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Award Number: DAMD17-01-1-0360

TITLE: Effects of Moderate Aerobic Exercise Combined with Calorie Restriction on Circulating Estrogens and IGF-I in Premenopausal Women

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CONTRACTING ORGANIZATION: The Pennsylvania State University
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PREPARED FOR: U.S. Army Medical Research and Materiel Command
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13. ABSTRACT (Maximum 200 Words)

This proposal entitled "Effects of moderate aerobic exercise combined with caloric restriction on circulating estrogens and IGF-1 in premenopausal women" will provide important contributions regarding the primary prevention of breast cancer in women. This study has examined the effects of exercise training combined with caloric restriction, resulting in weight loss, on two hormonal biomarkers for breast cancer i.e., circulating estrogens and insulin-like growth factor I (IGF-I). As expected, exercise training 4 times per week combined with an 20-30% decrease in caloric intake over four menstrual cycles has produced significant increases in aerobic capacity (28-33%), weight loss ranging from 1.0 to 9 kg, and loss of body fat ranging from 5 to 12% of initial percent fat. Light conditioning resulted in significant gains in aerobic capacity (33%), but only produced a trend toward a decrease in body fat percent (-3.1%), and no changes in body weight. Despite the highly significant changes in body composition and body weight in the exercising group, preliminary results indicate no significant changes in serum estradiol or serum estrone. IGF-I did not change significantly either, indicating that chronic exercise and dieting do not result in favorable changes in two hormonal biomarkers for breast cancer.

14. SUBJECT TERMS
Breast cancer, menstral cycle, IGF-1, estradiol, exercise

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INTRODUCTION

This proposal entitled " Effects of moderate aerobic exercise combined with caloric restriction on circulating estrogens and IGF-I in premenopausal women" will provide important scientific contributions with respect to the primary prevention of breast cancer in women. Specifically, this ongoing study will examine potential mechanisms relating to the role of physical activity in the reduction of the risk of breast cancer by testing whether moderate aerobic exercise can reduced the levels of two hormonal biomarkers, circulating estrogens and insulin-like growth factor I (IGF-I). Since elevated levels of both of these hormones have been associated with an increased risk of breast cancer, and because exercise may modulate circulating levels, we wish to extend previous findings from epidemiological and cross-sectional studies by performing a tightly controlled, prospective clinical study that addresses previously unanswered questions related to the role of exercise in the modulation of estrogen and IGF-I. Although previous studies have shown that negative energy balance, and not other stressful aspects of physical exercise, can modulate reproductive function and therefore circulating estrogen levels, no studies to date have determined the magnitude of energy deficit required for these changes during long-term training, and no studies have attempted to differentiate between the exercise-induced changes in ovarian versus adipose sources of circulating estrogens. Since both estradiol (ovarian) and estrone (adipose tissue) are biologically active, and because the importance of estrone as a risk factor increases with age and adiposity, it is important to consider the degree to which exercise which creates a negative energy balance affects both of these sources of circulating estrogens.

Circulating levels of IGF-I correlate with breast cancer risk, yet studies examining the responses of this hormone and its binding proteins to chronic exercise are lacking. Since IGF-I levels are very sensitive to nutritional status, previously reported stimulatory effects of exercise on IGF-I can be overridden if exercise is performed in the face of negative energy balance. In this regard, exercise that promotes weight loss can be viewed as a way to reduce levels of IGF-I, and therefore potentially reduce the risk of breast cancers. To date, no studies have addressed whether a program of moderate aerobic exercise and dietary restriction producing a negative energy balance that is carried out over a long duration will significantly alter IGF-I levels. Further, the degree to which these levels might be altered in individuals of differing initial energy stores has not been addressed.

Metabolic energy availability is an important contributing factor in the development of reproductive cancers. However, current methods for assessing energy availability, which include anthropometric measures, calculations of energy balance, evaluation of various serum and urinary biomarkers are prone to measurement error, not sensitive to alterations in energy availability, and are sometimes affected by disease states. The current project includes an introduction of a novel approach to estimating energy status by measuring metabolic hormones in plasma, insulin, IGF-I, IGFBP-1 and leptin. Recently, dried blood spot (DBS) sample collection techniques have allowed for endocrine based population studies examining a wide variety of ecological factors that contribute to variation in human reproduction. In order to use the proposed method of energy status assessment in large population-based applications, such as those addressing the role of physical activity and or diet in the risk of breast cancer, the battery of metabolic hormones that comprise the proposed method must be amenable to collection and assays. Although the DBS technique has been partially validated for some hormonal assays, it has not yet been properly validated for insulin, IGF-I, IGFBP-1 and leptin, and it is unclear whether the technique is responsive to physiological changes of these compounds. Therefore, the current work calls for the validation of the DBS sampling technique for these assays under physiological conditions.

The proposed studies will yield new and important information regarding the degree to which an exercise and diet program that results in an energy deficit will reduce the risk of breast cancer.

BODY

Study Design: The study utilizes a prospective, randomized design that tests the effects of a moderate exercise program (4X/wk; 4 months) combined with moderate dietary restriction that results in an average daily energy

deficit of -20%-30% kcals (Figure 1). Previously sedentary, eumenorrheic women aged 25-40 years will be assigned to exercise or light conditioning groups. Both normal weight (BMI 21-25 kg/m^2) and overweight (BMI 26-30 kg/m^2) will be assigned to either exercise or light conditioning group (exercise 2X/wk; no dietary restriction) groups; 4 groups, n=15 each group. Subjects will be studied for a total of six menstrual cycles, i.e., 2 control followed by 4 cycles with training and dietary restriction.

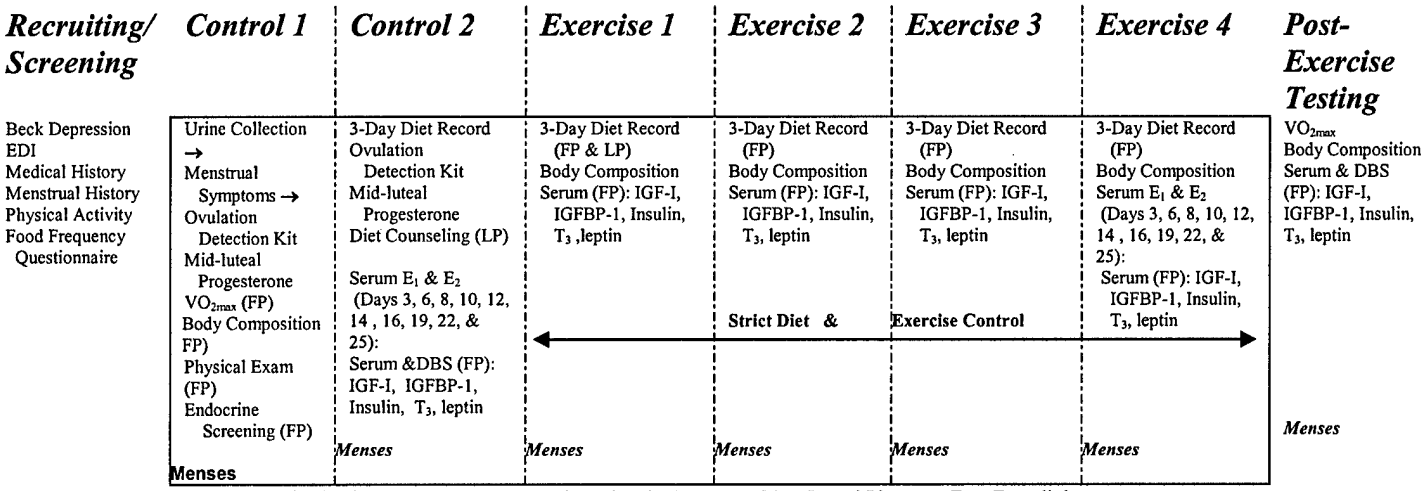

Figure 1. Study Design

Progress According to the Approved Statement of Work:

(See previous Annual Summary for 2002-2003)

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Proposed Months 25-28

1. Repeat Steps above for year 3 recruiting and beginning testing (n=5 in each of 4 groups)
2. Perform assays on metabolic hormones in serum
3. Send serum and blood spot samples from year 2 subjects to DSL

Actual Month 25, September, 2003: Enrollment increased dramatically, fourfold increase in enrollment; assays completed, T3, and continued for IGF-1; arrangements made with Salimetrics Laboratory, University Park, PA to develop blood spot assays for Leptin, T3, and IGF-I (See Appendix); begun assays on urinary LH to document LH surges.

Actual Month 26, October, 2003: Continued with rolling recruitment, began screening procedures on recently enrolled subjects, completed IGF-I assays on completed subjects, continued with urinary LH assays to document LH surges

Actual Month 27, November, 2003: Continued with recruitment and testing, continued LH urinary assays

Actual Month 28, December, 2003: Continued with recruitment and testing, completed urinary LH assays on first cohort of completed subjects

Proposed Months 29-36:

1. Continue year 3 recruitment efforts only if necessary
2. Continue year 3 subject screening/initial testing

3. Complete year 3 subject exercise training/experimental testing
4. Perform urinary assays on LH, E3G, PdG urinary
5. Send serum and blood spot samples from year 3 subjects to DSL.
5. Perform data analysis and statistics

Actual Month 29, January, 2004: Continued testing and recruiting
Actual Month 30, February, 2004: Continued testing and recruiting
Actual Month 31, March, 2004: Continued testing and recruiting
Actual Month 32, April, 2004: Continued testing and recruiting
Actual Month 33, May, 2004: Continued testing and recruiting
Actual Month 34, June, 2004: Performed assays on next cohort of completed subjects for T3, leptin, and IGF-I; continued testing and recruiting.
Actual Month 35, July, 2004: Continued to perform assays for T3, leptin, and IGF-I. continued testing and recruiting; began database checking and data reduction; preliminary data analysis

Actual Month 36, August, 2004: Stopped recruitment of subjects, continued with testing of currently enrolled subjects; Finished assays for T3, leptin, and IGF-I for most recently finished cohort. Performed assays for estradiol for most recently completed cohort.
Actual Month 37, September, 2004: Continued with testing, preliminary data analysis and database management; perform preliminary statistics for annual report; examine results from Salimetrics thus far

Newly Proposed Months 38-42, October, 2004-February, 2005:

Request extension for final report for this study (IDEA Award) from DAMD; perform urinary LH, E1G, and PDG assays, and serum metabolic assays when final cohort is finished; perform insulin, IGFBP-2, estradiol, and estrone on remaining completed subjects; send completed DBS samples from completed subjects to Salimetrics; perform data analysis; obtain results of DBS samples from Salimetrics, submit abstract for ERA of HOPE Meeting in December, 2004

Newly Proposed Months 43-48, March 2005- May 2005:

Write and submit manuscripts

Preliminary Results From Years 1, 2, and 3:

Subject Recruitment:

We have accumulated approximately 269 phone and e-mail contacts since September 03, bringing our 3 year total number of contacts up to 571. In the last 3 years seventy-eight women have begun the study and 52 have dropped out or been excluded for the following reasons: 14 with menstrual abnormality detected in the control months, 10 for medical reasons, 21 self –drop-out (time, intervention), 2 non-compliance, 2 with pregnancies during the study, and 3 because of weight/body composition measures outside inclusion criteria during screening. Although this represents a high drop-out rate (66%) prior to screening, our drop-out rate after screening procedures have been performed (including two control menstrual cycles to determine normal menstrual cyclicity) is 52%. That is, 52% of the women that made it through out screening procedures have dropped out of the study. This rate is much higher than predicted (20%).

Our recruitment efforts were stepped up beginning September 2003. Although we generally see do well with inquiries about the study, we had an especially disheartening recruitment effort this year, as our dropout rate

was double what it has been in the past two years. Therefore, our current subject numbers are reflected in Table 1. Descriptive characteristics of these subjects are shown in Table 2.

Table 1. Current Enrollment and Completed Subjects

Experimental Group	Initially Began Study After Screening (N)	Currently Enrolled (N)	Finished Study (N)	Potential Final (N)
Light Conditioning-low BMI	8	0	6	6
Light Conditioning-high BMI	6	1	2	3
Exercisers-low BMI	20	3	14	17
Exercisers-high BMI	11	2	5	7

Table 2. Initial Characteristics of Subjects Completed or Currently Enrolled in the Study

Variable	Light Conditioning-low BMI (LCLB)	Light Conditioning-high BMI (LCHB)	Exercisers-low BMI (ELB)	Exercisers-high BMI (EHB)
Age (yrs)	33.63 ± 3.34	34.83 ± 4.26	32.00 ± 4.75	31.73 ± 2.90
Weight (kg)	61.43 ± 3.70	68.88 ± 3.73	60.05 ± 6.12[d]	73.56 ± 9.04[c,f]
Height (cm)	166.46 ± 5.27	160.97 ± 6.88	163.64 ± 5.90	163.08 ± 6.73
BMI (kg/m^2)	22.21 ± 1.93	27.35 ± 2.16[a]	22.27 ± 1.75[d]	27.95 ± 2.09[c,f]
Body Fat (%)	31.10 ± 4.03	39.20 ± 4.07[a]	29.96 ± 3.50[d]	37.78 ± 4.62[c,f]
VO_2 Max (mg/kg/ml)	30.36 ± 1.99	26.43 ± 4.14	33.88 ± 5.19[d]	27.63 ± 6.43[f]

One-way ANOVA; Post-hoc: LSD; $P<0.05$
[a]LCLB vs LCHB
[b]LCLB vs ELB
[c]LCLB vs EHB
[d]LCHB vs ELB
[e]LCHB vs EHB
[f]ELB vs EHB

Preliminary Results:

Aerobic Capacity, Body Weight and Body Composition: Our light conditioning group exhibited a trend toward a decrease in percent body fat of -3.1% ($P< 0.072$), but no significant changes in body weight or BMI. The exercising group experienced significant declines in both body weight (-6.2%) and percent body fat (-15.7% of initial percent fat), fat mass (-20.6%) and in BMI (-6.8%). Both groups significantly increased their aerobic capacity, i.e., Light conditioning increased by 33% and exercising group increased by 28% (Tables 3 and 4).

Estradiol and Estrone: When serum measurements of these hormones across Control Cycle 2 (n=10), and Exercise 4 cycles (n=10) are averaged, and then compared with paired samples T-tests, no differences are observed in either the light conditioning or exercising groups, despite the loss of body fat (Tables 3 and 4). A

composite graph of these changes, depicted according to cycle day is illustrated in Figure 2. A representative depiction of the changes in both serum estrone and estradiol and urinary E1G is depicted in Figure 3.

Table 3. Paired-Samples T-Tests Comparing Pre to Post Intervention in Light Conditioning Group

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean	Sig. (2-tailed)
Pair 1	Pre VO2 Max (ml/kg/min)	28.3500	6	3.56693	1.45619	
	Post VO2 Max (ml/kg/min) (Ex 3 BIOEY1; Post BIOEY2&3)	37.7667	6	4.17069	1.70268	.001
Pair 2	Pre UWW Weight (kg) (control month BIOEY 1-3)	63.1429	7	4.37516	1.65365	
	Post UWW Weight (kg)(Ex 3 BIOEY 1; Post BIOEY 2&3)	62.3071	7	4.62911	1.74964	.114
Pair 3	Pre UWW % Body Fat (control month BIOEY 1-3)	33.4514	7	4.71277	1.78126	
	Post UWW % Body Fat(Ex 3 BIOEY1; Post BIOEY2&3)	32.2000	7	5.53164	2.09076	.072
Pair 4	Pre UWW BMI (control month BIOEY 1-3)	23.4186	7	3.52394	1.33193	.
	Post UWW BMI (Ex 3 BIOEY1; Post BIOEY2&3)	23.1386	7	3.56102	1.34594	.104
Pair 5	Pre Month RMR (kcal/min)	.9045	6	.06965	.02844	
	Post Exercise Month RMR (kcal/min)	.9778	6	.05128	.02094	.066
Pair 6	EstradiolAvePRE	70.3756	5	13.53968	6.05513	
	EstradiolAVERAGEPOST	80.4066	5	16.36771	7.31986	.161
Pair 7	Pre UWW Ave FFmass (kg)(control month BIOEY 1-3)	41.8900	7	2.10473	.79551	
	Post UWW Ave FFmass (kg) (Ex 3 BIOEY1; Post BIOEY2&3)	42.0729	7	2.25627	.85279	.146
Pair 8	Pre UWW Ave Fatmass (kg) (control month BIOEY 1-3)	21.1643	7	4.29164	1.62209	
	Post UWW Ave Fatmass (kg) (Ex 3 BIOEY1; Post BIOEY2&3)	20.2343	7	4.82436	1.82344	.107

Table 4. Paired-Samples T-Tests Comparing Pre to Post Intervention in Exercising Group

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean	Sig. (2-tailed)
Pair 1	Pre VO2 Max (ml/kg/min)	32.9938	16	5.36675	1.34169	
	Post VO2 Max (ml/kg/min) (Ex 3 BIOEY1; Post BIOEY2&3)	42.1938	16	9.80064	2.45016	.001
Pair 2	Pre UWW Weight (kg) (control month BIOEY 1-3)	63.7590	20	9.50026	2.12432	
	Post UWW Weight (kg)(Ex 3 BIOEY 1; Post BIOEY 2&3)	59.7575	20	9.03649	2.02062	.000
Pair 3	Pre UWW % Body Fat (control month BIOEY 1-3)	31.6030	20	5.20520	1.16392	
	Post UWW % Body Fat(Ex 3 BIOEY1; Post BIOEY2&3)	26.6530	20	6.28069	1.40440	.000
Pair 4	Pre UWW BMI (control month BIOEY 1-3)	23.5036	20	3.09325	.69167	
	Post UWW BMI (Ex 3 BIOEY1; Post BIOEY2&3)	21.9395	20	2.66114	.59505	.000
Pair 5	Pre Month RMR (kcal/min)	.9231	20	.09858	.02204	
	Post Exercise Month RMR (kcal/min)	.8964	20	.11824	.02644	.146
Pair 6	EstradiolAvePRE	95.0502	12	21.46584	6.19665	
	EstradiolAVERAGEPOST	93.3349	12	28.63159	8.26523	.828
Pair 7	Pre UWW Ave FFmass (kg)(control month BIOEY 1-3)	43.3275	20	5.13945	1.14922	
	Post UWW Ave FFmass (kg) (Ex 3 BIOEY1; Post BIOEY2&3)	43.5390	20	5.48725	1.22699	.460
Pair 8	Pre UWW Ave Fatmass (kg) (control month BIOEY 1-3)	20.4070	20	5.92869	1.32570	
	Post UWW Ave Fatmass (kg) (Ex 3 BIOEY1; Post BIOEY2&3)	16.2185	20	5.47167	1.22350	.000
Pair 9	EstroneAVERAGEPRE	58.7406	7	15.66615	5.92125	
	EstroneAVERAGEPOST	56.7727	7	13.95731	5.27537	.765

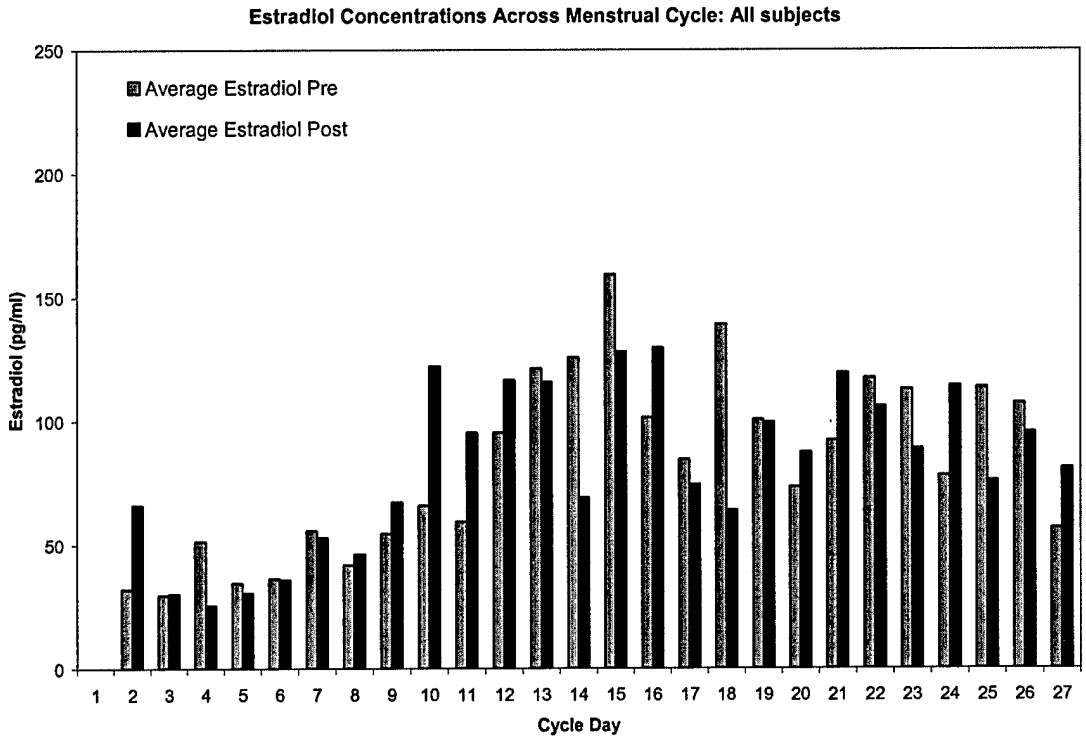

Figure 2. Composite graph of estradiol measurements from Control Cycle 2 (Pre) and Exercise 4 (Post) cycles.

Figure 11

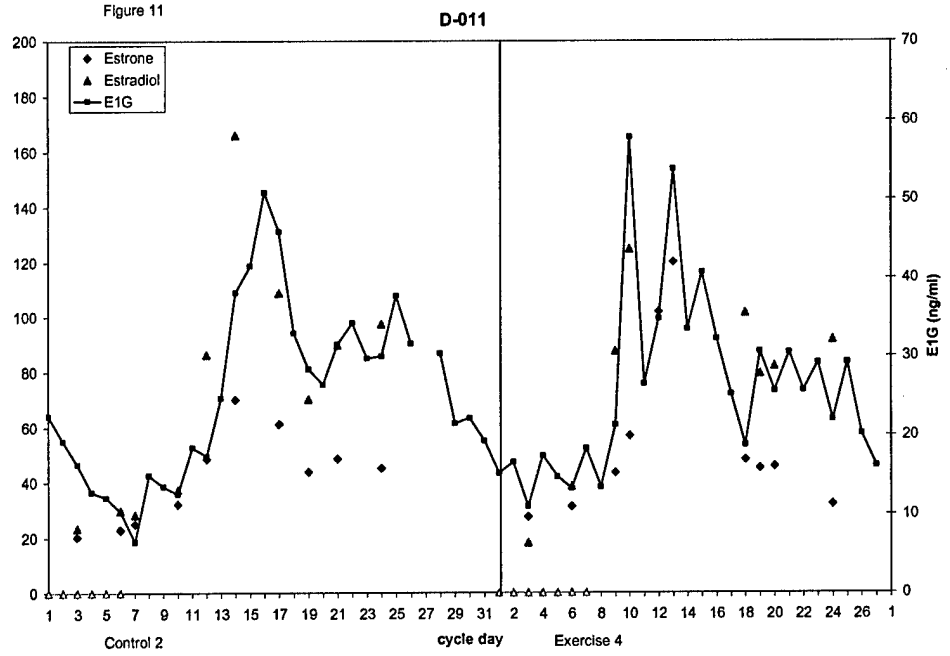

Figure 3. Representative example of a single subject's urinary (E1G) and serum estrogens (estrone and estradiol) before (Control 2) and after (Exercise 4) exercise training combined with caloric restriction.

Serum Leptin, T3, and IGF-I: A significant decrease ($P < 0.05$) was observed in measurements for leptin (Table 5), primarily accounted for by the changes in the exercising group ($P < 0.05$ group X time interaction). Serum T3 decreased significantly overall ($P<0.05$) (Table 6). No significant differences were observed in either group for IGF-I (Table 7).

Table 5. Serum Leptin for Light Conditioning (0) and Exercisers (1) Pre and Post study

	Groupsbasedonexercise	Mean	Std. Deviation	N
Pre Leptin (ng/ml)	.00	13.0750	6.40459	6
	1.00	15.9233	11.82781	18
	Total	15.2113	10.67270	24
Post Leptin (ng/ml)	.00	15.0050	9.24739	6
	1.00	7.4656	7.21061	18
	Total	9.3504	8.25476	24

Table 6. Serum T3 for Light Conditioning (0) and Exercisers (1) Pre and Post study

	Groupsbasedonexercise	Mean	Std. Deviation	N
Total T3 Pre (ng/dl)	.00	107.0380	24.17636	5
	1.00	104.0635	14.02287	17
	Total	104.7395	16.21055	22
Total T3 Post (ng/dl)	.00	96.1460	22.05372	5
	1.00	95.1106	16.04316	17
	Total	95.3459	16.99823	22

Table 7. Serum IGF-I for Light Conditioning (0) and Exercisers (1) Pre and Post study

	Groupsbasedonexercise	Mean	Std. Deviation	N
IGF-1Pre (ng/ml)	.00	238.3740	56.80587	5
	1.00	211.4859	50.48205	17
	Total	217.5968	51.85874	22
IGF-1 Post (ng/ml)	.00	230.6080	26.58635	5
	1.00	203.6382	58.94881	17
	Total	209.7677	54.00045	22

Results for Dried Blood Spot Samples: Thus far, Salimetrics has provided us with results for leptin DBS samples. In comparison to the simultaneous venipuncture measurement of leptin as assayed in our laboratory, a significant correlation exists ($P<0.05$; Pearson Correlation) (Table 8, and Figure 4)

Table 8. Correlation between serum and DBS sample for leptin

		Av Control Month Leptin (ng/ml)	PreLeptinBlood Spot(ng/ml)
Av Control Month Leptin (ng/ml)	Pearson Correlation	1	.677(*)
	Sig. (2-tailed)	.	.011
	N	36	13
PreLeptinBloodSpot (ng/ml)	Pearson Correlation	.677(*)	1
	Sig. (2-tailed)	.011	.
	N	13	13

* Correlation is significant at the 0.05 level (2-tailed).

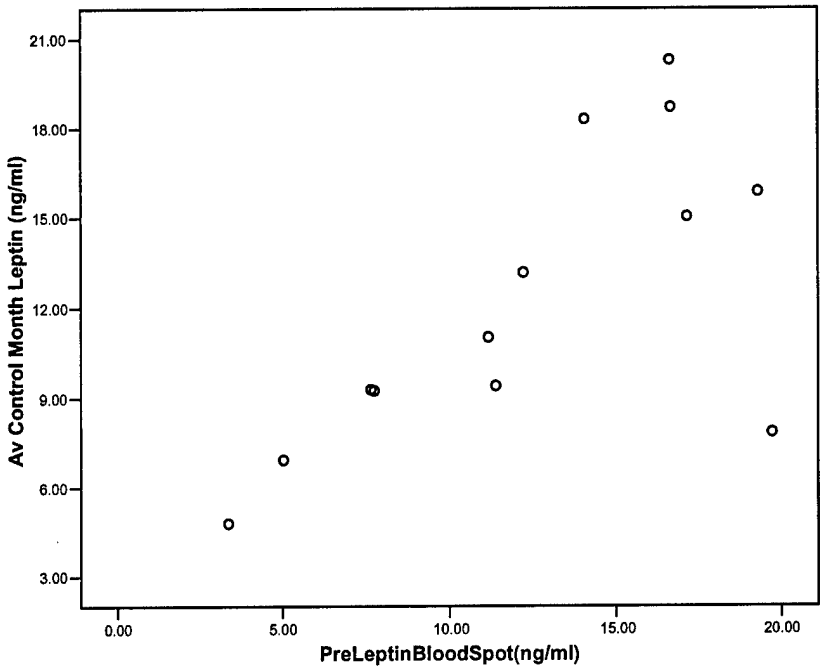

Figure 4. Scatterplot of leptin DBS vs venipuncture results

Overall Results from Years 1-3: Although our data set is not yet complete, it appears as though there are no dramatic changes in circulating estradiol, estrone, or in urinary E1G in our subjects, despite significant loss of weight and decrease in body fat. Preliminary results comparing DBS technique to venipuncture as assayed by RIA are very promising.

KEY ACCOMPLISHMENTS

This is an ongoing study, so preliminary publication of the data is not feasible.

REPORTABLE OUTCOMES

Training:
The following individuals have been supported by DAMD17-01-1-0360:
Faculty:
Nancy Williams, Sc.D.
Undergraduate Kinesiology Students:
Carmon Communale 3/04-5/04
Kristin Gross 2/04-9/04

The following students received degrees in the past year under the direction of Dr. Williams. These students all assisted with the current project.

Kelly Dougherty, MS Kinesiology
Brian Frye, MS Kinesiology

Heather Leidy, PhD Physiology
Michael Perry, MS Kinesiology

Publications:
To date, no publications have resulted from the project supported by these funds because the data set is not yet complete. However, Dr. Williams has produced the following publications while being supported by this Career Award:

Published Manuscripts:
Williams, NI. Experimental disruptions of the menstrual cycle: Lessons from long-term prospective studies. Med Sci Sports Exerc 35 (8): 1564-1572, 2003.

De Souza, M.J., H. McConnell, E. O'Donnell, B. Lasley, and **Williams NI**. Fasting Ghrelin Levels in Physically Active Women: Relationship with Menstrual Disturbances and Metabolic Status. J Clin Endocrinol Metab. Jul;89(7):3536-42, 2004.

McConnell HJ, Gardner JK, Frye BR, Snook ML, Schuchert MK, Richard EL, and **Williams NI.** Circulating ghrelin is sensitive to changes in body weight during a diet and exercise program in normal weight young women (Special edition: J Clin Endocrinol Metab. Jun;89(6):2659-64, 2004.

De Souza, M.J., and **N.I. Williams**. Physiological Aspects and Clinical Sequelae of Energy Deficiency and Hypoestrogenism in Exercising Women. Hum Reprod Update. Sep-Oct;10(5):433-48, 2004

Williams, NI and De Souza, MJ. "Exercise-associated menstrual cycle disturbances: practical and clinical considerations", Endocrinology of Physical Exercise and Sport as part of the series "The Encyclopedia of Sports Medicine" for the International Olympic Committee (In Press, for 2005).

Manuscripts in Review:

De Souza MJ, and **Williams NI.** Beyond Hypoestrogenism in Amenorrheic Athletes: Energy Deficiency as a Contributing Factor for Bone Loss (Submitted to Currrent Sports Medicine Reports)

Mastro AM, Williams NI, Kraemer WJ et al. Exercise Intervention and Plasma Levels of IFN-, and IL-6 following Chemotherapy for Breast Cancer. (submitted to the Journal of Clinical Oncology).

Manuscripts in Progress:
Williams NI, Perry MD, Kraemer WJ, and Mastro AM. "Effects of chemotherapy followed by exercise training on reproductive status and stress hormones in breast cancer patients"

Williams, N.I. Williams, N.I. , Berga S.L., and Cameron, J.L. Synergism of multiple sub-threshold stressors: effects of diet, exercise, and psychosocial stress on menstrual cyclicity

Leidy HJ, Frye BR, Duke KM, Albert AE, Snook ML, **Williams NI**. Changes in ghrelin are concomitant with changes in body weight, leptin, and IGF-1 during an energy deficit-imposing diet and exercise program in normal weight, healthy young women

Leidy HJ, Frye BR, Duke KM, Albert AE, Snook ML, **Williams NI**. Meal Calorie Content and Meal Timing Affect Specific Meal Response Characteristics of Total Ghrelin in Normal Weight Healthy Young Women

Leidy HJ, Frye BR, Duke KM, Albert AE, Snook ML, **Williams NI.** The Meal Related Pattern and Diurnal Rhythm of Ghrelin are Elevated Following an Energy Deficit-imposing Diet and Exercise Intervention

Cancer Grants:

Active: The following grant was awarded for additional studies to be undertaken in collaboration with Dr. Kimberly Westerlind at the AMC Cancer Research Center in Denver, Colorado. This work will examine the effects of exercise on the ratios of urinary estrogen metabolites.

AMC Cancer Research Center
Co-Investigator (Williams)
PI (Westerlind) 1/04-12/05
$76,865

"Exercise and Estrogen Metabolism: Implications for Breast Cancer Prevention"

Pending: The principal investigator plans to submit an NIH R01 grant to secure funding to perform additional analyses on serum samples collected from the current project. This grant will be in response to PA-04-124 (Studies of Energy Balance and Cancer in Humans) July 7, 2004 -Sept 2, 2006.

"Effects of energy deficiency on hormonal and immunological biomarkers for cancer"

Other Grants:

(Active Support)

1. **NIH**
   1 RO1 HD39245-01 (Williams) 5/1/01 - 4/30/04
   (currently in 1 yr no cost extension) 30%
   PHS/NICHD **$ 1,538,361**
   Principal Investigator:
   "Bioenergetics of Exercise-induced Menstrual Disturbances"

2. **US Army Medical Research and Materiel Command** 9/17/01- 9/16/05 15%
   US Army Breast Cancer Program (IDEA AWARD) **$408,878**

   Principal-Investigator:
   "Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-1 in Premenopausal Women (IDEA Award) "

3. **US Army Medical Research and Materiel Command** 9/17/01- 9/16/05 50%
   US Army Breast Cancer Program **$312,081**
   (CAREER DEVELOPMENT AWARD)

   Principal-Investigator:
   "Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-1 in Premenopausal Women (Salary Only)

4. Retirement Research Foundation 2000-2004 2%
$56,832

Co-Investigator: (PI is J.L. Cameron, PhD)
"Physical Exercise and Brain Aging"

5. National Institutes of Health (NIH) 2003-2008
HD-02-012 Cooperative Reproductive Science Research Centers at Minority Institutions
Co-Investigator: $ 1,160,204 5%
"The efficacy and safety of metformin and lifestyle factors in the amelioration of hyperandrogenemia and its associated symptomology"

6. Cancer Research and Prevention Foundation
Co-Investigator (PI is Kim Westerlind, AMC Cancer Research Center, Denver, CO)
1/04-12/05 0%
$76,865
"Exercise and Estrogen Metabolism: Implications for Breast Cancer Prevention"

7. NASA
Co-Investigator (PI is James Pawelczyk, PSU) 4/1/05-3/31/06 5%
$1,144,613
"Improving Orthostatic Tolerance in Women: Control of Splanchnic and Cutaneous Vascular Capacitance"

****

(Pending)

1. National Institutes of Health (NIH) 4/1/05-3/31/09 28.8%
Co-Principal Investigator (PI is Susan Bloomfield, Texas A&M)
$2,000,000
"Impact of Food Restriction on Bone Health in Active Females

****

(Not funded)

1. National Institutes of Health (NIH)
1 RO1 (**Co –Principal Investigator** with Mary Jane De Souza, Univ. Toronto)
7/01/02 - 6/30/07 15%
PHS/NICHD **$ 2,433,044**
" Clinical Sequelae Exercise-Induced Hypoestrogenism"

2. National Insitutes of Health (NIH)
Co-Investigator (PI is Terryl Hartman, PSU) 4/01/04-3/31/08 20%
$2,085,448
"Female Cancer Survivors Weight and Activity Intervention"

3. Dairy Farmers of Canada 1/1/05-12/31/06 10%
Co- Principal Investigator (PI is Mary Jane De Souza, University of Toronto)

"Can Increased Dietary Calcium Improve Recovery of Bone Health in Exercising Women Undergoing a Lifestyle Intervention for Severe Menstrual Disturbances?"

4. National Institutes of Health (NIH) 4/1/05- 3/31/09 15%
Co-Investigator (PI is Terryl Hartmen, Dept. Nutrition, Penn State) $856,295

"Antioxidant Status, Diet and Early Pregnancy"

Presentations:

J K Gardner, H J McConnell, B R Frye, K A Dougherty, T S Parrott, E L Richard, M L Snook, M Schukert, **Williams, NI**. Validation of an Improved Method to Estimate Energy Requirements in College-aged Women: The PERK method (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S79, 2004)

K Dougherty , H J McConnell, J Gardner, B Frye, E Richard, M Snook, M Schucert, A Albert, T Parrott and **Williams, NI.** Effects of Diet and Exercise on Leptin Levels In Women: Dependence on Body Composition Changes (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S80, 2004)

Williams, NI, HJ McConnell, JK Gardner, BR Frye, EL Richard, ML Snook, KL Dougherty, TS Parrott, A Albert, M. Schukert. Exercise-associated menstrual disturbances: dependence on daily energy deficit, not body composition or body weight changes. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004.

De Souza, M.J., E. O'Donnell, R. Hontscharuk, T. Burke, J. Goodman, **Williams, NI.**
Diagnosis of Osteopenia May Indicate the Presence of Increased Cardiovascular Risk in Female Athletes. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004.

R. Hontscharuk, E. O'Donnell, **Williams, NI** T. Burke, M.J. De Souza. Dietary Cognitive Restraint: A Marker for Altered Energy Homeostasis and Menstrual Disturbances in Athletic Women (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S33, 2004.

McConnell, H., **Williams, NI**, E. O'Donnell, B. Lasley, M.J. De Souza. Fasting Ghrelin Levels in Physically Active Women: Relationship with Menstrual Disturbances and Metabolic Status. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004)

CONCLUSIONS:

We are making good progress toward the completion of this study. Preliminary examination of the data look interesting but thus far analyses do not support the hypothesis that circulating biomarkers of breast cancer are altered by diet and exercise. The DBS technique looks promising as a potential field marker for energy availability, based on a favorable correlation between serum and DBS samples.

REFERENCES:

NONE

APPENDIX

1. Letter from Salimetrics
2. T3 performance and quality control characteristics
3. IGF-I performance and quality control characteristics

Dr. Nancy I. Williams
Associate Professor
Room 267Q
Recreation Building
Department of Kinesiology
& Noll Physiological Research Center
Penn State University
University Park, PA 16802

Dear Dr. Williams,

At Dr. Granger's request, I am writing to outline the basic objectives for our development of blood spot assays for Total T3 and IGF-1 for your project. You should have received quotes for these projects from Martha Orland last weekend. As you are aware, we have already developed similar assays for testosterone, leptin, estradiol, and progesterone. Based on our previous experience I don't expect protocol development for these markers will be problematic. Nevertheless, as with any research project a specific timeline is difficult to predict. We hope the development work will take no longer than 3 months time.

As in the past, our approach will be to begin by modifying commerically available enzyme immunoassay protocols. The assay development will include determination of assay range, lower limit of sensitivity, linearity and spike recovery, and confirmation that intra- and inter-assay coefficients of variation are within acceptable limits outlined by Chard (1990). We will also provide recommendations regarding sample collection, preparation, and the amount of sample needed to perform each assay.

In a previous note to Dr. Granger, you mentioned having matched serum/plasma samples. Once the assay is internally validated we highly recommend comparing values from the blood spot assay protocols with results you obtain from the serum tests. We can arrange those serum tests for you if you don't already have a source for those assays.

Once completed, we can provide testing services for your project at a cost of $25.00 per sample for T3 and
>$30.00 per sample for IGF-1.

If you have any questions or are just interested in a progress report, please don't hesitate to call (800-790-2258 ext. 207) or email me (Ebs@salimetrics.com).

Best Regards,

Eve Schwartz

T3 BLOOD SPOT PERFORMANCE CHARACTERISTICS

LINEARITY OF DILUTION :

A plasma sample was diluted linearly and each dilution was mixed with equal parts of RBCs. 50 ul of each mixture was pipetted onto blood spot papers, frozen, thawed, and then assayed.

DILUTION FACTOR	EXPECTED ng/dL	OBSERVED ng/dL	RECOVERY %
0		287.75	
x2	143.88	135.20	94.0%
x4	71.94	77.84	108.2%

PRECISION:

The intra-assay precision was determined from the mean of 10 replicates each.

SAMPLE	N	MEAN ng/dL	STANDARD DEVIATION ng/dL	COEFFICIENT OF VARATION %
C I	10	140.32	12.45	8.9
C II	10	70.07	4.43	6.3

The inter-assay precision was determined from the mean of average duplicates for 4 separate runs.

SAMPLE	N	MEAN ng/dL	STANDARD DEVIATION ng/dL	COEFFICIENT OF VARATION %
C I	4	146.65	8.71	5.9
C II	4	64.73	6.42	9.9

SPIKE AND RECOVERY:

The zero calibrator was spiked with three different levels of T3 and mixed with equal parts of RBCs. 50 ul of each mixture was pipetted onto blood spot papers, frozen, thawed, and then assayed.

Endogenous (ng/dL)	Added (ng/dL)	Expected (ng/dL)	Observed (ng/dL)	Recovery (%)
0	37.5	37.5	34.7	92.5
0	112.5	112.5	94.9	84.3
0	187.5	187.5	157.5	84.0

SENSITIVITY:

The low limit of sensitivity of the assay was determined by mixing equal parts of the zero calibrator and red blood cells and spotting 50 uL onto blood spot papers. The spots were frozen and thawed before assay. The lower limit of sensitivity was determined by interpolating the mean minus 2 SD for eleven zeros. The minimal concentration of T3 that can be distinguished from 0 is 30 ng/dL

SALIMETRICS LLC

IGF-1 BLOOD SPOT PERFORMANCE CHARACTERISTICS

LINEARITY OF DILUTION :

A plasma sample was diluted linearly and each dilution was mixed with equal parts of RBCs. 50 ul of each mixture was pipetted onto blood spot papers, frozen, thawed, and then assayed.

DILUTION FACTOR	EXPECTED ng/mL	OBSERVED ng/mL	RECOVERY %
0		270.17	
x2	135.09	133.04	98.5
x4	67.54	57.27	84.8

PRECISION:

The intra-assay precision was determined from the mean of 10 replicates of low, mid and high concentrations of IGF-1.

SAMPLE	N	MEAN ng/mL	STANDARD DEVIATION ng/mL	COEFFICIENT OF VARATION %
Low	10	25.0	1.75	7.0
Mid	10	59.14	3.19	5.4
High	10	129.96	8.87	6.8

The inter-assay precision was determined from the mean of average duplicates for 4 separate runs.

SAMPLE	N	MEAN ng/mL	STANDARD DEVIATION ng/mL	COEFFICIENT OF VARATION %
Low	4	93.13	4.44	4.8
High	4	166.85	7.55	4.5

SPIKE AND RECOVERY:

The zero calibrator was spiked with three different levels of IGF-1 and mixed with equal parts of RBCs. 50 ul of each mixture was pipetted onto blood spot papers, frozen, thawed, and then assayed.

Endogenous (ng/mL)	Added (ng/mL)	Expected (ng/mL)	Observed (ng/mL)	Recovery (%)
0	55.0	55.0	64.3	116.9
0	110.0	110.0	117.1	106.5
0	165	165	158.7	96.2

SENSITIVITY:

The low limit of sensitivity of the assay was determined by mixing equal parts of the zero calibrator and red blood cells and spotting 50 uL onto blood spot papers. The spots were frozen and thawed before assay. The lower limit of sensitivity was determined by interpolating the mean minus 2 SD for 10 zeros. The minimal concentration of IGF-1 that can be distinguished from 0 is < 20 ng/mL

NANCY I. WILLIAMS
Curriculum Vitae

BIOGRAPHICAL

PII Redacted

University Address
Department of Kinesiology
Room 267Q Recreation Building
Penn State University
University Park, PA 16802

Phone: 814-865-1346
Fax: 814-865-1275
Email: niw1@psu.edu

EDUCATION

1984	B.S.	Biology, Bucknell University, Lewisburg, PA
1986	M.S.	Exercise Physiology, The Ohio State University, Columbus, OH
1992	Sc.D.	Applied Anatomy & Physiology, Boston University, Boston, MA
1992-1996		Postdoctoral fellowship, University of Pittsburgh School of Medicine, Center for the Study of Reproductive Physiology (Judy L. Cameron PhD, mentor)

PROFESSIONAL EXPERIENCE

2003-present	Associate Professor	Department of Kinesiology and Noll Physiological Research Center Joint Appointments: Intercollege Program in Physiology, Department of Nutrition, Life Science Consortium (Nutrition Science Option); Penn State University University Park, PA
1997-2003	Assistant Professor	Department of Kinesiology and Noll Physiological Research Center Joint Appointments: Intercollege Program in Physiology, Department of Nutrition, Life Science Consortium (Nutrition Science Option); Penn State University University Park, PA
1996-1997	Visiting Assistant: Professor	Human Anatomy & Physiology Department of Biological Sciences Ohio University

Athens, Ohio

1992-1996 Postdoctoral Fellow: Center for the Study of Reproductive Physiology
School of Medicine
University of Pittsburgh
Pittsburgh, Pennsylvania

1987-1992 Graduate Fellow: Department of Health Sciences
Sargent College
Boston University
Boston, Massachusetts

Research Projects: NIH grant: "Effects of exercise on pituitary hormone secretion"
NIH grant: "Exercise as an adjunct therapy for persons with mental illness"

Health/Fitness Center Coordinator: Faculty/Staff Fitness Program
Department of Health Sciences
Sargent College
Boston University
Boston, Massachusetts

1986-1987 Project Director: Exercise Physiology Laboratory
Department of Exercise Science
The Ohio State University
Columbus,Ohio

NIH Grant: "Effects of chronic exercise training on aging"

1984-1986 Research Assistant: Exercise Physiology Laboratory
Department of Exercise Science
The Ohio State University,
Columbus, Ohio

NIH Grant: "Effects of chronic exercise training on aging"

HONORS AND AWARDS

Canada Research Chair Nomination (declined), York University, Toronto, Ontario, Canada 2003

Department of Defense Breast Cancer Research Program, Career Development Award, 2001

Fellowship Status: American College of Sports Medicine, 1998

NIH Individual National Research Service Award (NRSA), 1994-1996

Endocrine Society; Women in Endocrinology Travel Award, 1995

Association of Women in Science Education Foundation Award, 1990

American Association of University Women Predoctoral Fellowship, 1990

American College of Sports Medicine, New England Chapter Scholarship Award; 1989

Phi Sigma Biological Honor Society; 1984

Scholar/Athlete of the Year, Southern New Jersey Courier Post, 1980

PROFESSIONAL MEMBERSHIPS/AFFILIATIONS

Collaborative Scientist, Oregon National Primate Research Center	2003-present
American College of Sports Medicine	1984-present
Endocrine Society	1996-present
New England Chapter ACSM	1987-1992
Association for Women in Science	1987-1992
Mid-Atlantic Chapter ACSM	1997-present
Female Athlete Triad Coalition	2004-present

TEACHING

COURSES TAUGHT AT BOSTON UNIVERSITY:

HS 276 *Physiology of Exercise Laboratory*
HS 302 *Exercise Physiology(Lecture)*
HS 535 *Clinical Fitness Evaluation*
HS 573 *Physiology of Activity (Lecture)*
HS 573 *Physiology of Activity (Laboratory)*

COURSES TAUGHT AT OHIO UNIVERSITY:

BIOS 450/550 *Principles of Endocrinology (section on neuroendocrinology)*
BIOS 446/546 *Exercise Physiology Laboratory*
BIOS 345 *Human Physiology*
BIOS 346 *Human Physiology Laboratory*

COURSES TAUGHT AT PENN STATE UNIVERSITY:

Sem/Year	Course	Title	Credits	Enrollment
Fall 1997	Kines 481W	Scientific basis of Exercise for Older Adults	3	50
	Kines 496C	Independent Study	3	1
Spring 1998	Kines 456	Fitness Appraisal	4	96
	Kines 496C	Independent Study	3	5
	Kines 395b	Practicum	3	2
Summer 1998	Kines 496C	Independent Study	1-3	3
Fall 1998	Kines 456	Fitness Appraisal	4	86
	Kines 456h	Fitness Appraisal (honors option)*	4	1
	Kines 496c	JumpStart to Health/Fitness	3	6
	Kines 496c	Independent Study	3	5
	Kines 496c	Independent Study (Schreyer Student)**	3	1
	Kines 596c	Supervised Teaching	3	1
	Kines 597i	Neuroendocrine-Immune Interactions	1	4
	Kines 395b	Practicum	3	1

COURSES TAUGHT ...cont.

Sem/Year	Course	Title	Credits	Enrollment
Spring 99	Kines 456	Fitness Appraisal	4	103
	Kines 424	Female in Exercise and Sport	3	36
	Kines 496c	Independent Study	3	16
Summer 99	Kines 456	Fitness Appraisal	4	14
Fall 99	Kines 424	Female in Exercise and Sport	3	16
	Kines 496c	Independent Study**	3	5
	Physio/Bio 572	Animal Physiology	3	12
Spring 00	Kines 456	Fitness Appraisal	4	78
	Kines 424	Female in Exercise and Sport	3	33
	Kines 496c	Independent Study**	3	5
Summer 00	Kines 456	Fitness Appraisal	4	12
Fall 00	Kines 424	Female in Exercise and Sport	3	35
	Physio/Bio 572	Animal Physiology	3	25
	Kines 496c	Independent Study**	3	5
Spring 01	Kines 424	Female in Exercise and Sport	3	35
	Kines 496c	Independent Study**	3	5
Fall 01	Kines 424	Female in Exercise and Sport	3	35
	Kines 496c	Independent Study**	3	5
Fall 02	Kines 424	Female in Exercise and Sport	3	35
Fall 03	Kines 424	Female in Exercise and Sport	3	40
Fall 04	Kines/WMST 424	Female in Exercise and Sport	3	40

*Supervised the writing of new laboratory experiment and handout for Kines 456

** Supervise students who work in my laboratory on research project examining the interactions between reproductive function disturbances, eating habits, and body image

STUDENT TRAINING

Preceptor NIH GM08619-07 Research Training in Physiological Adaptations to Stress. National Insititute of General Medical Sciences, 1996-2005. Director is PA. Farrell, PhD, Noll Physiological Research Center, Penn State University

Committee Chair- Undergraduate Honors Thesis Students

2000 Kathleen Flecker – Shreyer's Honor's College: "Weight and diet concerns among female athletes with menstrual cycle irregularities" (Winner 3rd place Undergraduate Research Exhibition; attended medical school)

2003 Meredith Snook- Shreyer's Honor's College: "Effects of a diet and exercise on interationcs between thyroid hormone, resting metabolic rate, and anthropometric measurements in normal weight healthy young women" (Earned full scholarship to University of Pittsburgh Medical School in a special clinical program designed to train clinicians to conduct clinical research)

Committee Chair- Masters Students

1999 Paula Wilkins "Body Image, Social Physique Anxiety, and Menstrual Dysfunction in the Female Athlete" (Physiology)
2000 Heather McConnell "Determining the validity of ovulation detection methods in an athletic population" (Physiology)
2000 Angelique Matuch "Quantifying physiological responses prior to competitive exercise" (Kinesiology)
2002 Megan Senior "Screening for Subclinical Eating Disorders in Female Athletes: The Use of an Indirect Interview Technique " (Nutrition)
2004 Michael Perry " Effects of chemotherapy followed by exercise training on reproductive status and stress hormones in breast cancer patients" (Kinesiology)
2004 Kelly Dougherty "No relation between leptin and exercise-associated reproductive disturbances in healthy normal weight young women" (Kinesiology)
2004 Brian Frye "Predictors of weight loss in a diet and exercise intervention in young women" (Kinesiology)

Committee Chair - Doctoral Students

1999 *Jill Bush "Proenkephalin peptide F concentrations in different blood bio-compartments: The effect of an acute resistance exercise protocol" (Kinesiology)
2004- Heather Leidy "Role of ghrelin in energy homeostasis"(Physiology)

*= co-chaired this committee in lieu of the early departure of her major advisor, William Kraemer

Committee Member- Masters Students

1997 Scott Mazetti "The influence of direct supervision of heavy resistance training on muscular performance and hormonal responses" (Kinesiology)

1998 Sang Kyung Kim "The effects of menstrual function on plasma peptide F immunoreactivity in response to high intensity cycle exercise" (Kinesiology)

1998 Jennifer DeSanto "Body Composition and energy balance: Comparison between eumenorrheic and amenorrheic athletes" (Kinesiology)

1998 Wallace Baker "Characterization of leukocyte infiltration after muscle damage" (Kinesiology)

1998 Steve Tokeshi "Maximal isokinetic force generation in upper body musculature during concentric and eccentric actions: a gender comparison" (Kinesiology)

1999 Jannell MacAulay "Submaximal cycle ergometry as a predictor of maximal aerobic capacity in women on oral contraceptives" (Kinesiology)

2000 Brittney Salkeld "The effect of oral contraceptive use on measures of fatigue and energy metabolism" (Kinesiology)

2003 James Butler (Media Studies)

2003 Micheal Curren "Octreotide improves orthostatic tolerance in women" (Physiology)

Committee Member- Doctoral Students

1998 Jeff Volek "Fasting and postprandial serum lipoprotein responses to a hypocaloric low carbohydrate diet rich in monounsaturated fat and supplemented with n-3 fatty acids" (Kinesiology)

2002 Greg Daniels "Walking and running: Information and energetics" (Kinesiology)

2002-present Nancy Johnston "Bio-markers of pre-term labor" (Nursing, Physiology minor)

Undergraduate Research Advising:

Summer 1998 Minority High School Student Research Apprentice Program at Penn State University
*Mentored student who helped with research projects in laboratory

Fall 98 to 2001 WISE program; Women in Science in Engineering
*Have averaged two female students per year who have worked in laboratory

Summer 2001 Minority Access to Research Careers (MARC)
*Mentored student who helped with research projects in laboratory

Summer 2002 McNair Scholars Programs
*Mentored first generation college student who performed research project

RESEARCH

INTRAMURALLY FUNDED GRANTS

(Completed)

1. **Dudley Allen Sargent Research Fund** (intramural): 1988, 1989, 1990
Sargent College of Allied Health Professions
Boston University, Boston, Massachusetts

Principal Investigator:
"Effects of exercise and caloric restriction upon luteinizing hormone secretion"

2. Penn State University
College of Health and Human Development
Interdisciplinary Seed Grant Program , 1997-1998;
$5000

Principal Investigator:
"Prevalence of Female Athlete Triad Disorders: Estimation by Questionnaires and Subsequent Follow-up with Clinical and Laboratory Assessments of Physiological Status"

3. Penn State University
College of Health and Human Development
Interdisciplinary Seed Grant Program , 1998-1999;
$6000

Principal Investigator:
"Disturbances in Reproductive Function caused by Metabolic Stress: Possible Increased Susceptibility in Individuals with Elevated Levels of Perceived Psychological Stress "

4. Penn State University
College of Health and Human Development
Interdisciplinary Seed Grant Program , 1999-2000;
$6000

Co- Investigator: (PI Jay Hertel)
"Changes in risk factors of anterior cruciate ligament ruptures in female collegiate athletes across the menstrual cycle"

5. Penn State University
Pathology Initiation Grant January 2002-January 2003 5%
Hershey Medical Center, Dept. Pathology **$15,170**

Co-Investigator (PI is Williams' Doctoral student, Thomas Whipple, MS, PT)
"The Role of Resistance Exercise and Energy Availability on Bone Metabolism"

6. Penn State University
Children's Youth and Family Consortium January 2002- January 2003 5%
Penn State University, CHHD **$13, 925**

Co-Principal Investigator (with Moira Petit, PhD (PSU-Hershey))
"Designing Intervention Programs to Optimize Bone Development: Application of Bone Markers to Monitor the Short-term Response to Exercise"

EXTRAMURALLY FUNDED GRANTS

(Completed)

1. NIH National Research Service Award (NRSA), 1994-1996
Center for the Study of Reproductive Physiology
School of Medicine
University of Pittsburgh
Pittsburgh, Pennsylvania

Principal Investigator:
"Metabolic cues governing reproductive hormone secretion"

2. Pharmavite Corporation, Seattle, Washington
Research Grant-in-Aid, 1998-1999; $20,000

Principal Investigator:
" Consumer Taste and Education of a Nutritional Sports Supplement"

3. US Army Medical Research and Materiel Command 1998-2001 5%
US Army Breast Cancer Program **$292,539**

Co-Investigator:
"Use of Exercise to Increase CD4 Lymphocytes following Chemotherapy Treatment for Breast Cancer "

****

(Active Support)

1. NIH
1 RO1 HD39245-01 (Williams) 5/1/01 - 4/30/04
(currently in 1 yr no cost extension) 30%
PHS/NICHD **$ 1,538,361**

Principal Investigator:
"Bioenergetics of Exercise-induced Menstrual Disturbances"

2. US Army Medical Research and Materiel Command 9/17/01- 9/16/05 15%
US Army Breast Cancer Program (IDEA AWARD) **$408,878**

Principal-Investigator:
"Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-1 in Premenopausal Women (IDEA Award) "

3. US Army Medical Research and Materiel Command 9/17/01- 9/16/05 50%
US Army Breast Cancer Program **$312,081**
(CAREER DEVELOPMENT AWARD)

Principal-Investigator:
"Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-1 in Premenopausal Women (Salary Only)

4. Retirement Research Foundation 2000-2004 2%
$56,832

Co-Investigator: (PI is J.L. Cameron, PhD)
"Physical Exercise and Brain Aging"

5. National Institutes of Health (NIH) 2003-2008
HD-02-012 Cooperative Reproductive Science Research Centers at Minority Institutions
Co-Investigator: $ 1,160,204 5%
"The efficacy and safety of metformin and lifestyle factors in the amelioration of hyperandrogenemia and its associated symptomology"

6. Cancer Research and Prevention Foundation
Co-Investigator (PI is Kim Westerlind, AMC Cancer Research Center, Denver, CO)
1/04-12/05 0%
$76,865
"Exercise and Estrogen Metabolism: Implications for Breast Cancer Prevention"

7. NASA
Co-Investigator (PI is James Pawelczyk, PSU) 4/1/05-3/31/06 5%
$1,144,613
"Improving Orthostatic Tolerance in Women: Control of Splanchnic and Cutaneous Vascular Capacitance"

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(Pending)

1. National Institutes of Health (NIH) 4/1/05-3/31/09 28.8%
Co-Principal Investigator (PI is Susan Bloomfield, Texas A&M)
$2,000,000
"Impact of Food Restriction on Bone Health in Active Females

****

(Not funded)

1. National Institutes of Health (NIH)
1 RO1 (**Co –Principal Investigator** with Mary Jane De Souza, Univ. Toronto)
7/01/02 - 6/30/07 15%
PHS/NICHD **$ 2,433,044**
" Clinical Sequelae Exercise-Induced Hypoestrogenism"

2. National Insitutes of Health (NIH)
Co-Investigator (PI is Terryl Hartman, PSU) 4/01/04-3/31/08 20%
$2,085,448

"Female Cancer Survivors Weight and Activity Intervention"

3. Dairy Farmers of Canada 1/1/05-12/31/06 10%
Co- Principal Investigator (PI is Mary Jane De Souza, University of Toronto)

"Can Increased Dietary Calcium Improve Recovery of Bone Health in Exercising Women Undergoing a Lifestyle Intervention for Severe Menstrual Disturbances?"

4. National Institutes of Health (NIH) 4/1/05- 3/31/09 15%
Co-Investigator (PI is Terryl Hartmen, Dept. Nutrition, Penn State) $856,295

"Antioxidant Status, Diet and Early Pregnancy"

****

RESEARCH REPORTS

Williams NI, Christante DH, Swavely K, Laufer E, McBrearty C, and Clark KC. Penn State Univeristy JogMate Study: Product Effectiveness and Consumer Appeal
Submitted to Pharmavite Corp, Seattle, WA, July 15, 1999

PUBLISHED MANUSCRIPTS

Skrinar, G.S., **N.I. Williams**, B.A. Bullen, J.W. McArthur, and N.M. Mihok. Changes in body consciousness relate to regularity of exercise training. *Perceptual and Motor Skills.* 75: 696-698, 1992

Bloomfield, S.A., **N.I. Williams**, D.R. Lamb, FACSM, and R.D. Jackson. Non-weight bearing exercise may increase lumbar spine bone mineral density in healthy post menopausal women. *Amer. J. Phys. Med. Rehabil.* 72: 204-209, 1993

Williams, N.I. , J. McArthur, B. Turnbull, B. Bullen, G. Skrinar, I.Z Beitins, G.M. Besser, L.H. Rees, I. Gilbert, D. Cramer, L. Perry, D.S. Tunstall-Pedoe. Effects of follicular phase exercise on LH pulse characteristics in sedentary eumenorrheic women. *Clinical Endocrinology* 41: 787-794, 1994

Williams, N.I., J. Young., J. McArthur, B. Bullen, G. Skrinar, and B. Turnbull. Strenuous exercise with caloric restriction: Effect on luteinizing hormone secretion. *Med. Sci. Sports Exerc.* 27 (10): 1390-1398, 1995

Williams, N.I., M.J. Lancas, and J.L. Cameron. Stimulation of luteinizing hormone (LH) secretion in male rhesus monkeys by food intake: Evidence against a role for insulin. *Endocrinology* 137(6): 2565-2571, 1996

Williams, N.I. Low energy availability and reproductive disturbances: a review of clinical and hormonal effects. *Dance Medicine and Science* 2:(1) 19-31, 1998

Williams, N.I., B.A. Bullen, J.W. MacArthur, G.S. Skrinar, and B.A. Turnbull. Effects of short-term strenuous endurance exercise upon corpus luteum function". *Med. Sci. Sports Exerc* 31(7): 949-958,1999.

Sharkey, N.A., **Williams, N.I.**, Guerin, J.B.: The role of exercise in the prevention and treatment of osteoporosis and osteoarthritis. *Nursing Clinics of North America*, 35 (1): 209-221, 2000

Williams, N.I., Caston-Balderrama, A.L. Helmreich, D.L., Parfitt, D.B., Nosbisch C, Cameron, J.L. Longitudinal changes in reproductive hormones and menstrual cyclicity in cynomolgus monkeys during strenuous exercise training: rapid transition to exercise-induced amenorrhea *Endocrinology* 142: 2381-2389, 2001

Williams N.I., DL Helmreich DL, DB Parfitt, Caston-Balderrama AL, JL Cameron. Evidence for a causal role of low energy availability in the induction of menstrual cycle disturbances during strenuous exercise training. *J Clin Endocrinol Metab* 86: 5184-5193, 2001

Miles MP, Mackinnon LT, Grove DS, **Williams NI**, Bush JA, Marx JO, Kraemer WJ, Mastro AM. The relationship of natural killer cell counts, perforin mRNA and CD2 expression to post-exercise natural killer cell activity in humans. *Acta Physiol Scand* 174: 1-9, 2002.

McConnell HJ, KA O'Connor, E Brindle, and **NI Williams**. Validity of methods for analyzing urinary steroid data to detect ovulation in athletes. *Med. Sci. Sports Exerc,* 34(11): 1836-1844, 2002

Whipple TJ, Petit Moira, Sharkey N, Demers L, **Williams NI**. Leptin and the skeleton. *Clin. Endocrinol.* 57: 701-711, 2002.

Williams, NI. Experimental disruptions of the menstrual cycle: Lessons from long-term prospective studies. *Med Sci Sports Exerc* 35 (8): 1564-1572, 2003.

De Souza, M.J., H. McConnell, E. O'Donnell, B. Lasley, and ***Williams NI****. Fasting Ghrelin Levels in Physically Active Women: Relationship with Menstrual Disturbances and Metabolic Status. (*J Clin Endocrinol Metab. *Jul;89(7):3536-42, 2004.*

McConnell HJ, Gardner JK, Frye BR, Snook ML, Schuchert MK, Richard EL, and **Williams NI.** Circulating ghrelin is sensitive to changes in body weight during a diet and exercise program in normal weight young women (Special edition: *J Clin Endocrinol Metab.* Jun;89(6):2659-64, 2004.

De Souza, M.J., and ***N.I. Williams****. Physiological Aspects and Clinical Sequelae of Energy Deficiency and Hypoestrogenism in Exercising Women (*Hum Reprod Update. *Sep-Oct;10(5):433-48, 2004*

BOOK CHAPTERS

Williams, NI and De Souza, MJ. "Exercise-associated menstrual cycle disturbances: practical and clinical considerations", Endocrinology of Physical Exercise and Sport as part of the series "The Encyclopedia of Sports Medicine" for the International Olympic Committee (In Press, for 2005).

MANUSCRIPTS IN REVIEW

De Souza MJ, and **Williams NI.** Beyond Hypoestrogenism in Amenorrheic Athletes: Energy Deficiency as a Contributing Factor for Bone Loss (Submitted to *Currrent Sports Medicine Reports*)

MANUSCRIPTS IN PROGRESS

Williams, N.I. Williams, N.I. , Berga S.L., and Cameron, J.L. Synergism of multiple sub-threshold stressors: effects of diet, exercise, and psychosocial stress on menstrual cyclicity

Leidy HJ, Frye BR, Duke KM, Albert AE, Snook ML, **Williams NI**. Changes in ghrelin are concomitant with changes in body weight, leptin, and IGF-1 during an energy deficit-imposing diet and exercise program in normal weight, healthy young women

Leidy HJ, Frye BR, Duke KM, Albert AE, Snook ML, **Williams NI**. Meal Calorie Content and Meal Timing Affect Specific Meal Response Characteristics of Total Ghrelin in Normal Weight Healthy Young Women

Leidy HJ, Frye BR, Duke KM, Albert AE, Snook ML, **Williams NI.** The Meal Related Pattern and Diurnal Rhythm of Ghrelin are Elevated Following an Energy Deficit-imposing Diet and Exercise Intervention

ABSTRACTS

N.I. Williams, K.A. Greaves, G.R. Brodowicz, T.E. Kirby, and D.R. Lamb, FASCM. Cardiovascular effects of endurance training during submaximal exercise in elders. Exercise Physiology Laboratory, The Ohio State University, Columbus, Ohio, 43210. (research abstract presented at the *Midwest American College of Sports Medicine Winter Meeting*, Boyne Mountain, Michigan, February, 1986)

N.I. Williams, K.A. Greaves, and D.R. Lamb, FACSM. "Cardiovascular function in lean and obese children during acute submaximal exercise". Exercise Physiology Laboratory, The Ohio State University, Columbus, Ohio, 43210. (research abstract presented at the *Midwest American College of Sports Medicine Winter Meeting*, Boyne Mountain, Michigan, February, 1987)

Williams, N.I., K.A. Greaves, T.E. Kirby and D.R. Lamb. Exercise training and cardiovascular function in the elderly. (presented at *Federation for the Society of Experimental Biology* meetings in Washington, DC, 1987) *FASEB Proceedings,* Vol. 46, p. 492, 1987

Williams, N.I. , J. McArthur, B. Turnbull, B. Bullen, G. Skrinar, I. Gilbert, G.M. Besser, and L.H. Rees. Early effects of follicular phase exercise on LH pulse characteristics in sedentary eumenorrheic women.

(presented at the *American College of Sports Medicine Annual Meeting,Orlando, FL, May 29-June1, 1991) Med. Sci. Sports Exerc.* 23(4), p. S93, 1991

Williams, N.I., J. McArthur, B. Bullen, G. Skrinar, B. Turnbull, and J. Young. Slowed LH pulse frequency in trained eumenorrheic women due to caloric restriction combined with heavy training. (presented at the *American College of Sports Medicine Annual Meeting, Dallas, TX, May 27-May 30,1992) Med. Sci. Sports Exerc.* 24(5), p. S36, 1992

Peachey, S., G. Skrinar, E. Kuligowska, B. Bullen, **N. Williams**, B. Turnbull, and J. McArthur. Effect of enhanced follicular phase endurance training on follicular maturation in women. (presented at the *American College of Sports Medicine Annual Meeting, Dallas, TX May 27-May 30, 1992) Med. Sci. Sports Exerc.* 24(5), p. S171, 1992

Skrinar, G.S., D. Hutchinson, and **N. Williams**. Exercise: An adjunct therapy for persons with psychiatric disabilities. (presented at the *American College of Sports Medicine Annual Meeting, Dallas, TX, May 27-May 30, 1992) Med. Sci. Sports Exerc.* 24(5), p. S36, 1992

Bullen, B., B. Turnbull, J. McArthur, G. Skrinar, **N. Williams**, and I. Beitins. Exercise and Diet: Correlates with the onset of menstrual disorders. *Proceedings of the Second IOC World Congress on Sport Sciences,* Barcelona, Spain. p. 155, 1992

Williams, N.I., A.L. Caston, and J.L. Cameron. Induction and reversal of exercise-induced amenorrhea: Temporal correlation with plasma T3 levels. (presented at the *76th Proceedings of the National Endocrine Society, Anaheim, CA, June, 1994) Endocrine Society Abstract*, #1775, 1994

Williams, N.I., M.J. Lancas, and J.L. Cameron. Stimulation of luteinizing hormone (LH) secretion in male rhesus monkeys by food intake: Evidence against a role for insulin. (presented at the *77th Proceedings of the National Endocrine Society, Washington, DC, June, 1995*) *Abstract,* #OR22-3, 1995

Williams, N.I., and J.L. Cameron. Stimulation of luteinizing hormone (LH) secretion in male rhesus monkeys by food intake: Role of circulating triiodothyronine (T3) (presented at the *10th International Congress of Endocrinology/78th Proceedings of the National Endocrine Society, San Francisco, CA, June, 1996*) *International Congress of Endocrinology/Endocrine Society, #P2-505, 1996.*

Williams, N.I., Berga, S.L., and J.L. Cameron. Mild metabolic stress potentiates the suppressive effect of psychological stress on reproductive function in female cynomolgus monkeys. (presented at the *79th Proceedings of the National Endocrine Society, Minneapolis, MN, June, 1997 Endocrine Society Abstract* #P1-367, 1997.

Williams, N.I., Bullen B.A., McArthur J.W., Skrinar G.S., and Turnbull B.A. Effects of short-term strenuous exercise on corpus luteum function. (presented at the *American College of Sports Medicine Annual Meeting, Orlando, FL June 3-6, 1998) Med. Sci. Sports Exerc.* 30 (5), p. S324, 1998

Williams, N.I. Bullen B.A., McArthur J.W., Skrinar G.S., and Turnbull B.A. Effects of short-term strenuous exercise on corpus luteum function. (presented at the *American College of Sports Medicine Annual Meeting, Orlando, FL June 3-6, 1998 Med. Sci. Sports Exerc.* 30 (5), p. S324, 1998

Williams NI, Clark KL, Mihalko SL, Matuch AN, McConnell HJ. Body image, disordered eating, exercise, and depression in athletes and non-athletes: association with menstrual status. (presented at the *American*

College of Sports Medicine Annual Meeting, Seattle, WA June 3-6, 1999 Med Sci Sports Exerc 31(5), S65, 1999

Miles MP, Mackinnon LT, **Williams NI**, Bush JA, Marx JO, Mastro AM, Kraemer WJ. NK cell activity and LFA-2 expression after running (presented at the *American College of Sports Medicine Annual Meeting, Seattle, WA June 3-6, 1999)*

Mackinnon LT, Miles MP, **Williams NI**, Bush JA, Mastro AM. Effects of prolonged exercise on natural killer (NK) cell cytotoxic activity and LFA-2 expression. Book of abstracts. *Fifth IOC World Congress*, Sydney, Australia, Oct 31-Nov 5, 1999, p. 51.

Mackinnon LT, Miles MP, Grove DS, **Williams NI**, Bush JA, Marx JO, Kraemer WJ. Effects of prolonged exercise on expression of perforin mRNA in peripheral blood natural killer (NK) cells (presented at *Sports Medicine Australia*, 1999)

Williams NI, Clark KL, McConnell, Matuch A, O'Connor KA. Menstrual irregularities and disordered eating in female athletes: survey vs follow-up physiological studies (presented at the *American College of Sports Medicine Annual Meeting, Indianapolis, IN, June 3-6, 2000 Med Sci Sports Exerc* 32 (5), S64, 2000

Mastro AM, **Williams NI,** et al. Exercise and Recovery of CD4 (+) cells after chemotherapy for breast cancer (*presented at Era of Hope Meeting of US Army Medical Research and Materiel Command,* June 8-12, 2000, Atlanta, GA)

Flecker KA, **Williams NI.** Body Image, disordered eating and menstrual status in collegiate athletes. (*presented at the National Conference for Undergraduate Research (NCUR),* University of Montana, Missoula, Montana, April 27-29, 2000)

Miles MP, MacKinnon LT, Grove DS, **Williams NI**, Bush JA, Marx JO, Kraemer WJ, Mastro AM. Potential mechanisms of post-exercise Suppression of NK cell activity: Cell number, Perforin mRNA and CD2. (research abstract presented at the 2000 American Physiological Society Meeting "The Integrative Biology of Exercise", Portland, ME, September 20-23, 2000.

Mastro AM, **Williams NI**, Kraemer WJ, Orsega-Smith EM, Perry MD, Dixon RH, Bleznak AD, Underwood J. Exercise, quality of life, and the recovery of CD4 (+) lymphocytes following chemotherapy for breast cancer *Proceedings of the American Association for Cancer Research 92nd Annual Meeting,* New Orleans, LA , 42 : 331, March 24-28, 2001

Perry MD, Mastro AM, Orsega-Smith E, Miles MP, Kraemer WJ, **Williams NI**. Exercise training and immune function following chemotherapy for breast cancer. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001

Orsega-Smith E, **Williams NI** (FACSM), Perry MD, Mastro AM, Kraemer WJ, Bleznak A, Dixon R, Underwood J. Fatigue, quality of life and physical function after chemotherapy for breast cancer. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001

Galucci, AN, **Williams NI**. Physiological indicators of psychological stress prior to competitive exercise. *Proceedings of the American College of Sports Medicine Annual Meeting*, Baltimore, MD, June 2-6, 2001

McConnell HJ, O'Connor KA, Brindle E, **Williams, NI**. Assessing reproductive function in exercising women: validity of ovulation detection algorithms. *Proceedings of the Endocrine Society Annual Meeting, Abstract* #P2-408, 2001

Senior MK, **Williams NI**, McConnell HJ, Clark KC. Screening for subclinical eating disorders in female athletes: validation of an indirect interview technique. *(Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001).*

McConnell HJ, **Williams NI**, O'Connor KA, Clark KL, Putukian M. Menstrual irregularities and disordered eating in female athletes: survey vs follow-up clinical and physiological studies. *(Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001).*

Mastro AM, **Williams NI**, Ford J, Fuener K, Orsega-Smith E, Kraemer WJ, Bleznak AD, Dixon RH, Underwood J, Miles M, Wagner K. IL-6 and interferon-gamma levels following chemotherapy for breast cancer. *Proceedings of the American Association for Cancer Research Annual Meeting*, San Francisco, CA, April 6-10, 2002

Hertel J, **Williams NI**, Gribble PA, McConnell HJ, DiPasquale AA, Putukian M. Changes in risk factors of ACL injuries across the menstrual cycle: A pilot study. *Proceedings of the American College of Sports Medicine Annual Meeting*, St. Louis, MO, May 29-June 1, 2002

Williams NI, McConnell HM, Gardner JK, Albert AC, Cameron JL. Lifestyle factors such as exercise, caloris intake, and psychological stress: relationship to reproductive hormones and possibly the risk of breast cancer. *Era of Hope* meeting, Department of Defense Breast Cancer Research Program, Orlando, FL, September 25-28, 2002

Dougherty, K., Galucci AN, McConnell HJ, **Williams NI.** Cortisol and testosterone levels prior to competitive exercise. *Proceedings of the American College of Sports Medicine Annual Meeting* , San Francisco, May 28-June 1, 2003, *Med. Sci. Sports Exerc.* 35 (5), p. S1837, 2003.

Williams NI, McConnell HJ, Gardner JK, Cameron JL, Schuchert MK, Richard EL, Snook ML. Susceptibility of menstrual cycle to various stressors: correlation with baseline luteal progesterone levels. *Proceedings of the American College of Sports Medicine Annual Meeting* , San Francisco, May 28-June 1, 2003, *Med. Sci. Sports Exerc.* 35 (5), p. S12, 2003.

McConnell HJ, Schuchert MK, Gardner JK, Frye BR, **Williams NI**. Basal Ghrelin is sensitive to changes in body weight during a controlled diet and exercise program in normal weight young women. (Presentated at the 2003 Endocrine Society Meeting, Philadelphia, PA, June 2003).

Whipple TJ, Le, B., Demers, L., Petit M.A., Sharkey N. **Williams, NI**. Acute Effects of Moderate Intensity Resistance Exercise on Bone Cell Activity. (*Presented at Association for Bone and Mineral Research Meeting, 2003*).

J K Gardner, H J McConnell, B R Frye, K A Dougherty, T S Parrott, E L Richard, M L Snook, M Schukert, **Williams, NI**. Validation of an Improved Method to Estimate Energy Requirements in College-aged Women: The PERK method (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S79, 2004)

K Dougherty , H J McConnell, J Gardner, B Frye, E Richard, M Snook, M Schucert, A Albert, T Parrott and **Williams, NI.** Effects of Diet and Exercise on Leptin Levels In Women: Dependence on Body Composition Changes (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S80, 2004)

Williams, NI, HJ McConnell, JK Gardner, BR Frye, EL Richard, ML Snook, KL Dougherty, TS Parrott, A Albert, M. Schukert. Exercise-associated menstrual disturbances: dependence on daily energy deficit, not body composition or body weight changes. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004.

De Souza, M.J., E. O'Donnell, R. Hontscharuk, T. Burke, J. Goodman, **Williams, NI.** Diagnosis of Osteopenia May Indicate the Presence of Increased Cardiovascular Risk in Female Athletes. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004.

R. Hontscharuk, E. O'Donnell, **Williams, NI** T. Burke, M.J. De Souza. Dietary Cognitive Restraint: A Marker for Altered Energy Homeostasis and Menstrual Disturbances in Athletic Women (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S33, 2004.

McConnell, H., **Williams, NI**, E. O'Donnell, B. Lasley, M.J. De Souza. Fasting Ghrelin Levels in Physically Active Women: Relationship with Menstrual Disturbances and Metabolic Status. (*Proceedings of the American College of Sports Medicine meeting, Indianapolis, IN, 2004 Med. Sci. Sports Exerc.* 36 (5), p. S280, 2004)

INVITED PRESENTATIONS

"Cardiovascular/Medical Applications for Aerobic Exercise", *Aerobics and Fitness Association of America (AFAA), National Primary Certification Workshop*, Boston, Massachusetts, October 3, 1987.

"Principles and Benefits of Exercise Training for Seniors", *Annual Health Program, Leo Yasenoff Jewish Community Center*, Columbus, Ohio, June 6, 1987.

"ACSM Certification, Tracts Offered and Benefits Provided", *American College of Sports Medicine, New England Chapter Annual Meeting*, Worcester, Massachusetts, November 2-3, 1989.

"Special Topics for Students", *American College of Sports Medicine, New England Chapter Annual Meeting*, Worcester, Massachusetts, November 2-3, 1989.

"Exercise Testing and Prescription", *Harvard Medical School Department of Continuing Education Conference: "Current Advances in Nutritional Medicine and Disease Prevention: Medical Treatment Strategies"*, Boston, Massachusetts, April 25, 1991

"Eating Disorders and Body Image With Special Emphasis on the Female Athlete", *New York State Association of Physician's Assistants*, Calicoon, NY, April 18, 1998.

"Exercise and Female Hormones: What are the Health Risks and Benefits?" *American College of Sports Medicine Health Fitness Summit*, April 14-18, 1999, New Orleans, LA

"Women's Health and Fitness Issues" *Panel Discussion atAmerican College of Sports Medicine Health Fitness Summit*, April 14-18, 1999, New Orleans, LA

"Modulation of Reproductive Runction by Metabolic Cues", invited speaker for *Bucknell University Biology Department Seminar Series*, March 3, 2000. Bucknell University, Lewisburg, PA

"Career Development for Women" *Women and Sciences and Engineering* (WISE) program for potential college students from surrounding area and other states, June 19, 2000, Penn State University

"Low Energy Availability and the Menstrual Cycle: Clinical and Physiological Implications" *Society for the Study of the Menstrual Cycle, Bi-Annual meeting*, June, 2001, Hartford Connecticut

"Physiological Connections Between Factors of the Female Athlete Triad" *Penn State Athletic Training Conference*", April 12, 2002, Penn State University, University Park, PA

"Exercise and Women's Health: Lessons from the Female Athlete Triad", Department of Health and Exercise Science, April 25, 2002, *Wake Forest University*, Winston-Salem, NC

"Subclinical Eating Disorders and Menstrual Cycle Irregularities in Female Athletes" *Eating Disorders on Campus, The Institutional Response*, June 7, 2002, Eighth Annual Conference, Penn Stater Conference Center Hotel, Penn State University, University Park, PA

"Effects of Exercise on the Menstrual Cycle: Physiological mechanisms and practical considerations" February, 2003, *School of Kinesiology and Health Science*, York University, Ontario, Canada.

"Effects of Estrogen on Vascular Function", February, 2003, *School of Kinesiology and Health Science*, York University, Ontario, Canada.

"Exercise and the Menstrual Cycle: Psychological, sociological, and physiological factors. June, 5, 2003, Keynote for *Society for Menstrual Cycle Research* meeting, Pittsburgh, PA

"Exercise-associated Menstrual Disturbances: Role of Energy Availability", October 10, 2003. *Faculty of Health and Physical Education*, University of Toronto, Toronto, Ontario, Canada.

"Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction", November 24, 2003, *Department of Health and Kinesiology, Texas A and M University*, College Station, TX

"Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction", November 25, 2003, *Department of Nutrition, Texas A and M University*, College Station, TX

"Exercise-associated menstrual disturbances: Physiological mechanisms and role of caloric restriction", December 4, 2003, *Department of Endocrinology, Endocrine Research Conference*, Hershey Medical Center, Penn State University, Hershey, PA

"Exercise-associated menstrual disturbances: Phyiological mechanisms and clinical sequelae", March 2, 2004, Department of Exercise Science, University of Massachusetts, Amherst, MA)

"Exercise-associated menstrual disturbances: Phyiological mechanisms and clinical sequelae", April 30, 2004, Department of Physical Therapy, Faculty of Medicine, University of Toronto, Toronto, Ontario)

SYMPOSIUM PRESENTATIONS

Chairperson, Symposium on "Special Topics of Interest to Students in ACSM", *American College of Sports Medicine, New England Chapter Annual Meeting*, Worcester, Massachusetts, November 2-3, 1989.

"Menstrual Disturbances in Athletes: Lessons from Prospective Experiments on Animals and Humans (Chairperson Anne B. Loucks, PhD) Lessons from Experimental Disruptions of the Menstrual Cycle in Primates and Humans, N. Williams (*American College of Sports Medicine Annual Meeting*, St. Louis, MO, May 30, 2002)

Chairperson, Symposium on "Current Practices for Screening and Prevention of the Female Athlete Triad" (*American College of Sports Medicine Annual Meeting*, San Fransisco, CA, May 31, 2003).

Co-Chairperson, Symposium on "Assessing Endocrine Alterations in Exercising Women". Weight loss and changes in circulating metabolic hormones and metabolic rate as biomarkers for exercise-associated menstrual disturbances: evidence from prospective studies. Proceedings of the *American College of Sports Medicine Annual Meeting*, Indianapolis, IN, 2004)

WORKSHOPS ATTENDED

The X and Y: Current Topics in Gender – Specific Medicine, April 6-7, 2001
Harvard Medical School, Department of Continuing Education, Boston, Massachusetts

SERVICE

PROFESSIONAL SERVICE

COMMITTEES

American College of Sports Medicine Student Affairs Committee,
Student Representative for New England Chapter, 1988-1990

American College of Sports Medicine Executive Committee,
Member at Large, New England Chapter, 1990-1991

American College of Sports Medicine, Strategic Health Initiative Committee: Women, Sports and Physical Activity, June 2000-2002

American Collge of Sports Medicine, Credentials Committee, Spring 2003-present

American College of Sports Medicine, Position Stand Review Committee, "Female Athlete Triad," Spring 2002-present

REVIEWER

Journals *Journal of Applied Physiology, ACSM Health Fitness Journal Medicine, Science, Sports and Exericse, Journal Clinical Endocrinology and Metabolism*

Grants Dissertation Awards, Susan B. Komen Foundation for Breast Cancer Research (2001-2002)

Editorial Board American College of Sports Medicine *Health and Fitness Journal* (2002-present)

Fellow American College of Sports Medicine, June, 1998

Participant "Biopsychology of Infertility Workshop" Sponsored by National Institutes of Health (National Institute of Child Health and Human Development); September 21-22, 1995; NIH Campus, Bethesda, Maryland

UNIVERSITY SERVICE

Advisory Board: The Tremin Trust Research Program on Women's Health, Penn State University, University Park, PA, 2001-present

University Committees

Faculty Senate (Spring 2002)-Senate Committee on Intra-University Relations

College Committees (College of Health and Human Development)

College of Health and Human Development Seed Grant Review Committee (Fall 00)
Faculty Council (Fall 00- Spring 2001)

Intercollege Program Committee (Physiology)

Candidacy Exam Committee (Intercollege Program in Physiology) (Spring 01-present)

Department Committees (Department of Kinesiology)

Curriculum Committee	Fall, 1998 to Spring 2002
Candidacy Committee	Fall, 1998 to 2002
Search Committee (Noll Laboratory Exercise Physiology positions)	Fall, 1998
Search Committee (General Education Fitness Position)	Spring 99
Search Committee (Department of Kinesiology Chair)	Fall 01-Spring 02
Curriculum Revisions (ad hoc)	Spring 01-Spring 02
Advisory Committee for Fitness Assessment Program	Spring 02-present
Search Committee (Director, Noll Laboratory)	Fall 02-Spring 04)
Advisory Committee	Fall 02-present
Search Committee	Spring 2003-present

(Pedagogy Positions)
Search Committee
(Noll Endowed Professorship) Summer 04-present

University Presentations

Fall 1997	Kinesiology Proseminar	"Professional Development"
Fall 1998	Kinesiology Proseminar	"Professional Development"
Fall 1997	Nutrition Ingestive Behavior Journal Club	"Reproductive disturbances and low energy availability: aberrant eating habits"
Fall 1997	Kinesiology Colloguium	"Low energy availability and the female athlete: Clinical and Hormonal Effects"
Fall 1997	Population Research Institute	"Modulation of Reproductive Function by Metabolic Cues"
Spring 1998	Nutrition Dept. Colloquium	"Modulation of Reproductive Function by Metabolic Cues"
Spring 1998	Biobehavioral Health Dept. Colloquiium	"Reproductive disturbances caused by low energy availability: Interaction with psychological stressors"

OTHER SERVICE

News article, Kinesiology Today, Spring 1999 issue, "Study links Body Image to Athletes' Fertility"

Interview/article, The Penn Stater, September/October 1999 issue "Research and Discovery Section" by Nick McCarthy

Interview/article, The Penn Stater, 2000 issue of undergraduate research, "Research and Discovery"

Interview/article, Intercom, July, 1999. featured in "Focus on Research" article, by Barbara Hale.

2000 Undergraduate Exhibition
Served as Judge for the 2000 Undergraduate Exhibition in April, 2000.