Collaborating Clinical Site Facilities & Resources

Part I: Contact Information

Please include NIH Biosketches for the PI and Co-Investigators with submission.

Principal Investigator

Name Erin S. LeBlanc, MD, MPH
Position/Title Investigator
Institution/Center Kaiser Center for Health Research
Email Erin.S.LeBlanc@kpchr.org
Address 3800 North Interstate Avenue
Phone 503-528-3996
Fax 503-335-2424
City Portland State OR Zip 97227

How long have you been affiliated with your current institution/center? 42 Months

In the event that you leave your institution before completion of the active phase of the D2d study, please provide a succession plan regarding local leadership for the D2d study:

Dr. Hillier, co-investigator, would be able to take over responsibility for overseeing the trial. There are also several other physician investigators at CHR who could take over leadership of this trial if necessary.

Research Coordinator

Name Lucy Fulton and Suzanne Jones, RN
Email Lucy.Fulton@kpchr.org/Suzanne.M.Jones@kpc
Institution/Center Kaiser Center for Health Research
Phone 503-335-2424
Address 3800 North Interstate Avenue
Fax 503-335-2424
City Portland State OR Zip 97227

Please describe previous research coordination experience, with emphasis on multi-center trials:

We have two excellent clinical staff with long-term experience in clinical trials and research (Ms. Lucy Fulton and Suzanne Jones, R.N.) who will work as a team to coordinate the overall study. Ms. Fulton will serve as the Project Manager while Ms. Jones will serve as Clinic Coordinator. Ms. Fulton has 10 years of experience managing multi-site studies including the MY-FIT study, a study focused on maximizing the yield of the Fecal Immunochemical Test.

Co-Investigators

1) Name Teresa A. Hillier, MD, MS
Email Teresa.Hillier@kpchr.org
Institution/Center Kaiser Center for Health Research
Phone 503-335-2478
Position/Title Senior Investigator
Fax 503-335-2424

Please describe expected roles in the D2d study (*e.g. recruitment, participant management, study physician, etc)*:

Dr. Hillier will serve as Co-Investigator for this project, including supporting overall PI Dr. LeBlanc as needed for recruitment and conduct of the trial. As Co-I, Dr. Hillier will also supervise the acquisition of data and participate in monitoring and ensuring protocol adherence.

2) Name
Email
Institution/Center
Phone
Position/Title
Fax

Please describe expected roles in the D2d study (*e.g. recruitment, participant management, study physician, etc)*:

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Part II: Site-specific Recruitment Strategy and Patient Population

1. Please provide a site-specific recruitment strategy for the D2d trial. Please include methods the site has successfully used in the past for similar trials, including the use of electronic databases to identify participants, outreach efforts etc.
Details about electronic databases will be provided in the next question.

At the Center for Health Research (CHR), we have been successfully recruiting participants into large multi-center trials for over 30 years. One of these large multi-center studies (Study of Osteoporotic Fractures, SOF), for which CHR investigators recruited 2,579 post-menopausal women in 1986-88, is still ongoing with excellent retention (met 95% of target for recent questionnaire completion); Dr. Hillier has been PI for SOF at CHR since 2000. We have recruited as few as 30 and as many as 3,000 participants for studies of multiple types of interventions including menopausal hormone therapy (e.g., Women's Health Initiative), weight loss programs (e.g., Premier), and weight loss maintenance programs (e.g. Weight Loss Maintenance or WLM). In recent years, use of the Kaiser Permanente NW electronic medical record system to identify patients with specific diagnosis codes, labs, or medications has allowed us to successfully recruit very specialized populations (e.g., pregnant women in a certain trimester and women in a specific stage of menopause).

CHR researchers have been able to successfully meet recruitment goals because of our affiliation with KPNW. Currently, the KPNW health plan enrolls some 480,000 members in Oregon and southwest Washington. The ability to draw from this large population allows our researchers to generate sample sizes that are sufficiently powered to detect treatment effects. KPNW maintains comprehensive administrative and clinical electronic medical records (EMR) that track all of the medical care its members receive including outpatient visits, laboratory tests, and pharmacy dispenses. We have extensive experience with collecting, merging, and analyzing complex databases and we are expert at using the EMR to identify eligible participants.

We have designed the recruitment strategy based on our extensive experience with recruiting using the EMR. The first step will be to use the KPNW EMR to identify persons 30 years or older who meet BMI and pre-diabetes criteria (by ICD codes or by A1c levels); persons with orders or dispenses for diabetes medicines or other exclusion criteria will not be included in the potential participant pool. At the start of study recruitment, we will identify currently enrolled members who have met inclusion criteria in the previous 12 months. During the 17 months of recruitment, we will identify persons with newly diagnosed pre-diabetes by using bi-monthly EMR pulls. We expect this will easily give us adequate recruitment numbers, but if needed, we could extend the pull further back (e.g. to persons with prediabetes in the 3 years prior).

To decrease the number of screening visits that end in screen failure, we will conduct a brief chart review to look for excluded conditions (expected number of chart reviews=950). CHR staff have more than 30 years of medical record review experience and can efficiently check for ineligibility prior to further outreach. We will send potentially eligible participants a personalized letter explaining the study and contact them within 7 days to briefly screen them for eligibility and interest (focusing on criteria not captured in EMR or chart abstraction). A tracking system will provide efficient communication in the timing of call attempts to ensure properly timed calls and calls at various times and days (including weekends and evenings). In a recent large CHR study, MY-FIT (described below), CHR staff have achieved an overall success rate of ~97% in reaching participants and ~60% of those contacted have agreed to participate in the trial. Based on our experience, we estimate that 56% of those who are potentially eligible after the chart review will move on to the next stage of recruitment.

Potentially eligible and interested participants without two positive screening laboratory results documented in the EMR within the time window will undergo verbal consent and then be asked to have a screening test (fasting plasma glucose and/or hemoglobin A1c) done at a local Kaiser laboratory. We have used verbal consent for pre-screening laboratory testing in previous CHR studies with good success (see letter from Dr. Plaut, IRB chair). Only participants who meet full laboratory criteria for study eligibility will be invited to a screening visit (estimated to be 56% of participants who get screening labs done).

There are currently 43,598 KPNW patients aged 30 or over with a BMI greater than 25 and A1C levels consistent with pre-diabetes but no dispenses for diabetes medications within the last three years. We will therefore need a recruitment rate of only 0.04% to recruit 160 participants (9 to 10 per month). We have used similar recruitment techniques in previous studies with a 10-14% recruitment rate.

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Part II: Site-specific Recruitment Strategy and Patient Population

2a. Existing Databases. Please provide a detailed description of databases the investigative team **can access** to identify potentially eligible participants for the D2d study (e.g. electronic medical records, research participant registries). Please describe whether databases include relevant information such as age, gender, ethnicity, BMI, current medication use and results of recent laboratory tests (e.g. fasting glucose, hemoglobin A1c) that will help the investigators identify potential participants by querying the database. Please describe any barriers in accessing the databases (e.g. access processes that are time consuming, costly, etc).

Please attach to the application a letter from the appropriate institution official (e.g. IRB, information technology, Chief of Primary Care) stating support for the use of EMR.

We routinely use the KPNW EMR to identify potential participants for studies by identifying medical conditions, laboratory tests, and medications that meet inclusion and exclusion criteria. KPNW maintains administrative and clinical databases that are available to CHR investigators. In addition, CHR has developed and continues to maintain other databases that are used exclusively for research purposes. These databases are populated by data from KPNW's electronic administrative systems, from CHR's research data systems, and from the health plan's computerized clinical information system, HealthConnect. These systems are linked using members' unique health record numbers, which never change. KP HealthConnect is the automated clinical information system used in all Kaiser Permanente medical facilities across the organization's seven regions. It is the world's largest private deployment of an electronic medical record system, providing direct, immediate, and easily accessible information on the medical histories, diagnostic findings, and treatments of 9.1 million patients, who are securely connected to more than 16,000 physicians in almost 600 medical offices and 37 hospitals. The KPNW region's HealthConnect system contains the medical records of about 480,000 members. KP HealthConnect automatically links a patient's record with other databases, such as the laboratory information system and inpatient and outpatient pharmacy databases (described below) to provide complete health and medical history. This system contains information on health problems, physical findings, tests ordered, medications prescribed, therapies ordered, and progress notes. KP HealthConnect facilitates large-scale research by providing CHR scientists with an automated source of diagnoses and procedures. The automated outpatient pharmacy system records all prescriptions dispensed by KPNW outpatient pharmacies. KPNW pharmacies dispense more than two million outpatient prescriptions annually. An estimated 90% of all prescriptions are filled at a health plan pharmacy, including those for members without a prepaid drug benefit. While KPNW has a formulary of recommended medications, physicians may prescribe any marketed drug. The outpatient pharmacy system tracks over-the-counter medications, such as aspirin and niacin, to monitor adverse effects. Data from this system are linked to administrative and research databases containing detailed information on the patient, clinician, and medication for each dispensed prescription. The integrated laboratory information system database includes all KPNW laboratory procedures, including test orders and specimen tracking, results interpretation and reporting, cumulative patient reporting, anatomical pathology, and clinical laboratory test results, blood bank testing results, and cytogenetics test results and interpretations. A relational research database provides CHR researchers with data elements for each procedure.

2b. Estimated number of available participants.

Please query your institution's electronic medical record database for all active (within the last three years) patients and complete the following table. Please provide as much information as possible.

Total active patients	
Age > 30	311,065
Age > 30 **and** BMI > 25	207,117
Age > 30 **and** BMI >25 **and** no diabetes medications	288,083
Age > 30 **and** BMI >25 **and** no diabetes medications **and** 5.8 < HbA1c < 6.5%	43,598

Please query your research participant registry (if available) and complete the following table.

Total volunteers	
Age > 30	
Age > 30 **and** BMI > 25	
Age > 30 **and** BMI >25 **and** no diabetes medications	
Age > 30 **and** BMI >25 **and** no diabetes medications **and** 5.8 < HbA1c < 6.5%	

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Part II: Site-specific Recruitment Strategy and Patient Population

3a. Targeted/Planned Enrollment Table

Study Title: **D2d study at** (*please insert name of site*)	Center for Health Research NW, Kaiser Permanente
Total Planned Enrollment:	160

TARGETED/PLANNED ENROLLMENT: Number of Subjects

Ethnic Category	Females	Males	Total
Hispanic or Latino	5	5	10
Not Hispanic or Latino	75	75	150
Ethnic Category: Total of All Subjects *	80	80	160
Racial Categories			
American Indian/Alaska Native	1	1	2
Asian	5	5	10
Native Hawaiian or Other Pacific Islander	1	1	2
Black or African American	3	3	6
White	70	70	140
Racial Categories: Total of All Subjects *	80	80	160

The "Ethnic Category: Total of All Subjects" must be equal to the "Racial Categories: Total of All Subjects."

3b. Please provide a brief justification of the planned ethnic/racial distribution of the target population, including availability of interpreter services.

Based on the current ethnic breakdown of our health plan membership, we would anticipate that approximately 6% of those recruited would be Hispanic/Latino and 13% non-White. However, we are able to identify race and gender through the KPCHR EMR. Given our large recruitment pool, we can easily over-recruit minorities or target recruitment of particular race/ethnic groups if desired.

Each study at CHR determines its ability to recruit non-English speaking participants. If the decision is to reach out to members who may not speak English, then the study provides translated documents and staff with appropriate language skills. For MY-FIT, documents were translated into Spanish, and a Spanish-speaking staff member was deployed as needed for phone calls. CHR has also prepared for in-person clinic visits with non-English speaking participants (De Por Vida study). For that study, a Spanish speaking staff person handled all visits.

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Part III: Clinical Trial Experience

Have you ever been involved in a clinical trial enrolling participants with pre-diabetes? Yes ☐ No ☑

Please provide the following information for up to five relevant (pre-diabetes, obesity, type 2 diabetes, vitamin D) trials the* PI, Coordinator or Co-Investigator *was involved in during the past five years, with emphasis on multi-center trials in the current institution. If the PI is new to the institution, please provide experience at his/her previous institution.

1) Trial name Early Screening for Gestational Diabetes (EarlyGDM)

Institution/Center KPNW Center for Health Research

Sponsor NICHD

Role in study: Principal Investigator

Multi-center trial? Yes ☐ No ☑

Participant population (key eligibility criteria):

Clinicaltrials.gov #

For this study, we demonstrated successful recruitment using a very difficult recruitment strategy to find the eligible population from a very small recruitment pool. This indicates that with a large recruitment pool (i.e., >43,000 for the proposed D2D), our site can clearly be successful.

For this EarlyGDM study, we initiated a new screening program for all high-risk obese pregnant women in both KPNW and KP-Hawaii regions that was done by 2-step screening (50g 1 hour nonfasting glucose challenge test [GCT], followed by 3-hour fasting OGTT if GCT+). We wanted to evaluate the

Recruitment methods:

For the D2d study, we will be able to start with one large initial EMR pull of >43,000 eligible members to begin recruitment.

In contrast, for EarlyGDM, our statistician had to do weekly pulls to identify new pregnant women who had also completed early GCT screening, so our recruiter could quickly confirm their continuing pregnancy in the EMR, then recruit them to have 3-hour OGTT testing before they "timed out" on potential eligibility (were 18 weeks gestation or greater). For the OGTT testing, this was only an eligible pool of 191 women over 13 month period. It was thus

Intervention:

This was not a recruitment for intervention, but for additional laboratory testing to evaluate sensitivity and specificity of lab testing. Recruitment is totaled for both groups below, but detailed by group in the primary outcome section. We are still doing final analyses for this study, so have not calculated ethnic breakdown but typically for KPNW would be 80-85% Caucasian, with Hispanic, African American, and Asian, Native Hawaiian and Pacific Islander

Primary outcome(s):

Despite the challenges of only having a total recruitment pool of 191 women over more than year period, we successfully recruited 22 women (>10%) to have OGTT. For those +GCT that only needed a HbA1c (pool of 74 women), we recruited 30 (41%). Both of these represent extraordinary recruitment percentages given the challenge of a couple week window in early pregnancy, especially for the OGTT which required dedicating an entire morning during

Recruitment breakdown:

Number of participants:

Targeted	265	
Enrolled	52	
Enrolled:Targeted rate (%)	21	%
Recruitment period:	13	Months

Please provide explanation below if final enrollment was lower than originally anticipated.

The number 265 represents the total number of women at KPCHR and KP-Hawaii who met our inclusion criteria in the EMR. We were able to recruit 21% of them for this study. This represents an extraordinary recruitment percentage given the challenge of the very short time window during which we had to recruit them and the significant amount of additional laboratory testing they had to undergo.

This was recruitment for one lab test (no follow-up), which is why retention for this study was 100%.

Completed follow-up*	100	
Retention rate (%) (Completed : Enrolled)	100	%
Duration of follow-up:		Months

**Number of participants reached outcome or completed last visit*

Gender, ethnicity and race breakdown:

Female		%
Hispanic or Latino		%
Unknown		%
American Indian/Alaska Native		%
Asian		%
Native Hawaiian or other Pacific Islander		%
Black or African American		%
White		%
More than one race		%
Unknown		%

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Part III: Clinical Trial Experience

2) Trial name Pilot trial of effects of vitamin D on menopausal symptoms

Institution/Center KPNW Center for Health Research

Sponsor Oregon Clinical & Translational Research Insti

Role in study: Principal Investigator

Multi-center trial? Yes ☐ No ☑

Participant population (key eligibility criteria):

Clinicaltrials.gov # _____

We recruited a highly selected population for this small pilot randomized clinical trial of the effects of vitamin D vs placebo on body composition and menopausal symptoms. We studied overweight and obese women in the menopausal transition or early postmenopause (based on menstrual cycle changes) who had vitamin D levels between 10-30 ng/ml and suffered from menopause-related symptoms. Other inclusion criteria included weight stability (+/- 5%) for 3-months, non-smoking, not taking medications that affect body weight, no prior bariatric surgery, no contraindications to vitamin D

Recruitment methods:

Unlike the proposed D2d trial that will have a large recruitment pool identified by the EMR, this pilot trial had extremely difficult recruitment because the main inclusion criteria (being in the menopausal transition with menopausal symptoms) were not easily identifiable through the EMR (most women do not see their physicians about their menopausal stage or symptoms). We first used the EMR to identify women who were aged 40-55, overweight or obese, and did not meet exclusion criteria (e.g., non-smoking, not taking medications that affect body weight, without prior bariatric surgery). We sent letters to

Intervention:

This was a randomized clinical trial of vitamin D tablets vs matching placebo.

Primary outcome(s):

Despite the challenges of needing a highly selected population of women in a particular stage of life (and not being able to identify this criteria through the EMR), we were able to recruit 6 to 7 women per month. We will have no problem recruiting 5-10 participants per month for the D2d trial given the much

Recruitment breakdown:

Number of participants:

Targeted	50	
Enrolled	33	
Enrolled:Targeted rate (%)	66	%
Recruitment period:	5	Months

Please provide explanation below if final enrollment was lower than originally anticipated.

This was a pilot study with limited funds for a short time. Therefore, given the highly selected study population and the inability to identify potentially eligilible subjects using the EMR, we did not meet our target (which was based on our funding amount).

Because of problems with the pharmacy that compounded our vitamin D pills, we had to pause the study and re-randomize women. Several participants chose to drop out at this point leading to a lower retention rate than is usual for trials conducted at CHR (see other studies described in this section and CHR facilities section for description of excellent retention in previous CHR studies)

Completed follow-up*	23	

**Number of participants reached outcome or completed last visit*

Retention rate (%) (Completed : Enrolled)	70	%
Duration of follow-up:	9	Months

Gender, ethnicity and race breakdown:

Female	100	%
Hispanic or Latino		%
Unknown		%
American Indian/Alaska Native		%
Asian		%
Native Hawaiian or other Pacific Islander		%
Black or African American		%
White	80	%
More than one race		%
Unknown		%

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Part III: Clinical Trial Experience

3) Trial name MY-FIT (Maximizing the Yield of Fecal Immunochemical Tests)

Institution/Center CHR

Sponsor NCI

Role in study: Coordinator

Multi-center trial? Yes ☐ No ☑

Participant population (key eligibility criteria):

Clinicaltrials.gov # NCT01634126

Ms. Fulton, the proposed project manager for D2d at CHR, is the study coordinator of MY-FIT. This study of the predictive value of Fecal Immunochemical Tests (FIT) tests recruited KP health plan members aged 50-75 with a screening colonoscopy referral from their Primary Care Physician. Those with a recent colonoscopy or flexible sigmoidoscopy, certain medical conditions (e.g. colorectal cancer, history of adenoma, Irritable Bowel Syndrome (IBS), rectal bleeding, weight loss/iron deficiency of unknown cause, active cancer treatment) were excluded.

Recruitment methods:

Potentially eligible KP participants were identified through the EMR. It was a complicated identification process involving over 100 diagnosis codes. After eligible patients identified by the EMR were loaded into a dedicated tracking system, they were contacted by phone and, after informed consent, asked additional questions regarding medical history and symptoms, medications, and family history.

Intervention:

Patients with a colonoscopy referral are asked complete 2 FIT tests prior to the procedure. The goal was to compare sensitivity, specificity and positive/negative predictive value of the FIT KITS vs. colonoscopy.

Primary outcome(s):

Ms. Fulton's success in the MY-FIT study reflects the great potential of our proposed recruitment method (EMR identification with follow-up letters and phone calls) for the D2d study.

Recruitment breakdown:

Number of participants:

Targeted	2100	
Enrolled	2919	
Enrolled:Targeted rate (%)	139	%
Recruitment period:	30	Months

Please provide explanation below if final enrollment was lower than originally anticipated.

Recruitment is still ongoing with recruitment ending on 10/2014. There are no follow-up data yet as the study is still in the recruitment phase.

Completed follow-up*		
Retention rate (%) (Completed : Enrolled)		%
Duration of follow-up:		Months

*Number of participants reached outcome or completed last visit

Gender, ethnicity and race breakdown:

Female	54	%
Hispanic or Latino		%
Unknown		%
American Indian/Alaska Native		%
Asian		%
Native Hawaiian or other Pacific Islander		%
Black or African American		%
White	82	%
More than one race		%
Unknown		%

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Part III: Clinical Trial Experience

4) Trial name Healthy Moms

Institution/Center KPNW Center for Health Research

Sponsor NICHD

Role in study: Select One:

Multi-center trial? Yes ☐ No ☑

Participant population (key eligibility criteria):

Clinicaltrials.gov # NCT00950235

This trial was conducted at CHR by close collaborators of Drs LeBlanc and Hillier. We describe the study because it used EMR to identify potential participants similar to the recruitment procedure that we propose for our site for the D2d trial. We regularly consult with our colleagues on studies and the support staff (programmers and research analysts) who assist with recruitment through the EMR worked on Healthy Moms. Healthy Moms was a randomized clinical trial of a behavioral weight loss intervention during pregnancy. Obese women before 21 weeks gestation were eligible. Women with

Recruitment methods:

KPNW's electronic medical record was used to identify potentially eligible participants. Eligible participants were then sent invitations by mail and followed up by telephone. Of the 2,279 identified as being potentially eligible through the EMR, 2,166 (95%) completed a screening phone call. Of these, 55% were verified to be eligible at the screening phone call and 10% of these were interested in joining the intervention.

Intervention:

Those randomized to the intervention had two individual nutritional counseling sessions followed by weekly 90 minute group meetings throughout their pregnancy.

Primary outcome(s):

The Healthy Moms study staff, which was targeting a much smaller pool (approximately 2,300 women in early pregnancy) than the untreated prediabetic pool at KPNW (>43,000), were able to identify and contact close to 60 eligible participants per month. The inability to meet their target recruitment was

Recruitment breakdown:

Number of participants:

Targeted	160	
Enrolled	116	
Enrolled:Targeted rate (%)	73	%
Recruitment period:	20	Months

Please provide explanation below if final enrollment was lower than originally anticipated.

The low recruitment rate was not due to a lack of being able to identify potential participants by using the KPNW EMR; rather, it was due to women's resistance to joining a study that involved an intense intervention of weekly meetings focused on lifestyle changes.

Completed follow-up*	112	

**Number of participants reached outcome or completed last visit*

Retention rate (%) (Completed : Enrolled)	95	%
Duration of follow-up:	6	Months

Gender, ethnicity and race breakdown:

Female	100	%
Hispanic or Latino		%
Unknown		%
American Indian/Alaska Native		%
Asian		%
Native Hawaiian or other Pacific Islander		%
Black or African American		%
White	85	%
More than one race		%
Unknown		%

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Part III: Clinical Trial Experience

5) Trial name LIFE

Institution/Center KPNW Center for Health Research

Sponsor NIH

Role in study: Select One:

Multi-center trial? Yes ☐ No ☑

Participant population (key eligibility criteria):

Clinicaltrials.gov # NCT00526565

This is a study conducted by close collaborators of Drs LeBlanc and Hillier at CHR. This is another example of a recent trial that used similar recruitment techniques to what we propose to use in the D2d study. LIFE recruited obese adults who had successfully completed a weight loss program. There were multiple exclusions including having particular medical conditions (e.g. cancer treatment) or diabetes, use of weight loss medications, or history of bariatric surgery.

Recruitment methods:

The first step was a query of the KPNW EMR to identify those who met eligibility requirements. Potentially eligible participants were sent letters inviting them to participate in the study. Participants had to call CHR or access a study website in order to schedule an information session.

Intervention:

Participants were randomized into one of two weight loss maintenance interventions: tapas acupressure technique vs social support.

Primary outcome(s):

14,750 potentially eligible participants were identified through the EMR and sent brochures. 2122 potential participants expressed interest in the study by either calling CHR or accessing a website. 1344 people went on to schedule an information session, 428 (32%) by calling into the research center about

Recruitment breakdown:

Number of participants:

Targeted	288	
Enrolled	285	
Enrolled:Targeted rate (%)	99	%
Recruitment period:	13	Months

Please provide explanation below if final enrollment was lower than originally anticipated.

Completed follow-up*	250	

**Number of participants reached outcome or completed last visit*

Retention rate (%) (Completed : Enrolled)	88	%
Duration of follow-up:	12	Months

Gender, ethnicity and race breakdown:

Female	80	%
Hispanic or Latino		%
Unknown		%
American Indian/Alaska Native		%
Asian		%
Native Hawaiian or other Pacific Islander		%
Black or African American		%
White	94	%
More than one race		%
Unknown		%

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Part IV: Competing Trials

Please provide information for each clinical trial being conducted within your institution or catchment area recruiting participants with pre-diabetes in the next four years.

1) Name of competing clinical trial _____

Principal Investigator _____ Sponsor _____

Participant population (key eligibility criteria):

Intervention:

Primary outcome(s):

Enrollment period: _____/_____ to _____/_____
Month Year Month Year

2) Name of competing clinical trial _____

Principal Investigator _____ Sponsor _____

Participant population (key eligibility criteria):

Intervention:

Primary outcome(s):

Enrollment period: _____/_____ to _____/_____
Month Year Month Year

3) Name of competing clinical trial _____

Principal Investigator _____ Sponsor _____

Participant population (key eligibility criteria):

Intervention:

Primary outcome(s):

Enrollment period: _____/_____ to _____/_____
Month Year Month Year

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Part V: Description of Local Clinical Facilities

Please provide the following information about existing clinical site facilities at the site. All necessary facilities and equipment should be available for the D2d trial. No additional facilities or equipment will be requested during the grant application.

1. Please describe where participants will be seen for visits (*e.g. office space, examination rooms, phlebotomy chairs, secure areas for study files)*:

The Center for Health Research Northwest has an onsite clinic to collect specimens and measurements for research protocols. The clinic occupies 4,000 square feet at CHR. It includes a reception and waiting area, a lab, a pharmacy space, and 15 private rooms for interviews, physical exams, blood pressure monitoring, spirometry, abdominal ultrasound, bone density measurement by DXA, and general data collection. Staff provide a full range of clinical trial services including trial management, recruitment, clinical measures, telephone and in person follow-up, and data entry. Clinic staff also see study participants at community sites and conduct home visits. The clinic laboratory is fully equipped so that staff can perform phlebotomy, blood processing, specimen storage, and CLIA-waived laboratory testing. A key element of the research clinic is a scalable model for staffing. This means that the clinic can quickly expand its capacity through its network of trained nurses, nurse practitioners, project managers, physician assistants, clinical trial research assistants, and other health care providers in order to rapidly meet the needs of a given study. Currently, there are 13 full and part-time staff in the clinic, but this number varies a great deal depending on study needs. Several clinic features, such as integrated recruitment and follow-up activities, a robust appointment system, and retention best practices, support high follow-up and retention rates. The appointment system tracks visit outcomes, ensures that appointments are made within protocols, and provides reports on individual and trial-wide visit completion. The system includes online tools that support creation of reminder post cards, visit-related mailings, and completion of reminder phone calls. The system also provides online tools for case management of missed visits and integrates with trial-wide tracking systems to share demographic data, visit-scheduling data, and visit-outcome data.

2a. Please describe laboratory facilities (*e.g. processing, storage, shipping of biological material; experience of laboratory staff*):

The clinic laboratory is fully equipped so that staff can perform phlebotomy, blood processing, specimen storage, and CLIA-waived laboratory testing. The laboratory is equipped with two -70 freezers, a -20 freezer, a refrigerator/freezer, two refrigerated centrifuges, and one room-temperature centrifuge. All freezers, refrigerators, and the pharmacy space temperature are monitored continuously by the TempTrak® system, and the KP regional security dispatch office provides round-the- clock reporting if an alarm goes off. Research clinic staff have access to KP HealthConnect, Kaiser Permanente's electronic medical record system. Study staff can order a range of clinical tests, and samples can be taken for studies either in CHR's clinical area or in medical offices throughout the region. Samples can be analyzed in KP labs, and results reported through KP HealthConnect.

2b. Do you have a frozen centrifuge that can be used for D2d? Yes ☐ No ☑

2c. Do you have a -80°C freezer that can be used for D2d? Yes ☐ No ☑

3a. Does your site have an investigational pharmacy? Yes ☐ No ☑

3b. Please describe the procedures established for secure storage and dispensation of study pills:

Our site has experience with drug accountability on clinical trials. Currently we have a double-blinded trial where study medications are stored and distributed. We have utilized the Kaiser Permanente Northwest region's pharmacies for dispensing prescription medications; pharmacists have received both protocol-specific and GCP training. Non-prescription drugs are stored in a locked, temperature monitored/controlled room at the Research Clinic. Drug accountability logs document the date study drug is received, the drug number, the date dispensed, to whom, the date returned to clinic and the date the medications are returned to sponsor. Visit-specific source documents note the drug assignment number from the IVRS system, the date/visit dispensed, the number of drug returned from the previous visit with a pill count and compliance. The staff is familiar with the use of an IVRS system for randomization assignment of study medications. Quality assurance methods are in place to ensure the correct bottles are dispensed. Storage is available

4. Please describe experience with electronic data capture systems:

The CHR Research Clinic staff are well versed in the collection and maintenance of data via electronic data capture (EDC) systems. We are currently using four unique EDC systems on four separate clinical trials. The data management process begins with the development of source documents that correspond with EDC pages and meet good clinical practice (GCP) guidelines for our participants and staff. Timely data entry following visits allows for quality control of the data collected identifying inconsistencies, transcription errors, deviations from the protocol and any potential adverse events. Bi-weekly checks of the EDC system ensure an up-to-date data base. We provide prompt and accurate response to data queries (usually within 48 hours) by working with the coordinating center, CRA, or sponsor directly as needed.

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Part V: Description of Local Clinical Facilities

5a. Name of local IRB: KPNW IRB

5b. How often does the local IRB meet? 1 times per Month

5c. Please describe protocol submission process and timeline for approval by local IRB:

The full IRB meets monthly on the 3rd Wednesday of the month. Studies needing full IRB review that are submitted by the first of the month will be reviewed at that month's meeting. Investigators will be notified within one week of the status of their application. Revisions are reviewed on a rolling basis and do not have to go to full board if they meet the requirements of being expeditable per federal guidelines. Studies that are deemed minimal risk are evaluated on a rolling basis by the IRB chair and do not require full IRB board review.

Please consult with your IRB before responding to the following two questions:

5d. Can the site use a Central IRB *specifically for the D2d study*? Yes ☐ No ☑
Please note that some institutions utilize a central IRB but only select studies qualify for a Central IRB.

If yes, name of central IRB: _____

5e. Would your institution consider ceding IRB oversight to another academic IRB via an IRB Authorization Agreement (IAA)?

☐ Yes, my institution would consider an IAA

☑ No, my institution would not consider an IAA

Please return completed form with PI and Co-Investigator Biosketches to D2d@tuftsmedicalcenter.org.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Erin S. LeBlanc, MD, MPH	Investigator
eRA COMMONS USER NAME LEBLANC	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Stanford University, Palo Alto, CA	B.S.	06/91	Biology
Yale University School of Medicine, New Haven, CT	M.D.	05/95	Medicine
Stanford University, Palo Alto, CA	Residency	06/95-06/98	Internal Medicine
Portland VA Medical Center, Portland, OR	Fellowship	07/98-06/00	Women's Health
Oregon Health & Science University, Portland, OR	M.P.H.	06/00	Epidemiology
Oregon Health & Science University, Portland, OR	Fellowship	07/00-06/03	Endocrinology and Metabolism

A. Personal Statement

I am a board-certified adult endocrinologist with more than 10 years of clinical experience in managing endocrinology issues, including vitamin D deficiency and diabetes, and I am an investigator at the Center for Health Research. My post-graduate training in women's health and epidemiology has guided my research focus on women's health issues across the lifespan, including obesity, dyslipidemia, type 2 diabetes, dementia, osteoporosis, and menopausal symptoms. I am also an MPH-level epidemiologist with experience in designing and running randomized controlled trials (RCTs). As a Fellow in Building Interdisciplinary Research in Women's Health, and as part of my K-23 award, I designed and implemented an RCT examining estrogen's effects on cognition and menopausal symptoms in early menopausal women. I also designed and implemented FLASH, a pilot randomized clinical trial examining the effects of vitamin D on menopausal symptoms and body composition. In these studies, I successfully recruited menopausal women, randomized them to treatment arms, followed them during the study, and oversaw data collection and analysis. I will serve as site PI for the D2d trial.

I have been an investigator on several multicenter trials, including site PI of the Women's Health Initiative and co-investigator on the Study of Osteoporotic Fractures (SOF), a long-term prospective cohort study of bone health and aging in 9,704 women. I have led the USPSTF review on screening and treatment of adult obesity and am currently leading the 2012-2014 USPSTF review of screening for Vitamin D for disease prevention. I joined CHR three years ago and through my research efforts there have greatly expanded my population, outcomes, and epidemiology expertise. Teresa Hillier, MD (PI of the Study of Osteoporotic Fractures) actively mentored me during my Vitamin D RCT pilot study, including helping to ensure successful recruitment and completion of study visits. In the D2d trial, I will be able to use, and extend, my considerable expertise to lead the D2d RCT, while still being supported by a senior mentor with complementary expertise, and by the extensive infrastructure to support clinical trial research at CHR that will include utilizing the KPNW membership as our population for EMR recruitment.

B. Positions and Employment

2012-present	Investigator, Kaiser Permanente Center for Health Research (TCHR)
2009-2012	Contract Investigator, Kaiser Permanente Center for Health Research (TCHR), Portland, OR
2012-present	Affiliate Assistant Professor of Medicine, Division of Endocrinology and Metabolism, Oregon Health & Science University, Portland, OR
2009-2012	Adjunct Assistant Professor of Medicine, Division of Endocrinology and Metabolism, Oregon Health & Science University, Portland, OR
2008-2009	Clinical Investigator, Kaiser Permanente Center for Health Research (TCHR), Portland, OR
2003-2009	Assistant Professor of Medicine, Division of Endocrinology and Metabolism, Oregon Health & Science University, Portland, OR

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. LeBlanc ES, Kubo J, Desai M, Perrin N, Wactawski-Wende J, Manson JE, Cauley JA, Michael YL, Tang J, Womack C, Song Y, Johnson KC, O'Sullivan MJ, Woods N, Stefanic ML. Vitamin D levels and menopause-related symptoms. Menopause. (in press)
2. LeBlanc E, Rizzo JH, Pedual KL, Ensrud KE, Cauley J, Hochbert M. Hillier for the Study of Osteoporotic Fractures TA. Associations between 25-hydroxyvitamin D and weight gain in elderly women. *J Womens Health (Larchmt)* 2012 2012 Oct; 21(10):1066-73. [Epub 2012 Jun 25] PMCID: PMC3466912
3. LeBlanc ES, Perrin N, Johnson JD Jr., Ballatore A, Hillier T. Over-the-counter and compounded vitamin D: Is potency what we expect? *JAMA Intern Med* 2013 Apr 8; 173(7):585-6 PMID:23400578
4. Ryckman KK, Rillamas-Sun E, Spracklen MS, Wallace RB, Garcia L, Tylavsky FA, Howard BV, Liu S, Song Y, LeBlanc ES, White MV, Parikh NI, Robinson JG. Ethnic Differences in the Relationship between Birth weight and Type 2 Diabetes Mellitus in Postmenopausal Women. *Diabetes and Metabolism.* (in press)
5. Prentice RL, Pettinger MB, Jackson RD, Wactawski-Wende J, LaCroix AZ, Anderson GL, Chlebowski RT, Manson JE, Van Horn L, Vitolins MZ, Datta M, LeBlanc ES, Cauley JA, Rossouw J. Health risks and benefits from calcium and vitamin D supplementation: Women's Health Initiative clinical trial and cohort study. *Osteoporos Int* 2013 Feb; 24(2):567-80. [Epub 2012 Dec 4] PMCID: PMC3557387
6. Engelman CD, Meyers KJ, Iyengar SK, Liu Z, Karki CK, Igo RP Jr, Truitt B, Robinson J, Sarto GE, Wallace R, Blodi BA, Klein ML, Tinker L, LeBlanc ES, Jackson RD, Song Y, Manson JE, Mares JA, Millen AE. Vitamin D intake and season modify the effects of the GC and CYP2R1 genes on 25-hydroxyvitamin D concentrations. *J Nutr* 2013 Jan; 143(1):17-26. [Epub 2012 Nov 28] PMCID: PMC3521459 Rossom RC,
7. Espeland MA, Manson JE, Dysken MW, Johnson KC, Lane DS, LeBlanc ES, Lederle FA, Masaki KH, Margolis KL. Calcium and vitamin D supplementation and cognitive impairment in the Women's Health Initiative. *J Am Geriatr Soc* 2012 Dec; 60(12):2197-205. [Epub 2012 Nov 23] PMCID: PMC3521077
8. Neuhouser ML, Manson JE, Millen A, Pettinger MB, Margolis K, Jacobs ET, Shikany JM, Vitolins M, Adams-Campbell L, Liu S, LeBlanc E, Johnson KC, Wactawski-Wende J. The influence of health and lifestyle characteristics on the relationship of serum 25-hydroxyvitamin D with risk of colorectal and breast cancer in postmenopausal women. *Am J Epidemiol* 2012 Apr 1; 175(7):673-84. [Epub 2012 Feb 22] PMCID: PMC3324430
9. Tang JY, Fu T, Leblanc E, Manson JE, Feldman D, Linos E, Vitolins MZ, Zeitouni NC, Larson J, Stefanick ML. Calcium plus vitamin D supplementation and the risk of nonmelanoma and melanoma skin cancer: Post hoc analyses of the Women's Health Initiative Randomized Controlled Trial. *J Clin Oncol* 2011 Aug 1; 29(22):3078-84. [Epub 2011 Jun 27] PMCID: PMC3157967
10. Slinin Y, Paudel ML, Taylor BC, Fink HA, Ishani A, Canales MT, Yaffe K, Barrett-Connor E, Orwoll ES. Shikany JM, LeBlanc ES, Cauley JA, and Ensrud KE. 25-hydroxyvitamin D levels and cognitive performance and decline in elderly men. *Neurology* 2010; 74(1):33-41. PMCID: PMC2809025

Recent publications of importance to the field (in chronological order)

11. Lee CG, Schwartz AV, Yaffe K, Hillier TA, LeBlanc ES, Cawthon PM. Changes in physical performance in older women according to presence and treatment of diabetes mellitus. *J Am Geriatr Soc.* 2013 Nov;61(11):1872-8. [Epub 2013 Oct 28] PMCID: PMC3827698
12. LeBlanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary-care-relevant treatments for obesity in adults: A systematic evidence review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2011 Oct 4; 155(7):434-47.
13. LeBlanc ES, Hillier TA, Pedula KL, Rizzo JH, Cawthon PM, Fink HA, Cauley JA, Bauer DC, Black DM, Cummings SR, Browner WS. Hip fracture and increased short-term but not long-term mortality in healthy older women. *Arch Intern Med* 2011 Nov 14; 171(20):1831-7. [Epub 2011 Sep 26] PMCID: PMC3576923
14. Everson-Rose SA, Paudel ML, Taylor BC, Dam T, Cawthon PM, LeBlanc E, Strotmeyer ES, Cauley JA, Stefanick ML, Barrett-Connor E, Ensrud KE. Metabolic syndrome and physical performance in elderly men: The osteoporotic fractures in men (MrOS) study. *J Amer Geriatr Soc* 2011 Aug; 59(8):1376-84. PMCID: PMC3545517
15. Hillier TA, Pedula KL, Vesco KK, Schmidt MM, Mullen JA, LeBlanc ES, Pettitt DJ. Excess gestational weight gain: Modifying fetal macrosomia risk associated with maternal glucose. *Obstet Gynecol* 2008; 112(5):1007-14.

D. Research Support

Ongoing Research Support

290-2007-10057I, Task Order 13
Whitlock (overall PI); LeBlanc PI for Vitamin D review 09/11–9/14
AHRQ
EPC Technical Support of the U.S. Preventive Services Task Force (PTF-2)
The Oregon Evidence-based Practice Center has conducted systematic reviews in support of U.S. Preventive Services Task Force recommendations for more than a decade. This project is one of 15 current reviews; *Dr. LeBlanc is the PI of the 2014 screening for Vitamin D USPSTF review*.
Role: Co-Investigator

R01DK099277 Lindberg (PI) 04/14–03/18
NIDDK
Culturally competent behavioral intervention for diabetes risk reduction (De Por Vida)
The prevalence of type 2 diabetes and prediabetes is disproportionately high in obese Hispanic women, compared to non-Hispanic whites. Prevention of diabetes among pre-diabetic individuals, and self-management of diabetes among those with the diagnosis is critical. Lifestyle interventions focused on weight loss, physical activity, and nutrition have been shown to have a positive effect on preventing the onset of diabetes, and for achieving glycemic control among diabetic individuals. This project will test the efficacy of two evidence-based weight-loss interventions into a program designed for a low-income Hispanic population to be delivered in a community health clinic.
Role: Co-Investigator

R01 AG027574 Hillier (PI) 09/11–08/16
NIA
4 of 4: Study of Osteoporotic Fractures (SOF)
This project continues the prospective Study of Osteoporotic Fractures (SOF) and links the comprehensive SOF database with Medicare claims data to determine if age-related trajectories in cognitive function, physical performance, bone mineral density, body weight and positive affect predict phenotypes of optimal aging defined by longevity (including survivorship into the 10th decade of life), active lifespan (survival free of major disability), exceptional health span (survival free of major disease events) and rates of inpatient and residential health care utilization. Role:
Co-Investigator

Sanofi #EFC11319 Elder (PI) 12/12–11/15

Sanofi-Aventis
Lixisenatide as an Add-On to Standard-of-Care Treatment in Type 2 Diabetic Patients After an Acute Coronary Syndrome (SANOFI ELIXA)
This project, a randomized, double-blind, placebo-controlled, parallel-group, multicenter study, is evaluating the cardiovascular outcomes during treatment with lixisenatide as an add-on to standard-of-care treatment in type 2 diabetic patients after an acute coronary syndrome.
Role: Co-Investigator

Completed Research Support (arranged by relevance to D2d trial)

LeBlanc (PI) 06/10–5/11
KP Internal CBI
The Role of Vitamin D in Menopause: Relationship to Menopausal Symptoms and Body Composition (OCTRI CBI Vitamin D)
This randomized, placebo-controlled clinical trial (RCT) evaluated the treatment effect of Vitamin D on body composition and menopausal symptoms in women transitioning to menopause or in early menopause.
Role: Principal Investigator

R01 HS019859 Selby (PI) 09/10–09/13
AHRQ
Multi-Institutional Consortium for CER in Diabetes Treatment and Prevention (Prospect DM)
This project built a comprehensive, standardized, longitudinal diabetes registry and a parallel registry of non-diabetic patients enriched with patients at high risk for developing Type 2 diabetes in the membership of each of 12 participating health systems. The project included surveillance of obesity and diabetes incidence, diabetes treatment patterns, and outcomes. It also created new process variables using natural language processing (NLP) and develops new patient-reported information for use in comparative effectiveness research.
Role: Site Principal Investigator

Nichols (PI) 10/12–12/14
Bristol-Meyers Squibb
Understanding Clinician Response to Loss of Glycemic Control: Action and Reasons for Inaction (BMS Clinician Study)
The objectives of this project are to conduct: (1) an observational, data-only analysis of clinician characteristics associated with clinical inaction when patients with diabetes are not in glycemic control; (2) detailed interviews with a small subset of clinicians to collect information about inaction when patients are not in glycemic control to aid in development of a clinician questionnaire; and (3) a clinician survey of Kaiser Permanente Northwest primary care clinicians to determine and quantify reasons for clinical inaction when patients are not in glycemic control.
Role: Co-Investigator

K23-RR020049 LeBlanc (PI) 07/04–06/11
The Role of Estradiol in Menopause
This project examined the role of endogenous and exogenous estradiol in symptoms, sleep, mood, and cognition during the transition to menopause.
Role: Principal Investigator

N01-WH-4-2114 LeBlanc (PI) 09/94–09/10
NIH
Clinical Centers for the Clinical Trial and Observational Study of the Women's Health Initiative−West (WHI)
This project tested the benefits and risks of hormone replacement therapy, low-fat dietary modification, and supplementation with calcium and Vitamin D on the overall health of postmenopausal women ages 50-79.
Role: Site Principal Investigator (starting in 2009)

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Teresa Anne Hillier	Senior Investigator
eRA COMMONS USER NAME TAHILLIER	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Northwest Nazarene College, Nampa, ID	BS	06/86	Biology
Oregon Health & Science University, Portland, OR	MD	06/90	Medicine
University of Virginia, Charlottesville, VA	MS	06/98	Epidemiology

A. Personal Statement

I am an Endocrinologist and Senior Investigator at the Center for Health Research, with a dual appointment in Northwest and Hawaii. With post-graduate training in epidemiology, I focus my research on how modifiable risk factors earlier in life can impact future risk of endocrine diseases across the lifespan, including gestational diabetes, obesity, metabolic syndrome, type 2 diabetes, and osteoporosis. I have over 10 years' experience as PI of multi-center trials, including extensive experience with recruitment and safety and procedural issues for clinical measurements in clinical trials. As PI for one of the four sites of the Study of Osteoporotic Fractures, I recently oversaw a 4-hour clinical exam of 1,385 surviving participants that included development of the clinic's Manual of Procedures for site-specific laboratory collection; my site also exceeded recruitment goals. I also have over 10 years' experience overseeing projects at CHR-Hawaii, including recruitment for multi-center trials with a clinical exam component. I evaluated the parallel obesity and diabetes epidemics with an internationally recognized diabetes epidemiology research group at France's *Institut national de la santé et de la recherche médicale* (INSERM) during my sabbatical in 2004-5, funded by a fellowship from the American Diabetes Association-European Association for the Study of Diabetes. My recent diabetes expertise has focused on partnering with the Kaiser Permanente Northwest (KPNW) and Hawaii (KPH) regions to implement early gestational diabetes (GDM) screening of high-risk obese women. We are just beginning a randomized study of two methods of GDM screening to evaluate outcomes in all pregnant women and their offspring (over 17,500 pregnant women and their babies—more than 35,000 total participants) will be randomized in the next three years as part of their clinical care).

Particularly relevant to this proposal, I have worked closely with Dr. LeBlanc for over 5 years, transitioning from her active mentor to her collaborator as she continues to emerge as a PI. She has led several important publications about Vitamin D that we have collaborated on over the last several years. She has been developing an increasing interest and momentum in Vitamin D research, which is why she is now leading the current USPSTF review for Vitamin D screening. This, combined with her recent involvement with SUPREME-DM, make her a perfect fit as PI for this trial. Moreover, as we are both well grounded in our research within the KPNW health plan, we are also perfectly poised to utilize the EMR to easily recruit a small sample from our identified sample of over 43,000 KPNW members that meet A1C criteria for pre-diabetes, but are currently not on medications.

B. Positions and Honors

Positions and Employment

1993–1994 Physician, Good Samaritan Convenience Care Center, Portland, OR.
1993–1994 Physician, Osteoporosis Research Center, Portland, OR.
1997–1998 Instructor, Division of Endocrinology, Department of Medicine, University of Virginia, Charlottesville, VA.
1998–1999 Senior Research Associate, Center for Health Research, Kaiser Permanente Northwest, Portland, OR.
1999–2006 Investigator, Center for Health Research, Kaiser Permanente Northwest/Hawaii.
1999–present Clinical Assistant Professor, Division of Endocrinology, Department of Medicine, Oregon Health & Science University, Portland, OR.

2006–present Senior Investigator, Center for Health Research, Kaiser Permanente Northwest/Hawaii.

Honors

July 2004 American Diabetes Association-European Association for the Study of Diabetes Fellowship
June 2005 Title of Project: *The Pathogenesis of Early Obesity in France: Implications for Altering Our Worldwide Obesity Epidemic*
Fellowship Location: INSERM Unit 258, Cardiovascular and Metabolic Epidemiology, 16 Avenue Paul Vaillant Couturier, 94807 Villejuif cedex, FRANCE

Training

1994–1997 Fellow, Division of Endocrinology, Dept. of Medicine, University of Virginia, Charlottesville, VA
1991–1993 Resident, Internal Medicine, Providence Medical Center, Portland, OR
1990–1991 Intern, Internal Medicine, Providence Medical Center, Portland, OR

Board Certification

1997 Diplomate, Endocrinology, Diabetes, and Metabolism, (Subspecialty within American Board of Internal Medicine). Re-certified 2003; Certificate now active through 2017.
1993 Diplomate, American Board of Internal Medicine. Re-certified 2003; Certificate now active through 2013.

C. Selected Peer-reviewed Publications (*Selected from over 100 peer-reviewed publications*)

Most relevant to the Current Application

1. **LeBlanc ES**, Perrin N, Johnson JD Jr., Ballatore A, **Hillier T**. Over-the-counter and compounded vitamin D: Is potency what we expect? *JAMA Internal Med* 2013 Apr 8; 173(7):585-6.
2. **LeBlanc ES**, Rizzo JH, Pedula KL, Ensrud KE, Cauley J, Hochberg M, **Hillier TA**; Study Of Osteoporotic Fractures. Associations between 25-hydroxyvitamin D and weight gain in elderly women. *J Womens Health* (Larchmt) 2012 2012 Oct; 21(10):1066-73. PMCID: PMC3466912 [Available on 2013/10/1]
3. **LeBlanc ES, Hillier TA**, Pedula KL, Rizzo JH, Cawthon PM, Fink HA, Cauley JA, Bauer DC, Black DM, Cummings SR, Browner WS. Hip fracture and increased short-term but not long-term mortality in healthy older women. *Arch Intern Med* 2011 Nov 14; 171(20):1831-7. [Epub 2011 Sep 26] PMCID: PMC3576923
4. Hillier TA, Pedula KL, Vesco KK, Schmidt MM, Mullen JA, LeBlanc ES, Pettitt DJ. Excess gestational weight gain: Modifying fetal macrosomia risk association with maternal glucose. *Obstet Gynecol* 2008; 112(5):1007-14.

Additional Recent Publications of Importance to the Field (in chronological order)

5. Hillier TA, Ogasawara K, Pedula K, Vesco KK. Markedly different rates of incident insulin treatment based on universal GDM screening in a diverse HMO population. *Am J Obstet Gynecol.* 2013 Nov;209(5):440. [epub 2013 June 28]
6. Hillier TA, Lui LY, Kado DM, LeBlanc ES, Vesco KK, Bauer DC, Cauley JA, Ensrud KE, Black DM, Hochberg MC, Cummings SR. Height loss in older women: Risk of hip fracture and mortality independent of vertebral fractures. *J Bone Miner Res* 2012;27(1):153-9.
7. Hillier TA, Cauley JA, Rizzo JH, Pedula KL, Ensrud KE, Bauer DC, Lui LY, Vesco KK, Black, DM, Donaldson MG, LeBlanc ES, Cummings SR. The WHO absolute fracture risk models (FRAX): Do clinical risk factors improve fracture prediction in older women with normal or low bone mass? *J Bone Miner Res 2011* Aug; 26(8):1774-82.
8. Hillier TA, Vesco KK, Pedula KL, Beil T, Whitlock E, Pettitt DJ. Screening for gestational diabetes: A systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2008; 148(10):766-75.
9. Hillier TA, Stone KL, Bauer DC, Rizzo JH, Pedula KL, Cauley JA, Ensrud KE, Hochberg MC, Cummings SR. Repeat bone mineral density measurement and prediction of fractures in older women: Is more better? The Study of Osteoporotic Fractures. *Arch Int Med* 2007; 167(2):155-60.
10. Hillier TA, Pedula KL, Schmidt MM, Mullen JA, Charles MA, Pettitt DJ. Childhood obesity and metabolic imprinting: The ongoing effects of maternal hyperglycemia. *Diabetes Care* 2007; 30(9):2287-92.
11. Hillier TA, Fosse S, Balkau B, Simon D, Eschwège E, Fagot-Campagna A. Weight, the metabolic syndrome, and coronary heart disease in type 2 diabetes: Associations among a national French sample-The ENTRED Study. *J CardioMetabolic Syndr* 2006; 5(1):318-25.
12. Hillier TA, Rousseau A, Lange C, Lepinay P, Cailleau M, Novak M, Calliez E, Ducimetiere P, Balkau B. Practical way to assess metabolic syndrome using a continuous score obtained from principal components analysis: The D.E.S.I.R. Cohort.* *Diabetologia* 2006; 49(7):1528-35.

13. Hillier TA, Fagot-Campagna A, Eschwège E, Vol S, Cailleau M, Balkau B, and the D.E.S.I.R. Study group. Weight change and changes in the metabolic syndrome as the French population moves towards overweight: The D.E.S.I.R. Cohort. *Int J Epidemiol* 2006 Feb; 35(1):190-6.
14. Hillier TA, Rizzo JH, Pedula KL, Cauley JA, Schwartz AV, Ensrud KE, Browner WS. Increased mortality associated with the metabolic syndrome in older women with diabetes. *Diabetes Care* 2005; 28(9):2258-60.
15. Hillier TA, Pedula KL. Complications in young adults with early onset Type 2 Diabetes: Losing the relative protection of youth. *Diabetes Care* 2003; 26(11):2999-3005.

D. Research Support

Ongoing Research Support

(Hillier, Teresa A., M.D.) 09/12 - 08/17
NIDDK
Comparing Two Gestational Diabetes Screening Methods: A Pragmatic Outpatient RCT (ScreenR2 GDM/3517)
This project randomizes two different screening strategies for diabetes in pregnancy, among a study population of over 17,500 pregnant women and their babies (over 35,000 total) in a large diverse HMO, to determine how diagnosis and treatment based on these two strategies in routine clinical care affects complications for the baby and the mother.
Role: Principal Investigator

R01 HD058015 Hillier (PI) 08/09–05/14
NICHD
Impact of Early Gestational Diabetes Screening in High-Risk Populations (Early GDM)
Screens for early diabetes in pregnancy in all high-risk obese pregnant women at the first prenatal visit and compares outcomes prior to the new screening program among a longitudinal study population of over 59,000 pregnant women and their babies (118,000 total) in an HMO, to determine if early GDM diagnosis and treatment reduces maternal and perinatal complications.
Role: Principal Investigator

R01 AG027574 Hillier (PI) 09/11–08/16
NIA
4 of 4: Study of Osteoporotic Fractures (SOF)
Continues the prospective Study of Osteoporotic Fractures (SOF) and links the comprehensive SOF database with Medicare claims data to determine if age-related trajectories in cognitive function, physical performance, bone mineral density, body weight, and positive affect predict phenotypes of optimal aging defined by longevity (including survivorship into the 10th decade of life), active lifespan (survival free of major disability), exceptional health span (survival free of major disease events) and rates of inpatient and residential health care utilization.
Role: Principal Investigator

R01 AG020048 Hampson (PI) 09/07–08/17
NIA
Personality and Health: A Longitudinal Study (LCH III)
Integrates endocrinology, epidemiology, and behavioral science within a life-span perspective. Findings may enable us to identify individuals with personality traits that put them at higher risk for metabolic syndrome and mediating lifestyle risk factors. Such findings would initiate a transdisciplinary, life-span approach for future interventions to prevent metabolic syndrome that would combine medical and behavioral science in tailoring interventions to individuals' risk factors.
Role: Co-Investigator

Fredman (PI) 07/11–06/15
NIA
Health Decline in Aged Caregivers: Epidemiologic Study (SOF Caregiver 3)
The Study of Osteoporotic Fractures (SOF) Caregiver study is an ancillary study that recruited a sample of SOF women who were caregivers and non-caregivers to compare health outcomes. This study has been ongoing for the past 10 years, and has had separate clinic visits associated with it at the SOF sites.
Role: Site Principal Investigator

Completed Research Support *(Selected from past three years)*

R01 AG027574-25 Hillier (PI) 09/09–08/11
NIA
4 of 4: Study of Osteoporotic Fractures (SOF)–Portland Clinical Center (SOF YEAR 25)
Studied why some women in the SOF cohort achieve and maintain high cognitive and physical function and low risk of falls and fractures in the 9th and 10th decade of life; allowed the SOF clinical centers to conduct new analyses related to this recently completed clinic visit of the cohort.
Role: Principal Investigator

R01 AG028254 Michael (PI) 02/07–01/12
NIA
Neighborhood Design and Obesity in Older Women (NEIGHBORHOOD OBESITY)
Sought to determine whether neighborhood characteristics are associated with more active lifestyles in addition to the effect of individual-level characteristics in older women among the SOF Portland cohort.
Role: Co-Investigator

R34 AG033669 Bauer (PI) 06/10–05/11
NIA
Planning a Multi-center Trial of Subclinical Hypothyroidism in Older Adults
Piloted the feasibility of point-of-care thyroid screening in 600-800 KPNW adults; surveyed a sub-sample by a questionnaire and followed up with confirmatory testing at the KPNW labs.
Role: Site Principal Investigator for pilot study