balance versus nutrient balance. In: Kinney JM, Tucker HN, eds. Energy metabolism: tissue determinants and cellular corollaries. New York: Raven Press, 1992.

Jesus P, Achamrah N, Grigioni S, Charles J, Rimbert A, Folope V, Petit A, Dechelotte P, Coeffier M. Validity of predictive equations for resting energy expenditure according to the body mass index in a population of 1726 patients followed in a Nutrition Unit. Clin Nutr 2015;34:529-535.

Jeukendrup AE, Wallis GA. Measurement of substrate oxidation during exercise by means of gas exchange measurements. Int J Sports Med 2005;26:S28-37.

Jiang M, Gao H, Vinyes-Pares G, Yu K, Ma D, Qin X, Wang P. Association between breastfeeding duration and postpartum weight retention of lactating mothers: A meta-analysis of cohort studies. Clin Nutr 2018;37:1224-1231.

Johannsen DL, Knuth ND, Huizenga R, Rood JC, Ravussin E, Hall KD. Metabolic slowing with massive weight loss despite preservation of fat-free mass. J Clin Endocrinol Metab 2012;97:2489-2496.

Johnstone AM, Murison SD, Duncan JS, Rance KA, Speakman JR. Factors influencing variation in basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex, circulating leptin, or triiodothyronine. Am J Clin Nutr 2005;82:941-948.

Kac G, Benicio MH, Velasquez-Melendez G, Valente JG. Nine months postpartum weight retention predictors for Brazilian women. Public Health Nutr 2004;7:621-628.

Katzmarzyk PT, Perusse L, Tremblay A, Bouchard C. No association between resting metabolic rate or respiratory exchange ratio and subsequent changes in body mass and fatness: 5-1/2 year follow-up of the Quebec family study. Eur J Clin Nutr 2000;54:610-614.

Keesey RE, Powley TL. Body energy homeostasis. Appetite 2008;51:442-445.

Kennedy GC. The role of depot fat in the hypothalamic control of food intake in the rat. Proc R Soc Lond B Biol Sci 1953;140:578-596.

Ketterl TG, Dundas NJ, Roncaioli SA, Littman AJ, Phipps AI. Association of pre-pregnancy BMI and postpartum weight retention fefore second pregnancy, Washington State, 2003-2013. Matern Child Health J 2018;22:1339-1344.

King NA, Hopkins M, Caudwell P, Stubbs RJ, Blundell JE. Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss. Int J Obes (Lond) 2008;32:177-184.

Kirkegaard H, Stovring H, Rasmussen KM, Abrams B, Sorensen TI, Nohr EA. How do pregnancy-related weight changes and breastfeeding relate to maternal weight and BMI-adjusted waist circumference 7 y after delivery? Results from a path analysis. Am J Clin Nutr 2014;99:312-319.

Kirkegaard H, Stovring H, Rasmussen KM, Abrams B, Sorensen TI, Nohr EA. Maternal weight change from prepregnancy to 7 years postpartum--the influence of behavioral factors. Obesity (Silver Spring) 2015;23:870-878.

Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA 2009;301:2024-2035.

Kominiarek MA, Rajan P. Nutrition Recommendations in Pregnancy and Lactation. Med Clin North Am 2016;100:1199-1215.

Kopp-Hoolihan LE, van Loan MD, Wong WW, King JC. Longitudinal assessment of energy balance in well-nourished, pregnant women. Am J Clin Nutr 1999;69:697-704.

Krummel DA, Semmens E, Boury J, Gordon PM, Larkin KT. Stages of change for weight management in postpartum women. J Am Diet Assoc 2004;104:1102-1108.

Krummel DA. Postpartum weight control: a vicious cycle. J Am Diet Assoc 2007;107:37-40.

Kuhlmann AK, Dietz PM, Galavotti C, England LJ. Weight-management interventions for pregnant or postpartum women. Am J Prev Med 2008;34:523-528.

Labbok M, Krasovec K. Toward consistency in breastfeeding definitions. Stud Fam Plann 1990;21:226-230.

Lakoski SG, Barlow CE, Farrell SW, Berry JD, Morrow JR, Jr., Haskell WL. Impact of body mass index, physical activity, and other clinical factors on cardiorespiratory fitness (from the Cooper Center longitudinal study). Am J Cardiol 2011;108:34-39.

Lam YY, Ravussin E. Analysis of energy metabolism in humans: A review of methodologies. Mol Metab 2016;5:1057-1071.

Lam YY, Ravussin E. Indirect calorimetry: an indispensable tool to understand and predict obesity. Eur J Clin Nutr 2017;71:318-322.

Larson-Meyer DE, Ravussin E, Heilbronn L, DeJonge L. Ghrelin and peptide YY in postpartum lactating and nonlactating women. Am J Clin Nutr 2010;91:366-372.

Larson-Meyer DE, Schueler J, Kyle E, Austin KJ, Hart AM, Alexander BM. Do lactation-induced changes in ghrelin, glucagon-like peptide-1, and peptide YY influence appetite and body weight regulation during the first postpartum year? J Obes. 2016;2016:ID 7532926.

Lazzer S, Agosti F, Resnik M, Marazzi N, Mornati D, Sartorio A. Prediction of resting energy expenditure in severely obese Italian males. J Endocrinol Invest 2007;30:754-761.

Lee D, Artero EG, Sui X, Blair SN. Mortality trends in the general population: the importance of cardiorespiratory fitness. J Psychopharmacol 2010;24:27-35.

Lee DC, Sui X, Artero EG, Lee IM, Church TS, McAuley PA, Stanford FC, Kohl HWr, Blair SN. Long-term effects of changes in cardiorespiratory fitness and body mass index on all-cause and cardiovascular disease mortality in men: the Aerobics Center Longitudinal Study. Circulation 2011;124:2483-2490.

Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. N Engl J Med 1995;332:621-628.

Levine JA. Measurement of energy expenditure. Public Health Nutr 2005;8:1123-1132.

Levine JA. Non-exercise activity thermogenesis (NEAT). Best Pract Res Clin Endocrinol Metab 2002;16:679-702.

Li C, Chen P, Smith MS. Neuropeptide Y and tuberoinfundibular dopamine activities are altered during lactation: role of prolactin. Endocrinology 1999;140:118-123.

Lim S, O'Reilly S, Behrens H, Skinner T, Ellis I, Dunbar JA. Effective strategies for weight loss in post-partum women: a systematic review and meta-analysis. Obes Rev. 2015;16:972-987.

Linne Y, Barkeling B, Rossner S. Long-term weight development after pregnancy. Obes Rev 2002;3:75-83.

Linne Y, Dye L, Barkeling B, Rossner S. Weight development over time in parous women--the SPAWN study--15 years follow-up. Int J Obes Relat Metab Disord 2003;27:1516-1522.

Lipsky LM, Strawderman MS, Olson CM. Maternal weight change between 1 and 2 years postpartum: the importance of 1 year weight retention. Obesity (Silver Spring) 2012;20:1496-1502.

Liu Y, Dai W, Dai X, Li Z. Prepregnancy body mass index and gestational weight gain with the outcome of pregnancy: a 13-year study of 292,568 cases in China. Arch Gynecol Obstet 2012;286:905-911.

Livingston EH, Kohlstadt I. Simplified resting metabolic rate-predicting formulas for normal-sized and obese individuals. Obes Res 2005;13:1255-1262.

Lopez-Olmedo N, Hernandez-Cordero S, Neufeld LM, Garcia-Guerra A, Mejia-Rodriguez F, Mendez Gomez-Humaran I. The associations of maternal weight change with breastfeeding, diet and physical activity during the postpartum period. Matern Child Health J 2016;20:270-280.

Lovelady CA, Meredith CN, McCrory MA, Nommsen LA, Joseph LJ, Dewey KG. Energy expenditure in lactating women: a comparison of doubly labeled water and heart-rate-monitoring methods. Am J Clin Nutr. 1993;57:512-518.

Lovelady CA, Nommsen-Rivers LA, McCrory MA, Dewey KG. Effects of exercise on plasma lipids and metabolism of lactating women. Med Sci Sports Exerc 1995;27:22-28.

Lowell H, Miller DC. Weight gain during pregnancy: adherence to Health Canada's guidelines. Health Rep 2010;21:31-36.

Lu GC, Rouse DJ, DuBard M, Cliver S, Kimberlin D, Hauth JC. The effect of the increasing prevalence of maternal obesity on perinatal morbidity. Am J Obstet Gynecol 2001;185:845-849.

Ma D, Szeto IM, Yu K, Ning Y, Li W, Wang J, Zheng Y, Zhang Y, Wang P. Association between gestational weight gain according to prepregnancy body mass index and short postpartum weight retention in postpartum women. Clin Nutr 2015;34:291-295.

Mamun AA, Kinarivala M, O'Callaghan MJ, Williams GM, Najman JM, Callaway LK. Associations of excess weight gain during pregnancy with long-term maternal overweight and obesity: evidence from 21 y postpartum follow-up. Am J Clin Nutr 2010;91:1336-1341.

Mannan M, Doi SA, Mamun AA. Association between weight gain during pregnancy and postpartum weight retention and obesity: a bias-adjusted meta-analysis. Nutr Rev 2013;71:343-352.

Marra M, Scalfi L, Covino A, Esposito-Del Puente A, Contaldo F. Fasting respiratory quotient as a predictor of weight changes in non-obese women. Int J Obes Relat Metab Disord 1998;22:601-603.

Martin JE, Hure AJ, Macdonald-Wicks L, Smith R, Collins CE. Predictors of post-partum weight retention in a prospective longitudinal study. Matern Child Nutr 2014;10:496-509.

Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-419.

Matthews JN, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. British Medical Journal 1990;300:230-235.

Matu J, O'Hara J, Hill N, Clarke S, Boos C, Newman C, Holdsworth D, Ispoglou T, Duckworth L, Woods D, et al. Changes in appetite, energy intake, body composition, and circulating ghrelin constituents during an incremental trekking ascent to high altitude. Eur J Appl Physiol 2017;117:1917-1928.

Mayer J, Marshall NB, Vitale JJ, Christensen JH, Mashayekhi MB, Stare FJ. Exercise, food intake and body weight in normal rats and genetically obese adult mice. Am J Physiol 1954;177:544-548.

Mayer J, Roy P, Mitra KP. Relation between caloric intake, body weight, and physical work: studies in an industrial male population in West Bengal. Am J Clin Nutr 1956;4:169-175.

Mayer J. Glucostatic mechanism of regulation of food intake. N Engl J Med 1953;249:13-16.

McArdle WD, Katch FI, Katch VL. Sports and exercise nutrition. 3rd ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009.

McBain RD, Dekker GA, Clifton VL, Mol BW, Grzeskowiak LE. Impact of inter-pregnancy BMI change on perinatal outcomes: a retrospective cohort study. Eur J Obstet Gynecol Reprod Biol 2016;205:98-104.

McInnis KJ, Balady GJ. Comparison of submaximal exercise responses using the Bruce vs modified Bruce protocols. Med Sci Sports Exerc 1994;26:103-107.

Mellinkoff SM, Frankland M, Boyle D, Greipel M. Relationship between serum amino acid concentration and fluctuations in appetite. J Appl Physiol 1956;8:535-538.

Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr 1990;51:241-247.

Miles CW, Wong NP, Rumpler WV, Conway J. Effect of circadian variation in energy expenditure, within-subject variation and weight reduction on thermic effect of food. Eur J Clin Nutr 1993;47:274-284.

Montgomery KS, Best M, Aniello TB, Phillips JD, Hatmaker-Flanigan E. Postpartum weight loss: weight struggles, eating, exercise, and breast-feeding. J Holist Nurs 2013;31:129-138.

Morton GJ, Cummings DE, Baskin DG, Barsh GS, Schwartz MW. Central nervous system control of food intake and body weight. Nature 2006;443:289-295.

Morton GJ, Schwartz MW. The NPY/AgRP neuron and energy homeostasis. Int J Obes Relat Metab Disord 2001;25:S56-62.

Most J, Vallo PM, Gilmore LA, St Amant M, Hsia DS, Altazan AD, Beyl RA, Ravussin E, Redman LM. Energy expenditure in pregnant women with obesity does not support energy intake recommendations. Obesity (Silver Spring) 2018;26:992-999.

Motil KJ, Montandon CM, Garza C. Basal and postprandial metabolic rates in lactating and nonlactating women. Am J Clin Nutr 1990;52:610-615.

Muller MJ, Bosy-Westphal A, Klaus S, Kreymann G, Luhrmann PM, Neuhauser-Berthold M, Noack R, Pirke KM, Platte P, Selberg O, et al. World Health Organization equations have shortcomings for predicting resting energy expenditure in persons from a modern, affluent population: generation of a new reference standard from a retrospective analysis of a German database of resting energy expenditure. Am J Clin Nutr 2004;80:1379-1390.

Muller MJ, Enderle J, Pourhassan M, Braun W, Eggeling B, Lagerpusch M, Gluer CC, Kehayias JJ, Kiosz D, Bosy-Westphal A. Metabolic adaptation to caloric restriction and subsequent refeeding: the Minnesota Starvation Experiment revisited. Am J Clin Nutr 2015;102:807-819.

Muller MJ, Geisler C. From the past to future: from energy expenditure to energy intake to energy expenditure. Eur J Clin Nutr 2017;71:358-364.

Murgatroyd PR, Davies HL, Prentice AM. Intra-individual variability and measurement noise in estimates of energy expenditure by whole body indirect calorimetry. Br J Nutr 1987;58:347-356.

National Institutes of Health. Body weight planner.Available from: https://www.niddk.nih.gov/bwp (acessed March 29, 2019).

Ndahimana D, Kim E-K. Measurement Methods for Physical Activity and Energy Expenditure: a Review. Clin Nutr Res 2017;6:68-80.

Nehring I, Schmoll S, Beyerlein A, Hauner H, von Kries R. Gestational weight gain and long-term postpartum weight retention: a meta-analysis. Am J Clin Nutr 2011;94:1225-1231.

Nelson KM, Weinsier RL, Long CL, Schutz Y. Prediction of resting energy expenditure from fat-free mass and fat mass. Am J Clin Nutr 1992;56:848-856.

Neville MC: Determinants of milk volume and composition. In: Jensen RG, ed. Handbook of Milk Composition. San Diego, CA: Academic Press, 1995; 87-113.

Ng SW, Popkin BM. Time use and physical activity: a shift away from movement across the globe. Obes Rev 2012;13:659-680.

Nohr EA, Vaeth M, Baker JL, Sorensen TI, Olsen J, Rasmussen KM. Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy. Am J Clin Nutr 2008;87:1750-1759.

Norman AW, Henry HL: III. Structure, synthesis, secretion, and target cells of the hypothalamic releasing hormones: E. Hypothalamic control of prolactin secretion. In: Hormones: Academic Press, 2014; p. 66.

Ohlin A, Rossner S. Maternal body weight development after pregnancy. Int J Obes 1990;14:159-173.

Ohlin A, Rossner S. Trends in eating patterns, physical activity and socio-demographic factors in relation to postpartum body weight development. Br J Nutr 1994;71:457-470.

Ohnhaus EE, Alder R. Methodological problems in the measurement of pain: a comparison between the verbal rating scale and the visual analogue scale. Pain 1975;1:379-384.

Olson CM, Strawderman MS, Hinton PS, Pearson TA. Gestational weight gain and postpartum behaviors associated with weight change from early pregnancy to 1 y postpartum. Int J Obes Relat Metab Disord 2003;27:117-127.

Ostbye T, Peterson BL, Krause KM, Swamy GK, Lovelady CA. Predictors of postpartum weight change among overweight and obese women: results from the Active Mothers Postpartum study. J Womens Health (Larchmt) 2012;21:215-222.

Ostendorf DM, Melanson EL, Caldwell AE, Creasy SA, Pan Z, MacLean PS, Wyatt HR, Hill JO, Catenacci VA. No consistent evidence of a disproportionately low resting energy expenditure in long-term successful weight-loss maintainers. Am J Clin Nutr 2018;108:658-666.

Ovesen P, Rasmussen S, Kesmodel U. Effect of prepregnancy maternal overweight and obesity on pregnancy outcome. Obstet Gynecol 2011;118:305-312.

Owen OE, Kavle E, Owen RS, Polansky M, Caprio S, Mozzoli MA, Kendrick ZV, Bushman MC, Boden G. A reappraisal of caloric requirements in healthy women. Am J Clin Nutr 1986;44:1-19.

Pannacciulli N, Salbe AD, Ortega E, Venti CA, Bogardus C, Krakoff J. The 24-h carbohydrate oxidation rate in a human respiratory chamber predicts *ad libitum* food intake. Am J Clin Nutr 2007;86:625-632.

Pansini F, Bonaccorsi G, Genovesi F, Folegatti MR, Bagni B, Bergamini CM, Mollica G. Influence of estrogens on serum free fatty acid levels in women. J Clin Endocrinol Metab 1990;71:1387-1389.

Parker JD, Abrams B. Differences in postpartum weight retention between black and white mothers. Obstet Gynecol 1993;81:768-774.

Patel SR, Malhotra AF, White DP, Gottlieb DJ, Hu FB. Association between reduced sleep and weight gain in women. Am J Epidemiol 2006;164:947-954.

Pedersen P, Baker JL, Henriksen TB, Lissner L, Heitmann BL, Sorensen TI, Nohr EA. Influence of psychosocial factors on postpartum weight retention. Obesity (Silver Spring) 2011;19:639-646.

Pelletier C, Imbeault P, Tremblay A. Energy balance and pollution by organochlorines and polychlorinated biphenyls. Obes Rev. 2003;4:17-24.

Pennington Biomedical Research Center. Gestational weight gain calculator.Available from: https://www.pbrc.edu/research-and-faculty/calculators/gestational-weight-gain/ (acessed March 29, 2019).

Pennington Biomedical Research Center. Weight loss predictor.Available from: https://www.pbrc.edu/research-and-faculty/calculators/weight-loss-predictor/ (acessed March 29, 2019).

Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Khanh V, Bell G, Robson PJ, ENRICH Study Team. The influence of energy metabolism on postpartum weight retention. Am J Clin Nutr 2019;https://doi.org/10.1093/ajcn/nqy389.

Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Prado CM. Changes in energy metabolism from prepregnancy to postpartum: a case report. Can J Diet Pract Res 2018;79:191-195.

Pereira LCR, Purcell SA, Elliott SA, McCargar LJ, Bell RC, Robson PJ, Prado CM. The use of whole body calorimetry to compare measured versus predicted energy expenditure in postpartum women. Am J Clin Nutr 2019;109:554-565.

Phillips J, King R, Skouteris H. A conceptual model of psychological predictors of postpartum weight retention. Journal of Reproductive and Infant Psychology 2012;30:278-288.

Piaggi P, Thearle MS, Bogardus C, Krakoff J. Lower energy expenditure predicts long-term increases in weight and fat mass. J Clin Endocrinol Metab 2013;98:E703-707.

Picciano MF. Pregnancy and lactation: physiological adjustments, nutritional requirements and the role of dietary supplements. J Nutr 2003;133:1997s-2002s.

Piers LS, Soares MJ, Makan T, Shetty PS. Thermic effect of a meal. 1. Methodology and variation in normal young adults. Br J Nutr 1992;67:165-175.

Pinheiro Volp AC, Esteves de Oliveira FC, Duarte Moreira Alves R, Esteves EA, Bressan J. Energy expenditure: components and evaluation methods. Nutr Hosp 2011;26:430-440.

Pontzer H. Energy expenditure in humans and other Primates: a new synthesis. Ann Rev Anthropol 2015;44:169-187.

Poston L, Caleyachetty R, Cnattingius S, Corvalan C, Uauy R, Herring S, Gillman MW. Preconceptional and maternal obesity: epidemiology and health consequences. Lancet Diabetes Endocrinol 2016;4:1025-1036.

Provencher V, Drapeau V, Tremblay A, Despres JP, Lemieux S. Eating behaviors and indexes of body composition in men and women from the Quebec family study. Obes Res 2003;11:783-792.

Public Health Agency of Canada, Canadian Institute for Health Information. Obesity in Canada: A joint report from the Public Health Agency of Canada and the Canadian Institute for Health Information. Ottawa: Public Health Agency of Canada; 2011. Available from: https://www.canada.ca/en/public-health/services/health-promotion/healthy-living/obesity-canada.html (accessed March 13, 2019).

Ravn AM, Gregersen NT, Christensen R, Rasmussen LG, Hels O, Belza A, Raben A, Larsen TM, Toubro S, Astrup A. Thermic effect of a meal and appetite in adults: an individual participant data meta-analysis of meal-test trials. Food & Nutrition Research 2013;57:10.3402/fnr.v3457i3400.19676.

Ravussin E, Bogardus C. Relationship of genetics, age, and physical fitness to daily energy expenditure and fuel utilization. Am J Clin Nutr 1989;49:968-975.

Ravussin E, Burnand B, Schutz Y, Jequier E. Twenty-four-hour energy expenditure and resting metabolic rate in obese, moderately obese, and control subjects. Am J Clin Nutr 1982;35:566-573.

Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. J Clin Invest 1986;78:1568-1578.

Ravussin E, Lillioja S, Knowler WC, Christin L, Freymond D, Abbott WG, Boyce V, Howard BV, Bogardus C. Reduced rate of energy expenditure as a risk factor for body-weight gain. N Engl J Med 1988;318:467-472.

Ravussin E, Ryan Donna H. Three New Perspectives on the Perfect Storm: What's Behind the Obesity Epidemic? Obesity 2017;26:9-10.

Redman LM, Smith SR, Burton JH, Martin CK, Il'yasova D, Ravussin E. Metabolic slowing and reduced oxidative damage with sustained caloric restriction support the rate of living and oxidative damage theories of aging. Cell Metab 2018;27:805-815.

Reid CA, Harbron CG, Blundell JE, Stubbs RJ. What are psychometric assessments of appetite asking A preliminary multivariate analysis. International Journal of Obesity 1998;22:151A.

Rong K, Yu K, Han X, Szeto IM, Qin X, Wang J, Ning Y, Wang P, Ma D. Pre-pregnancy BMI, gestational weight gain and postpartum weight retention: a meta-analysis of observational studies. Public Health Nutr 2015;18:2172-2182.

Rooney BL, Schauberger CW. Excess pregnancy weight gain and long-term obesity: one decade later. Obstet Gynecol 2002;100:245-252.

Rosenbaum M, Hirsch J, Gallagher DA, Leibel RL. Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. Am J Clin Nutr 2008;88:906-912.

Rossner S, Ohlin A. Pregnancy as a risk factor for obesity: lessons from the Stockholm Pregnancy and Weight Development Study. Obes Res 1995;3:267s-275s.

Ruddick-Collins LC, King NA, Byrne NM, Wood RE. Methodological considerations for meal-induced thermogenesis: measurement duration and reproducibility. Br J Nutr 2013;110:1978-1986.

Sayer RD, Peters JC, Pan Z, Wyatt HR, Hill JO. Hunger, food cravings, and diet satisfaction are related to changes in body weight during a 6-month behavioral weight loss intervention: The Beef WISE Study. Nutrients 2018;10:700.

Schmitt NM, Nicholson WK, Schmitt J. The association of pregnancy and the development of obesity - results of a systematic review and meta-analysis on the natural history of postpartum weight retention. Int J Obes (Lond). 2007;31:1642-1651.

Schoffelen PF, Westerterp KR. Intra-individual variability and adaptation of overnight- and sleeping metabolic rate. Physiol Behav 2008;94:158-163.

Schoffelen PFM, Plasqui GA-Ohoo. Classical experiments in whole-body metabolism: open-circuit respirometry-diluted flow chamber, hood, or facemask systems. Eur J Appl Physiol. 2018;118:33-49.

Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. Hum Nutr Clin Nutr 1985;39 Suppl 1:5-41.

Schwartz MW, Woods SC, Porte DJ, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature 2000;404:661-671.

Shechter A, Rising R, Wolfe S, Albu JB, St-Onge MP. Postprandial thermogenesis and substrate oxidation are unaffected by sleep restriction. Int J Obes (Lond) 2014;38:1153-1158.

Sichieri R, Field AE, Rich-Edwards J, Willett WC. Prospective assessment of exclusive breastfeeding in relation to weight change in women. Int J Obes Relat Metab Disord 2003;27:815-820.

Siervo M, Faber P, Lara J, Gibney ER, Milne E, Ritz P, Lobley GE, Elia M, Stubbs RJ, Johnstone AM. Imposed rate and extent of weight loss in obese men and adaptive changes in resting and total energy expenditure. Metabolism 2015;64:896-904.

Singh J, Huang CC, Driggers RW, Timofeev J, Amini D, Landy HJ, Miodovnik M, Umans JG. The impact of pre-pregnancy body mass index on the risk of gestational diabetes. J Matern Fetal Neonatal Med 2012;25:5-10.

Smith DE, Lewis CE, Caveny JL, Perkins LL, Burke GL, Bild DE. Longitudinal changes in adiposity associated with pregnancy. The CARDIA Study. Coronary Artery Risk Development in Young Adults Study. JAMA 1994;271:1747-1751.

Smith MS, True C, Grove KL. The neuroendocrine basis of lactation-induced suppression of GnRH: role of kisspeptin and leptin. Brain Res 2010;1364:139-152.

Smith SR, de Jonge L, Zachwieja JJ, Roy H, Nguyen T, Rood JC, Windhauser MM, Bray GA. Fat and carbohydrate balances during adaptation to a high-fat. Am J Clin Nutr 2000;71:450-457.

Snoek HM, L. H, Van Gemert LJ, De Graaf C, Weenen H. Sensory-specific satiety in obese and normal-weight women. Am J Clin Nutr 2004;80:823-831.

Sorbye LM, Skjaerven R, Klungsoyr K, Morken NH. Gestational diabetes mellitus and interpregnancy weight change: A population-based cohort study. PLoS Med 2017;14:e1002367-e1002367.

Spaaij CJ, van Raaij JM, de Groot LC, van der Heijden LJ, Boekholt HA, Hautvast JG. Effect of lactation on resting metabolic rate and on diet- and work-induced thermogenesis. Am J Clin Nutr 1994;59:42-47.

Speakman JR, Selman C. Physical activity and resting metabolic rate. Proc Nutr Soc 2003;62:621-634.

Sports Medicine Australia. SMA statement the benefits and risks of exercise during pregnancy. Sport Medicine Australia. J Sci Med Sport 2002;5.

Statistics Canada. Table 13-10-0096-20 Body mass index, overweight or obese, self-reported, adult, age groups (18 years and older). Available from:

https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009620 (acessed March 29, 2019).

Stubbs RJ, Hopkins M, Finlayson GS, Duarte C, Gibbons C, Blundell JE. Potential effects of fat mass and fat-free mass on energy intake in different states of energy balance. Eur J Clin Nutr 2018;72:698-709.

Stubbs RJ, Hughes DA, Johnstone AM, Rowley E, Reid C, Elia M, Stratton R, Delargy H, King N, Blundell JE. The use of visual analogue scales to assess motivation to eat in human subjects: a review of their reliability and validity with an evaluation of new hand-held computerized systems for temporal tracking of appetite ratings. Br J Nutr 2000;84:405-415.

Stuebe AM, Mantzoros C, Kleinman K, Gillman MW, Rifas-Shiman S, Gunderson EP, Rich-Edwards J. Duration of lactation and maternal adipokines at 3 years postpartum. Diabetes 2011;60:1277-1285.

Stuebe AM, Rich-Edwards JW. The reset hypothesis: lactation and maternal metabolism. Am J Perinatol 2009;26:81-88.

Sunehag AL, Louie K, Bier JL, Tigas S, Haymond MW. Hexoneogenesis in the human breast during lactation. J Clin Endocrinol Metab 2002;87:297-301.

Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. J Am Coll Cardiol 2001;37:153-156.

Tataranni PA, Harper IT, Snitker S, Del Parigi A, Vozarova B, Bunt J, Bogardus C, Ravussin E. Body weight gain in free-living Pima Indians: effect of energy intake vs expenditure. Int J Obes Relat Metab Disord 2003;27:1578-1583.

Thomas DM, Martin CK, Heymsfield S, Redman LM, Schoeller DA, Levine JA. A simple model predicting individual weight change in humans. J Biol Dyn 2011;5:579-599.

Thomas DM, Navarro-Barrientos JE, Rivera DE, Heymsfield SB, Bredlau C, Redman LM, Martin CK, Lederman SA, M Collins L, Butte NF. Dynamic energy-balance model predicting gestational weight gain. Am J Clin Nutr 2012;95:115-122.

Thomas EA, McNair B, Bechtell JL, Ferland A, Cornier MA, Eckel RH. Greater hunger and less restraint predict weight loss success with phentermine treatment. Obesity (Silver Spring) 2016;24:37-43.

Tigas S, Sunehag A, Haymond MW. Metabolic adaptation to feeding and fasting during lactation in humans. J Clin Endocrinol Metab 2002:302-307.

Torloni MR, Betran AP, Horta BL, Nakamura MU, Atallah AN, Moron AF, Valente O. Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis. Obes Rev 2009;10:194-203.

Tremblay A, Pelletier C, Doucet E, Imbeault P. Thermogenesis and weight loss in obese individuals: a primary association with organochlorine pollution. Int J Obes Relat Metab Disord 2004;28:936-939.

Tremblay, A. Personal communication. Canadian Nutrition Society 2018 Annual Conference. May 5, 2018.

Treuth MS, Butte NF, Puyau M. Pregnancy-related changes in physical activity, fitness, and strength. Med Sci Sports Exerc 2005;37:832-837.

Tschöp M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. Diabetes 2001;50:707-709.

Tschöp MH, Speakman JR, Arch JRS, Auwerx J, Brüning JC, Chan L, Eckel RH, Farese RVJ, Galgani JE, Hambly C, et al. A guide to analysis of mouse energy metabolism. Nat Methods 2011;9:57-63.

U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans, 2nd edition. Washington, DC: U.S. Department of Health and Human Services; 2018. Available from: http://www.health.gov/paguidelines/ (accessed March 13, 2019).

Vandenbroeck P, Goossens J, Clemens M. Foresight Tackling Obesities: Future Choices—Building the Obesity System Map. Government Office for Science, UK Government's Foresight Programme 2007. Available from: http://www.foresight.gov.uk/Obesity/12.pdf (acessed April 30, 2019).

Vila G, Hopfgartner J, Grimm G, Baumgartner-Parzer SM, Kautzky-Willer A, Clodi M, Luger A. Lactation and appetite-regulating hormones: increased maternal plasma peptide YY concentrations 3-6 months postpartum. Br J Nutr 2015;114:1203-1208.

Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. Lancet 2006;368:1164-1170.

Viswanathan M, Siega-Riz AM, Moos MK, Deierlein A, Mumford S, Knaack J, Thieda P, Lux LJ, Lohr KN. Outcomes of maternal weight gain. Evid Rep Technol Assess (Full Rep) 2008;168:1-223.

Walker LO, Wilging S. Rediscovering the "M" in "MCH": maternal health promotion after childbirth. J Obstet Gynecol Neonatal Nurs 2000;29:229-236.

Warburton DER, Jamnik VK, Bredin SSD, Gledhill N. The Physical Activity Readiness Questionnaire (PAR-Q+) and electronic Physical Activity Readiness Medical Examination (ePARmed-X+) Health Fitness J Can 2011;4:3-17.

Weijs PJ, Kruizenga HM, van Dijk AE, van der Meij BS, Langius JA, Knol DL, Strack van Schijndel RJ, van Bokhorst-de van der Schueren MA. Validation of predictive equations for resting energy expenditure in adult outpatients and inpatients. Clin Nutr 2008;27:150-157.

Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1-9.

Weise CM, Hohenadel MG, Krakoff J, Votruba SB. Body composition and energy expenditure predict *ad libitum* food and macronutrient intake in humans. Int J Obes (Lond) 2014;38:243-251.

Weng HH, Bastian LA, Taylor DHJ, Moser BK, Ostbye T. Number of children associated with obesity in middle-aged women and men: results from the health and retirement study. J Womens Health (Larchmt) 2004;13:85-91.

Westerterp KR. Doubly labelled water assessment of energy expenditure: principle, practice, and promise. Eur J Appl Physiol 2017;117:1277-1285.

Westerterp KR. Metabolic adaptations to over--and underfeeding--still a matter of debate? Eur J Clin Nutr 2013;67:443-445.

Whitaker K, Young-Hyman D, Vernon M, Wilcox S. Maternal stress predicts postpartum weight retention. Maternal and child health journal 2014;18:2209-2217.

Williamson DF, Madans J, Pamuk E, Flegal KM, Kendrick JS, Serdula MK. A prospective study of childbearing and 10-year weight gain in US white women 25 to 45 years of age. Int J Obes Relat Metab Disord 1994;18:561-569.

Wing RR, Phelan S. Long-term weight loss maintenance. Am J Clin Nutr 2005;82:222S-225S.

Woods SC, Ramsay DS. Food intake, metabolism and homeostasis. Physiol Behav 2011;104:4-7.

Woodside B, Popeski N. The contribution of changes in milk delivery to the prolongation of lactational infertility induced by food restriction or increased litter size. Physiol Behav 1999;65:711-715.

Woodside B. Prolactin and the hyperphagia of lactation. Physiol Behav 2007;91:375-382.

Woolridge MW, Butte N, Dewey KG: Methods for the measurement of milk volume intake in the breast-fed infant. In: Jensen RG, Neville MC, eds. Human Lactation: Milk Components and Methodologies. New York: Plenum Press, 1985;5-21.

World Health Organization. Global Health Observatory data: overweight and obesity. Geneva (Switzerland): WHO; 2014.

World Health Organization. Indicators for assessing infant and young child feeding practices: conclusion of a consensus meeting held 6–8 November 2007. Geneva: WHO; 2008.

World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:i-xii, 1-253.

Yu Z, Han S, Zhu J, Sun X, Ji C, Guo X. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: a systematic review and meta-analysis. PLoS One 2013;8:e61627.

Zanotti J, Capp E, Wender MC. Factors associated with postpartum weight retention in a Brazilian cohort. Rev Bras Ginecol Obstet 2015;37:164-171.

Zourladani A, Zafrakas M, Chatzigiannis B, Papasozomenou P, Vavilis D, Matziari C. The effect of physical exercise on postpartum fitness, hormone and lipid levels: a randomized controlled trial in primiparous, lactating women. Arch Gynecol Obstet 2015;291:525-530.

Appendices

Appendix 1. Changes in Energy Metabolism from Prepregnancy to Postpartum: A Case Report

1. Preface

A version of this appendix has been published. Pereira LCR, Elliott SA, McCargar LJ, Bell RC, Prado CM. Changes in Energy Metabolism from Prepregnancy to Postpartum: A Case Report. Can J Diet Pract Res. 2018;79(4):191-195, https://doi.org/10.3148/cjdpr-2018-016.

2. Introduction

The estimation of energy needs during pregnancy and lactation is challenging. Recommendations were derived from high-quality studies but many years ago and based on a limited number of scientific studies (1-6) It is therefore reasonable to expect that current recommendations for energy may not reflect the needs of contemporary women who generally are older (7), more sedentary and of different body composition (8) compared to data from older studies. This in turn can impact weight gain/retention throughout pregnancy and postpartum.

In an effort to explore the energy needs of these women, we assessed changes in energy expenditure using a state-of-the-art technique (whole body calorimetry unit [WBCU]) at four time points: one month prepregnancy ("baseline"), pregnancy (33 weeks), and at three and nine months postpartum of a primigravida woman. We also compared measured and estimated energy expenditure using common equations.

3. Presentation of the Case

The unique data presented was acquired as the same individual participated in two unrelated studies, thus allowing the opportunistic investigation of energy expenditure changes. Informed consent was obtained according to the University of Alberta Health Research Ethics Board (Pro20408 and Pro42267).

The married, university educated, Caucasian participant was 30 years of age, and working full time prior to maternity leave. Her prepregnancy weight and height were 58.06kg and 1.64m, respectively. Resting blood pressure and heart rate were within normal ranges with no adverse health problems (**Table 1**).

4. Activities undertaken

Total energy expenditure (TEE) was measured for 24 hours by indirect calorimetry using a WBCU at all but the three months postpartum time point – the latter due to exclusive breastfeeding. However, all time points included a measure of resting energy expenditure (REE). While in the WBCU, individual components of TEE were assessed: REE (30 minutes), exercise energy expenditure (35 minutes treadmill walking at 2.5 mph and 5% incline, reflective of a low- to moderate-intensity walk), and energy expended while pumping breastmilk (five times/day via electric pump). Respiratory Quotient (RQ) was also assessed within the WBCU, and calculated from the ratio of carbon dioxide produced to oxygen consumed by the body.

Body composition was measured by dual energy X-ray absorptiometry (GE Medical Systems; WI, USA, enCORE 9.20 software). Energy intake was assessed using 3-day food records, (ESHA-Food Processor v.10.12.0; OR, USA), including one weekend and two weekdays, and directed by experienced research staff with extensive nutrition background. Baecke questionnaire (9) was used to assess physical activity, with the following categories: "at work", "sport", and "nonsport leisure" time. Scores for each of these three categories range from one to five and the total physical activity score (sum) range from three to fifteen. A higher score represents a higher level of physical activity.

Exclusively breastfeeding was reported at three months postpartum, with both breastmilk and complementary foods given at nine months. Breastmilk volume was estimated based on 24-hours infant test-retest weighing, in which the infant was weighed before and after each breastfeeding session. Breastmilk volume was used to estimate breastfeeding energy expenditure according to the FAO/WHO/UNU Human Energy Requirements report (10), with breastmilk volume corrected for insensible water losses (5%). The energy content of breastmilk was assumed to be 0.67 Kcal/g; and an efficiency factor of 80% was applied.

Mifflin-St Jeor equation (11), commonly used in practice (12), was used to compare measured (WBCU) and estimated REE. Dietary References Intakes (DRIs) (13) and the Factorial Method (14) (using measured and estimated REE and breastfeeding energy expenditure) were used to compare measured (WBCU) and estimated TEE (**Table 2**).

5. Outcomes

Changes in measured TEE and REE are shown in **Figure 1.** REE was similar at baseline, three and nine months postpartum. As expected, REE and TEE increased during pregnancy. Baseline and 9-month TEE were also similar, despite additional energy expended through pumping. While in the WBCU, 410mL of breastmilk was pumped which equated to an estimated energy cost of ~360 kcals (10). Interestingly, according to the WBCU, 1.5kcal/min was expended on average while pumping, totaling 180 kcals for five sessions. Fasting RQ was higher at baseline than during pregnancy or postpartum, likely due to underlying metabolic changes or differences in macronutrient intake during those periods (Table 1).

Although body weight returned to prepregnancy values at nine months postpartum, waist circumference was higher compared to prepregnancy. No change in lean tissue occurred in the postpartum period, although fat mass increased by 2% (1.5kg) between three and nine months. Energy intake was similar between both postpartum time points, and physical activity increased in the postpartum period compared with pregnancy, remaining stable postpartum (Table 1).

Measured REE was higher than estimated at all four time points. Minimal differences in measured and estimated TEE were observed at baseline (<100 kcal). During pregnancy, measured TEE was lower than predicted by the DRIs (13), and by the two Factorial Methods (measured and estimated). Differences between measured versus predicted TEE were more pronounced at nine months postpartum, in which the current DRIs recommendations for energy (13) overestimated TEE by 350 kcal (Table 2).

6. Discussion

We believe this case report was the first to assess TEE in three stages of woman's life (prepregnancy, pregnancy, and postpartum) using WBCU. Although this study carries unique and accurate information, findings are not meant to be generalized due to the intrinsic limitations of a case report. However, our results highlight the need for further research re-evaluating current recommendations for energy, especially for postpartum women.

Here we reported a woman's TEE returns to prepregnancy values by nine months postpartum, despite additional costs of breastfeeding. Similarly, REE was ~75% of TEE throughout pregnancy and the postpartum period, even with significant burden of energy deposition (during pregnancy) and energy stores mobilization (during lactation). It suggests that adaptations in energy metabolism may occur throughout the postpartum period, thus facilitating achievement of prepregnancy metabolic state. Likewise, current DRIs recommendations for energy (13) overestimated actual needs for this individual by 350 kcal/d at nine months postpartum.

Additionally, pumping milk inside the WBCU is different compared to the milk supply-demand cycle of infant feeding. However, our precise WBCU data showed that energy expended in pumping milk was 50% lower than estimated by the FAO/WHO/UNU Human Energy Requirements Report (10). Likewise, discrepancies between recommended and estimated breastfeeding energy expenditure values were observed. As this accounts for ~40% of her TEE, its accuracy should be considered when examining energy requirements. Lactating women are suggested to expend ~400 kcal/d during 7-12 months postpartum (13); however, our estimated value was ~700 kcal/d at 9-months postpartum based on 24-hour infant test-retest weighing.

A pattern of altered body composition emerged (higher fat/lean ratio) between three and nine months postpartum without changes in physical activity and energy intake. Therefore, the postpartum period may involve increases in fat mass that are not reflected in overall weight change (15). Although some women may return to their prepregnant weight and energy expenditure values, the increase in fat mass and waist circumference may be persistent, with longer term health effects. Similar to what we observed in this woman, maternal adiposity was not associated with breastmilk volume, after correction for multiple comparisons in another study (16); however, the impact of breastfeeding patterns on body composition changes should be further investigated. Finally, body composition and more accurate approaches to estimate energy needs may improve nutritional assessment during the postpartum period.

7. Relevance to Practice

Pregnancy and postpartum energy needs may not be accurately depicted by current equations. Likewise, weight change is not reflective of body composition change. Accurately determining energy needs during these periods is essential for providing adequate dietary advice and promoting a healthy body weight and composition, avoiding any adverse maternal/infant outcomes. Further research is required to re-evaluate and revise current energy recommendations for pregnant and postpartum women.

Table 1. Descriptive characteristics of anthropometrics, measured energy expenditure and respiratory quotient, body composition, energy intake, breastfeeding, and physical activity, prepregnancy, during pregnancy and at three and nine months postpartum.

Participant's characteristics	Prepregnancy	Pregnancy (33 weeks)	3 months Postpartum	9 months Postpartum
Anthropometrics				
Weight (kg)	58.06	72.00	59.20	57.90
BMI (kg/m^2)	22.2	–	22.1	21.6
Waist circumference (cm)	70.6	–	80.4	76.3
Weight change (kg)[a]	–	–	1.14	-0.16
Blood pressure (diastolic/systolic, mmHg)	104/69	107/68	112/72	107/72
Resting Heart rate (bpm)	63	78	78	74
Measured energy expenditure and respiratory quotient				
Resting energy expenditure (kcal/day)	1389	1767	1346	1449
Fasting respiratory quotient	0.93	0.83	0.84	0.78
Total energy expenditure (kcal/day)	1847	2226	–	1919
24-hour respiratory quotient	0.90	0.88	–	0.82
Exercise energy expenditure (kcal)	151	191	–	157
Exercise respiratory quotient	0.94	0.93	–	0.87
Body composition				
Fat mass (kg)	–	–	14.43	15.91
% Fat mass	–	–	24.70	26.74
Lean soft tissue (kg)	–	–	41.66	41.15
Fat-free mass (kg)	–	–	44.09	43.62
Fat:Lean ratio	–	–	0.35	0.39
Energy intake	–	–		
Energy Intake (kcal/day)	–	–	2321	2365
Energy Intake (kcal/kg)	–	–	39	41
Breastfeeding	–	–		
24-hours infant test-retest weighing	–	–		
.. Total milk volume expressed (mL/day)	–	–	722	822
.. Estimated energy expended in breastfeeding (kcal)[b]	–	–	635	723
Energy expended pumping breast milk while in the WBCU	–	–		

.. Total milk volume pumped while in the WBCU (mL/day)	–	–	–	410
.. Based on the WBCU data points (kcal)	–	–	–	180
.. Based on the FAO/WHO/UNU (kcal)[b]	–	–	–	360
Physical activity scores				
Baecke questionnaire total	–	7.2	8.5	8.5
Baecke questionnaire work	–	2.0	3.1	3.1
Baecke questionnaire sports	–	2.5	2.5	2.8
Baecke questionnaire leisure	–	2.7	2.9	3.0

Note: Energy expenditure and respiratory quotient were measured by indirect calorimetry using a WBCU; body composition was measured by dual energy X-ray absorptiometry; energy intake was assessed using 3-day food records; physical activity was assessed using Baecke Questionnaire (9). BMI, body mass index; WBCU, whole body calorimetry unit. [a]Change in weight compared to prepregnancy weight. [b]Based on the FAO/WHO/UNU Human Energy Requirements report (10).

Table 2. Comparison of estimated and measured energy expenditure variables.

Energy Expenditure	Equation	Estimated EE (kcal/day)	Measured EE (kcal/day)	Difference between estimated and measured EE (kcal)
REE				
Mifflin-St Joer [a]	10 × weight (kg) + 6.25 × height (cm) – 5 × age (y) - 161 [b]	–	–	–
Nonpregnant	–	1296	1389	-93
Pregnant	–	1432	1767	-335
3 months postpartum	–	1302	1346	-44
9 months postpartum	–	1277	1449	-172
TEE				
DRI [c]				
Nonpregnant	354 – (6.91 x age [y]) + PA × {(9.36 × weight [kg]) + (726 × height [m])} [d]	1869	1847	22
Pregnant	Nonpregnant EER + 272 + 180	2321	2226	95
3 months postpartum	Nonpregnant EER + 500 – 170	2199	–	N/A
9 months postpartum	Nonpregnant EER + 400 – 0	2269	1919	350
Factorial Method (measured)				
Nonpregnant	Measured REE × PAL 1.4	1945	1847	98
Pregnant	Measured REE × PAL 1.4 + 452 [e]	2926	2226	700
3 months postpartum	Measured REE × PAL 1.4 + 635 [f]	2519	–	N/A
9 months postpartum	Measured REE × PAL 1.4 + 723 [f]	2752	1919	833
Factorial Method (estimated)				
Nonpregnant	Estimated REE × PAL 1.4	1814	1847	-33
Pregnant	Estimated REE × PAL 1.4 + 272 + 180 [e]	2457	2226	231
3 months postpartum	Estimated REE × PAL 1.4 + 500 – 170 [g]	2153	–	N/A
9 months postpartum	Estimated REE × PAL 1.4 + 400 – 0 [g]	2188	1919	269

Note: EE, energy expenditure; REE, resting energy expenditure; TEE, total energy expenditure; DRI, dietary references intakes; EER, estimated energy requirements; PA, Physical Activity Coefficient; PAL, physical activity level.

Positive value denotes overestimation by predictive equation. N/A, not available, no comparisons could be made between two data points.

[a] Mifflin-St Jeor equation (11).

[b] The same equation was used at all four measurement time points

[c] DRI equations (13).

[d] Physical activity coefficient of 1 was used in the DRI equations (13), which is consistent with PAL of 1.4 used in factorial method. This PAL (1.4) was chosen based on the participant's self-reported physical activity level (lightly active).

[e] Additional pregnant-related calories were estimated based on the DRI equations (13), which takes into account energy expended during pregnancy (272 kcal) plus pregnancy energy deposition (180 kcal).

[f] Energy expended breastfeeding as measured by breastfeeding diaries and calculated based on the FAO/WHO/UNU Human energy requirements report (10).

[g] Energy expended breastfeeding as estimated by DRI equations (13) which takes into account milk energy output (3 months postpartum: 500 kcal, and nine months postpartum: 400 kcal), and weight mobilization (3 months postpartum: 170 kcal, and 9 months postpartum: 0 kcal).

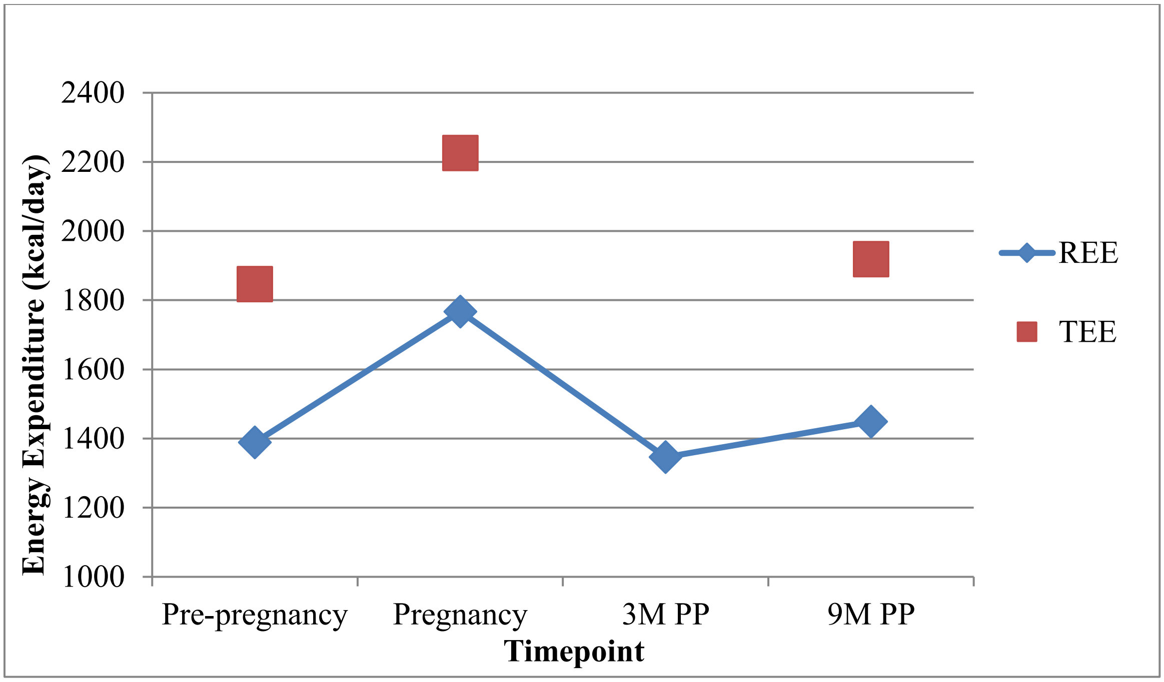


Figure 1. **Changes over time in resting and total energy expenditure measured using the whole body calorimetry unit.** REE, resting energy expenditure; TEE, total energy expenditure; 3M PP, three months postpartum; 9M PP, nine months postpartum.

8. References

1. Butte NF, Wong WW, Hopkinson JM. Energy requirements of lactating women derived from doubly labeled water and milk energy output. J Nutr 2001;131:53-58.
2. Forsum E, Kabir N, Sadurskis A, Westerterp K. Total energy expenditure of healthy Swedish women during pregnancy and lactation. Am J Clin Nutr 1992;56:334-342.
3. Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Sawyer MB, Ashford J, Black AE. Longitudinal assessment of the components of energy balance in well-nourished lactating women. Am J Clin Nutr 1991;54:788-798.
4. Kopp-Hoolihan LE, van Loan MD, Wong WW, King JC. Longitudinal assessment of energy balance in well-nourished, pregnant women. Am J Clin Nutr 1999;69:697-704.
5. Lovelady CA, Meredith CN, McCrory MA, Nommsen LA, Joseph LJ, Dewey KG. Energy expenditure in lactating women: a comparison of doubly labeled water and heart-rate-monitoring methods. Am J Clin Nutr 1993;57:512-518.
6. Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Wensing C, Black AE, Harding M, Sawyer M. Longitudinal assessment of energy expenditure in pregnancy by the doubly labeled water method. Am J Clin Nutr 1993;57:494-505.
7. Mills M, Rindfuss RR, McDonald P, te Velde E. Why do people postpone parenthood? Reasons and social policy incentives. Hum Reprod Update 2011;17:848-860.
8. Church TS, Thomas DM, Tudor-Locke C, Katzmarzyk PT, Earnest CP, Rodarte RQ, Martin CK, Blair SN, Bouchard C. Trends over 5 decades in U.S. occupation-related physical activity and their associations with obesity. PLoS One 2011;6:e19657.
9. Pols MA, Peeters PH, Bueno-De-Mesquita HB, Ocke MC, Wentink CA, Kemper HC, Collette HJ. Validity and repeatability of a modified Baecke questionnaire on physical activity. Int J Epidemiol 1995;24:381-388.
10. FAO/WHO/UNU. Human energy requirements: report of a joint FAO/WHO/UNU Expert Consultation, Rome 17-24 October 2001. Rome: Food and Agriculture Organization of the United Nations; 2004.
11. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr 1990;51:241-247.

12. Frankenfield D, Roth-Yousey L, Compher C. Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review. J Am Diet Assoc 2005;105:775-789.
13. Institute of Medicine. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: The National Academies Press, 2005.
14. Vinken AG, Bathalon GP, Sawaya AL, Dallal GE, Tucker KL, Roberts SB. Equations for predicting the energy requirements of healthy adults aged 18–81 y. Am J Clin Nutr 1999;69:920-926.
15. Elliott SA, Pereira LCR, Guigard E, McCargar LJ, Prado CM, Bell RC. Association between breastfeeding, maternal weight loss and body composition at 3 months postpartum. FASEB J 2016;30:45.44.
16. Gridneva Z, Rea A, Hepworth AR, Ward LC, Lai CT, Hartmann PE, Geddes DT. Relationships between breastfeeding patterns and maternal and infant body composition over the first 12 months of lactation. Nutrients 2018;10:E45.