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PI: <b>Demark-Wahnefried, Wendy</b>	Title: Vegetable garden feasibility trial to promote function in older cancer survivors	
	FOA: PA12-135	
	FOA Title: TRANSLATIONAL RESEARCH AT THE AGING/CANCER INTERFACE (TRACI) (R21)	
<b>1 R21 CA182508-01</b>		
IPF: 1288803	Organization: UNIVERSITY OF ALABAMA AT BIRMINGHAM	

## RESEARCH & RELATED Other Project Information

1. \* Are Human Subjects involved?  Yes  No

1.a If YES to Human Subjects

Is the Project Exempt from Federal regulations?  Yes  No

If yes, check appropriate exemption number.  1  2  3  4  5  6

If no, is the IRB review Pending?  Yes  No

2. \* Are Vertebrate Animals Used?  Yes  No

3. \* Is proprietary/privileged information included in the application?  Yes  No

4.a. \* Does this project have an actual or potential impact on the environment?  Yes  No

5. \* Is the research performance site designated, or eligible to be designated, as a historic place?  Yes  No

6. \* Does this project involve activities outside of the United States or partnerships with international collaborators?  Yes  No

## **Vegetable Garden Feasibility Trial to Promote Function in Older Cancer Survivors**

There are currently over 13.7 million cancer survivors in the U.S., and the number is steadily increasing. While the rising number of cancer survivors is cause for celebration, cancer survivors are at much greater risk for second malignancies, cardiovascular disease, osteoporosis, and functional impairment. Functional decline, especially that which results in a loss of independence, contributes substantially to the economic burden and also reduces quality of life among cancer survivors and their family members. This is of particular concern among older cancer survivors who comprise the majority (>60%) of all cancer survivors, and whose numbers are expected to exceed 14 million by the year 2030. Thus, there is large public health potential for targeted interventions that stabilize or positively reorient the steep trajectory of functional decline among older cancer survivors. This exploratory study is in response to the Translational Research at the Aging/Cancer Interface (TRACI) (PA-12-135) announcement. and proposes a novel and holistic approach, i.e., gardening, as a way to cultivate long-term adherence to an improved diet and increased physical activity, with the anticipation that it may slow the decline of health and function in this vulnerable population, and promote more successful aging.

The proposed feasibility study relies on the extant infra-structure of the Alabama Cooperative Extension Master Gardener Program. A total of 46 older ( $\geq 65$  years) cancer survivors recently diagnosed with a loco-regionally staged cancer with a good prognosis (i.e.,  $\geq 80\%$  5-year survival) and with 2 or more physical function limitations will be recruited from select rural and urban counties in Alabama and randomized to 1-of-2 study arms: 1) an intervention group that receives a 1-year mentored vegetable gardening intervention that pairs cancer survivors with certified Master Gardeners, or 2) a usual care control group. Aims of this study are to: 1) explore the feasibility and acceptability of a mentored vegetable gardening intervention by assessing accrual, retention, adherence, fidelity, and possible adverse events, 2) obtain means and precision estimates, and explore between-arm differences on pre-post changes in physical function and secondary endpoints (e.g., quality of life, fruit & vegetable intake, physical activity, biomarkers of successful aging), and 3) to explore participant factors associated with program efficacy (e.g., gender, comorbidity). The proposed vegetable gardening intervention is a novel and feasible strategy to reduce functional impairment and improve quality of life in elderly cancer survivors. The Master Gardener Program exists in all 50 United States, with a large proportion of these states (84%) having the capacity for 2-to-3 growing seasons a year. Thus, there is both an infrastructure and capacity for sustainability and wide-scale dissemination which ultimately could have great public health significance.

Cancer survivors are at increased risk for age- and treatment-related comorbidities, including second cancers, cardiovascular disease, and impaired physical functioning. This project will explore the feasibility of a vegetable gardening intervention that pairs older cancer survivors with community-based Master Gardeners. We also will explore the impact of this holistic intervention that targets the aging-cancer interface and obtain parameter estimates on physical functioning, biomarkers of successful aging, and behaviors affecting cancer control.

## **FACILITIES**

### **Outline**

#### **University of Alabama at Birmingham (UAB)**

1. UAB

#### **UAB Centers**

1. UAB Comprehensive Cancer Center
2. UAB Center for Clinical and Translational Science (CCTS)
3. Nutrition and Obesity Center
4. Minority Health Research Center

#### **UAB Schools**

1. School of Medicine
2. School of Public Health
3. School of Health Professions

#### **UAB Departments/Divisions**

1. School of Medicine
2. School of Public Health
3. School of Health Professions

#### **UAB Departments**

1. Nutrition Sciences
2. Preventive Medicine

#### **UAB Programs and Shared Facilities**

1. Program of Cancer Control and Population Sciences
2. Biostatistics Shared Facilities
3. Clinical Trials Shared Facilities
4. Community Recruitment and Retention Shared Facilities

#### **Other UAB Resources**

1. Deep South Network for Cancer Control
2. UAB/ Morehouse/ Tuskegee Partnership

#### **Auburn University**

1. Auburn University
2. Alabama Cooperative Extension Offices (ACES; 14 off campus offices)

#### **Auburn Colleges and Units**

1. College of Agriculture
2. Alabama Ag Experiment Station (Auburn U)

#### **Auburn Departments/Divisions**

1. Department of Horticulture
2. Home Grounds Team (ACES)
3. Alabama Master Gardeners

#### **Shared Facilities and Cores**

1. Alabama Ag Experiment Station, Fairhope (Auburn U)
2. County Extension Offices

***The University of Alabama at Birmingham (UAB) ([www.uab.edu](http://www.uab.edu))*** UAB is a comprehensive teaching and research-intensive university with an exceptionally strong Academic Health Center and graduate programs in a wide variety of disciplines. Medically related schools are the Schools of Medicine, Public Health, Health Professions, Dentistry, Nursing, and Optometry. The University offers 35 doctoral programs and 45 master's

programs. Student enrollment exceeds 17,000 and currently more than 16,000 people work at UAB. The university is proud of its minority (31.6%) and female (60.2%) enrollment. The academic medical center has grown rapidly from its beginnings only four decades ago, due in large measure to a strong commitment to biomedical research. The campus occupies more than 82 city blocks and has an operating annual budget of \$2.3 billion, making it the largest employer in the State. UAB's aggregate economic impact for Birmingham and the State of Alabama exceeds \$3 billion. The flagship UAB Medical Center and the associated Children's Hospital of Alabama and Birmingham Veterans' Affairs Medical Center, are the primary institutions that have led the extraordinary transformation of Birmingham into one of the leading biomedical centers in the U.S. UAB faculty members have successfully competed for \$460 million in extramural grants and contracts. UAB now ranks in the top tier in extramural support for biomedical research from the National Institutes of Health. The UAB Academic Health Center is home to a diverse range of interdisciplinary centers that focus on extraordinary research strengths and a culture that encourages and nurtures interdisciplinary interactions and scholarship among scientists in over 70 Research Centers. UAB has been successful in breaking down departmental barriers to collaborative research, a feature that attracts outstanding faculty and students to Birmingham, and makes UAB-initiated biomedical research projects highly competitive for federal funding. UAB is a national leader for multi-institutional investigations and clinical trials.

### **UAB Centers**

***Comprehensive Cancer Center (CCC)*** ([www.ccc.uab.edu](http://www.ccc.uab.edu)) The UAB CCC was one of the first eight comprehensive cancer centers established by NCI. In 2005, the Cancer Center renewed its designation as "comprehensive" and is now in its 40<sup>th</sup> year of NCI support. Since 1998, UAB has received NCI funding for SPORES in five important NCI and CCC priority areas for interdisciplinary, multi-institutional, translational cancer research: ovarian, prostate, breast, brain and pancreas. The Cancer Center's research activities are divided into nine major programs. Of note, Dr. Demark-Wahnefried is Associate Director of Cancer Prevention and Control, and both she and Dr. Locher are members of the Cancer Control and Population Sciences Program (CCPS). This program encompasses efforts in cancer outreach, epidemiology, and behavioral intervention, and thus the proposed project will be housed within this program. Other programs include Tumor Immunology, Structural Biology, Virology, and Tumor Biology with interdisciplinary, laboratory research-based projects overseen by basic science and clinical investigators pursuing molecular mechanisms relevant to normal and neoplastic cell growth and behavior. The Center supports 14 shared facilities which provide investigators with convenient access to cost-effective services, equipment, and consulting expertise that enhance their research productivity. The Shared Facilities are Biostatistics & Bioinformatics, Clinical Protocol & Data Management, Comprehensive Genomics, DNA Sequencing, High Resolution Imaging, Human Imaging, Mass Spectrometry/Proteomics, Microarray, Molecular NMR, Recruitment and Retention, Small Animal Imaging, Tissue Procurement, Transgenic Animal, and X-ray Crystallography. The Recruitment and Retention Shared Facility, funded by NCI, is a central resource for clinical trials recruitment throughout the Medical Center. One of the primary missions of the Cancer Center is to provide community outreach services to minority and underserved populations. The Cancer Center has traditionally been a pacesetter for UAB interdisciplinary research efforts in an institution with an international reputation for scholarly contributions based on collaborative, interdisciplinary research.

***UAB Center for Clinical and Translational Science (CCTS)*** The Center for Clinical and Translational Science (CCTS) is a designated University-Wide Interdisciplinary Research Center. The CCTS was developed in response to NIH applications for Clinical and Translational Science Awards (CTSAs). UAB was officially funded for the CCTS in 2008. CCTS enhances human health by driving scientific discovery and dialogue across the bench, bedside and community continuum. The vision of the Center is to speed the translational of research into improved human health. The Center is comprised of eight Components and a Research Commons: Biomedical Informatics; Pilots; Drug Discovery; Research Education and Training; Clinical Research Unit (CRU); Cores; Regulatory and Research Ethics; and One Great Community. The CCTS has become a dynamic, physical and virtual hub through which investigators, trainees, and community members interact and collaborate. The Research Commons provides services that are especially useful for this project. Research Commons staff serve as Investigator Advocates for scientists and trainees using CCTS resources, and provide input on crafting effective career development plans. The Center supports translational research with methodological expertise in epidemiology, biostatistics, outcomes and effectiveness research, and data management. CPCTP trainees are encouraged to take full advantage of all CCTS resources and services.

**Nutrition and Obesity Research Center (NORC)**, funded by NIH, fosters a multidisciplinary approach to basic, clinical and translational research with an emphasis on understanding the metabolic, environmental, and genetic factors underlying nutrition and obesity-related disorders; to better understand the consequences of these disorders; and ultimately to lead to better methods for treatment and prevention. The NORC is supported by an NIH center grant (P30DK056336) and currently has over ~70 appointed faculty representing more than 19 departments and 8 schools at UAB with ~ \$44 million in direct funding for nutrition/obesity research. Both Drs. Locher and Demark-Wahnefried are members of this center. The Center's research focuses on nutrition and obesity. It also maintains several labs and has access to specialized equipment, including: a respiration chamber to measure 24-hour energy expenditure and substrate oxidation, an underwater weighing system, a BodPod system for measuring whole-body density using air displacement plethysmography, several dual-energy x-ray absorptiometers, a SensorMedics 2900 Metabolic Cart, an exercise testing facility, a hormone substrate assay facility, a muscle biopsy facility, and an animal studies facility. While many of these resources will be untapped for this study, the potential support for add-on studies and the expertise of the faculty bring added support to this project.

**Minority Health & Health Disparities Research Center (MHRC)** provides UAB and community researchers with an infrastructure to develop and conduct innovative research for improving the health status of minority groups, to increase community outreach and education, and to expand the participation of minorities in biomedical and behavioral research. The MHRC's mission is guided by the themes of building trust, sharing power, and reducing racial bias within UAB, the greater Birmingham community and, ultimately, the state of Alabama. The MHRC is sponsored by the UAB Schools of Public Health, Nursing, Health Related Professions, Optometry, and Medicine and has an Academic Council that represents nine Minority Serving Institutions in Alabama. As with the UABNCC, this also will be an instrumental center for enhancing accrual to our trial. Health Smart, is a newly created facility within downtown Birmingham which is key component of the MHRC and allows for community-based recruitment in an urban setting.

### **UAB Schools**

**School of Medicine (UASOM) ([www.medicine.uab.edu](http://www.medicine.uab.edu))** UAB is among a select group of universities recognized for both high research activity and significant community engagement. UAB ranks 27<sup>th</sup> among academic institutions in federal research funding and 20<sup>th</sup> in funding from NIH. Total research funding exceeds \$460 million annually and over \$250 million can be attributed to the School of Medicine alone. As one of the leading public medical schools in the Southeast, it has been responsible for educating and training medical students, for providing knowledge in basic and clinical sciences, and for understanding and appreciating the socioeconomic factors involved in providing both primary and specialized medical care. In addition to the medical education program, SOM faculty conduct research in university-wide interdisciplinary research centers. The UAB interdisciplinary culture presents the medical and scientific community with opportunities to collaborate with colleagues from other schools, departments and disciplines who have comparable or complementary research interests. UAB offers an NIH-funded Medical Scientist Training Program (MSTP) that offers a combined MD/PhD program designed to prepare students for careers that combine laboratory investigation of disease mechanisms with the practice and teaching of clinical medicine in an academic setting. The MSTP enrolls about nine new students each year. The SOM faculty represents a variety of disciplines with diverse educational and research backgrounds. The School has an earned tradition of excellence in research and clinical care and is recognized as a leader in many fields. It currently has 1200 funded research grants and contracts, which represent \$273 million in peer-reviewed research. The SOM has ranked as high as 17<sup>th</sup> in the nation based on research awards received from the National Institutes of Health. The Department of Nutrition Sciences dually reports to the UASOM and the School of Health Professions (below).

**School of Public Health ([www.uab.edu/PublicHealth](http://www.uab.edu/PublicHealth))** The UAB School of Public Health (SPH) includes approximately 85 full-time primary faculty members plus 40 secondary, adjunct and emeritus faculty members, housed in five academic Departments: Biostatistics, Environmental Health Sciences, Epidemiology, Health Behavior, and Health Care Organization and Policy. The SPH supports six multi-disciplinary centers that play key roles in the School's research and disease control missions: the Center for Health Promotion, the Center for Community Health Resource Development, the Deep South Center for Occupational Health and Safety, the John J. Sparkman Center for Global Health, the South Central Center for Public Health Preparedness, and the Lister Hill Center for Health Policy. The SPH has a strong research program, ranking second among UAB Academic Health Center schools in research dollars. The SPH also has a strong teaching program and



through its education and training mission serve the public health needs of Alabama and assist UAB in carrying out its mission as an international university. The SPH's student body of approximately 300 includes students from Alabama (50%), other U.S. states (25%) and other countries (25%).

**School of Health Professions (SHP) ([www.uab.edu/shp/](http://www.uab.edu/shp/))** The UAB School of Health Professions has 21 academic programs at the baccalaureate, master's, and doctoral levels within six departments: Critical Care, Diagnostic Care, Health Services Administration, Nutrition Sciences, Occupational Therapy, and Physical Therapy. It has 89 full-time faculty and nearly 1350 students. The School educates health professionals to enhance and improve health care services and the systems through which these services are administered. In keeping with the mission of UAB, the resources of the programs of SHP are dedicated to excellence in teaching, research, scholarly activity, and service to the institution, community, and the professions. For most of its history, the School has ranked number one or two in total research support provided by the NIH to Allied Health Schools. A recent *U.S. News and World Report* ranking placed SHP's nutrition sciences program 2<sup>nd</sup> nationally, its health services administration program 8<sup>th</sup>, its physical therapy program 19<sup>th</sup>, and its occupational therapy program 40<sup>th</sup>. The School enjoys a national and international reputation in research, diagnostic and rehabilitative care, and in clinical and didactic education.

### **UAB Programs and Shared Facilities**

**Department of Nutrition Sciences (DNS)** was created in 1977 and is jointly administered by three health schools (Health Professions, Medicine, and Dentistry) within the UAB Academic Medical Center. The Department has a distinguished history, and is currently comprised of over 20 primary full-time faculty members and more than 90 staff, students, and postdoctoral fellows. The faculty includes a multidisciplinary team of physician-scientists, PhD scientists, registered/licensed dietitians, and nurses working together in patient care, research, and education programs. The Department is organized into four Divisions: Molecular Nutrition and Genetics, Physiology and Metabolism, Clinical Nutrition and Dietetics, and Pediatric Nutrition. Drs. Demark-Wahnefried has an appointment in this department. Departmental faculty members are housed in the Susan Mott Webb Nutrition Sciences Building and in the adjacent Learning Resources Center, both centrally located within the UAB medical center complex. Dr. Demark-Wahnefried has private office space with dedicated telephone lines and networked Pentium computers through the DNS. The Susan Mott Webb (Dr. Demark-Wahnefried is the Webb Chair of Nutrition Sciences) Building provides more than 60,000 square feet of space dedicated to teaching, community service activities, and nutrition research – including world-class core facilities for metabolic assessments in humans. Research programs within the Department encompass basic, clinical, and translational research. Research interests pertain to diseases that account for a major burden of patient suffering and social costs, with expertise in obesity, diabetes, energy metabolism and body composition, cancer, nutrient metabolism, arthritis and osteoporosis, and genetic susceptibility to disease. The Department's current annual extramural research funding exceeds \$5 million and it consistently ranks among the top human nutrition departments in the country in terms of research funding from the National Institutes of Health. In addition, the Department provides an academic home for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)-funded The *Energy Metabolism/Body Composition Core Laboratory (EM/BMI:CL)* is located within this department and occupies approximately 44,000 sq. ft. of space in the Susan Mott Webb Nutrition Sciences Building, which is centrally located in the UAB Health Sciences Center. Approximately 15,000 sq. ft. of space in the Nutrition Sciences building are dedicated to laboratories, including the 3,500 sq. ft. Energy Metabolism/Body Composition Core Laboratory of the NORC. This Core Laboratory provides assessments of energy expenditure (short-term and free-living), fuel utilization, body composition (4-compartment model), hormone/substrate assays, insulin sensitivity testing, exercise testing, and muscle metabolism (histochemistry and enzyme activities from biopsy). All of the above assessments are performed routinely in pediatric, adult, and older adult subjects. Approximately 1,500 sq. ft. of adjacent space for offices are dedicated to the Division of Physiology & Metabolism, which houses this laboratory. Blood processing, serum assays, resting metabolic rates and DXA scans will be performed on our study sample at multiple timepoints, thus the proposed study will benefit greatly from the infrastructure that currently exists. The *Exercise Laboratory (EL)* is an 1800 sq ft exercise testing and training facility is located on the ground floor of the Nursing Bldg. immediately adjacent to the Webb Bldg.

**Department of Preventive Medicine (DPM)** serves as the major integrating foci for preventive medicine activities within the Department of Medicine at the University of Alabama at Birmingham (UAB). The Department's broad, varied scope of interests and activities provide a unique resource within the UAB Medical

Center for disease prevention. The Division is committed to: (1) providing clinical and preventive medical services; (2) serving as a resource to industry, business, and individuals to aid in creating and evaluating innovative clinical services, preventive medicine, addiction medicine and behavioral medicine programs; (3) developing and conducting research programs primarily related to clinical services and disease prevention with particular focus on underserved populations and women; and (4) providing training in preventive medicine, clinical epidemiology and behavioral medicine with broad experiences in clinical research.

### **UAB Programs and Shared Facilities**

**Cancer Control and Population Sciences Program (CCPS)** The goal of the CCPS is to reduce cancer incidence, morbidity and mortality through prevention and control measures. Alabama's high-incidence cancers and medically underserved populations are high priority areas for research and service activities of the CCPS; thus, the proposed project fits well within that mission. CCPS scientists are actively involved in laboratory investigations in chemoprevention and nutrition, comparative effectiveness studies, observational studies, surveillance, clinical trials of cancer survivorship, and community education and research. Approximately 49 investigators have appointments to this program, and their grant support totals approximately \$28 million in annual direct funding.

**Biostatistics and Bioinformatics** – The primary objective of the Biostatistics and Bioinformatics Shared Facility (BBSF) is to serve as a focal point from which the UAB Comprehensive Cancer Center's investigators may draw statistical and bioinformatics expertise for planning, management and analysis of their studies. Dr. Cantor directs this shared resource and the developmental time spent on this grant was covered from this resource.

**Clinical Protocol and Data Management** – The Clinical Protocol and Data Management Shared (CPDM) Facility provides central management for the implementation, coordination, and conduct of clinical trials developed by the Cancer Center faculty and by extramural collaborators associated with SPOREs, other cancer centers, the National Cancer Institute, industry and cooperative groups. The CPDM will support the randomization of the proposed study participants.

**Community Recruitment and Retention** – The Community Recruitment and Retention (CRR) Shared Facility is an infrastructure designed to facilitate and assist Cancer Center investigators in recruiting subjects to participate in clinical research and to provide linkage between the community and UAB Researchers. The CRR is particularly focused on efforts to refine recruitment strategies, particularly for population-based studies, among minority participation in clinical trials. This resource provides guidance to enhance accrual and retention and many of the strategies used in this proposal are a result of such guidance.

### **Other UAB Resources**

***Deep South Network (DSN) for Cancer Control*** The proposed project interfaces with UAB's mission regarding the elimination of unnecessary and unacceptable disparities in cancer death rates between blacks and whites in Alabama and the Deep South. The DSN was created to meet the needs of the underserved African-American community in this region. The purpose of the DSN is to build community, institutional capacity, and the infrastructure necessary to eliminate cancer health disparities. DSN goals are to improve access to and utilization of proven beneficial cancer interventions and to conduct community-based participatory education, training and research. The DSN builds upon community infrastructures, state partnerships and coalitions to: (1) provide cancer awareness activities; (2) support minority enrollment in clinical trials; and (3) promote the development of minority junior biomedical researchers. The Community Health Advisor (CHA) model is utilized to train women who are natural helpers to provide cancer awareness messages and resources to their communities. The CHAs are trained as research partners (CHA-RPs) to enhance African-American participation in clinical trials. The DSN targets breast, cervical and colon cancers in two underserved rural areas - the Black Belt of Alabama and the Delta region of Mississippi - and two urban underserved areas - Jefferson County, Alabama, and Hattiesburg/Laurel Metro, Mississippi. The DSN is one of 25 Cancer Network Programs funded by the NCI Center to Reduce Cancer Health Disparities. While we will be recruiting survivors through the cancer registry, the additional support of this network will be helpful.

***Morehouse/Tuskegee/UAB CCC Partnership.*** The Morehouse School of Medicine (MSM)/ Tuskegee University (TU)/ UAB CCC partnership facilitates research and training collaborations between the three

institutions. The partnership strengthens all three universities in areas of weakness while continuing to enhance and upgrade the cancer research capabilities of each. This partnership is composed of two NCI-funded grants: a U56 with MSM and a P20 planning grant with TU. The partnership has led to development of programs in the following areas: (1) Research; (2) Research Training and Career Development; (3) Education and (4) Community Outreach. The development of these programs enhances the promise of success for investigators at all three institutions to become independent and culturally sensitive researchers. Furthermore, this partnership: (1) provides MSM and TU researchers with training opportunities in cancer research being conducted at UAB; (2) increases the number of MSM and TU students in cancer research; (3) increases the number of minority researchers with Bioethics training and (4) exposes researchers at all three institutions to training in the areas of Bioethics in research, cultural sensitivity and community outreach research. The partnership is making significant contributions to the elimination of the gap in cancer incidence, morbidity and mortality between whites and African Americans in urban and rural African American communities. It is entirely possible that trainees affiliated with this partnership will help to work on the proposed project.

## **Auburn University (AU)**

1. **Auburn University** was established in 1856 as the East Alabama Male College, 20 years after the city of Auburn's founding. In 1872, under the Morrill Act, the school became the first land-grant college in the South and was renamed the Agricultural and Mechanical College of Alabama. In 1899 the name again was changed, to the Alabama Polytechnic Institute. Finally, in 1960 the name of the school was changed to Auburn University, a title more in keeping with its location, and expressing the varied academic programs and larger curriculum of a major university.

Today, Auburn is one of the few universities to carry the torch as a land, sea and space grant university. Our Fall 2010 semester enrollment was 25,078. Students can choose from more than 140 degree options in 13 schools and colleges at the undergraduate, graduate and professional levels.

Auburn University's mission is defined by its land-grant traditions of service and access. The University will serve the citizens of the State through its instructional, research and outreach programs and prepare Alabamians to respond successfully to the challenges of a global economy. The University will provide traditional and non-traditional students broad access to the institution's educational resources. In the delivery of educational programs on campus and beyond, the University will draw heavily upon the new instructional and outreach technologies available in the emerging information age.

As a comprehensive university, Auburn University is committed to offering high-quality undergraduate, graduate, and professional education to its students. The University will give highest priority for resource allocation for the future development of those areas that represent the traditional strengths, quality, reputation, and uniqueness of the institution and that continue to effectively respond to the needs of students and other constituents.

Because research is essential to the mission of a land-grant university, Auburn University will continue development of its research programs. The primary focus of this research will be directed to the solution of problems and the development of knowledge and technology important to the state and nation and to the quality of life of Alabama citizens. The University's research programs will make important contributions to instructional programs through the involvement of graduate and undergraduate students and the renewal of the faculty. Research will also provide the knowledge base for outreach programs. In carrying out its research mission, the University will emphasize established areas of strength and will focus available resources in those areas of research and doctoral study that are, or have the potential to develop into nationally and internationally recognized centers of excellence. Extension and outreach programs are fundamental to the land-grant mission because these programs directly affect the lives of all citizens in the state. The University will maintain the strengths of its traditional outreach programs and will increasingly involve the broader University in outreach

programs that respond to the changing needs of the society in which we live. The University will continue to seek new and innovative ways to reach out to the people it serves.

## **2. Alabama Cooperative Extension System (ACES)**

The Alabama Cooperative Extension System (ACES) operates as the primary outreach organization for the land-grant functions of Alabama A & M and Auburn Universities. The Alabama Cooperative Extension System collaborates with many partners to help people and communities improve their quality of life and economic well-being. ACES accomplishes this mission by providing educational opportunities and information grounded in research based science in six program areas.

Extension programming provides educational opportunities to help people, individually and collectively, make sound decisions about their lives, businesses, and communities and develop economically, socially, and culturally.

The Alabama Cooperative Extension System offers Specialists and programming in the following areas: Agriculture, Forestry- Wildlife and Natural Resources, Urban Affairs and New Nontraditional Programs, Family and Consumer Sciences, Economic and Community Development, 4-H and Youth Development.

The System employs more than 800 faculty, professional educators, and staff members operating in offices in every one of Alabama's 67 counties and in nine urban centers covering the major regions of the state. In conjunction with the Alabama Agricultural Experiment Station, the system also staffs six Extension and Research Centers located in the state's principal geographic regions.

County Offices — Agents in all 67 county offices offer educational programs adapted to the needs and interests of local residents. Regional agents work in teams across county lines to provide specialized knowledge in a wide range of subjects.

Online Services — Our web site at [www.aces.edu](http://www.aces.edu) offers Extension articles, publications, and blogs written by specialists and researchers, with links to additional information.

Videoconference sites — Extension has 54 video-conference sites around the state enabling clients to participate in educational and certification programs close to home.

## **Colleges & Units**

### **1. College of Agriculture (CoA)**

The College of Agriculture at Auburn University is dedicated to educating people and discovering knowledge that improves the lives of all Alabama citizens through our research, instruction and outreach programs.

The College of Agriculture traces its roots back to 1872 with the establishment of the Alabama Agricultural and Mechanical College as a land-grant college. Throughout its -year history, the college has helped advance Alabama's agricultural economy while improving the nutrition, health and standard of living for all citizens.

### **2. Alabama Agricultural Experiment Station (AAES)**

As part of the land-grant system, the AAES coordinates research for scientists in five schools and colleges on the AU campus as well as scientists at Alabama A&M and Tuskegee universities.

For more than 125 years, the Alabama Agricultural Experiment Station (AAES) has provided scientific research to support Alabama's agricultural industries and businesses and to benefit Alabama citizens. AAES is headquartered at Auburn University one of Alabama's three land-grant universities ; it includes units of the Colleges of Agriculture, Sciences and Mathematics, Human Sciences, Veterinary Medicine, and the School of Forestry and Wildlife Sciences as well as several outlying research units. Historically, these outside facilities, located in 16 counties throughout the state, have hosted the majority of AAES research. In recent decades, AAES has added a number of research laboratories at both Auburn University and the outlying units.

During the early years of the twenty-first century, AAES has continued research on cultivation practices, management of pests and diseases, and variety selection. In addition, AAES is engaged in research related to food, food safety and security, and nutrition; agricultural biosecurity, bioenergy, and bioproducts; the environment and climate change; and water and other natural resources. Working closely with the Alabama Cooperative Extension System, AAES is developing and disseminating technologies to make Alabama's agribusinesses sustainable and competitive in the global marketplace.

## **Departments/Divisions**

### **1. Horticulture Department**

The Auburn University Department of Horticulture was formed in 1906, although horticulture classes were first taught at Auburn University in the 1890's. Since that time we have grown into one of the largest and oldest horticulture departments in the United States with over 200 students enrolled each year since 1996.

Departmental research is focused on: plant management via growth regulators and herbicides, variety development in food crops (fruit and vegetable), native plant selections and tolerances for urban settings, pecans and greenhouse crops. The sustained growth of undergraduate enrollment in the Department of Horticulture can be attributed to many factors, including demand for Auburn Horticulture graduates nationwide.

Courses prepare Horticulture graduates for the landscaping industry, nursery and greenhouse production, fruit and vegetable production, and pre-landscape architecture. The Horticulture curriculum at Auburn University offers the student a wide range of opportunities. Some of the opportunities for jobs in the field include: landscape designer, botanical gardens manager/curator, research, retail sales, Extension educator, landscape care professional, municipal horticulturist, landscape contractor, nursery manager, or farm producer.

While at Auburn, students participate in many campus and departmental club activities. As well the department provides opportunities in internships, study abroad and study tours.

### **2. Home Grounds Team**

The Home Grounds team is comprised of Extension Agents representing both Alabama A&M University (6 Agents) and Auburn University (12 Agents). Auburn University Extension Agents work with traditional programs and audiences, while Alabama A&M University Agents work with non-traditional programs and audiences. The Master Gardener Program is directed by Auburn Agents. Our goal with all Home Grounds programs is to improve the knowledge, enjoyment and safety of the home environment while ensuring the safety of Alabama's environment. The Home Grounds Team Agents teach practical problem-solving for the home, lawn, and garden.

### **3. Alabama Master Gardener Association (AMGA)**

The Master Gardener Program is a public service program offered by the Cooperative Extension Service that provides university training to volunteers for the purpose of enabling them to serve their communities through horticulture, gardening, and pest management. The first Master Gardener Program was initiated in the state of Washington in 1973 by Extension agents in response to a burgeoning interest in horticulture from citizens in the urban areas. The program's objective was to train volunteers to help Extension meet the overwhelming demand for information on horticulture, gardening, and plant problems. Volunteers participated in a series of science-based educational sessions that included many aspects of horticulture and related topics. Then, in return for this training, they assisted local Extension personnel in providing information and education.

The Master Gardener training program started in 1981 in Huntsville Alabama. The Alabama Master Gardeners Association (AMGA) was incorporated in 1993 and the Officers and Board of Directors are comprised of representatives from many of the counties in the State of Alabama. The mission of the Alabama Master Gardeners Association is to assist and support the Alabama Cooperative Extension System in its education outreach program and to support the local Master Gardener Associations in their pursuit of continuing education in the field of horticulture and providing volunteer service through horticultural based assistance, education and community projects.

AMGA presently has more than 2000 members statewide representing approximately 40+ counties. Thousands of volunteer hours were reported to the Alabama Cooperative Extension Agents during 2010. Alabama Master Gardeners currently support public outreach in conjunction with Auburn University and the Alabama Cooperative Extension System in community projects, the Master Gardener telephone hotline, municipal events and fairs, public education programs, distributing education materials, community gardens and food safety, demonstrations gardens, horticultural therapy and youth education.

## EQUIPMENT

**Computer:** All investigators and study staff have access networked (wireless and hard-wired) computers that are Pentium based or higher and units are continuously being upgraded. New units run at 3.2 Ghz or higher and are Dell workstations that include the necessary software for conducting research. Wireless access is available throughout the UAB campus. All computers are linked to each School's network, which has a dedicated server for faculty and for data storage and manipulation. There is direct connection to on-line Libraries, including the Medical Center Library. In addition, the faculty and staff can connect to the networks from offsite locations using secure VPN connections.

Software resources available include but are not limited to Microsoft Windows Vista, Microsoft Windows XP, 2000 Server, 2003 Server, Linux, Microsoft SQL, Exchange, FoxPro, Borland DBase & Paradox, Microsoft Excel, SPSS, Stata, PASS, SAS, BMDP, NCSS, StatXact, MapInfo, NQuery Advisor, DBMSCopy, Harvard Graphics, CorelDraw, Ethnograph, WordPerfect, Endnote, Microsoft Office including Outlook 2003 and 2007, Star Office, DICOM image software to include Desacc Digital Jacket, Personnel Server, DICOM Gateway, Verity Tele-Forms, MacAfee Virus protection, NOD32, COMODO Firewall, Ghost Firewall and Microsoft Desktop Firewall, TeleForm 10.2, Studytrax, Redcap, Cytel StatXact 8, StatXact Procs for SAS, Cytel LogXact 8, East 5, MathType 6, Rightfax Business Server 11.0., S-Plus 2000, P-Pharm 1.5.1, Kinetica 2000, Mathematica, arcGOS. EpilInfo 6.0, Cart, Rancode, Scientific Work Place 2.5, PASS, EquivTest, LISrel 8.0, IMSL, SUDAAN, Costart, Scientific Word 3.0, Wusage 7.1, Omni Page Pro v10.0, Macromedia DreamWeaver 8.0, Fireworks 8.0, Microsoft GeneSpring 6.0, JRUN 3.0, JRE 3.1, Tomcat 6.0, SUN Fortran Suite, SQL, C+, Visual Basic, Visual Studio, MedQuest, HTML, Java, ASP, and Adobe Acrobat.

Servers (maintained at departmental levels) are racked and made redundant, with continuous power supply, running a switched DHCP network at 100 MB per second to workstations, and connected to the network backbone by 1GB fibre. At a minimum there are 11 servers at each departmental level, including intranet servers, file and print servers, CND computer lab servers, and media servers. Servers and systems are backed up data according to each institution's Systems Security protocols and procedures, and disaster recovery plans are in place.

**Office:** All investigators and study staff at a project manager or higher position who are involved in this project have private offices that are wired for phone and internet through their departments.

**Laboratory:** The laboratory includes Eppendorf 5810 and 5804 plate centrifuges, and other standard laboratory equipment. There are 20 cubic foot, ultra-low freezers, as well as -20 °C freezers that will be used for the storage of biospecimens collected during home visits (sera, plasma, and buffy coat). Each of these freezers is hard wired to both an alarm system and emergency power. There is also a computerized bar-code based inventory system for tracking all specimens.

<b>1. Project Director / Principal Investigator (PD/PI)</b>	
Prefix:	Dr.
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Middle Name:	
* Last Name:	Demark-Wahnefried
Suffix:	Ph.D.
<b>2. Human Subjects</b>	
Clinical Trial?	<input type="checkbox"/> No <input checked="" type="checkbox"/> Yes
* Agency-Defined Phase III Clinical Trial?	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<b>3. Applicant Organization Contact</b>	
Person to be contacted on matters involving this application	
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## Vegetable Garden Feasibility Trial to Promote Function in Older Cancer Survivors

*Life begins the day you plant a garden" - Chinese Proverb*

**Specific Aims:** The therapeutic benefits of gardening were noted by Cicero in 60 BC. More recently, research shows that individuals who garden, and especially those who grow their own fruits and vegetables (F&V), are more physically active,<sup>1,2</sup> and tend to have healthier diets,<sup>3,4</sup> body weight status,<sup>5</sup> and better mental health and acuity.<sup>6-15</sup> To date, a handful of community-based F&V gardening interventions have demonstrated benefit for improving diet quality in healthy populations.<sup>16-19</sup> In a study by Brown et al. of 66 nursing home residents, a 5-week gardening intervention significantly improved the ability of older adults to perform three activities of daily living, i.e., transferring, eating and toileting, and also enhanced reassurance of worth.<sup>20</sup> These results may apply to cancer survivors as they are at far greater risk for many health conditions that are influenced by health behaviors (e.g., second cancers, cardiovascular disease [CVD] and diabetes).<sup>21-48</sup> Moreover, since accelerated functional decline is an acknowledged concern among cancer survivors,<sup>49,50</sup> the findings of Brown et al.<sup>20</sup> are compelling, and suggest that a gardening intervention may hold particular promise for older cancer survivors.

Last year, we piloted a gardening intervention that paired cancer survivors with Cooperative Extension Master Gardeners (MG).<sup>51</sup> Vegetable gardens were established at survivors' homes, and a yearlong intervention involving bimonthly contact between survivors and MGs to plan and plant gardens, check plant status, harvest, and rotate plantings was conducted. Though the study only enrolled 8 adult cancer survivors, data show trends toward improved F&V intake and physical activity (PA). Similar to Brown et al.,<sup>20</sup> we observed improvements in objective measures of strength, agility, and endurance. Based on these exciting findings, we attempted an R01 application which was well-scored, but criticized for two reasons: 1) a lack of focus solely on older cancer survivors; and 2) reliance on a pilot study that was too broad and scant to yield reliable parameter estimates.

Totally revamping our approach, we now propose a feasibility study among 46 older cancer survivors of locoregionally staged cancers with good prognosis residing in select urban and rural counties in Alabama. Participants will be randomized to 1-of-2 study arms: 1) an intervention group that receives a 1-year mentored vegetable gardening intervention, or 2) a usual care control group. Home visits will occur at baseline and 1-year follow-up to assess weight status, physical performance, and perform phlebotomy; self-report data on diet, PA, physical functioning, and quality of life also will be assessed. Our research team, comprised of investigators with expertise in cancer survivorship, aging, community-based interventions, oncologic care, and biostatistics, as well as agriculture and gardening, is well-poised to pursue the following specific aims:

### **Primary Aims:**

**(a) To explore the feasibility and acceptability of a mentored vegetable gardening intervention.** This aim will be accomplished by collecting detailed process data, which will allow the assessment of accrual, retention, adherence/fidelity, and adverse events; and **(b) To quantify (mean change scores and precision estimates) and compare between-arm differences in physical function as measured by the Short Form 36 Physical Function Subscale (SF36-PFSS).** We hypothesize that by using methods similar to our smaller pilot, we will be able to recruit (within a 6 month window) 46 older cancer survivors who will be paired with geographically-matched MGs, retain >80% of the sample, invoke >80% adherence/fidelity to the intervention and protocol, while at the same time observing no serious adverse events directly attributable to the intervention. We also hypothesize that the intervention arm will show more favorable SF35-PFSS change scores than the control arm over the 1-year study period. The trial will be declared a success if feasibility benchmarks are met, and the hypothesized directionality of effects on physical function as measured by the SF36-PFSS are observed.

### **Secondary Aims:**

- 1. To obtain means and precision estimates and explore between-arm differences on pre-post changes in secondary endpoints:** (a) physical performance tests (Short Physical Performance Battery (SPPB)<sup>52,53</sup> & Senior Fitness Tests<sup>54,55</sup>), (b) biomarkers of physical function and healthful aging (e.g. IL-6, D-dimer, sVCAM, & telomerase), (c) F&V intake and diet quality (DQ), (d) accelerometer measured PA, (e) BMI, (f) health-related quality of life (HRQoL), and (g) reassurance of worth.
- 2. To explore participant factors associated with program efficacy, e.g., gender, and comorbidity.**

Cancer survivors suffer from a host of long-term adverse effects that reduce HRQoL and physical functioning. These downstream effects result in an annual burden of approximately \$130 Billion.<sup>56,57</sup> Thus, there is an urgent need to develop interventions that are effective, durable and disseminable. Gardening interventions may hold particular promise in these domains; thus, if the data from the proposed study continue to show feasibility and benefit, the effect estimates will be used to power future trials to discern efficacy.

## RESEARCH STRATEGY

**A. Significance:** There are 13.7 million cancer survivors in the US, comprising ~4% of the population.<sup>58</sup> The number of cancer survivors is skyrocketing due to a confluence of the following factors: 1) the US population is aging; 2) cancer is an age-related disease (>60% of cancer survivors are age 65+); and 3) improvements in early detection and treatment have resulted in many common cancers having 5-year cure rates that surpass 90%.<sup>59-61</sup> Rising numbers of cancer survivors is good news, but over \$130 billion annually is needed to address their long-term health and psychosocial sequelae.<sup>57</sup> Compared to others, cancer survivors are at higher risk for other cancers, CVD, osteoporosis, and diabetes.<sup>21-48</sup> Accelerated functional decline also is a major problem among cancer survivors,<sup>62-65</sup> especially those who are older.<sup>50,66-71</sup> Baker et al. found that compared to age-matched controls, cancer cases (n=45,494) had significantly lower physical and social functioning, vitality, mental health, and HRQoL (p<0.001).<sup>63</sup> Results of others are similar and suggest that cancer survivors face functional decline that threatens their ability to live independently, posing a burden to themselves, their families and the health care system.<sup>50,62-71</sup> Thus, cancer survivorship is claimed as a national priority,<sup>32</sup> and there is a call for interventions that target markedly vulnerable subsets.<sup>72</sup>

Prior interventions to improve PA and DQ have proven effective in improving functional status and other health outcomes in cancer survivors.<sup>73-75</sup> The 2 largest RCTs to date aimed at physical function, RENEW (Reach-out to ENhancE Wellness, n=641) and Project LEAD (Leading the way in Exercise And Diet, n=182), were led by Demark-Wahnefried (PI) and tested home-based interventions. Both RCTs resulted in significant improvements in DQ, PA and physical function, with few adverse events and low rates of attrition, but there was little capacity for dissemination once funding ended. Thus, we have sought to develop interventions that build on existing programs and that have a high likelihood of translation into the community. The proposed intervention relies on: (a) the extant infrastructure of the Cooperative Extension, (b) our mini-pilot work and collaboration with MGs, (c) data that show that gardening consists of low-to-moderate PA that combines aerobic and strength training activities associated with improved health,<sup>76</sup> and (d) new observational data published in 2012 that show that gardeners have significantly better gait speed, balance, and significantly fewer chronic conditions, functional limitations and falls.<sup>77</sup>

MG Programs exist in land grant universities in all 50 United States. Certified MGs complete  $\geq 60$  hrs. of instruction and community service (CS) and 25 hrs./year of CS to maintain active status. In surveying 184 MGs in AL, we found that 71% were “extremely interested” in mentoring a cancer survivor on vegetable gardening for their CS, and an extra 26% stated that “they were interested and wanted to learn more.” Thus, the project is of great interest and builds on an extant infrastructure for sustainability. Ultimately, this intervention could be disseminated to states with 3 growing seasons and adapted to colder weather in those with 2 growing seasons (42 states in total – see Appendix A). The intervention also could be adapted for persons with other types of chronic disease in which physical functioning and lifestyle behaviors are key. Finally, this project is significant because the intervention has great potential for sustainability since gardening: (a) involves many activities which prevent satiation common with other forms of exercise; (b) provides a sense of achievement and zest for life that come from nurturing and observing new life and growth;<sup>78</sup> and (c) imparts natural prompts since plants require regular care (watering) and attention (harvesting) and serve as continual and dynamic behavioral cues.

**B. Innovation:** The proposed RCT is innovative because...

- 1) It will be one of the first gardening interventions in a patient population - the very first for cancer survivors.
- 2) It represents a behavioral intervention that will assess behavior and functional change both by self-report and objective measures, e.g., physical function (self-report using the SF36-PFSS) and physical performance (objective battery of tests),<sup>52,53</sup> PA 7-day recall and accelerometry.
- 3) It uses a novel, holistic approach to improve physical function and performance, and QoL.
- 4) It will be one of the few RCTs conducted in a diverse and broad-based sample of older survivors of various cancers for which 5-year survival is  $\geq 80\%$ . Thus, it differs from previous research which has been largely limited to young, white, breast cancer survivors.<sup>21</sup> Given our focus on health behaviors and physical function, our broad sample of older survivors is justified and enhances generalizability (vital for future dissemination). Our RCT also will include survivors in rural and urban settings, men and women, and include 27% minority.
- 5) It advances the science of successful aging by gauging changes in interleukin-6 (IL-6), soluble vascular cell adhesion molecule (s-VCAM), D-dimer, and telomerase since other studies suggest that these biomarkers relate to physical function, and are influenced by diet and exercise (though more data are needed).<sup>1-10</sup>
- 6) It is a pioneering effort and community-based partnership between health care and agriculture, and brings together cancer survivors, researchers at UAB, and agents of the AL Cooperative Extension.

## C. Approach:

**C.1 Preliminary Research:** The proposed RCT builds upon our successful track record of developing, delivering, and testing home-based interventions to improve the health behaviors and outcomes among cancer survivors (Appendix B),<sup>73,75,79-94</sup> and a previous community-based intervention that partnered MGs with rural church parishioners to establish victory gardens in the Black Churches United for Better Health Project.<sup>95-99</sup> The intervention also is based on our mini-pilot study that assessed the feasibility of a vegetable gardening intervention that paired 8 adult cancer survivors (4 breast/4 prostate) with MGs to explore effects on F&V intake,<sup>100</sup> PA,<sup>101</sup> HRQoL,<sup>102</sup> and physical function<sup>102</sup> and performance.<sup>54,51</sup> MGs worked with survivors to plan and then plant 3 gardens, harvest and rotate plantings, and troubleshoot as needed.

**Table 1. Comments by Mini-Pilot Survivors(#1-2) & MGs (#3-4)**

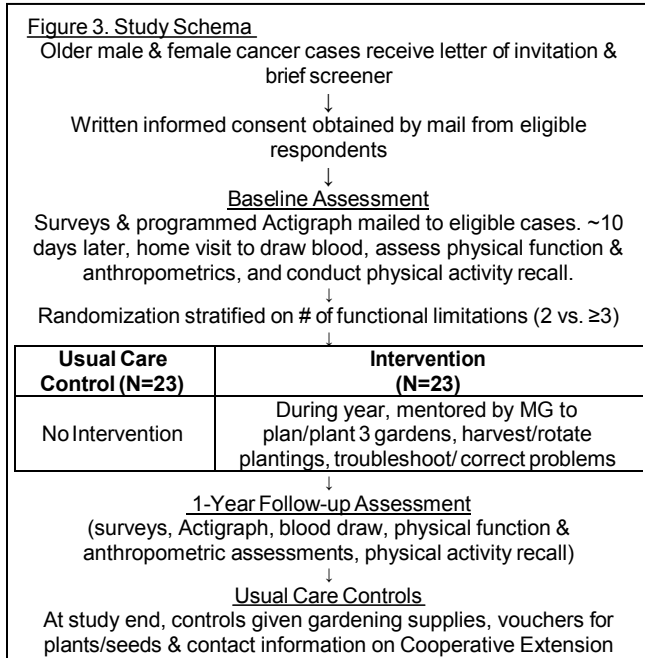
1. "I feel so much better since starting the study and I have lost 5 or 6 pounds as a result of the extra [physical] activity"
2. "I may not always feel up to it, but if I know there's a tomato to be picked, I am not going to sit here and let it rot."
3. "In my 14 years as a master gardener, this has been the most exciting and rewarding project I have participated in."
4. "I believe I have gotten far more from this program than I ever gave. This experience has filled me with joy."

Results suggest that the 1-year intervention was feasible (robust enrollment; minimal attrition) and well-received by cancer survivors and MGs (Table 1; also see letters of support). Improvement in 3 of 4 objective measures of strength, agility & endurance was observed in all survivors, with the following pre-post change scores (median [interquartile range]): hand grip test (+4.5 [3.0, 6.7] kg), 30-sec. chair stand (+1.5 [-1.0, 5.0] stands), 8 foot Get Up and Go (-1.5 [-2.1, -0.2]

sec.), and 6-minute walk (+38 [20, 120] ft). Also, 50% of survivors increased their F&V intake by  $\geq 1$  serving/day and 67% increased their PA by  $\geq 30$  minutes/week. While two of our cancer survivors were displaced by the EF-5 tornados that tore through AL in April 2011, no adverse events were noted. Of note, 100% of survivors plan to continue gardening and also to expand their gardens, and one has even completed the MG certification process. A paper detailing these findings is in press in *Acta Oncologica* (see Appendix C for galley proofs).<sup>51</sup>

**C.2 Community-Based Partnership:** Like our mini-pilot study, the proposed intervention is a community-

based partnership between UAB and the Alabama Cooperative Extension System (ACES), the lead education outreach arm of Auburn University. The MG Program recruits and trains volunteer leaders to assist Extension agents in disseminating research-based information on landscaping and gardening to the general public. There are 44 MG associations within defined regions in AL, with widespread coverage throughout the state. In 2012, there were >2,500 active certified MGs and interns who clocked >190,000 volunteer hours (~90 hours/MG). For the proposed project, we will focus on Cullman and Mobile counties that have 163 MGs in total. These counties were chosen specifically because: 1) they both have vibrant MG programs; 2) they are well-separated geographically and will well-prepare us for a future R01 that will encompass the entire state; and 3) these northern and southern counties provide good variation in soil-type (clay vs. sand), elevation (mountain vs. sea-level), and rural vs. urban (see map Appendix D). As in our mini-pilot, our collaborators at ACES will be responsible for recruiting, training, and



supporting the MG volunteers who agree to be mentors in the proposed intervention (training program outline - Appendix E). ACES will organize training to teach principles of F&V gardening. Regionally-based ACES Agents will be available via telephone, e-mail, and face-to-face to assist mentors with gardening support and offer print, web-based and other resources. MGs will be paired with cancer survivors based on proximity, and once paired, every effort will be made to maintain that relationship until the intervention is completed. However, as in the pilot study if illness, personal issues, or personality conflicts arise, a substitute MG will be found.

**C.3. Overview of the Mentored Vegetable Gardening RCT:** This randomized controlled feasibility trial employs a usual care control arm (rather than an attention control) given the holistic nature of our intervention (study schema - Fig. 3). Gardening supplies however, will be provided to controls at study completion in order to improve recruitment and retention. We will enroll 46 older (aged 65+) survivors of loco-regionally staged cancers with good prognoses ( $\geq 80\%$  5-year relative survival). Outcome measures will be assessed at baseline and 1-year follow-up on all study participants (regardless of arm and adherence); home visit assessments are planned to reduce barriers to participation by underserved (older, rural, lower SES) survivors. Data collection includes subjective (diet, PA, HRQoL), objective (accelerometry, physical performance tests), biologic (blood biomarkers), and qualitative (process data & post-intervention debriefings) data (Table 4).

**C.4. Recruitment and Consent:**

As in our current ENERGY trial,<sup>103,104</sup> cases will be ascertained using the Gold Certified, population-based AL Statewide Cancer Registry (ASCR) (see letter of support from registrar). A purchased service agreement with ASCR will employ the following procedure: 1) Identify cases aged  $\geq 65$  years diagnosed within the past 5 years with one of the cancers listed in Table 2; 2) Contact oncologists of cases to obtain permission to contact; 3) If approved or non-response (ASCR accepts passive consent), case contact data sent to study staff; & 4) If not approved, forward aggregate demographic (age, sex, race-ethnicity) and cancer data (type/stage, diagnosis year) at enrollment completion (to assess potential selection bias).<sup>105</sup>

This trial will recruit men and women recently diagnosed with a cancer of favorable prognosis from both rural (Cullman:n=16; 8/arm) and urban (Mobile:n=30;15/arm) counties (representative cancers-Table 2 and eligibility criteria-Table 3). Our sample will represent the state population for race-ethnicity (27% minority). Our accrual target is 46 cases, which is attainable given an estimated pool of 2956 cases. This allows for a 91% contact rate (as in our ENERGY trial)<sup>104</sup> and affords a joint eligibility-response rate as low as 2%.

Cullman and Mobile MGs will be identified, and then cancer cases residing within a 15-mile radius of MGs will be approached for possible enrollment. As in our previous studies,<sup>51,73-75</sup> potentially eligible cases will be mailed a letter of invitation along with a brief screener to assess eligibility (Appendix F), 2 consent forms (one to sign, one to keep), and a preaddressed, postage paid envelope for return. Eligible cases will be contacted via telephone by study staff to schedule the baseline assessment. Response rates (cases responding/cases ascertained [minus dead letters]), reasons for ineligibility or disinterest, and proportional accrual (cases enrolled/cases ascertained) will be carefully tracked.

**Table 2. Estimates of cancer cases ( $\geq$  age 65) with cancer-free relative survival  $\geq 80\%$**

Cancer Site	Stage(s) at Diagnosis	5-year Relative Survival	Adj. Ave. Count
Bladder	In situ	96.6%	129
Breast (female)	Localized, Regional	98.6%, 83.8%	762
Cervix	Localized	90.9%	11
Colon & rectum	Localized	90.1%	333
Corpus & uterus	Localized	95.8%	88
Kidney/renal pelvis	Localized	90.8%	130
Hodgkin Lymphoma	Localized, Regional	89.8%, 90.4%	7
Non-Hodgkin Lymphoma	Localized	81.1%	63
Oral cavity/pharynx	Localized	82.3%	50
Ovary	Localized	92.4%	12
Prostate	Localized, Regional	99.9%	1305
Small intestine	Localized	80.1%	7
Soft tissues	Localized	83.6%	17
Thyroid	Localized, Regional	99.8%, 96.9%	42
<b>Total Count</b>			<b>2956</b>

**Table 3. Adult ( $\geq 65$  years of age) men and women who meet the following criteria are eligible for this trial:**

<u>1</u>	Diagnosed with a loco-regionally staged cancer associated with an 80% or greater 5-year relative survival rate and residing in either Cullman (rural) or Mobile (urban) counties (see Table 2 above).
<u>2</u>	Within 5-years of diagnosis and completed primary curative treatment (surgery, chemotherapy, radiation).
<u>3</u>	<b>At higher risk for functional decline as shown by at least 2 physical function limitations on the SF36 PFSS.</b>
<u>4</u>	<u>Not</u> currently adhering to the recommended number of F&V servings/day ( $\geq 5$ ) and minutes of exercise/week ( $\geq 150$ )
<u>5</u>	No pre-existing medical condition(s) that precludes (a) increased consumption of F&Vs, e.g., pharmacologic doses of warfarin or (b) gardening, e.g., severe orthopedic conditions, pending hip/knee replacement (within 6 mo.), paralysis, dementia, blindness, untreated stage 3 hypertension, or MI, congestive heart failure, or conditions that required oxygen or hospitalization within 6 mo.
<u>6</u>	Community dwelling and residence within 15 miles of a MG volunteering in the study.
<u>7</u>	Reside in a location that can accommodate 4 or more Earthboxes or one 4'x8' foot raised bed with ample sunshine (i.e., 6 or more hours per day) and have ready access to water.
<u>8</u>	No previous experience with vegetable gardening, e.g., planting a vegetable garden annually.
<u>9</u>	English-speaking & writing (some of our scales are not validated in other populations/languages)
<u>10</u>	Willingness to be randomized to either study arm and participate in the 1-year follow-up assessment.

**C.5. Baseline Assessment:** Roughly 10-12 days prior to the baseline visit,<sup>73</sup> participants will be mailed questionnaires and a programmed accelerometer with instructions for a 7-day collection. These materials will be collected by study staff during the baseline visit conducted in participants' homes (similar to our prior

epidemiology studies)<sup>106-108</sup> and will also include anthropometrics, PA recall, physical performance tests, and phlebotomy (10 cc EDTA treated tube)(C.9/Table 4). During the home visit, study staff will confirm the garden-based eligibility criteria (#7 & #8; initially assessed prior to scheduling home visit) prior to conducting any study measures. Ineligible individuals will receive the \$10 study visit incentive, but will not be tested nor enrolled.

**C.6. Randomization:** Subjects will be block randomized within 2 strata defined by the number of physical function limitations as assessed by the SF36-PFSS (2 vs.  $\geq 3$ ).

### **C.7. Vegetable Gardening Intervention:**

**C.7.1. Theoretical Framework:** The proposed intervention will be guided primarily by Social Cognitive Theory (SCT),<sup>109,110</sup> which emphasizes self-efficacy and skills development to mediate behavior change.<sup>109-124</sup> MGs will be trained to promote self-efficacy by serving as role models, encouraging incremental goal setting, providing reinforcement/encouragement as appropriate, strategizing to overcome barriers, creating expectancy that gardening will result in desired outcomes, and skills training for high risk situations to enhance behavioral capability. Participants will be asked to keep a gardening journal (self-monitoring). The intervention also draws from the Social Ecological Model (SEM),<sup>125</sup> since we expect that effects on physical functioning, F&V intake, and PA, will be influenced by interactive relationships between the survivor and his/her social/physical environment. The practice of vegetable gardening is likely to have multiple levels of influence including individual factors (e.g., demographics), interpersonal factors (e.g., social support) and community factors (e.g., availability of gardening supplies/support).

**C.7.2. Intervention Elements: Gardening supplies:** At intervention start, participants will receive Earthboxes® (Scranton, PA) or raised bed kits (Home Depot, Inc. Atlanta, GA) via direct home delivery (our mini-pilot showed that ~25% of our sample will live in apartments/rentals and require Earthboxes). Gardening supplies, including watering cans, weeding hoes, transplanners, etc. also will be ordered via Home Depot and delivered to each study participant's home. Items that cannot be shipped (e.g., plants, seeds, soil mix, fertilizer, tomato cages) will be purchased by participant-MG dyads or by the MG (gift cards will be made available to cover purchases and receipts collected) at local gardening stores (C.7.3). **Study Binder (Appendix G):** Participants will receive binders with their MG contact information, articles on garden design, safety and health (e.g., protecting knees & back, sun protection), nutrition (e.g., cooking methods to preserve vegetable nutrients), information on their raised bed or Earthbox®, and instructions for keeping a gardening journal. MGs will receive a binder with their participant contact information, detailed information on raised bed and Earthbox® gardening, & a contact checklist to track home visits, follow-up telephone calls, and a list of topics to discuss with study participant (e.g., pest management, soil care, watering). Information will be provided in brief segments and ordered to promote self-mastery, thus adhering to the tenets of SCT. **Facebook:** As was observed in our mini-pilot, participants have an interest in sharing their gardening experiences, suggestions, and photos. Therefore, a dedicated and secured Facebook site will be set up, administered and maintained by ACES for interactive sharing of information among registered and interested study participants and MGs (using secure log-in).

**C.7.3. Intervention Delivery:** After the gardening supplies have been delivered to the participant's home, their MG mentor will make a home visit to help build the raised bed (from kit) or to assemble 4 Earthboxes®. An initial meeting between the participant-MG dyad will take place to discuss plans for establishing the first garden, e.g., location, types of F&Vs and herbs that the participant likes or is willing to try (Appendix E). The participant-MG dyad will then meet at the local garden store to select plants and seeds, and purchase remaining supplies, i.e., soil mix, fertilizer, tomato cages. Visits to the local gardening store will serve as opportunities for the MG to impart knowledge on plants and supplies and will occur at least once over the course of the 1-year intervention. Plants and supplies will be transported to the participant's home, and together the MG and participant will plant the garden. The MG will leave instructions on care of the garden, and follow-up with the participant via a series of alternating monthly telephone calls and home visits, with contact occurring every 2 weeks. At each visit, the MG will troubleshoot any problems and assist the participant in correcting them. Between visits, the MG will provide support via e-mail/telephone to discuss progress (status of plants, harvesting), review care of their garden (soil & pest management, watering), and answer questions and suggest solutions to problems (excessive heat, too much/little water). During monthly visits, as old plants expire, the MG will assist the participant in substituting new items. The temperate climate in AL (frost cloths provided) makes it possible to grow throughout the year and 3 gardens are planned: spring, summer & winter.

Education is a key component of the intervention, and to be sustainable, the participant will need to learn as much as possible about plants (e.g., purchasing, growing from seeds) and gardening (e.g., planting, maintaining, harvesting). There are many ways in which this will be accomplished: a) the MG will teach the participant about organic gardening and "soft chemistry" for fertilizing and pest control, b) the dyad will visit local garden

centers together at least once to impart knowledge on selecting healthy plants and additional supplies (e.g., extra soil or fertilizer), and c) Dr. Demark-Wahnefried and her staff will train MG on working with cancer survivors and engaging them in incremental goal setting. Thus, participants' first gardens will rely on elementary knowledge and skill levels, and as plants are rotated and gardens evolve, higher levels of skill will be called for.

**C.7.4. Monitoring Fidelity to Intervention Delivery/Gardening Activity:** Strategies to monitor and enhance fidelity to intervention delivery by MGs, and to gardening by cancer survivors are based on the NIH Behavior Change Consortium recommendations:<sup>126</sup> 1) **Treatment Design:** Our protocol specifies the schedule for home visits; however, as the need for gardening advice is driven by participants, the frequency, date and duration of follow-up contacts (telephone/e-mail) will be tracked. Log books kept by MGs will be collected monthly (Appendix G). 2) **Provider Training:** A review of vegetable & container gardening from the MG certification course (Appendix E) and training for working with cancer survivors will be provided to all MG mentors. Booster training sessions, easy access to project staff, and review of MG log books by staff will minimize recidivism over time in MG intervention skills and ensure MG adherence to the protocol. MGs will receive gardening support through the ACES Agents and intervention specific support through UAB staff. 3) **Treatment Delivery:** Consistency in intervention content & delivery will be ensured by using standardized procedures/materials. MGs will complete a checklist for gardening activities (e.g., plant rotation) and lessons (e.g., soil care), which will be reviewed by staff; standardized written materials will be provided. 4) **Treatment Receipt:** Participants' logs of MG contact (to verify #2 above) & time-stamped photographs of the garden (weekly) and at each MG visit will be submitted to the UAB study office. 5) **Enactment of Treatment Skills:** Adoption of skills learned during the intervention will be assessed from gardening journals, telephone contact with staff, photograph confirmation, and home visits.

**C.8. Safety:** Safety precautions include: 1) exclusion of individuals for whom unsupervised activity or gardening is unsafe; 2) written materials on safety will be provided to participants (e.g., the importance of wearing gloves and avoiding excessive arm strain to prevent lymphedema in breast cancer survivors) and reinforced by MGs (Appendix G); 3) participants will be advised to report adverse events (e-mail/ toll-free study phone #), and 4) well-trained staff in conducting physical performance tests, based on validated protocols.

**C.9. Measures & Measurement Points:** In addition to assessing response rates (C.4.), drop-out, and adverse events (Human Subjects), the data shown in Table 4 will be obtained at baseline and/or 1-year home visits

<b>Table 4. Measures at baseline (B) and 1-year follow-up (1Y) (See Appendix H for surveys/protocols)</b>	<b>B</b>	<b>1Y</b>
<b>SF36 Physical Function subscale (SF36 PFSS) (PRIMARY ENDPOINT):</b> This 10-item subscale assesses general physical function and is valid & reliable for use in healthy & chronically-ill adults. Internal consistency is excellent: $\alpha=0.89$ to $0.92$ . <sup>102</sup> It has published norms, is sensitive to change, & has performed well in our past studies; <sup>75,79,86</sup> we have found it free of ceiling effects. Two limitations (limited a little or limited a lot) are required at screening to be eligible for the study.	<b>X</b>	<b>X</b>
<b>Physical Performance Tests:</b> Short Physical Performance Battery (SPPB): the standard gerontology assessment tool of lower extremity function; includes tests of balance, gait (timed 8-ft walk at normal pace), & lower body strength (time to rise from a chair 5 times). This battery has strong predictive validity for disability, hospitalization, nursing home admission, & mortality. <sup>52,53,128</sup> <b>Senior Fitness Test Battery:</b> <sup>55</sup> is also sensitive to change & has normative scores & may have fewer ceiling effects, <sup>55</sup> & thus may be more responsive than the SPPB in our sample. Physical function domains: lower & upper body strength (30-sec chair stand, arm curl), endurance (2-min step test), flexibility (chair sit-&-reach, back scratch), & agility/dynamic balance (8-ft Get Up & Go). <sup>54,129</sup> Additionally, grip strength will be objectively measured by a dynamometer (predictive of functional limitations and disability). <sup>130,131</sup> Total performance test time: 20-25 minutes.	<b>X</b>	<b>X</b>
<b>Blood Draw &amp; Biomarkers of Physical Function &amp; Healthful Aging:</b> Blood will be drawn in a 10 cc EDTA-treated vacutainer, allowed to clot & centrifuged immediately (portable centrifuges will be used in the field as in our epidemiologic studies). <sup>106,107</sup> While our biomarkers are not influenced by fasting, <sup>127</sup> there may be some diurnal variation, thus time of the draw will be recorded along with wake time; baseline and follow-up visits will be scheduled at similar times of day ( $\pm 2$ hrs.) for each participant to reduce intra-individual variation. Blood will be configured into plasma (stored on dry ice), and buffy coat/peripheral blood mononuclear cells (PBMC)(stored at room temp), the latter of which will under-go RNA extraction. Upon return to UAB, samples will be stored at $-20^{\circ}\text{C}$ (PBMCS) & $-80^{\circ}\text{C}$ (DNA, plasma) until batch analysis at study end. Currently we have no specific plans for DNA; however, we will obtain permission to store it using a separate clause on the consent form as this is a valuable resource for future studies.	<b>X</b>	<b>X</b>
Growing evidence, including studies of Dr. Cohen (consultant and expert in gero-oncology), suggest that IL-6, s-VCAM, D-dimer and telomerase are responsive to diet and PA and related to better functional status and successful aging, <sup>132-141</sup> thus serving as useful & novel secondary endpoints. Plasma IL-6 and s-VCAM will be assessed via electrochemiluminescence in the UAB Core Laboratory of the Center for Clinical & Translational Science & the Nutrition Obesity Research Center. Plasma D-dimer will be assayed in the Coagulation Core Service Laboratory using enzyme-linked immunoassays (Dimertest Tripwell EIA kit). Mean intra- & inter-assay coefficients of variation for markers of inflammation are below 5% and 10%, respectively. Telomerase activity will be measured in PBMCS by the laboratory of Dr. Trygve Tollefsbol, a leader in the field of aging using the Telomerase PCR ELISA assay. <sup>142</sup> Assays will be performed in duplicate, & re-runs performed on samples providing discrepant readings (>25%).	<b>X</b>	<b>X</b>
<b>F&amp;V/Dietary Intake</b> will be assessed via self-report using the NCI Diet History Questionnaire (DHQ). <sup>143</sup> DQ will be derived using the Healthy Eating Index, 2005. <sup>144,145</sup> The mean energy adjusted correlation coefficient comparing the DHQ and 4 - 24-hr dietary recalls was 0.62, with similar or higher coefficients for F&Vs. <sup>146</sup>	<b>X</b>	<b>X</b>

<b>Table 4. Measures at baseline (B) and 1-year follow-up (1Y) (See Appendix H for surveys/protocols)</b>	<b>B</b>	<b>1Y</b>
<b>7-day PA Recall:</b> captures household & leisure activities, has a standardized script, & measures current & recent past PA & thus is sensitive to change. It also has been used successfully in many large trials. <sup>73,147-153</sup> Test-retest reliability separated by 2 weeks is 0.99; same day test-retest reliability with 2 different interviewers is 0.86. <sup>148</sup>	<b>X</b>	<b>X</b>
<b>Accelerometry:</b> PA will be objectively measured via accelerometry (Actigraph, Fort Walton Beach FL). Programmed units will be mailed to participants with instructions for 7 day collection, and then collected by staff during home visits. This unit was selected given its reliability & longstanding use in large scale trials <sup>152,153</sup> Accelerometers will be downloaded & processed using procedures & software supplied by the manufacturer.	<b>X</b>	<b>X</b>
<b>Health-Related Quality of Life</b> The SF36 (SF36v2r) provides a global measure of health related QoL, & each of the 8 subscales will be explored separately. The internal consistency & reliability for all 8 subscales is high, ICC 0.78- 0.93. <sup>63,154</sup>	<b>X</b>	<b>X</b>
<b>Anthropometrics:</b> Procedures delineated in the <u>Anthropometric Standardization Manual</u> <sup>155</sup> will be used to measure height, weight, and waist circumference during home assessments using a calibrated scale (to nearest 0.1 kg), portable stadiometer (nearest 0.5 cm), <sup>156</sup> and a non-stretch, tension-controlled tape measure (nearest 0.5 cm), respectively.	<b>X</b>	<b>X</b>
<b>Comorbidity:</b> Older Americans Resources & Services (OARS) Comorbidity Index <sup>157</sup> will assess the # of chronic medical conditions/ symptoms & their functional impact (severity). An item assessing falls in the past year will be added. <sup>77</sup>	<b>X</b>	<b>X</b>
<b>Reassurance of Worth:</b> One of 6 subscales of the Revised Social Provision Scale, this measure will be used to assess the psychosocial benefits of gardening. Several gardening studies have reported enhanced self-esteem, increased independence, and increased zest for life associated with gardening. <sup>10,20</sup> Reliability estimates: 0.60 to 0.70. <sup>158</sup>	<b>X</b>	<b>X</b>
<b>Mediators: Interpersonal:</b> We will use the Social Support & Eating Habits (10 items) & Exercise Surveys (13 items) <sup>159</sup> since they have been widely used in diverse samples & have strong psychometric properties ( $\alpha=.70$ ). Surveys will be adapted for gardening using identical anchors. <b>Individual:</b> Self-efficacy beliefs are domain-specific; thus, for this RCT, self-efficacy is survivors' beliefs in their ability to maintain a successful vegetable garden. <b>Community-Level:</b> Participant-MG dyads will independently assess the participant's local environment for support of vegetable gardening considering the following factors: 1) availability of garden stores; 2) presence of pests (i.e., insects, deer); 3) neighborhood covenants that impose landscaping restrictions; and 4) sense of belonging with other gardeners in local community. (7-point Likert scale: environment is extremely unsupportive (1) to extremely supportive (7) for gardening)	<b>X</b>	<b>X</b>
<b>Intentions of Future Gardening:</b> Upon completion of the intervention, participants will be asked whether they intend to continue vegetable gardening and to expand their gardening space.	-	<b>X</b>
<b>Demographic &amp; Health-Related Characteristics:</b> Data will be collected on age, race/ethnicity, education, income range, marital status, occupation, and smoking status. Cancer related data will be obtained from both participants (treatment: surgery, radiotherapy, chemotherapy, hormone therapy) and the cancer registry (cancer site/stage, diagnosis year).	<b>X</b>	-
<b>Process Data</b> will be collected & used to evaluate adherence to & fidelity of the intervention (Primary Endpoint): <b>Gardening Activities:</b> Photographs of the garden & of the survivor-MG dyad posing together in front of the garden (during monthly visits) will be collected quarterly (e-mailed or postage-paid envelope for disposable cameras). Additionally, data will be extracted from gardening journals. <b>MG Mentoring:</b> MGs will report via email or phone during scheduled calls with Regional Agents the status of participant contact (home visits and telephone calls) (See MG binder, Appendix G).	<b>X</b>	<b>X</b>

**C.10. Hypotheses, Power and Statistical Analyses:** For this feasibility study, we hypothesize that we will meet the accrual target of 46 cancer survivors, retain  $\geq 80\%$  of our sample, evoke 80% adherence/fidelity with contacts and logs, and experience no serious adverse events attributable to the intervention. These hypotheses will not require formal statistical analysis. While establishing efficacy is a primary concern for feasibility studies, we still will explore whether a higher proportion of participants in the intervention arm as compared to the control arm show improvements in physical function (SF36-PFSS) of 5 points or more by testing for differences between groups with the Fisher's exact test for proportions. Using 1-sided testing (appropriate for pilots),  $\alpha = 0.05$ , and 20 subjects/arm (assumes 13% attrition), we have 79% power to detect a response difference between groups assuming underlying proportions of 15% in the control arm and 55% in the intervention arm. Analyses: Differences between refusers and enrollees and drop-outs vs. completers will be compared by chi-square (categorical variables) and t-tests (continuous variables). Adverse events will be summed as frequencies along with 95% confidence intervals. To provide estimates of efficacy for a larger RCT, between group differences in baseline to 1-year change in physical performance tests, biomarkers of physical function & aging, F&V intake, diet quality, PA, and HRQoL will be quantified using means and standard deviations and compared using pooled t-tests. Logistic regression will be used to evaluate subject characteristics (e.g., age, education, # of comorbidities, sex) associated with adherence to gardening and with improvements in F&V intake, PA, and improvement of physical function of 5 points or more on the SF36-PFSS.

**C.11. Study Timeline:** Given our mini-pilot experience, development time (obtain regulatory approvals, train MGs & study staff, finalize study materials) is substantially reduced. Participants will be accrued into Cohort 1 (Rural county; n=16) or Cohort 2 (Urban county; n=30). The intervention is divided into 3 periods or seasonal gardens: Summer (Apr-Jul), Fall (Aug- Nov), Spring (Dec-Mar). For each gardening season: month-1: planning meetings between MG-survivor dyads (e.g., Dec. for spring garden); month-2: garden is planted (e.g., Jan. for spring garden).

	Year 1 (2013-14)			Year 2 (2014-15)		
	Dec-Mar	Apr-Jul	Aug-Nov	Dec-Mar	Apr-Jul	Aug-Nov
Development						
Cohort 1						
Cohort 2						
Data entry/cleaning						
Analyses/Reports						



## **PROTECTION OF HUMAN SUBJECTS:**

Human Subjects Involvement and Participation: Cancer survivors are at significantly increased risk of developing progressive disease, comorbidity, and functional decline. Interventions that promote a healthy diet (ideally  $\geq 5$  servings/day of fruits and vegetables [F&V]) and increased physical activity (PA; ideally  $\geq 150$  minutes/week of moderate or vigorous activity) may improve the overall health and physical functioning of this vulnerable population. Our results from our vegetable gardening mini-pilot intervention suggest that gardening is a holistic approach to improving and sustaining health behaviors. In addition, this intervention holds particular promise for improving physical functioning, where improvements were observed after only 6 months of the intervention, and sustained at 1-year follow-up. The purpose of the proposed pilot/feasibility study is to expand this gardening intervention to a larger sample of adult cancer survivors in order to assess accrual, retention, adherence and fidelity, as well as potential adverse events. Additionally, the larger sample will provide mean change scores and precision estimates that are needed to power future trials to discern efficacy.

Half of the study sample will be randomly assigned to receive the mentored vegetable gardening intervention (intervention group); the other half will be observed during the 1-year study (usual care control group). Study participants will be provided with basic gardening supplies (e.g., hoses, weeding hoes), either a 4'x8' raised bed garden kit or 4 Earthboxes®, and plants and seeds for 3 seasonal gardens during the year-long intervention. Additionally, study participants will be paired with a certified Master Gardener from the Alabama Cooperative Extension System (ACES), who will mentor the participants on how to plant and maintain a productive garden. To enhance accrual and retention, individuals in the control group will receive gardening supplies and access to information from the master gardening program at study completion. Outcome measures (physical function tests, diet, PA, anthropometrics, Health-related Quality of Life (HRQoL), and biomarkers associated with physical functioning and healthy aging, i.e., IL-6, D-dimer, sVCAM, and telomerase) will be assessed during home visits at baseline and 1-year follow-up. We will quantify (mean change scores and precision estimates) and explore between-arm differences on pre-post changes in physical functioning, biomarkers, F&V intake, overall diet quality, PA, overall quality of life, BMI, and other indices of health and well-being.

In an effort to pursue these aims, the proposed study will accrue 46 adult cancer survivors aged 65 years or older in select rural and urban counties in Alabama (i.e., Cullman and Mobile counties). Additional eligibility criteria (with accompanying rationale) are as follows:

- diagnosed with a cancer that offers a 5-year relative survival  $\geq 80\%$ ;
- No evidence of progressive cancer (recurrence) or other cancers (except non-melanoma skin cancer), i.e., survivors who are “cured,” but at high risk for other cancers & co-morbidity;
- Within 5 years of diagnosis, but must have completed primary treatment (surgery, radiation or chemotherapy);
- At higher risk for functional decline, with at least two physical function limitations (limited a little or limited a lot) on the SF-36 Physical Function Subscale;
- English-speaking and writing;
- Not told by a physician to limit physical activity and no pre-existing medical condition(s) that would preclude (A) an increased consumption of fruits and vegetables, e.g., pharmacologic doses of warfarin or (B) gardening, e.g., severe orthopedic conditions, impending hip or knee replacement (within 6 months), end-stage renal disease, paralysis, dementia, blindness, unstable angina, untreated stage 3 hypertension, or recent history of myocardial infarction, congestive heart failure, or pulmonary conditions that required oxygen or hospitalization within 6 months. To date our home-based interventions have experienced few attributable side effects. We aim to continue our safe track record;
- Community dwelling and not residing in a skilled nursing or assisted living facility (We seek subjects who are able to pursue lifestyle changes independently and not as the result of institutional control);
- Must reside within 15 miles of one of the Master Gardener volunteer mentors;

- Not adhering to the recommended number of fruit and vegetable servings per day ( $\geq 5$ ) or minutes of exercise per week ( $\geq 150$  minutes/week). This intervention is aimed at those who do not adhere to recommended guidelines, since this population is most in need of intervention and is more likely to experience potential physiological benefits; and
- Willingness to be randomly assigned to either study arm and undergo baseline and follow-up assessments spanning a 1-year time frame.

A racially and ethnically representative sample of adult (age 65+ years) male and female survivors of cancer will be recruited using the Alabama State Cancer Registry, a method we have used successfully in the past. We will not exclude any ethnic or minority group, but will exclude children given our focus on adult cancer survivors, and physical function limitations that are prevalent in this age group. Our previous trials for home-based programs have always had low rates of attrition, i.e., 4.4% in FRESH START and 12.9% in RENEW during baseline to 1-year follow-up. Our high retention rates are likely due to regularly “checking-in” with participants (as we propose in this study), but not requiring that they come to see us. We will implement a similar strategy for the proposed trial, where data will be collected during home visits (baseline and 1-year follow-up) and will entail simple anthropometrics (weight, height, and waist circumference), conducting the Short Physical Performance Battery ( $\leq 15$  minutes) and the Senior Fitness Test Battery ( $\leq 15$  minutes) as well as grip strength (predictive of functional limitations and disability), and a blood draw (10 cc purple top vacutainer). Participants will receive \$10 for completing each home visit.

**Sources of Materials:** Cases will be identified using the Alabama Statewide Cancer Registry (ASCR) and permission to contact will be obtained from cases’ oncologists. If approved or non-response (the ASCR uses a passive consent method), case contact information will be forwarded to study staff. If not approved, aggregate (i.e., de-identified) demographic (age group, gender, race-ethnicity) and cancer data (type/stage, year of diagnosis) will be returned to study staff at completion of enrollment in order to generate CONSORT diagrams and compare characteristics of respondents with non-respondents (to assess potential selection bias). For patients that express interest in participation and who provide signed consent, we will collect other data (i.e. dietary and physical activity information, health and well-being, social support, self-efficacy, and other demographic information). All individuals who meet the study criteria will receive a thorough explanation of the study and given ample opportunity to ask questions. Signed informed consent will be obtained on all study subjects. Data regarding functional status, lifestyle behaviors and quality of life will be obtained during home visits, in which trained study staff will travel to the participant’s home, where their height, weight, waist circumference, and physical performance will be assessed, and a blood sample of 10 cc. will be collected. All measures performed at baseline will be repeated at the 1-year follow-up assessment. Blood samples will be configured into plasma and buffy coat from which DNA and PBMCs will be separated and stored until trial completion at which time they will be batch analyzed for *biomarkers of functional status and successful aging* (*IL-6, D-dimer, sVCAM, and telomerase*). Note: DNA will only be stored if the participant provides permission in a clause that will be stated on the consent form (the participant will be required to check a box that indicates approval or disapproval for this component). Blood is likely to be analyzed for other biomarkers (in remaining stored plasma) and for genetic studies (in stored DNA); however we have postponed all tests that are not strongly associated with our specific aims that will assess *physical functioning and successful aging*. As samples are collected, ancillary funding will be sought. Such an approach has worked for us in previous studies, such as FRESH START (CA81191) and our Prostate Cancer: Anthropometric Case: Control study (CA59263), in which both the Cancer Prevention Foundation and the American Institute for Cancer Research have provided additional funding. Brief surveys will be mailed to participants and collected during home visits (baseline and 1-year follow-up) to assess diet, QoL, comorbidities and symptoms, and reassurance of self-worth. All data will be used for research purposes and will be protected and kept strictly confidential (see Protection Against Risk Section below).

**Potential Risks:** This trial poses minimal risk; however, there still are some potential risks associated with the physical performance tests that are proposed to assess the impact of the intervention, as well as the intervention itself. Risks associated with the assessment of physical performance testing are

low given that the items assessed are normal daily activities and the eligibility criteria will exclude high risk individuals. The performance test batteries proposed for this study have been performed in a number of studies involving adults with a variety of comorbidities (e.g., chronic obstructive pulmonary disease, Alzheimer's disease, etc.) and typically performed in older/elderly adults with multiple comorbidities with no serious reported adverse events associated with performance testing. The purpose of performing two batteries of tests is to determine which battery is more responsive (i.e., fewer ceiling effects) in our sample. Dr. Demark-Wahnefried will oversee the training of the individuals performing the proposed physical performance testing. In addition, blood (10 cc in total) will be drawn from study participants during home visits at baseline, and 1- and 2-year follow-up. While blood will be drawn by trained phlebotomists, participants may still experience the small risks associated with phlebotomy, i.e. bruising, discomfort, etc. The potential benefits of a health promotion intervention are many and far outweigh any associated risks. The risks associated with the proposed study are minimal since moderate amounts of physical activity and a healthy diet generally promote good health, not endanger it. However, there are participants for whom such a tact is contraindicated. Our eligibility criteria are established to exclude individuals for whom unsupervised physical activity is not appropriate. We also will screen subjects directly using a mailed screener. Thus, using this multi-gated approach, we should be able to effectively screen-out any individuals for whom this intervention is contraindicated. We also will provide articles on gardening safety and health, e.g., protecting knees and back, sun protection, etc. in the study notebook that is delivered to participants prior to starting the intervention. *A private Facebook group will be created to allow interested cancer survivors and Master Gardeners enrolled in the study to obtain and/or share gardening related information, such as the status of their garden (e.g., pictures, what works well, what isn't working), problems they've encountered, solutions to problems, and different ways (e.g., recipes) to enjoy the produce from the garden. Participation in this forum is optional; the opportunity to interact with their fellow study participant-gardeners is being offered per the suggestion of the mini-pilot study participants.* The constructed Facebook page also will include a listing of warning signs with instructions should injury or other health problems occur. A toll-free number will be provided in order to communicate these with study staff. All health occurrences will be recorded and regularly reviewed by the study staff. Any serious adverse events will be immediately communicated to Dr. Demark-Wahnefried, who will confer with her co-Investigators – a procedure that has worked successfully in the past. All data will be used for research purposes and will be protected and kept strictly confidential (see Protection Against Risk Section below).

**Recruitment and Informed Consent:** IRB approval at UAB will be obtained in the months that precede funding. As described in section C.4 of this application, we will identify potential participants through the AL cancer registry (a process that we employed in our ENERGY trial). Permission to contact potentially eligible cases will then be sought from their oncology care physicians. All subjects will receive a letter of invitation from the study PI which will be cosigned by their oncology care physician. The letter will describe the study, including verbiage that this study is being done through a collaboration between UAB and the Alabama Cooperative Extension System (ACES), and will also include a toll-free study number (should patients have any questions or concerns). Included with this letter will be two copies of an informed consent form and if indeed subjects are interested in participating, they will be asked to return one of these forms in a pre-addressed, postage-paid envelope (along with a completed copy of the screening questionnaire), and to keep the other copy of the consent form for their files. Similar procedures have been used successfully in our previous trials, including the previous RENEW trial, as well as FRESH START, Project LEAD and DAMES.

**Protection Against Risk:** Protection against physical risk was previously covered under “potential Risks.” Given that there are risks associated with the collection of confidential information, the following paragraph is provided:

Since confidential information will be collected during the home visits, we will not directly link personal identifiers with the data collected, nor will we use personal identifiers in any reports, materials, or presentations that emanate from this work. All electronic files containing personal identifiers will be stored only within password protected files on the UAB file servers (located behind ample firewalls).

Information transferred to the server (for backup purposes) will be done via secure ftp. Files may be transferred to other computers via the Internet. When this is done, the files will be protected through a method that encrypts their contents during transfer and storage. The on-site file servers are physically accessible only to network support specialists (locked rooms). The on-site file server will be electronically accessible only to study staff through user/password protection. Non-electronic files (such as paper surveys, consent forms, authorization forms from physicians who approve patient contact, etc.) will be kept in a locked file cabinet, located in a locked room. Access to this room is limited to research staff only. In addition, all research staff are HIPAA certified and have completed and are current with regard to IRB training. Data sets provided as a function of the NIH Data Sharing Requirement will be stripped of identifying information according to HIPAA policy.

In addition, it should be noted that ALL individuals working on the pilot/feasibility study who have access to personal identifiers will have completed certified courses through the UAB IRB. The MGs who volunteer to mentor a study participant will also be required to complete Human Subjects training and will only begin to work with cancer survivors once their certification is submitted to the Study Research Office. A file of all MG Human Subjects certifications will be maintained in this office. Since training is available on-line this is fully executable and should not pose a significant barrier.

The Gardening Intervention Facebook group will be created as a private group, and thus the gardening information will only be shared amongst those participating in the study and not the public at large. Furthermore, participation by cancer survivors and Master Gardeners is optional. Nevertheless, individuals not familiar with Facebook will be informed about the nature of this interactive forum.

**Potential Benefit/Importance of Knowledge to be Gained:** Health promotion programs that support the achievement of increased F&V consumption and increased PA have been associated with improvements in functional status, health behaviors, QoL, co-morbidity, etc. Since cancer survivors are at greater risk of comorbidity and function decline, they have even a higher likelihood of benefiting from such programs, but travel and distance often pose barriers to participation (especially for cancer survivors who are elderly, rural, or lower SES). After the year-long mini-pilot study, we observed improvements in objective measures of physical functioning and trends in improved F&V consumption and PA. The proposed pilot/feasibility study is aimed at enrolling a larger sample in order to assess accrual, retention, adherence/fidelity, and adverse events. The larger study will also allow us to quantify (mean change scores and precision estimates) and compare between-arm differences in physical function and secondary endpoints in order to power future trials to discern efficacy. If successful, this program could be further disseminated to improve the lives of other cancer survivors across the state of Alabama, and ultimately across the nation. Additionally, it could be modified to address other high-risk populations of adults who suffer from co-morbidities that are also responsive to a healthy diet and increased physical activity, i.e., those with cardiovascular disease, diabetes, etc. Given that the Master Gardener Program is located in all 50 United States, the infrastructure for wide-spread dissemination exists. As is, the intervention could be disseminated in 22 states that have year round or 3 growing seasons; it also could be adapted with cold frames to 20 more. Thus, it is generalizable to a broad array of survivors residing in 84% of US states.

**Collaborating Sites:** This study will be performed through a community-based partnership between The University of Alabama at Birmingham and the Alabama Cooperative Extension System (ACES). However, ACES will not be responsible for accruing or monitoring participants; they only will assist with the intervention by providing support to the Master Gardeners. Thus, the identification of potential study participants, and subsequent accrual, consent, enrollment and in person visits to assess clinical outcomes will be conducted by UAB study staff. UAB also will perform specific functions that are key to the success of this trial, e.g., primary oversight, tracking, technical interface of the intervention and assessment materials, and overall data analysis. ACES will be responsible for recruiting (surveying all MGs in the state), training (to teach principles of vegetable/fruit gardening in residential landscape settings) and supporting the MG volunteers who agree to become “mentors” in this project (available to assist mentors via telephone, e-mail, or in-person). A detailed description of the scope of work provided by ACES is featured in the forerunning budget, grant application and under Consortium & Contracts.

## **DATA SAFETY AND MONITORING PLAN:**

**Trial Type/Level of Review:** Phase II – This study does not involve the testing of pharmacologic agents nor any therapeutic treatments. It is an educational intervention aimed at promoting healthy diet and physical activity. Thus, it is classified as a Type 3 Study (Non-therapeutic, non-physical intervention), a minimal risk level study that dictates annual review by the UAB Scientific Monitoring Subcommittee for scientific progress and IRB compliance. Furthermore, the UAB Scientific Monitoring Committee is comprised of seasoned investigators, clinicians and patient advocates. In addition, data will be reviewed by consultant Patrician Ganz, M.D. who is an expert in cancer survivorship.

### **Adverse Event Reporting:**

Study participants will be encouraged to report any “emergencies or events” by calling the toll-free study number. These instructions will be included on all cover letters that accompany the intervention materials and the toll-free number will also be prominently affixed to the study notebook that is provided at the start of the intervention period, as well as featured on the constructed Facebook page. The UAB project manager will record all reported events in the adverse event log (including the subject’s name, date, and event description). The project manager will inform the principal investigator, Wendy Demark-Wahnefried, PhD, immediately of any unanticipated study deaths or serious events that potentially jeopardize participation in the study. Dr. Demark-Wahnefried will consult with both Drs. De Los Santos and Ganz on the action that should be taken. This communication will occur within 24 hours (for an unanticipated study death), and 5 business days for an unanticipated serious event. This action and date of implementation also will be recorded in the adverse event log. The entire investigative team will participate quarterly in classifying any reported events as “serious” or “non-serious (see listing as follows),” as well as “non-attributable,” “possibly attributable” or “attributable” to the intervention (unlike a pharmaceutical trial where known side effects exist, the classification of “expected” vs. “unexpected” is inappropriate for this behavioral intervention).

**Serious—any event or condition that is life threatening, results in overnight hospitalization, cancer or a physical or cardiac event serious enough to require medical attention. A brief listing follows:**

- Fatal
- Life threatening
- Permanently disabling
- Required or prolonged (overnight) hospitalization (Admission—not ER visit)
- Overdose
- Significant hazard to patient

**Non-Serious—all other events.**

Furthermore, study staff, through bi-monthly telephone follow-up, and Master Gardeners, through monthly contact (in-person, and telephone and/or e-mail) will have an opportunity to assess the participants’ health status on a regular basis. Details of these events will be recorded. All adverse events will be reviewed on a quarterly basis by the research team and on a semi-annual basis by the UAB Scientific Monitoring Subcommittee. While the research team will be blinded to study condition, codes will be revealed to the UAB Scientific Monitoring Subcommittee. Also, in keeping with NIH guidelines, minority status and gender also will be included in these reports to allow for detection of differential effects.

### **Analysis Plan for Monitoring and Analyzing Incidence of Adverse Events**

While our previous FRESH START and RENEW studies have included an interim analysis, it has been clear given the low risk nature of our interventions that we have never even remotely approached significantly higher rates of adverse events with the intervention. In fact, in both these studies, adverse events have always been higher in either the attention control or the delayed intervention arms (prior to delivering the intervention). Thus, a formal interim analysis is not planned, though as stated, the UAB Review panel will conduct semi-annual reviews for safety.

The design of this monitoring plan makes the following assumptions. All patients will be asked if and when

they suffered adverse events during bi-monthly telephone contact with study staff and will be encouraged to report an event at any time during follow-up. Thus, at any given time, patients will have varying follow-up times. In practice, study participants will be encouraged to call-in on a toll-free number to report any adverse events that would preclude their participation in the study. Data from these phone calls will be included in the analyses along with data generated by the follow-up surveys (checking for any duplicates and cleaning the data as necessary). Within each arm, we assume independence of events.

**Data Monitoring:**

Enrolled subjects will be registered within the Clinical Trials Shared Resource, as well as with the UAB IRB. Thus, accrual and adverse events will be reviewed at least on an annual basis, if not more stringently (if unanticipated adverse events occur). In addition, these factions will specifically offer suggestions should accrual fall below 25% of the target by year 2, or if drop-out exceeds the projected 15%.

**INCLUSION OF WOMEN AND MINORITIES:** A stratified accrual strategy will assure equal numbers of men and women, thus 50% of our population will be female. We also plan to accrue a sample that is racially and ethnically representative of adult cancer cases in Alabama. NOTE: While the proportion of minorities is rising rapidly throughout the US, this trend is almost exclusively noted in younger, not older age groups. Because cancer is most prevalent after age 60 the racial/ethnic distribution of cancer cases must be taken into consideration. Within Alabama roughly 26.2% of cases are African American, and there is a far lower proportion of other ethnic groups, i.e., Hispanics, Native Americans, etc. Nonetheless, our sample will be comprised of roughly 73% Non-Hispanic Whites and 27% Minority (of which most will be African-American).

## Targeted/Planned Enrollment Table

See link below for updated notice:

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-086.html>



**INCLUSION OF CHILDREN:** The proposed study is exclusively aimed at older adults (age 65 and older) who have been diagnosed with adult onset cancers, as the primary focus of this proposal is on improving physical functioning; thus, children will be excluded from this study.

**RESOURCE SHARING PLAN:** Not applicable. The proposed R21-funded project falls below the \$500,000 cap where data sharing is required and the resources are available for such purposes. Additionally, the proposed project neither involves the development of model organisms nor is it a genome-wide association study.