Annals of Internal Medicine | Research and Reporting Methods

Reconsidering the Approach to Prevention Recommendations for Older Adults

Rosanne M. Leipzig, MD, PhD; Evelyn P. Whitlock, MD, MPH; Tracy A. Wolff, MD, MPH; Mary B. Barton, MD, MPP; Yvonne L. Michael, ScD, SM; Russell Harris, MD, MPH; Diana Petitti, MD, MPH; Timothy Wilt, MD, MPH; and Al Siu, MD, for the U.S. Preventive Services Task Force Geriatric Workgroup

The U.S. Preventive Services Task Force (USPSTF) bases its recommendations on an evidence-based model of clinical prevention that focuses on specific diseases, well-defined preventive interventions, and evidence of improved health outcomes. Applying this model to prevention for very old patients has been problematic for several reasons: Many geriatric disorders have multiple risk factors, interventions, and expected outcomes; older adults are not often represented in clinical trials; and important outcomes may not be measured and reported in ways that are conducive to evidence

Since its inception, the U.S. Preventive Services Task Force (USPSTF) has based its recommendations on an evidence-based model of clinical prevention that focuses on specific diseases, well-defined preventive interventions, and evidence of improved health outcomes. However, applying this model to prevention for very old patients has been problematic.

THE PROBLEM

Many USPSTF recommendations focus on prevention through the early identification of specific diseases with clearly defined risk factors or opportunities for early intervention. Using the current USPSTF approach for older adults has not been easy (1) because many geriatric disorders have multifactorial risk factors, interventions, and expected outcomes; older adults are not often represented in clinical trials; and important outcomes may not be measured and reported in ways that are conducive to evidence synthesis and interpretation.

Multifactorial Nature of Conditions

Disease or disability in geriatric populations can result from many small risks acting together, and different persons will have different component risks as part of a higher risk profile (2). Distinct clinical entities (such as functional decline, falls, osteoporosis, or vitamin D deficiency) may share risk factors and contribute to one another (3). Thus, interventions to reduce risk may benefit the patient through small improvements across several risk categories rather than a large improvement in a single risk category. Many of the more efficacious interventions for these conditions target multiple risk factors with multiple components (4, 5). Interventions with multiple, sometimes disparate, components may be difficult to synthesize into the systematic evidence reviews that are the basis for USPSTF recommendations.

Studies that evaluate the efficacy of these multifactorial interventions often measure more than 1 type of outcome

synthesis and interpretation. In 2005, the USPSTF convened a geriatrics workgroup to refine USPSTF methodology and processes to better address the preventive needs of older adults. The USPSTF has begun to apply these new approaches to the review and recommendation on interventions to prevent falls in older adults.

Ann Intern Med. 2010;153:809-814. For author affiliations, see end of text. www.annals.org

(for example, physical function, cognition, affect, and quality of life), which further complicates the synthesis and interpretation of results, including the fair valuation of cumulative small effects across disparate outcomes that may have different clinical importance to different patients. In addition, these types of outcomes commonly cut across multiple and seemingly unrelated clinical topics. For example, physical function may be measured as an end point in studies that aim to prevent immobility, falls, hospital complications, or cognitive decline. It is difficult to identify all of the relevant evidence and determine which interventions are similar enough to combine qualitatively or quantitatively. This can lead to different findings from different systematic reviewers of the same literature and can complicate efforts to assess net benefit and develop USPSTF recommendations on such topics as the prevention of functional decline. Furthermore, a piecemeal process (making separate recommendations for individual interventions or diseases) is inefficient and ineffective for health care providers and policymakers, who strive to develop multicomponent systems to improve the health of older adults.

Although screening is often performed in older adults to improve health outcomes, the pathway to improved outcomes may not be principally through preventing the associated disease. For example, the USPSTF recommendation on screening for cognitive impairment in older adults took evidence on the effect of interventions on both pa-

See also:

Print

Key Summary Points											810
Editorial comment											843
Related article											815

Web-Only

Conversion of graphics into slides

RESEARCH AND REPORTING METHODS | Reconsidering the Approach to Prevention Recommendations for Older Adults

Key Summary Points

U.S. Preventive Services Task Force (USPSTF) recommendations focus on specific diseases, well-defined interventions, and traditional health outcomes.

USPSTF recommendations are developed by using an evidence-based model (or framework) that relies on systematic reviews of appropriate evidence.

Developing recommendations for the geriatric population has been problematic because adverse clinical events that affect the geriatric population (such as falls or fall-related fractures) are:

Multifactorial in nature

Require interventions with multiple and sometimes disparate components

Include multiple domains of functional status and quality of life that are not easily expressed as discrete events

Older adults are not often represented in clinical trials Important outcomes in the geriatric population may not be measured and reported in ways that are conducive to evidence synthesis and interpretation

The USPSTF is developing new methods to review evidence and make recommendations for the geriatric population:

Addressing aging-specific issues for diseases prevalent in older adults

Expanding and adapting its typical analytic framework to better recognize the multifactorial nature of selected geriatric syndromes and their interventions Addressing the outcomes that are important to patients (including nontraditional outcomes, such as effect on caregivers)

Bundling recommendations on related topics

tients and caregivers into account (6). The considered benefits of this screening included nontraditional outcomes, such as improved ability to understand health instructions and participate in counseling or shared decision making on the patient's part and improved support and planning capability on the caregiver's part. Similarly, screening for functional status might be justified not only because it is a worthwhile method of optimizing patient function or an important goal of care in this population but also because of the prognostic value of the resultant information (for example, for risk stratification for other conditions closely tied to the desired outcome, such as falls, or for lifeplanning purposes). Thus, screening may be desirable for reasons other than the prevention of the specific disease or syndrome targeted in the screening. This rationale has not been easily incorporated into the USPSTF analytic framework for clinical prevention.

Measurement Issues

The USPSTF methods are designed to use evidence that preventive interventions improve traditional health outcomes. Often, these are discrete and well-understood outcomes, such as all-cause or cause-specific mortality or cardiovascular events. However, the most relevant health outcomes for very old patients (particularly those with serious chronic illness) may include multiple domains of functional status and quality of life that are not easily expressible as discrete events. These measures offer important and relevant considerations for setting goals of care, but they are not often reported as research outcomes that can be easily compared or combined. For example, the many available functional status or disease-specific quality-of-life instruments are not equally reliable, reproducible, or reflective of changes after treatment. Instruments that assess functional status and quality of life may assess overlapping domains. For example, physical function is one of many domains of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36), the most commonly used instrument to assess health-related quality of life in older adults, and researchers may choose to report either overall or domain-specific results. Although functional limitations and disability are conceptualized as distinct entities with clearly differentiated definitions (7), the research literature does not consistently distinguish between these terms (8). The clinical significance of the differences between these types of outcomes has not often been assessed and may vary by baseline characteristic. Many outcomes are continuous or ordinal measures, designed to be sensitive across a continuum, that are more difficult to express in terms of numbers needed to treat to avert an undesirable outcome. Thus, results for these types of outcomes are not easily summarized for systematic reviews and the development of recommendations.

Limited Data on Prevention Outcomes Specific to Older Adults

Even for prevention topics that can be approached with the traditional clinical prevention rationale and framework of the USPSTF, the nature of the evidence base complicates the derivation of preventive recommendations for older adults. Randomized trials (even for clinical topics prevalent in old age) sometimes exclude or include only a small proportion of patients at the extremes of old age or those who have short life expectancy. Thus, the USPSTF must often extrapolate results from middle-aged adults or younger older adults to much older persons and those with chronic conditions. Although the prevalence of the screening condition may actually increase with age, the risk for harm from the intervention may also increase, and the time until benefit may exceed the life expectancy of an older or frailer person. A common example of this problem is the dearth of evidence on the age or circumstances under which routine screening may be discontinued because of a lack of potential benefit. This issue is compounded in older

adults of certain ethnic and racial minority groups, because these groups are generally underrepresented in research.

As a result, previous USPSTF recommendations may not have fully explored or delineated important issues, such as multiple chronic health conditions more commonly encountered in an older patient population. Because of this paucity of evidence, USPSTF recommendations provide only limited guidance on what should be done in the case of serious comorbid conditions or limited life expectancy. For patients with multiple chronic conditions, it is difficult to prioritize preventive interventions; clinicians must balance the intervention with the diagnostic tests and treatments the patient already receives for chronic conditions (9).

New Methodology and Processes to Address Geriatric Topics

In 2005, the USPSTF convened a geriatrics subgroup of its Methods Workgroup to refine USPSTF methodology and processes to better address the preventive needs of older adults. On the basis of this group's work, the USPSTF proposes to address these shortcomings in its approach to topic prioritization, evidence review, and development of evidence-based recommendations on preventive services for older adults (see Key Summary Points).

Topic Prioritization

The USPSTF plans to prioritize topics that focus on preventive services of interest to clinicians who care for older adults. The process of prioritization occurs on an ongoing basis; the USPSTF regularly reconsiders its portfolio of recommendations, accepts nominations for new topics, and makes decisions about whether to update its reviews and recommendations. The prioritization of new and previous topics is based on several criteria, including burden of illness, expected effectiveness, potential impact of the recommendation on clinical practice, gap between evidence and practice, and relevance to primary or secondary prevention and primary care (10). In its new approach to geriatric topics, the USPSTF will modify its prioritization process to include considerations specific to older adults. The collection of information on burden of illness will include data, when available, on the burden of illness in older adults. The gap between evidence and practice is an especially important criterion to consider in geriatric care topics because of the potential differences in benefits and harms, patient preferences, and reported health status measures in this population.

Analytic Framework

Once a topic is prioritized by the USPSTF for review, it uses a systematic method to determine which questions need to be answered to make a recommendation. These questions are identified by developing an analytic framework. The USPSTF intends to address topics in older adults by using the following approaches when creating an analytic framework and evidence review. The USPSTF would ideally consider the burden of multiple comorbid conditions, multifactorial assessments, and comprehensive health outcomes when reviewing the evidence in older adults. Given the paucity of evidence for some of these dimensions, it is not appropriate or possible to take this approach for all geriatric topics. Therefore, the USPSTF proposes to take 1 of 3 approaches to developing the analytic framework and evidence review. The USPSTF will select the appropriate approach on the basis of the available evidence, understanding of natural history, pathophysiology of the disease, and understanding of potential effectiveness.

First, the USPSTF proposes to address aging-specific issues for diseases prevalent in older adults when using a more traditional disease-specific analytic framework for its systematic reviews. For example, in commissioning a systematic review to update the 2003 USPSTF recommendation on primary care screening for depression in adults, the USPSTF specifically considered evidence for screening, treatment effectiveness, and harms of treatment in adults 65 years or older. Similarly, the systematic review to update the 2003 recommendation on screening for obesity in adults uses an analytic framework that addresses the importance of elevated body mass index and the effect of obesity treatments in adults 65 years or older.

Second, the USPSTF proposes to expand and adapt its typical analytic framework approach for selected geriatric syndromes to better recognize the multifactorial nature of these syndromes and their interventions, as well as the expected outcomes that are important to patients. Figure 1 shows an ideal version of the usual analytic framework. This ideal geriatric version represents an approach to identifying high-risk patients with common risk factors for 1 or more geriatric syndromes, who could receive 1 of several interventions developed to reduce geriatric syndromes and related outcomes (such as falls or functional limitations), some of which could benefit more than 1 outcome. We simplified this approach for our systematic review for the USPSTF recommendation on prevention of falls, as we will discuss. A follow-up systematic review of multifactorial risk assessment and management interventions to improve functional limitations is currently under way.

Third, the USPSTF proposes to bundle recommendations on related topics to make recommendations more consistent, interlinked, and comprehensive. The bundling of recommendations will be done from the outset at the time of the update, so that the analytic framework, language, end points, and clinical approach will be consistent for each of the bundled topics. As an example, the USPSTF proposes to bundle its recommendations that address the prevention of bone fractures, which could include separate recommendations on calcium and vitamin D supplementation, screening for osteoporosis, and prevention of falls. Similarly, topics related to the prevention of falls, such as interventions to reduce disability, could be bundled to more clearly reflect how clinicians consider evi-

RESEARCH AND REPORTING METHODS | Reconsidering the Approach to Prevention Recommendations for Older Adults





* Risk factors include increasing age, baseline functional impairment and limitations, incontinence, polypharmacy, medical risks, or sensory and cognitive deficits.

dence in the care of an individual patient or groups of patients.

CLINICAL CONSIDERATIONS

When possible, the USPSTF intends to provide information in its recommendations on clinical considerations specific to older adults; this may include information that focuses on implementation or treatment in this population. Because sex, comorbid conditions, and small age increments may have a relatively large effect on health outcomes in older adults, the USPSTF will attempt to stratify recommendations according to these key components when the evidence permits.

FUTURE WORK IN PREVENTION IN OLDER ADULTS

The USPSTF geriatrics subgroup is working to more fully address other methodological issues critical to evidence-based recommendations. This includes further consideration of nontraditional outcomes, such as effect on caregivers, and determining approaches that allow more confident and consistent extrapolation of evidence from younger to older adult populations. Current projects of the geriatric workgroup include methods for evaluating evidence to determine whether screening continues to be beneficial in older adults, measures of quality of life, values and attitudes of older adults related to prevention, geriatric syndromes, and interventions that target functional limitations.

PREVENTION OF FALLS IN OLDER ADULTS: HOW THE USPSTF IS APPLYING NEW PROCESSES

Figure 2 shows the analytic framework used in the systematic review for the recommendation on the prevention of falls. Although this systematic review primarily used the typical USPSTF analytic framework approach (11), the USPSTF began to make some important adaptations for complex geriatric topics. In this analytic framework, the USPSTF specified a focus on the intervention rather than the traditional focus on screening, with the critical question, "Do primary care relevant interventions work?," because of the diversity in domains and measures used to identify patients at risk for falls. This analytic framework for fall prevention also explicitly acknowledged that older adults at risk for falls are also at risk for other negative outcomes, such as disability, and that interventions to reduce falls may thus result in other beneficial outcomes, including improvements of global health outcomes, such as quality of life. The USPSTF decided that modifying the analytic framework in this manner would be a start toward a more integrated consideration of interrelated geriatric syndromes. For example, a systematic review that also considers the effect of interventions that focus on functional limitations (as opposed to falls) would probably target similar patients and could complement the effect of fall interventions on morbidity, mortality, and quality of life. Future work by the USPSTF will seek ways to conduct rigorous reviews of interrelated geriatric topics by using clear and defensible methods to better define the benefits and harms of similar interventions and to

fairly value multiple related outcomes in assessing overall benefit.

In the recent review for fall prevention, the USPSTF encountered several challenges that will be important as it moves forward in addressing methods for geriatrics topics. Many of these challenges reflect the multifactorial nature of the risk factors, interventions, and outcomes. Multiple risk factors for falls can be specified at a population level and can act in an additive manner to increase risk for falls. However, the specific risks vary for the individual patient. The variation in approaches to risk assessment and the lack of validated risk instruments for fall prevention prohibited both the identification of a single approach that could be of robust use in primary care (12) and the assessment of conventional test performance characteristics (or at least of their reliability and validity).

This complexity in risk identification complicates evidence synthesis and is likely to occur with other complex geriatric syndromes. Synthesis is also a challenge because there is no consistent way to describe or categorize multifactorial interventions. The USPSTF also found in its review on fall prevention that researchers incorporated a greater diversity of measures for global outcomes, such as disability and quality of life, than they did for falls or fractures and that many of these outcomes were reported in ways that did not allow for the calculation of absolute risk. In addition, disability and quality of life were reported in only a few trials. Therefore, the USPSTF concluded that quantitative synthesis would not be useful and could be biased by selective reporting. The more complex approach set out in the ideal USPSTF analytic framework may remain unattainable for some time because of the lack of standardized measurement or reporting of disability and quality-of-life outcomes.

These issues influence the process of evidence review and synthesis conducted by the USPSTF, a process that often builds on previous systematic reviews (13). Differences in findings from previous reviews could reflect different inclusion or exclusion criteria (or the interpretation thereof) when selecting studies for review, as well as different approaches to categorizing interventions. Thus, more complicated interventions are both harder to synthesize





Key Questions

- KQ 1: Is there direct evidence that primary care interventions reduce fall-related injury, improve quality of life, reduce disability, or reduce mortality when used alone or in combination to reduce falls in community-dwelling older adults?
- KQ 1a: Do these interventions reduce injury, improve quality of life, reduce disability, or reduce mortality in older adults specifically identified as high risk for falls?
- KQ 2: Do primary care interventions used alone or in combination in community-dwelling older adults reduce risk for or rate of falls or fallers?
- KQ 2a: Do these interventions reduce falls in older adults specifically identified as high risk for falls?
- KQ 2b: Are there positive outcomes other than reduced falls, and related morbidity and mortality, that result from primary care fall interventions?
- KQ 3: What are the adverse effects associated with interventions to reduce falls?
- KQ 4: How are high-risk older adults identified for primary care fall interventions?
- * Expanded intervention list:
 - Multifactorial assessment and management includes multifactor risk assessment, comprehensive geriatric assessment, and ≥ 2 of the following screenings for fall risk: vision, gait, mobility, strength, medication review, cognitive impairment, orthostatic hypotension, and environmental risks.
 - Single clinical treatment (with or without screening) includes vision correction, medication optimization or adjustment, assistive device prescription, pharmacologic or nutritional interventions, treatment of orthostatic hypotension, urinary incontinence, and hip protectors.
 - Clinical education or behavioral counseling includes exercise, fall risk reduction, and a home-hazard checklist.
 - Home-hazard modification includes identifying and removing potential fall hazards, adding grab bars and handrails, and modifying the environment to improve mobility and safety.

Exercise or physical therapy includes physical exercise, mobility and gait training, muscle strengthening, balance training, and training for recurrent fallers.

KQ = key question; USPSTF = U.S. Preventive Services Task Force.

RESEARCH AND REPORTING METHODS | Reconsidering the Approach to Prevention Recommendations for Older Adults

and harder for the reader to understand and may show discrepancies between reviewers for reasons beyond the usual difference when a review is more current and therefore has newer studies to incorporate. Until the USPSTF has a more robust (and, ideally, empirically supported) mechanism for categorizing multifactorial interventions that address multiple risk factors as similar, and until global outcomes are consistently measured and reported, synthesizing results from interventions with related but distinct outcomes will be a challenge.

CONCLUSION

The USPSTF has begun developing methods for reviewing evidence and making recommendations specific to prevention in the geriatric population. This work is important because the anticipated, unprecedented growth of this population in the near future will result in increased attention to preventive services. In addition, the USPSTF will need to adjust its methodology because the benefits, harms, and preventive health care concerns of younger adults may not be entirely transferable to the older population. The public health sector and primary care systems need to offer effective services that maximize function and quality of life for an aging population. With the steps we have outlined, the USPSTF is committed to updating the methods of systematic evidence review to better meet the needs of the 21st century.

As new methods develop, the USPSTF expects to build a case for the research community to develop unified definitions of patients at risk, categorization of interventions, and standards of outcome measurement and reporting and to reduce the variability of these elements, especially for topics and populations in which standardization would be most valuable. The measurement of consistent outcomes, in addition to morbidity and mortality, is 1 element of the USPSTF plan; improved approaches to characterizing and describing interventions will probably be another. The USPSTF envisions an evolving process over the coming years as it addresses successive topics relevant to the geriatric population and further refines its methods to improve and maintain health for an aging population.

From Mount Sinai School of Medicine, New York, New York; Oregon Evidence-based Practice Center, Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon; Agency for Healthcare Research and Quality, Rockville, Maryland; University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; Arizona State University, Phoenix, Arizona; and Minneapolis Veterans Affairs Medical Center and University of Minnesota, Minneapolis, Minnesota. **Grant Support:** The general work of the USPSTF is supported by the Agency for Healthcare Research and Quality. This specific manuscript did not receive separate funding.

Potential Conflicts of Interest: Disclosures can be viewed at www.acponline .org/authors/icmje/ConflictOfInterestForms.do?msNum=M10-0472.

Requests for Single Reprints: Reprints will be available from the USPSTF Web site (www.uspreventiveservicestaskforce.org).

Current author addresses and author contributions are available at www .annals.org.

References

1. Cigolle CT, Langa KM, Kabeto MU, Tian Z, Blaum CS. Geriatric conditions and disability: the Health and Retirement Study. Ann Intern Med. 2007; 147:156-64. [PMID: 17679703]

2. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med. 1988;319:1701-7. [PMID: 3205267]

3. Tinetti ME, Inouye SK, Gill TM, Doucette JT. Shared risk factors for falls, incontinence, and functional dependence. Unifying the approach to geriatric syndromes. JAMA. 1995;273:1348-53. [PMID: 7715059]

4. **Tinetti ME, Baker DI, McAvay G, Claus EB, Garrett P, Gottschalk M, et al.** A multifactorial intervention to reduce the risk of falling among elderly people living in the community. N Engl J Med. 1994;331:821-7. [PMID: 8078528]

5. Inouye SK, Bogardus ST Jr, Charpentier PA, Leo-Summers L, Acampora D, Holford TR, et al. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med. 1999;340:669-76. [PMID: 10053175]

6. U.S. Preventive Services Task Force. Screening for dementia: recommendation and rationale. Ann Intern Med. 2003;138:925-6. [PMID: 12779303]

7. Institute of Medicine. The Future of Disability in America. Washington, DC: National Academies Pr; 2007.

8. Stuck AE, Walthert JM, Nikolaus T, Büla CJ, Hohmann C, Beck JC. Risk factors for functional status decline in community-living elderly people: a systematic literature review. Soc Sci Med. 1999;48:445-69. [PMID: 10075171]

 Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA. 2005;294:716-24. [PMID: 16091574]

10. Guirguis-Blake J, Calonge N, Miller T, Siu A, Teutsch S, Whitlock E; U.S. Preventive Services Task Force. Current processes of the U.S. Preventive Services Task Force: refining evidence-based recommendation development. Ann Intern Med. 2007;147:117-22. [PMID: 17576998]

11. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al; Methods Work Group, Third U.S. Preventive Services Task Force. Current methods of the U.S. Preventive Services Task Force: a review of the process. Am J Prev Med. 2001;20:21-35. [PMID: 11306229]

12. Michael YL, Whitlock EP, Lin JS, Fu R, O'Connor EA, Gold R. Primary care–relevant interventions to prevent falling in older adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2010;153: 815-25.

13. Whitlock EP, Lin JS, Chou R, Shekelle P, Robinson KA. Using existing systematic reviews in complex systematic reviews. Ann Intern Med. 2008;148: 776-82. [PMID: 18490690]

Annals of Internal Medicine

Current Author Addresses: Dr. Leipzig: Brookdale Department of Geriatrics and Adult Development, Mount Sinai School of Medicine, 1468 Madison Avenue, Box 1070, New York, NY 10029.

Dr. Whitlock: Center for Health Research, Kaiser Permanente, 3800 North Interstate Avenue, Portland, OR 97227.

Drs. Wolff and Barton: Center for Primary Care, Prevention, and Clinical Partnerships, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

Dr. Michael: Drexel University School of Public Health, 1505 Race Street, 6th Floor, MS 1033, Philadelphia, PA 19102.

Dr. Harris: University of North Carolina School of Medicine, Cecil G. Sheps Center for Health Services Research, CB 7590, Chapel Hill, NC 27599-7590.

Dr. Petitti: Arizona State University, 502 East Monroe C320, Phoenix, AZ 85004.

Dr. Wilt: Minneapolis Veterans Affairs Medical Center and University of Minnesota Department of Medicine, 1 Veterans Drive (111-0), Minneapolis, MN 55417.

Dr. Siu: Mount Sinai School of Medicine, Department of Geriatrics and Palliative Medicine, One Gustave Levy Place, Box 1070, New York, NY 10029.

Author Contributions: Conception and design: R.M. Leipzig, E. Whitlock, T.A. Wolff, Y.L. Michael, D. Petitti, A. Siu.

Analysis and interpretation of the data: Y.L. Michael, R. Harris, T. Wilt. Drafting of the article: R.M. Leipzig, E. Whitlock, T.A. Wolff, Y.L. Michael, A. Siu.

Critical revision of the article for important intellectual content: R.M. Leipzig, E. Whitlock, T.A. Wolff, M.B. Barton, Y.L. Michael, R. Harris, D. Petitti, T. Wilt, A. Siu.

Final approval of the article: R.M. Leipzig, T.A. Wolff, M.B. Barton, Y.L. Michael, R. Harris, D. Petitti, T. Wilt, A. Siu.

Administrative, technical, or logistic support: T.A. Wolff.

Collection and assembly of data: E. Whitlock, Y.L. Michael.