BIOGRAPHICAL SKETCH

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NAME: Stefanick, Marcia L.

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POSITION TITLE: Professor of Medicine and Professor of Obstetrics & Gynecology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Pennsylvania, Philadelphia, PA	B.A.	05/1974	Biology
Stanford University, Stanford, CA	Ph.D.	06/1982	Physiology
Stanford Center for Research in Disease Prevention, Stanford University, Stanford, CA	Postdoctoral Fellow	09/1983-86	Cardiovascular Disease Prevention (NHLBI)

A. Personal Statement

I am a Professor of Medicine at the Stanford Prevention Research Center (SPRC) and Professor of Obstetrics & Gynecology, with key leadership roles, including as founding Director of the Stanford Women's Health and Sex Differences in Medicine (WHSDM) Center and Co-leader of Stanford Cancer Institute's Population Science Program. I am PI of the Western Regional Center of the Women's Health Initiative (WHI) Extension Study (2010-2020), was PI of the Stanford WHI Clinical Center (1994-2010) and Chair of the WHI Steering and Executive Committees (SC, EC; 1998-2011), as well as Stanford's PI of WHI ancillary studies, e.g. Coronary Artery Calcification Study, Objective Physical Activity for Cardiovascular Health (OPACH) study, WHI Memory Study (WHIMS), Study of Cognitive Aging (WHISCA), WHI Brain MRI, WHIMS-Younger Cohort (WHIMSY). I am PI of the Current U01 Intervention site of the WHI Strong & Healthy (*WHISH*) pragmatic trial of physical activity (PA) which randomly assigned ~50,000 WHI participants to a PA intervention or "usual activity" control, with major CV events as the primary outcome. I have considerable expertise in lifestyle intervention trials, including single-site (Stanford) NHLBI randomized clinical trials (RCTs) of diet, exercise, and weight loss, i.e. the Stanford Weight Control Projects I & II and Diet and Exercise for Elevated (CV) Risk (DEER) trial, and as PI of the large WHI Diet Modification Trial and ~7-year NCI Women's Healthy Eating and Living (WHEL) trial of 3100 early stage breast cancer survivors. I have also been Stanford's PI of the Osteoporotic Fractures in Men Study (MrOS) since 2001, and PI of several MrOS ancillary studies, e.g. MrOS Sleep Study involving in-home polysomnography and a creatine dilution study of sarcopenia. I have considerable expertise in menopausal hormones and CVD, as PI or Co-PI of the NHLBI Postmenopausal Estrogen-progestin Interventions (PEPI) trial, the Heart and Estrogen-progestin Replacement Study (HERS), and andmark WHI hormone trials, and am now actively involved in research on long-term CV risks of adverse pregnancy, including an NHLBI study of preeclampsia. I direct many undergraduate courses on sex & gender in physiology and health and disease prevention and health promotion, and am core faculty of SPRC's Masters in Community Health and Prevention Research program. I mentor postdoctoral fellows in SPRC's T32 Cardiovascular Disease Prevention Training program, am faculty on T32s in Endocrinology and Nephrology, serve on a joint Advisory Committee for CV Medicine T32s, and have mentored junior faculty on K awards as well as many WHI and MrOS analyses.

1. **Stefanick ML**, Mackey S, Sheehan M, Ellsworth N, Haskell WL, Wood PD (1998). Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. *N Engl J Med*;339(1):12-20. PMID: 9647874
2. Manson JE, Greenland P, LaCroix AZ, **Stefanick ML**, Mouton CP, Oberman A, et al. (2002). Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med*;347(10):716-25. PMID: 12213942
3. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, **Stefanick ML**, Jackson RD, Beresford SA, Howard BV, Johnson KC, Kotchen JM, Ockene J. (2002) Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA*;288(3):321-33. PMID: 12117397

4. Manson JE, Chlebowski RT, **Stefanick ML**, Aragaki AK, Rossouw JE, Prentice RL, Anderson G, Howard BV, Thomson CA, LaCroix AZ, Wactawski-Wende Jean, Jackson RD, Limacher M, Margolis KL, Wassertheil-Smoller S, Beresford SA, Cauley JA, Eaton CB, Gass M, Hsia J, Johnson KC, Kooperberg C, Kuller LH, Lewis CE, Liu S, Martin LW, Ockene JK, O'Sullivan MJ, Powell LH, Simon MS, Van Horn L, Vitolins MZ, Wallace RB (2013). Menopausal hormone therapy and health outcomes during the intervention and extended post-stopping phases of the Women's Health Initiative randomized trials *JAMA* Oct 2;310(13):1353-68. - PubMed PMID: 24084921 PMCID: PMC3963523

B. Positions of Honor and Employment

Employment

1970-1974 Undergraduate work, Univ. of Penn.: German translator; Veterinary Research Assistant
1974-1975 Research Assistant, Oregon Regional Primate Research Center, Beaverton, OR
1975-1976 Research Assistant, Dept. of Physiology, Stanford University, Stanford, CA
1986-1987 Research Associate, Stanford Center for Research in Disease Prevention (SCRDP)
1988-1997 Senior Research Scientist, SCRDP, Dept. of Medicine, Stanford Univ., Stanford, CA
1997-2003 Associate Professor of Medicine, Stanford University, Stanford, CA
2003-present Professor of Medicine (Stanford Prevention Research Center), Stanford Univ,
2003-present Professor of Obstetrics and Gynecology, Stanford University

Other Experience and Professional Memberships and Honors

1976-1981 PHS-NRS Award - Training Grant in Systems Biology (GMO7181-02 thru-06)
1983-1986 Stanford Cardiovascular Disease Prevention Training Grant (T32 HL07034-09-12)
1987 (2001) Fellow of the (A.H.A. and) Council on Arteriosclerosis; Thrombosis, and Vascular Biology
1998-2011 Chair, Women's Health Initiative (Steering &) Executive Committee(s) [elected by WHI PIs]
2009-2010 Iris F. Litt Faculty Fellowship, Clayman Institute of Gender Research
2012-present Director, Stanford Women Health and Sex Differences in Medicine (WHSDM) Center

C. Contribution to Science

1. My early work consisted of a series of 1-2 year RCTs of overweight or high (CV) risk adults to determine independent and interactive effects of physical activity, diet, and weight loss on high and low density lipoprotein (HDL, LDL) cholesterol, with the findings that changes in diet composition (caloric restriction versus dietary fat reduction) strongly influenced weight loss effects of diet, particularly in women, and aerobic exercise, which generally increases HDL-C or prevents diet-induced reduction.
   a. Wood P, **Stefanick ML**, Dreon D, Frey-Hewitt B, et al. (1988) Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *N Engl J Med*;319 (18):1173-9. PMID: 3173455
   b. Wood PD, **Stefanick ML**, Williams PT, Haskell WL. (1991). The effects on plasma lipoproteins of a prudent weight-reducing diet, with or without exercise, in overweight men and women. *N Engl J Med*;325(7):461-6. PubMedID: 1852180
   c. Terry RB, **Stefanick ML**, Haskell WL, Wood PD. Contributions of regional adipose tissue depots to plasma lipoprotein concentrations in overweight men and women: possible protective effects of thigh fat. *Metabolism* 1991;40(7):733-40. PubMedID: 1870428
   d. King AC, Haskell WL, Young DR, Oka RK, **Stefanick ML**. Long-term effects of varying intensities and formats of physical activity on participation rates, fitness, and lipoproteins in men and women aged 50 to 65 years. *Circulation* 1995;91(10):2596-604. PMID: 7743622

2. A second line of research focused on effects of menopausal hormone therapy (MHT) on coronary heart disease, CHD, cognitive function CHD, and bone health in light of substantial observational study evidence of lower CHD, dementia, and osteoporosis in MHT users versus non-users, leading to increased MHT prescriptions older women. In contrast, WHI demonstrated no benefit to CHD (and early harm with combined estrogen and progestin therapy) and adverse effects on dementia, but did show benefit to bone.
   a. Shumaker SA, Legault C, Kuller L, Rapp SR, Thal L, Lane DS, Fillit H, **Stefanick ML**, Hendrix SL, Lewis CE, et al. Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study. *JAMA* 2004; 291(24): 2947-58. PMID: 15213206
   b. Rossouw JE, Prentice RL, Manson JE, Wu L, Barad D, Barnabei VM, Ko M, LaCroix AZ, Margolis KL, **Stefanick ML**. Postmenopausal Hormone Therapy and Risk of Cardiovascular Disease by Age and Years Since Menopause. *JAMA* 2007; 297(13):1465-77. PMID: 17405972

c. Robbins J, Aragaki AK, Kooperberg C, Watts N, Wactawski-Wende J, Jackson RD, LeBoff MS, Lewis CE, Chen Z, **Stefanick ML**, Cauley J. Factors Associated With 5-Year Risk of Hip Fracture in Postmenopausal Women. *JAMA*. 2007 November 28, 2007;298(20):2389-98.
d. Hlatky MA, Ray RM, Burwen DR, Margolis KL, Johnson KC, Kucharska-Newton A, Manson JE, Robinson JG, Safford MM, Allison M, Assimes TL, Bavry AA, Berger J, Cooper-DeHoff RM, Heckbert SR, Li W, Liu S, Martin LW, Perez MV, Tindle HA, Winkelmayer WC, **Stefanick ML**. Use of Medicare Data to Identify Coronary Heart Disease Outcomes In the Women's Health Initiative*. Circ Cardiovasc Qual Outcomes*. 2014 Jan 1;7(1):157-62. - PubMed PMID: 24399330

3. These results led to research on MHT effects on cancer outcomes, with strong evidence of increased breast cancer risk with E+P trial but a suggested reduced risk with E-alone trial.
   a. Chlebowski RT, Hendrix SL, Langer RD, **Stefanick ML**, Gass M, Lane D, et al. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative randomized trial. *JAMA* 2003; 289(24):3243-53. PMID: 12824205
   b. **Stefanick ML**, Anderson GL, Margolis KL, et al. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. *JAMA* 2006; 295(14): 1647-57. PMID: 16609086
   c. Chlebowski RT, Kuller LH, Prentice RL, **Stefanick ML**, Manson JE, Gass M, et al. Breast Cancer after Use of Estrogen plus Progestin in Postmenopausal Women. *N Engl J Med* 2009; 360(6):573-87. PMID: 19196674 PMCID: PMC3963492
   d. Chlebowski RT, Anderson GL, Gass M, Lane DS, Aragaki AK, Kuller LH, Manson JE, **Stefanick ML**, Ockene J, Sarto GE, Johnson KC, Wactawski-Wende J, Ravdin PM, Schenken R, Hendrix SL, Rajkovic A, Rohan TE, Yasmeen S, Prentice RL. Estrogen plus progestin and breast cancer incidence and mortality in postmenopausal women. *JAMA* 2010; 304(15):1684-1692. PMID: 20959578

4. Building on my diet (for CV risk) background, I focused on breast (and colorectal) cancer prevention in the ~8-year WHI Diet trial and breast cancer recurrence in the ~7-year WHEL plant-based diet trial in 3100 early stage breast cancer survivors.
   a. Prentice RL, Caan B, Chlebowski RT, Patterson R, Kuller LH, Ockene JK, Margolis KL, Limacher MC, Manson JE, Parker LM, Paskett E, Phillips L, Robbins J, Rossouw JE, Sarto GE, Shikany JM, **Stefanick ML**, Thomson CA, Van Horn L, et al. (2006). Low-fat dietary pattern and risk of invasive breast cancer: the Women's Health Initiative randomized controlled Dietary Modification trial. *JAMA*;295(6):629-42. PMID: 16467232
   b. Pierce JP, Natarajan L, Caan BJ, Parker BA, Greenberg ER, Flatt SW, Rock CL, Kealey S, Al-Delaimy WK, Bardwell WA, Carlson RW, Emond JA, Faerber S, Gold EB, Hajek RA, Hollenbach K, Jones LA, Karanja N, Madlensky L, Marshall J, Newman VA, Ritenbaugh C, Thomson CA, Wasserman L, **Stefanick ML** (2007). Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: the Women's Healthy Eating and Living (WHEL) randomized trial. *JAMA*; 298(3): 289-98. PMID: 17635889 PMCID: PMC2083253
   c. Pierce JP, **Stefanick ML**, Flatt SW, Natarajan L, et al. (2007). Greater survival after breast cancer in physically active women with high vegetable-fruit intake regardless of obesity. *J Clin Oncol*;25(17):2345-51. PMID: 17557947 PMCID: PMC2274898
   d. Thomson CA, McCullough ML, Wertheim BC, Chlebowski R, Martinez ME, **Stefanick ML**, Rohan TE, Manson JE, Tindle H, Ockene J, Vitolins M, Wactawski-Wende J, Sarto GE, Lane D, Neuhouser ML. (2014) Nutrition and physical activity cancer prevention guidelines, cancer risk, and mortality in the Women's Health Initiative. *Cancer Prev Res (Phila).* Jan; 7(1):42-53. - PubMed PMID:24403289 PMCID: PMC4090781

5. The relationship of physical activity and physical function to body composition, bone health and CVD, in aging adults and those with chronic disease, is a developing research interest. Multiple clinic weight and DXA measurements over decades in both the MrOS and WHI have revealed that loss of physical function and lean mass, not reduced bone mineral density, is the key to falls and fractures in older men and changes in body composition differ among younger versus older postmenopausal women..
   a. Sims ST, Kubo J, Desai M, Bea J, Beasley JM, Manson JM, Allison M, Sequin RA, Chen Z, Michael YL, Sullivan SD, Beresford S, **Stefanick ML**. (2013) Changes in physical activity and body composition in postmenopausal women over time. *Med Sci Sports Exerc*; 45(8):1486-92. [Epub ahead of print Feb 22] PMID: 23439422 PMCID: PMC3715578
   b. **Stefanick ML,** Brunner RL, Leng XI, PhD[3], Limacher MC, Bird CE, Garcia DO, Hogan PE, Mackey RH, Johnson KC, LaMonte MJ, LaCroix A, Robinson JG, Seguin RA, Tindle HA, Wassertheil-Smoller S. The

Relationship of Cardiovascular Disease to Physical Functioning in Women surviving to age 80 and over in the Women's Health Initiative J *Gerontology: Medical Sciences* 2016 Mar, 71 Suppl 1:S42-53. PMID: 26858324

c. Laddu DR, Wertheim BC, Garcia DO, Woods NF, LaMonte MJ, Chen B, Anton-Culver H, Zaslavsky O, Cauley JA, Chlebowski R, Manson JE, Thomson CA, **Stefanick ML**; Women's Health Initiative Investigators. 36-Item Short Form Survey (SF-36) Versus Gait Speed As Predictor of Preclinical Mobility Disability in Older Women: The Women's Health Initiative. J Am Geriatr Soc. 2018 Feb 10. PMID: 29427503

d. Saquib N, Brunner R, Desai M, Kroenke C, Daviglus M, Allen NB, Robinson J, Tindle H, **Stefanick ML**. Changes in physical and mental health are associated with cardiovascular disease incidence in postmenopausal women. *Age Ageing*. 2019 Feb 11. Doi: 10.1093/ageing/afy213. PMID: 30753250

D. Additional Information: Research Support and/or Scholastic Performance
Complete List of Published Work in **MyBibliography:**
http://www.ncbi.nlm.nih.gov/sites/myncbi/marcia.stefanick.1/bibliography/47580354/public/?sort=date&direction=ascending

Ongoing Research Support

HHSN268201100003C (Stefanick) 10/01/10-10/14/20
NIH/NHLBI
Women's Health Initiative Extension 2010-2015 and 2015-2020
Stanford is the Western Regional Center (WRC) of the Women's Health Initiative (WHI) 2010-2020 Extension, which is continuing to follow participants of the clinical trials (CT: hormone therapy; diet modification; and calcium/vitamin D) and observational study, (OS), (1993-2005), who consented to extended follow-up from 2010 on, with full outcome ascertainment of former HT trial and all African American and Hispanic CT and OS participants and cancer outcomes in all others. The WRC is playing a major role in facilitating scientific activities related to cardiovascular disease (with an emphasis on heart failure and atrial fibrillation, as well as CHD, stroke, VTE) and physical activity/body composition.
Role: PI, WHI Western Regional Center

U01HL122280-01 (Stefanick) 02/09/15-01/31/20
NIH/NHLBI
Physical Activity to Improve CV Health in Women: A Pragmatic Trial CCC-Lead
Stanford is the physical activity (PA) intervention site of the WHI Strong & Healthy (*WHISH)* Trial which is testing the hypothesis that a centralized, resource-efficient, and easily delivered public health intervention designed to improve physical activity levels (based on the NIA Go4Life® program) will reduce major cardiovascular disease events, fractures, and other outcomes, including cancer, in a multi-ethnic (particularly black and Hispanic) cohort of 52,000 older women (ages 65-99 years) over 4 -5 years.
Role: PI

5 U01 AG042143-16 (Stefanick) 09/30/99 - 04/30/20
NIH/NIAMS
Osteoporotic Fractures in Men
MrOS site continues to follow ~1000 men aged ≥ 65 yrs at baseline (minus deceased, discontinued) at each of 6 sites to determine: 1) the extent to which fracture risk is related to bone mass (by DEXA), bone geometry, lifestyle factors, biochemical measures, fall propensity and other variables; and 2) relationships between osteoporotic fracture (clinical, & by X-ray and CT) and osteoarthritis, prostate cancer & overall health.
Role: PI, Palo Alto MrOS Clinical Center

5P30CA12443508 (Mitchell) 06/04/07 - 05/31/21
NIH/NCI
Stanford University Cancer Center
The major goal of this project is to build on institutional strengths in both technology development and translational research to foster interdisciplinary collaborations amongst eight programs: Cancer Biology, Radiation Biology, Cancer Stem Cells, Cancer Imaging & Early Detection, Translational Oncology, Immunology & Cancer Immunotherapy, Lymphoma & Leukemia and Population Sciences. Shared resources will support the investigations in experimental and clinical research.

Role: Population Science Program Co-Leader

Stanford Project SPO# 124472 (Stefanick) 07/12/16 - 05/31/20
Transaction #637640 Mars Incorporated
Brigham and Women's Hospital
Randomized trial of cocoa flavanols and multivitamins in the reduction of cardiovascular disease and cancer. The WRC WHI site is responsible for obtaining medical records for WHI-COSMOS participants.
Role: Western Regional Center WHI Extension Study PI

1R01HL130591-01 (Eaton) 08/01/16 - 05/31/21
NIH/Brown University
WHISH 2 Prevent Heart Failure will evaluate the effect of this RCT on incident HF and HF burden (all heart failure hospitalizations and CVD death in those with antecedent HF) as well as perform dose-finding analyses. WHISH-2_Prevent Hearth Failure will be the first, largest, and longest primary prevention exercise trial ever performed in the highest risk group for HF-elderly women. An imbedded accelerometer study will allow for a dose-finding analysis regardless of the RCT results using newly developed MET –equivalent indices for elderly women. The WRC WHI site is responsible for obtaining medical records for Heart Failure reports.
Role: Western Regional Center WHI Extension Study PI

1R01HL136390-01 (Perez) 04/01/17 - 03/31/22
NIH/NHLBI
"The WHI Strong and Healthy SilenT Atrial Fibrillation Recording Study (WHISH STAR)"
Study Goals: To measure the effect of exercise intervention on clinical and asymptomatic forms of atrial fibrillation using loop recorders.
Role: Co-Investigator. Helped designed the project and will help analyze and interpret results of the study.

1R01 HL139844-01A1 (Hlatky) 07/01/18 - 06/30/23
NIH
Preeclampsia to Cardiovascular Disease: Life-Course Analysis of Biomarkers and Risk
The major goal of this study is to define the mediators of increased cardiovascular risk among women who developed preeclampsia during pregnancy (EPOCH).
Role: Principal Investigator

Completed Research Support (last 3 years)

UM1CA1736-02 (Caan) 02/01/15 - 01/31/18
National Cancer Institute/Kaiser Foundation Research Institute
The WHI Life and Longevity After Cancer (LILAC) study, funded by the National Cancer Institute, has been developing a unique resource to support studies of cancer survival, survivorship, and molecular epidemiology. The Stanford WHI team is collaborating by obtaining medical records and helping with the collection of tumor tissue and treatment data on women diagnosed with certain types of cancer, including breast cancer, colorectal cancer, endometrial cancer, ovarian cancer, lung cancer, melanoma, lymphoma, and leukemia.
Role: Principal Investigator of Stanford subcontract

R01 AR065268-02 (Cawthon) 09/16/13-08/31/17
NIH/NIGMS
Determination of Skeletal Muscle Mass by Creatine Dilution
This project was designed to assess skeletal muscle mass to enable us to better characterize aging muscle and its relationship with specific clinical outcomes (falls, mobility limitation). Labeled creatine dilution as a predictor of sarcopenia related outcomes will also be compared with DXA muscle mass data.
Role: Site PI