

Dietary Support of Extended-Duration Bed Rest Studies

AM Inniss¹, BL Rice², SM Smith³

¹General Clinical Research Center
University of Texas Medical Branch at Galveston
Galveston, TX 77555

²Enterprise Advisory Services, Inc.
Houston, TX 77058

³Human Adaptation and Countermeasures Office
NASA Lyndon B. Johnson Space Center
Houston, TX 77058

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ABSTRACT

Dietary control and nutrient intake are critical aspects of any metabolic study, but this is especially true in the case of bed rest studies. We sought to define nutrient requirements, develop menus, and implement them in a series of three long-duration bed rest studies. With regard to energy intake, the goal was to maintain subject body weight to within 3% of their body weight on day 3 of bed rest (after fluid shift had occurred). For other nutrients, intakes were based on the NASA space flight nutritional requirements (with some adaptations based on the ground-based model used here). A secondary goal was to develop menus with foods similar to those expected to be approved for space flight (however, this was relaxed to attain desired nutrient intakes). This paper also describes the role of the research dietitian as part of the multi-disciplinary team and the importance of the metabolic kitchen staff. It also provides insight into some of the dietary challenges that arise during extended-duration bed rest studies. Regardless of the overall objective of the study, nutrition must be carefully planned, implemented, and monitored for results to be uncompromised.

INTRODUCTION

Bed rest is an analog for simulating the effects of weightlessness on physiological systems (5). Nutrition and dietary support are critical for bed rest studies, and problems or issues can greatly affect even the best-designed study. Subject selection and retention may be adversely affected by the type and quantity of food. The fact that energy expenditure decreases during bed rest, and thus maintenance of body mass requires reduction of food intake, must be taken into account when controlling intake of specific nutrients. Although this is usually easy to accommodate, it can affect a researcher's ability to achieve constant total intake and a constant percent of the diet for the nutrient. Preventing subject boredom with menu cycles can also prove to be a difficult task.

ROLE OF THE RESEARCH DIETITIAN AND SUPPORT STAFF

The research dietitian is a valuable member of the research team and contributes to the success of the study. Before the study starts, the dietitian works with the investigator team(s) to ensure that all dietary restrictions are met, develops the menus to meet the nutrient requirements, purchases and manages food items for the metabolic kitchen, and works with the subject-screening team to address and resolve any dietary issues, such as subject food allergies or intolerances. Once the study starts, the dietitian interacts daily with the research subjects to discuss dietary issues, monitors subjects' weight, and ensures that subjects maintain maximum dietary compliance. This continuous interaction fosters a sense of rapport with the subjects and

may be psychologically beneficial to them, and thus promote their continued participation in the study. The dietitian also works closely with the nursing staff to communicate in a timely fashion any issues that may involve the medical care of the subjects.

The research dietitian is also responsible for overseeing the metabolic kitchen staff in the preparation of the meals, tracking caloric and nutrient intake for each subject via the nutrition database, and performing analysis of nutrient intake data.

The metabolic kitchen staff is responsible for preparing the meals, encouraging 100% compliance with the consumption of all meals, and ensuring that the subjects eat according to schedule.

METHODS

Eleven healthy subjects (8 men, 3 women) participated in the project, which was conducted in three studies (designated Study 1, 2, and 3). The subjects' mean age (\pm SD) was 34.8 ± 9.3 y. Average height of the study group was 169 ± 10 cm, and average weight was 73.6 ± 15.5 kg. Subjects had to successfully pass various physical and psychiatric examinations to be included in the study. As required by the NASA Bed Rest Standardization Protocol, subjects were excluded from the study if they did not meet the minimum testing requirements recently had sub-standard nutritional status, had gastro-esophageal reflux disease, had a history of diabetes, or took medication that would interfere with the interpretation of results. All subjects were given written and verbal explanation of testing and bed rest protocols, and signed documentation indicating

their understanding and consent. All protocols were reviewed and approved by the National Aeronautics and Space Administration (NASA) Johnson Space Center and the University of Texas Medical Branch at Galveston (UTMB) Institutional Review Boards. Bed rest was conducted under medically supervised conditions at the General Clinical Research Center at UTMB in Galveston, TX.

The ambulatory phase allowed subjects to become acclimated to the research environment and to the research diet. During the bed rest phase of the study, subjects were placed at a 6° head-down tilt. They were allowed to either elevate themselves on one elbow or turn over on their stomachs to consume meals; otherwise they were restricted to the head-down position.

Nutrient Requirements

The study diet was designed to approximate the diet consumed by space shuttle astronauts and consisted of standard foods. At baseline, its composition was 55% carbohydrates, 30% fat, and 15% protein. Dietary constraints included no caffeine, cocoa, chocolate, tea, or herbal beverages. Caloric requirements were individualized for each subject. The Harris-Benedict Equation (1) for calculation of resting energy expenditure was used to estimate caloric intake:

$$\text{Men: (kcal/d) = } 66.47 + (13.75 \times \text{weight (kg)}) + (5.00 \times \text{height (cm)}) - (6.76 \times \text{age})$$

$$\text{Women: (kcal/d) = } 655.10 + (9.56 \times \text{weight (kg)}) + (1.85 \times \text{height (cm)}) - (4.68 \times \text{age})$$

Activity factors of 1.6 and 1.3 were used for ambulatory and bed rest phases, respectively. These were based on data from previous bed rest studies. The primary goal of dietary support was for subjects to maintain pre-bed rest body weight. To this end, caloric intake was adjusted as

necessary to maintain body weight, which was recorded daily using a bed scale. Subjects were weighed each morning before they had breakfast. Dietary intervention to prevent weight loss occurred if a subject's body weight deviated by 3 or more percent from their weight on bed rest day 3, when the initial fluid shift and any diuresis resulting from postural change should have been completed. Caloric intake was manipulated by increasing carbohydrates and fat while keeping protein constant.

The target intake of nutrients (**Table I**) was based on the NASA space flight nutritional requirements, with some adaptations based on the ground-based model used here to make a set of Flight Analogs / Bed Rest Research Project nutrient intake requirements (NASA bed rest requirements). Calcium and phosphorus intake were targeted to be about 1400 mg/d. Sodium was targeted to be 2 mmol/kg·d⁻¹ and potassium, 1.2 mmol/kg·d⁻¹. Target fluid intake was 28.5 ml/kg body weight. Filtered water was provided for drinking and used in food preparation. For other nutrients, average intake was considered acceptable if it met 100-125% of NASA bed rest requirements, with daily intake not less than 80% of the requirement.

All diets were composed, and actual dietary intakes were determined, using the Nutrition Data System for Research (NDS-R) software, version 5.0_35, May, 2003, developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN (4).

Menu Development

A secondary goal of dietary support was to develop menus with foods similar to those expected to be approved for space flight. However, constraints on food for space flight

sometimes conflicted with another secondary goal of providing subjects with a product that was acceptable in variety, flavor, visual and aromatic appeal, texture, form, and shape, while at the same time achieving an acceptable nutrient value range. The amount of fresh foods is quite limited on a long-duration mission. Meat, fish, and poultry were provided to the bed rest subjects and prepared in various ways throughout the menu cycle, and a variety of fruits and vegetables were used. There was a shift from using frozen fruits in Studies 1 and 2 to using fresh fruits in Study 3. A greater variety of fresh fruit was also added to the menu for Study 3. This single change greatly improved the overall taste and visual appeal of the breakfast menus. The availability of fresh fruit throughout the year was an important consideration when designing the menu. The vegetables used during the studies were usually frozen because of the stability of frozen vegetables and their availability at any time of year.

Nutrient content was another important factor in the selection of food items and recipes. Certain drinks were chosen that were fortified with vitamins A, C, and E. Other juices, such as orange juice, were chosen because they were fortified with calcium and vitamin D. Other food items were selected because they were fortified with folic acid and vitamin D. Several ready-to-eat and heat-and-serve food items were incorporated into the menus. These quick and easy food items provided balance on days when extensive food preparation was required for other items. Several recipes for mixed dishes were chosen, as they incorporated more foods, such as fish and dairy products, that are high in calcium and vitamin D.

The sodium content of the food items was another important factor in composing menus and developing recipes. Many of the pre-packaged food items include some form of sodium as a preservative. Care was therefore taken to limit the amount of salt added to menu items. In

addition, minor changes were made to reduce the amount of sodium added throughout the studies. In Studies 1 and 2, regular salt was used. In an attempt to achieve an acceptable sodium intake range for Study 3, low-sodium salt was used in all recipes. Similarly, unsalted butter was used instead of salted butter.

The subject population was also a major consideration in the planning of the menus. The menus were devised to reflect the diversity of cultures and ethnicities in the subject population. Subjects had a variety of taste preferences and food aversions, and care was taken to create a menu cycle that would represent this diversity and accommodate all subjects. The meals were designed to provide as much color and contrast as possible to make each dish look attractive to the subjects. The menus included desserts such as cookies, pies, and ice cream.

Careful menu planning ensured that a particular food item was not served more than once in the same day. The menus were placed in order by meal and by day. This allowed the dietitian to see the layout of the menu cycle and to ensure that the same types of foods were not served at the same meal on consecutive days. After the menu cycle was set, the nutrient analysis was done to ensure that the nutrient requirements were met.

A 7-d menu cycle was implemented for the 60-d Study 1. For Studies 2 and 3 (90-d studies), a 10-d menu cycle was provided to coincide with the greater number of bed rest days and ensure that subjects did not receive the same meal on the same day of each week.

The menus were altered to accommodate certain study protocols. Tests that influenced the menus included the oral glucose tolerance test, the glucose breath test, and the cardiovascular test. Subjects were to avoid any gas-producing foods the night before they took the glucose breath test. To ensure that the overall carbohydrate intake remained stable, 50 g of carbohydrate

was eliminated from the diet on the days that the dextrose was given. Similarly, the oral glucose tolerance test required 75 g of glucose to be removed from the diet. Because both tests rarely fell on the same menu cycle day, two additional variations of the original 10-d menu cycle were created that reflected the changes in carbohydrate. This resulted in a total of three 10-d menu cycles per subject. The cardiovascular test required subjects to consume a light meal of predominantly complex carbohydrates before they participated in the test.

Subject Screening Process

Subject candidates were provided with sample menus before they met with the dietitian. They were instructed to identify foods to which they had allergies and foods that they absolutely could not tolerate throughout the study, by placing a check mark next to those foods on the menus.

Once the preference forms were completed, the information was forwarded to the dietitian and reviewed. On the day of subject screening at the Flight Analogs Research Center at UTMB, the dietitian visited each subject candidate to discuss food preferences and to get a better understanding of why certain foods were eliminated. During this time, it was discussed at length that the menus were standardized, but minor allowances would be made to accommodate subjects with adverse reactions to certain foods. Subjects were informed that all meals would be prepared in the metabolic kitchen, that they were expected to eat 100% of all meals, that no other food items were allowed in the rooms, and that visitors were not allowed to enter subjects' rooms with food. Any questions or concerns that the subject candidate had at this time were addressed. The dietary preference forms were then signed by the subject and the dietitian upon agreement that the

subject understood the dietary expectations. This dietary screening process was also discussed in an orientation session entitled “A Day in the Life”. This session introduced prospective subjects to the unit and allowed them to meet the nursing and dietary staff and ask questions about their stay on the unit. This orientation session was included in the consent process and was conducted by the nursing staff.

Kitchen Activity and Meal Serving Schedules

Menus prepared using NDS-R were converted into menu sheets using Microsoft™ Excel. The sheets were updated daily to reflect dietary changes and then were forwarded to the dietary staff. The updated sheets were placed in the appropriate subject’s binder. Each menu sheet was labeled with the subject’s name, date, bed rest day, the meals that were being prepared for the day, and the gram amount of each food item. Any discrepancies in the amount of foods consumed by each subject were recorded at the end of each meal. All foods were weighed to ± 0.1 g using Mettler Toledo scales.

All subjects received the same meal each day, except for minor variations that reflected each subject’s food preferences, or study protocol constraints as described earlier. Food portion sizes were different for different subjects because of different estimated caloric intake requirements. To ensure that each subject received the correct amount of each food item, each tray was labeled with the subject’s name and dated. The date on the tray was the day that the meal was to be consumed. Food items were prepared one day in advance, and a portion was weighed out for each subject and placed in a separate container until the time for meal preparation. In order for

each food item to be correctly identified and placed on the correct tray before the tray was served, each container was labeled with the name of the subject and the gram amount of the food item. Foods to be served hot were prepared a day in advance, pre-portioned, and heated before they were served. To ensure accuracy of measurements the weights of certain food items were randomly checked throughout the day.

The timing of meal service varied from day to day according to testing schedules. Schedules were checked a day in advance and noted on the diet board. The diet board was a bulletin board in the metabolic kitchen where daily sheets for each subject were posted that contained the date, the subject's name and ID number, the subject's room number, and the time each meal would be served. On the day of testing, the meal schedule was checked again. In many cases, meal times changed because tests were running behind schedule or a test had to be postponed or canceled.

The number of meals served for each study reflected the number of bed rest days for that study. A total of 2,847 meals were served for all three studies: 756 meals for Study 1; 1,368 meals for Study 2; and 723 meals for Study 3.

RESULTS

Nutrient intakes for ambulatory and bed rest phases are shown in **Table I**. The mean (\pm SD) intake for subjects at bed rest was 2208 ± 342 calories, with carbohydrates composing 56%, protein 15%, and fat 31% of the total (on average). Of the fat-soluble vitamins, the intake of vitamins D and E was below required values for both ambulatory and bed rest states.

Menu Palatability

The dietitian visited subjects frequently to address dietary issues and to elicit feedback about the quality of the meals. Subjects were asked which food items were the most and least acceptable and were asked to provide additional comments about their experiences to the dietary staff. Most of the subjects said the research diet was explained clearly to them and the overall appearance of the meal trays was good. Several subjects thought the portion sizes were either too large or too small. The subjects gave varied responses about the taste and acceptability of the food.

Body Weight

Sporadic spiking in subjects' weights was noted. It was concluded that the spikes were a result of measurement error, because several times spikes occurred for different subjects on the same day. If an unusual weight was noted before a subject consumed breakfast, the subject was re-weighed and the new weight recorded. If the subject had already consumed breakfast, the recorded weight remained. **Figure 1** shows the percent weight change throughout the study, relative to bed rest day 3.

The greatest weight loss observed was -4.0 kg. This weight loss was due in part to the subject not being able to consume 100% of meals because of medical issues throughout the study. The subject was encouraged to consume as much of each meal as possible, and the amount of

food consumed during each episode of low consumption was documented. The greatest weight gain observed was +2.3 kg. This occurred during the post-bed rest phase, when subjects were once again provided with the ambulatory diet. This diet provided about 370 more calories per day than the bed rest diet. The subject who gained 2.3 kg may have been more sensitive to the consumption of an increased number of calories than the other subjects and thus had a greater weight gain. In all, 8 out of 11 subjects experienced weight loss ranging from -0.2 kg to -4.0 kg. The remaining three subjects each had a weight gain of +0.2 kg to +2.3 kg.

DISCUSSION

Dietary challenges during bed rest studies included weight loss, menu fatigue, food allergies and intolerances, subjects not eating 100% of meals, and meeting the NASA bed rest requirements.

Weight Loss

During the bed rest phase of the studies, weight loss was observed in 8 out of 11 subjects. Dietary intervention was provided when a subject's weight changed by 3% of day 3 of bed rest. Calories were manipulated by increasing the amounts of carbohydrates and fats and keeping protein constant. Because many food items contained multiple energy sources, vitamins, and minerals, caloric manipulation of the diet became extremely challenging and time-consuming.

Menu Fatigue

A 7-d menu cycle was used for Study 1. The length of the bed rest phase for this study was 60 d. This allowed the subjects to predict which day of the week a certain menu would be served. When the length of the bed rest phase was extended to 90 d in subsequent studies, it was decided to add 3 additional menu days to provide less predictability. The menu cycle for Studies 2 and 3 was therefore increased to 10 d.

Food Allergies and Intolerances

During the screening process, subjects were asked to identify any foods to which they might be allergic. They were also asked if they were lactose intolerant. Subjects usually indicated that they were not allergic to, or were uncertain if they were allergic to food items listed. Thus, no food allergies were usually documented and the menus were devised with no consideration of them. As the study progressed, however, questions arose about whether a subject was allergic to a particular food or to some ingredient in a food. Once an allergy or sensitivity was verified by a physician, the food item was replaced with something comparable in calories and nutrients.

Subjects Not Eating 100% of Meals

During the study, a subject would sometimes notify the dietitian that he or she did not care for

a particular meal or food item. A general trend was noted that subjects who did not particularly care for a food item at the beginning of the study would develop a food aversion at the middle or toward the end of the study. The dietitian would remind the subject of the importance of eating all meals. At times, the subject would refuse to eat 100% of the particular food item or would strategically spread the food item over the plate as an indication that they had eaten all of it. In all cases, if the food item could be weighed, the leftover amounts were recorded. If the dietitian considered the amount to be significant, the food item would be portioned out and included with the next meal. If at the end of the day a subject had not consumed 100% of a meal, it was documented as a protocol deviation.

Meeting NASA Bed Rest Requirements

As the subjects transitioned from the ambulatory state to bed rest, their caloric requirements decreased. The decreased caloric intake had a direct effect on the micronutrient content of the diet. It was also evident that the smaller the size and body weight of the subject, the more challenging it was to meet the NASA bed rest requirements for vitamins and minerals when calories were further restricted. Having a larger body size and weight increased the likelihood that a subject's vitamin and mineral intakes would be within the required guidelines. The challenge of meeting these dietary guidelines was compounded further when changes were made in the diet to accommodate subjects' preferences, food allergies, or other medical conditions.

Some researchers (2, 3) have thought it essential to order same-lot food items to eliminate concerns about changes in nutrient intake and food availability throughout the duration of long-

term or crossover design studies. This is scientifically ideal, but it can greatly increase the budget for the experiment.

Achieving the NASA bed rest requirements for vitamin D and calcium was a challenge throughout the study. Calcium is found in a greater variety of foods than is vitamin D, and the major dietary sources of both are fortified foods. Great care was taken to include foods that were fortified with vitamin D or calcium, or both. Despite the addition of these foods, in most instances, vitamin D intake was still lower than the NASA bed rest requirements.

A related issue concerns the use of multivitamins during bed rest studies. In Study 1, multivitamins were provided to the subjects on orders from the attending physician. This is often done for these types of studies where diet and nutrition are not part of the primary hypothesis, the logic being that the supplement “ensures optimal vitamin status.” We chose not to continue this policy in Studies 2 and 3, and to strive for the diet to meet nutrient requirements, much as is done with the space food system. Although it may be possible to meet the vitamin D requirements in bed rest, the difficulties in accomplishing this goal highlight the general question of what is more important: should priority be given to the presentation, variety, and palatability of the meals, or to achieving the NASA bed rest requirements for the various nutrients? Is it possible to satisfy both requirements? This will continue to be a challenge in future studies.

As has been described in this paper, diet and nutrition are critical elements of bed rest studies. There are many facets to these, and a great deal of attention must be paid to the details. Although many options are available to choose from, having standardized, controlled dietary conditions is critical for experiment success.

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TABLE I. NUTRIENT INTAKE (MEAN VALUES \pm SD) FOR SUBJECTS (n = 11) BEFORE, DURING, AND AFTER BED REST, COMPARED WITH REQUIRED INTAKES.

Nutrient	Mean Intake Bed Rest Study 1, 2, 3	Mean Intake Pre Bed Rest Study 1, 2, 3	Mean Intake Post Bed Rest Study 1, 2, 3	Bed Rest Requirement	Acceptable Range	Flight Requirement
Energy, kcal	2208 \pm 342	2605 \pm 434	2437 \pm 333	Maintain BW		WHO (moderate activity)
Fat, g	76 \pm 12	90 \pm 16	83 \pm 11			
CHO, g	308 \pm 47	366 \pm 59	343 \pm 45			
Protein, g	85 \pm 15	99 \pm 17	92 \pm 15	12-15% of total energy	12-15% of total energy	12-15% of total energy
% kcal from fat	31% \pm 1%	31% \pm 1%	31% \pm 1%	30-35% of total energy	30-35% of total energy	30-35% of total energy
% kcal from CHO	56% \pm 1%	56% \pm 1%	56% \pm 1%			
% kcal from protein	15% \pm 1%	15% \pm 0%	15% \pm 1%	12-15% of total energy		12-15% of total energy
Vitamin A, μ g RE	1871 \pm 441	2167 \pm 526	1957 \pm 594	1000 μ g RE	1000-1500	1000 μ g RE
Vitamin D, μ g RE	6.2 \pm 1.3	6.9 \pm 1.7	8.2 \pm 4.3	10 μ g RE (400 IU)	8-12	10 μ g RE (400 IU)
Vitamin E, mg α -TE	13.4 \pm 2.8	16.2 \pm 3.4	12.9 \pm 4.9	20 mg α -TE	20	20 mg α -TE
Vitamin K, μ g	109 \pm 21	124 \pm 25	97 \pm 53	80 μ g (M), 65 μ g (F)		80 μ g (M) 65 μ g (F)

Vitamin C, mg	204 ± 35	208 ± 65	156 ± 59	100 mg		100 mg
Thiamin, mg	1.9 ± 0.3	2.3 ± 0.4	2.1 ± 0.5	1.5 mg		1.5 mg
Riboflavin, mg	2.1 ± 0.4	2.6 ± 0.4	2.4 ± 0.4	2.0 mg		2.0 mg
Niacin, mg	26.2 ± 4.0	30.2 ± 4.7	30.5 ± 5.5	20 mg	20	20 mg
Pantothenic acid, mg	5.7 ± 1.0	6.7 ± 1.4	5.6 ± 1.5	5.0 mg	5	5.0 mg
Vitamin B6, mg	2.5 ± 0.4	3.0 ± 0.5	3.2 ± 0.8	2.0 mg	2	2.0 mg
Folate, •g	486 ± 75	600 ± 92	621 ± 141	400 •g	400	400 •g
Vitamin B12, •g	6.2 ± 1.2	7.8 ± 1.4	8.6 ± 2.9	2.0 •g	2	2.0 •g
Calcium, mg	1188 ± 175	1400 ± 234	1159 ± 321	1000 – 1200 mg	900-1200	1000 – 1200 mg
Phosphorus, mg	1406 ± 256	1687 ± 262	1542 ± 289	1000 – 1200 mg	900-1200	1000 – 1200 mg
Magnesium, mg	327 ± 69	384 ± 68	349 ± 73	350 mg (M), 280 mg (F)		350 mg (M) 280 mg (F)
Iron, mg	16.6 ± 2.3	19.4 ± 2.7	16.9 ± 4.2	10 mg (M), 18 mg (F)	10-20 mg	10 mg
Zinc, mg	12.1 ± 1.8	14.8 ± 2.4	13.4 ± 2.4	15 mg	15	15 mg
Copper, mg	1.52 ± 0.27	1.79 ± 0.30	1.58 ± 0.32	1.5-3.0 mg	1.5-3.0	1.5-3.0 mg
Selenium, •g	130 ± 26	147 ± 26	138 ± 26	70 •g	70	70 •g
Sodium, mg	3176 ± 441	3736 ± 632	3033 ± 1056	<3500 mg	<3500 mg	<3500 mg
Potassium, mg	2856 ± 500	3438 ± 624	2841 ± 667	3500 mg	3000-3500	3500 mg

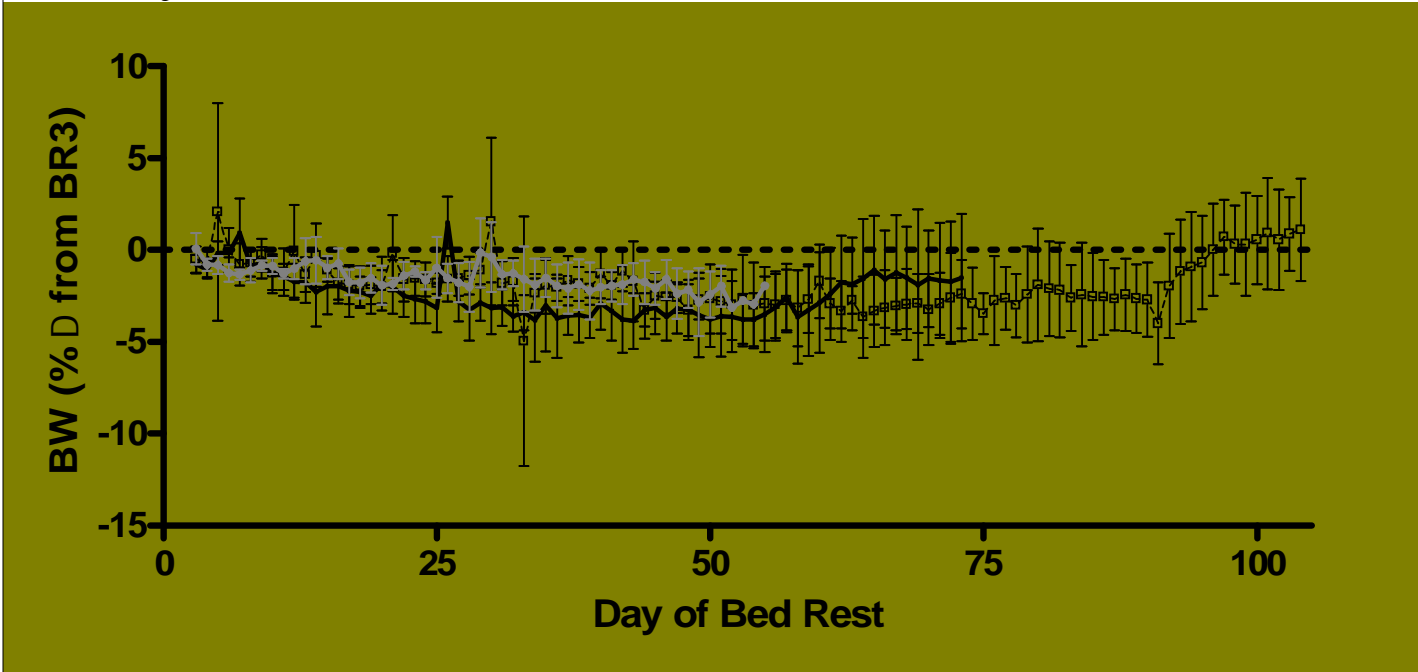
Fluid, mL	3903 ± 598	4179 ± 818	3880 ± 698	28.5 mL per kg	2L-4L	1.0-1.5 mL per kcal
Fiber, g	21.6 ± 4.7	25.1 ± 4.5	23.1 ± 5.3	10-25 g	10-25 g	10-25 g
Manganese, mg	4.3 ± 0.7	4.9 ± 0.7	5.0 ± 0.9	2.0-5.0 mg		2.0-5.0 mg

BW = body weight; CHO = carbohydrate; RE = retinol equivalent; TE = tocopherol equivalent; M = males; F = females.

FIGURE LEGENDS

Figure 1. Percent change in body weight of subjects (mean \pm SD) in three bed rest studies compared with day 3 of bed rest.

Figure 1.



FIGURES

Figure 1.