Official Title: Prevention of Fall in Older Adults with Overactive Bladder

NCT: NCT03946124

Document date: 03/29/2018

Protocol

Abstract
Older adults with overactive bladder (OAB) have reduced physical activity and are at increased risk for falls. Though recent studies suggest that treatment of OAB may improve physical activity, there is a lack of easily administered instruments for measuring physical activity in older adults. Furthermore, physical activity outcomes in older adults with OAB are affected by treatment preference and potential neurocognitive dysfunction caused by anti-cholinergic medication. The aims of the present proposal are 1) to validate an instrument to measure physical activity 2) to validate an instrument to measure preference for medication and 3) to determine the effect of preference for anti-cholinergic medication on adherence, physical activity, and falls risk. We plan a prospective cohort study of adults aged 65 or older with OAB undergoing treatment with anti-cholinergic medication. The primary outcome will be physical activity measured using a self-reported instrument and accelerometer at baseline and 8 weeks after treatment. Secondary outcomes will be fall risk defined by changes in neurocognitive testing, urinary symptoms, and medication adherence at 8 weeks after treatment. The findings of this study could provide a paradigm shift in the management of older adults with OAB and at increased risk for falls.

Objectives

Overall objectives
Our primary objective is to show that treatment preference and physical activity can be measured using patient-reported instruments. We also hypothesize that preference for anti-cholinergic medications is associated with higher adherence and improvement in domains relevant to falls in adults with OAB, including urgency, physical activity, and balance. Finally, we plan to show that treatment of urgency urinary incontinence with anti-cholinergic medication does not worsen neurocognitive function relevant to falls. Specifically, the overriding goal of this proposal is to validate patient-reported instruments that measure physical activity and preference for medication in elderly adults with overactive bladder, and examine the effect of treatment on physical activity and risk for falls (fall efficacy) in adults who prefer medication for the treatment of overactive bladder. Specific Aim 1: To determine the construct validity and responsiveness of physical activity instruments in older adults undergoing treatment for overactive bladder. We hypothesize that physical activity levels as measured by questionnaires will correlate with physical activity as measured by accelerometer. We will measure responsiveness of the instruments by comparing change in physical activity levels before and after treatment of OAB. The results will be informative as to which, if any, instrument is useful for measuring physical activity in adults with OAB. Specific Aim 2: To determine the construct validity of an instrument to measure preference for medication in older adults undergoing treatment for overactive bladder. We hypothesize that adults with preference for medication will have higher adherence to treatment at 8 weeks than adults who do not prefer medication. The results will enlighten us to which, if any, instrument, is useful for measuring preference for treatment with anti-cholinergic medication in adults with OAB. Specific Aim 3: To use the newly validated instruments to measure the impact of preference for medication on domains related to falls (physical activity, urinary symptoms, neurocognitive testing) in older adults undergoing treatment with anti-cholinergic medications for overactive bladder. We hypothesize that adults with preference for medications will have greater improvement in physical activity and urinary symptoms, and no difference in neurocognitive testing, than women who do not have preference for medications. This aim will establish if the new instruments are useful in measuring outcomes of preference and physical activity in the clinical setting and also provide preliminary data on the impact of treatment preference and anti-cholinergic medications on physical activity and falls risk in older adults with overactive bladder.

Primary outcome variable(s)
The primary outcome will be physical activity measured using a self-reported instrument and accelerometer at baseline and 8 weeks after treatment.

Secondary outcome variable(s)
Secondary outcomes will be fall risk defined by changes in neurocognitive testing, urinary symptoms, and medication adherence at 8 weeks after treatment.

Background
An estimated 29.8 million adults aged 40 and older in the United States suffer from overactive bladder

(OAB), a condition characterized by urgency to urinate.1 Overactive bladder is commonly associated with urgency urinary incontinence (UUI), and older adults with UUI are at twofold higher risk for falls. UUI is increasingly being recognized as a marker for musculoskeletal weakness.2, 3 According to the bio-psycho-ecological paradigm,4, 5 falls associated with overactive bladder are a combined result of the interaction between three elements: bladder urgency; mental abilities including anxiety and embarrassment related to bladder urgency; and physical difficulty in reaching the toilet in a timely fashion. Anti-muscarinic medications are the most common class of medication used for the treatment of UUI. Six main anti-muscarinic medications are available in the United States, with similar efficacy (Qaseem 2014, AUA/SUFU OAB guidelines), and are generally prescribed based on insurance coverage as well as tolerance of side effect profile. These medications are known to improve at least two of these domains: bladder urgency,6 and mental anxiety related to urinary incontinence.7 Prior studies also suggest that reduction of bladder urgency with medications may improve ability to reach the toilet by improving physical ability, which is the third domain associated with falls. In an abstract presented at AUGS 2014, we have shown that treatment of overactive bladder in adults (mean age 61.0 ± 13.8) with fesoterodine was associated with improved physical activity as measured by the two physical activity questions of the SF-12.8 Several studies have reported that treatment of overactive bladder is associated with improvement in physical activity related to travel, transportation, and planning to locate restrooms.9, 10, 11 While these activities do not necessarily correlate with physical activities known to reduce the risk of falls e.g. walking, climbing stairs, or participating in sports these studies provide promising evidence that treatment of OAB with anti-cholinergic medications could potentially reduce falls. However, though several physical activity questionnaires exist, none have been validated in older adults with urgency urinary incontinence. Finally, anti-cholinergic medications have been implicated in neurocognitive changes that could potentially increase the risk of falls.12 Therefore, there remains a key gap in knowledge regarding the effect of anti-cholinergic medications on physical activity and neurocognitive testing in older adults with urgency urinary incontinence. The efficacy of medications is closely related to adherence. Despite multiple benefits from anti-cholinergic treatment, the estimated adherence to anti-cholinergic medication is less than 10% at one year.13 Poor adherence carries the potential for wasted health care resources and continued suffering for patients. There is a lack of knowledge on how to best identify patients who will be adherent to anti-cholinergic treatment, and therefore derive the most benefit from medication. Recent studies in other conditions such as depression suggest that a key indicator for adherence is patient-expressed preference for treatment. We have previously shown that the health belief model is valid in women with OAB; women who believe in the intrinsic harm of medications have significantly worse adherence than those who believe in the benefit of medications.14 Urgency urinary incontinence is associated with increased risk of falls in older adults: Falls in the elderly have severe life-threatening consequences including injuries, immobility, and mortality.15 Several systematic reviews have confirmed that urgency urinary incontinence is an independent risk factor for falls.16, 17, 18 Gosch et al found that amongst patients admitted for fragility fractures, those with urinary incontinence displayed increased rates of cognitive dysfunction and depression compared to those without incontinence. Patients with incontinence were more likely to have musculoskeletal complaints that inhibit mobility, including lower back pain, weaker grip strength, and slower walking velocity.2 Despite the close relationship between UUI and falls, studies that determine if treatment of UUI can reduce fall risk are lacking. Improvement in physical activity can reduce the risk of falls in older adults: Women with UUI exhibit avoidance of physical exercise.20, 21, 22 One of the major risk factors for falls is decline in physical functioning, which is accelerated by lack of physical activity. In a meta-analysis of 30 studies, decline in lower extremity strength was associated with falls (odds ratio 1.76, 95% CI 1.3-2.4).23 On the other hand, improvement in physical activity by strength and balance training or simply by increased physical activity is effective in reducing fear of falling as well as actual falls.24, 25 The Nurses Health Study prospectively showed that older women who remained physically active longer were less likely to report the development of new onset UUI.26 However, it is not known if treatment of UUI can improve physical activity in older adults. Anti-cholinergic medications may improve physical activity in older adults with urgency urinary incontinence: Prior studies suggest that treatment of overactive bladder with anti-cholinergic medications is associated with improvement in physical activity associated with quality of life.9, 10, 27, 28 In these studies, activity was measured using the Physical Limitations domain of the Kings Health Questionnaire (KHQ) or the Coping score of the Overactive Bladder Questionnaire (OAB-q). However, these domains examine social-related activities such as planning for travel/transportation and locating of convenient restrooms, and are therefore quality-of-life rather than physical activity measures. This may not reflect change in actual physical activity such as walking, climbing stairs, or participating in sports. Data from our preliminary study at Penn presented at AUGS/IUGA 2014 suggest that treatment with fesoterodine, in combination with behavior modification and Kegel exercises, improves womens

ability to perform physical activities pertaining to leisure and moderate exercise. These studies suggest anti-cholinergic medications improve older adults physical activity and potentially reduce their risk for falls. Neurocognitive measures, anti-cholinergic medications and falls: Worsening functional and cognitive abilities are significantly associated with both falls and urinary incontinence. Anti-cholinergic medications may also cause neurocognitive dysfunction and potentially increase fall risk.12 Useful measures of neurocognitive function include: 1) the Mini-Cog Evaluation, the most studied screening instrument for cognitive impairment, with a 88.3% sensitivity and 86.2% specificity.29 2) Multiple studies show that the greatest factor predicting future falls is a history of a prior fall,30, 31, 32 3) Short Physical Performance Battery testing: the SPPB measures standing balance, walking speed, and ability to rise from a chair. Scores for each measure range from 0 to 4, with 4 indicating the highest level of performance and 0 the inability to complete the test. A summary score (range 0-12) is subsequently calculated by adding the three scores. The SPPB can be used to predict higher fall rates and recurrent fallers. Physical activity can be measured using self-reported questionnaires: Accurate and efficient measurement of activity in elderly subjects is complex. Accelerometers are considered reliable instruments for objective measurement of physical activity behavior.37 However, use is limited by expense, discomfort, shortcomings in measuring aquatic and static exercise activities, and non-compliance.38 Self-administered physical activity questionnaires are inexpensive, useful alternatives for measuring energy expenditure. Many physical questionnaires exist, but most are not validated in older adults and none have been validated in adults with UUI. The most widely used questionnaire, the International Physical Activity Questionnaire (IPAQ), has been validated only in subjects aged 15 to 69.39 Other potentially useful questionnaires are the Community Healthy Activities Model Program for Seniors (CHAMPS) questionnaire,40 and the Birmingham Bowel questionnaire. Both are validated in older adults but not in the OAB population. The ideal questionnaire to measure physical activity in older adults with OAB is not known. Adherence to anti-cholinergic medication is low: As mentioned above, despite the beneficial effects of anti-cholinergic medications, adherence is low. In two studies conducted at the University of Pennsylvania, adherence was associated with increased doubts in the efficacy and benefit of medicine as measured by the Belief Screen of the Brief Medication Questionnaire.14, 42 In this study, we choose to use a well-tolerated anticholinergic with fewer side effects: fesoterodine. Often, patients who had prior unsatisfactory symptom control and/or unacceptable adverse events with tolterodine or oxybutynin reported better efficacy and/or more acceptable adverse event profiles with fesoterodine. (AUA SUFU guidelines). Preferred treatments are associated with improved adherence: While adherence is the result of a complex interaction between psychological, socioeconomic, and clinical factors, there is a known connection between satisfaction with treatment and adherence.43 Patients beliefs of the necessity of is also important; indifference towards medications benefit as well as a greater ratio of concerns about medications versus necessity were associated with non-adherence in patients with rheumatoid arthritis.44 Additionally, patient participation in decisions regarding treatment are important for adherence. The shared decision-making framework, in which patient and physician discuss, share, and build consensus for a preferred treatment, may improve adherence.45 In patients with depression, self-reported adherence was significantly higher when there was concordance between preference for decision making and actual participation in decision making.46 A systematic review by Joosten et al found that in the limited literature that examined adherence as an outcome in shared decision-making models, patients who participated in decision making were more likely to adhere to medications at follow-up.47 There is a key gap in knowledge on how to measure preference for treatment for overactive bladder and the impact of these preferences on adherence. SUPPORTING DATA The studies below provide preliminary data for the proposed study and demonstrate the mentors expertise in mentoring fellows and in questionnaire validation. Preliminary Studies: 1. Physical Activity in Women Undergoing Treatment for Overactive Bladder. Mentored fellow: Chu. Funded: Pfizer-AUA. Presented at IUGA/AUGS Joint Conference, Washington DC, July 2014. The aim of this study is to determine if treatment of overactive bladder with anticholinergic medications has an impact on self-reported physical activity. Methods: 137 women with OAB symptoms treated with flexible-dose fesoterodine therapy, evaluated at baseline and 8 weeks post-treatment. Urinary symptoms and health beliefs were measured using validated questionnaires. Physical activity scores were calculated using the Short Form 12 (SF-12) Does your health now limit you in a) Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf? and b) Limit you in climbing several flights of stairs? Results: At 8 weeks, the proportion of women with no restriction in physical activity was higher in responders than non-responders (52% vs. 33%) while the proportion of women with severe restriction was lower in responders than non-responders (13% vs. 17%). Conclusion: Treatment of OAB in combination with behavior modification, Kegel exercises, and anti-cholinergic medication improves womens performance of physical activities pertaining to leisure and moderate exercise. 2. Exercise for the Prevention of Falls in Older Women with Urge Incontinence.

Funded: CTSA, Perelman School of Medicine of the University of Pennsylvania. We have an ongoing study to examine the efficacy of exercise for the prevention of falls in older women with urgency urinary incontinence. For this study we have recruited 36 community dwelling older women with UUI. Falls risk (using questionnaires and neurocognitive tests) and urinary symptoms were measured before and after the exercise intervention. This study shows 1) our ability to recruit older adults with urgency urinary incontinence and 2) feasibility of performing neurocognitive tests in older adults with urgency urinary incontinence. Related studies on Preference and Adherence: 3. Primary Adherence and Health Beliefs Regarding Anti-cholinergic Medications for Urge Incontinence.14 Mentored fellow: Saks. Funded: T32 HD007440, 10/1/00 - 4/30/11. Published. The aim of this prospective cohort study was to examine the role of health care beliefs in primary adherence to anti-cholinergic medications. Methods: 150 women with OAB prescribed anti-cholinergic medication were recruited from the Penn urogynecology clinic. Urinary symptoms and health beliefs were measured using validated questionnaires. Primary adherence (initial filling of a prescription) to medication was measured through pharmacy records. Results: The incidence of primary adherence was 73%. Patients beliefs in the general overuse/harm of medications were significant negative predictors of primary adherence (OR=0.35, 95% CI 0.16,0.79). Conclusion: Health care beliefs are strongly associated with primary adherence. 4. Validation of a Self-administered Instrument to Measure Adherence to Anti-cholinergic Drugs in Women with Overactive Bladder.42 Mentored fellow: Andy. Funded: Pfizer-AUA. Published. The aim of this study was to evaluate the validity of the MASRI for measuring adherence in women starting anti-cholinergic medications. Methods: Prospective study in 131 women with OAB treated with fesoterodine. Adherence was measured at 8 and 12 weeks using an interviewer administered Brief Medication Questionnaire (BMQ) that assesses barriers to adherence (criterion standard), the MASRI, and pill count. Results: Women diagnosed as non-adherent by the MASRI were more likely to report a belief barrier to taking medication as compared to adherent women at 8 weeks (80% vs. 38%, P0.001) and at 12 weeks (70% vs. 40%, P=0.003). The MASRI correctly identified 93% and 96% of non-adherent women at 8 and 12 weeks, respectively. Sensitivity, specificity, and positive likelihood ratio of the MASRI for predicting non-adherence was 91%, 82%, and 5.1% at 8 weeks and 90%, 85% and 6.1% at 12 weeks. Conclusion: The MASRI is a valid self-administered tool for measuring adherence to anti-cholinergic medication in women with OAB. Expertise in Questionnaire Validation: 5. Construct Validity of Utility Preference Score Instruments in Women with Urinary Incontinence.48 Mentored fellow: Harvie. Funded: International Urogynecology Association (IUGA). Published. The aim of this study was to evaluate the construct validity of three instruments for measuring utility preference scores in women with urinary incontinence. Methods: We recruited 260 consecutive women presenting to Penn urogynecology clinic with pelvic organ prolapse, stress, or urgency urinary incontinence. Utility scores were measured using the HUI-3, EQ-5D, SF-6D and a VAS. Results: The pattern of increasing (better) utility scores from UUISUIno incontinence persisted for all the health-status classification system instruments but not the VAS. Only the HUI-3 and SF-6D were able to discriminate between UUI and SUI. Utility scores from all four instruments were significantly negatively correlated with the UDI-6 and UIQ-7. Correlations were lowest for the VAS. Conclusion: Utility preference scores are valid quantitative measures of the negative impact of urinary incontinence on general health-related quality-of-life. The VAS and Euro-QOL provide poor discrimination for women with incontinence.

Study Design

Phase*
Not applicable

Design
Overall Study Design: All three aims are derived from the same prospective cohort design examining effects in adults aged 65 and older with OAB undergoing treatment with medication in a clinical setting. A follow up period of 8 weeks has been selected because this is the period of maximal drop in adherence.13, 49 Six anti-muscarinic medications are currently available for overactive bladder in the United States: darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, and trospium. There is no evidence to support that one anti-cholinergic medication is better than another. Literature indicates that no one treatment is clearly superior to another, (Qaseem 2014) and that selection of anti-muscarinic medication should be based on the physicians discretion based on tolerability of side effects and insurance costs. (AUA/SUFU OAB guidelines) In this study, patients will be provided medication free of costs, so insurance would not play a role in deciding medication type. Additionally, fesoterodine is an appropriate first choice for medication as it has comparable side effects to other anti-cholinergic medication typically used in overactive bladder, including dry mouth, constipation, and CNS effects.

(Tzefos 2009, AHRP reference guide) Additionally, fesoterodine has been compared to tolterodine, and may show greater efficacy. (Tzefos 2009) In fact, fesoterodine tends to have low incidence of dry mouth, and moderate incidence of constipation compared to other anti-muscarinics, making it a well-tolerated and appropriate first choice for most patients.(Ellsworth 2014) Low CNS penetration may also potentiate fewer CNS side effects.(Ellsworth2014) Additionally, our previously presented data on the potential positive effects of anticholinergic medication on physical activity was collected using fesoterodine, so there is a precedent for using this anticholinergic in a study examining changes in activity and sedentary behavior. Therefore, fesoterodine, the drug used in this study, is an appropriate medication for routine and standard care of overactive bladder. Fesoterodine is being supplied by Pfizer for the use of this study. As part of routine clinical care at the urogynecology clinics of the University of Pennsylvania Health System, all patients receive a pelvic exam, measurement of post-void residual by bladder ultrasound, and administration of four urinary questionnaires as part of evaluation of urinary symptoms. The OABq-SF and the UDI-6 will be used to screen patients. Inclusion Criteria: adults aged 65 or older, urinary urgency of quite a bit severity or more on the Overactive Bladder Questionnaire-Short Form (OABq-SF),50 who are eligible for pharmacologic therapy for overactive bladder Exclusion Criteria: predominant stress incontinence (on UDI-6), current/recent use (6 m) or contraindication to anti-cholinergic medication, severe voiding difficulties, men on 5-alpha reductase inhibitors, severe neurologic disease, recent anti-incontinence or prolapse surgery, other urinary tract conditions such as calculus or recurrent UTI. Recruitment/Retention Experience: The urogynecology/urology clinics of the Hospital of University of Pennsylvania are high volume referral clinics staffed by four urogynecologists and one urologist. We see 125 female and 50 male patients with OAB per month with eligibility:participation ratio of 1.5:1 in clinical trials.42, 48, 51 In recent trials, 50% of recruited adults were Caucasian and 45% African-American. We anticipate that the female:male ratio will be 2:1. Recruitment : Pre-screening will occur at a patients routine visit, or via chart review following clinical care. If a patient appears to be eligible, they will be referred to the study coordinator to schedule a baseline visit. Patients of urogynecology or other referring geriatrics/urology/primary care practices may also self-refer for participation, as long as their medical records are available for eligibility determination. Baseline visit: At this visit, the trained coordinator will obtain informed consent, administer physical activity and other questionnaires (see Instrument and Testing Schedule below). Routine pre-treatment counseling on medical treatment, as well as counseling on additional non-medical (biofeedback, behavioral strategies, pelvic floor muscle training) and interventional treatments (neuromodulation), will also be provided. Then the coordinator will administer the Preference instrument on a bidirectional scale with 0 being undecided, and either extreme (5 or -5) being a strong preference for that particular treatment. The Short Physical Performance Battery (SPPB) test will also be performed with the oversight of trained personnel for safety. Accelerometers and instructions for wearing the accelerometer will be provided at that time. The monitor will be retrieved from the patient by a study coordinator or investigator 1 week later. Intervention: All subjects (irrespective of preference) will receive a 90-day supply of open label fesoterodine 4 mg per day. They will start medication 1 week after the baseline visit. After 4 weeks of treatment, dose may be increased to 8 mg over the telephone based on symptom report. This dosing regimen is direct alignment with clinical care. Change of prescription to another anti-cholinergic may occur during the study period, if determined necessary by the physician. Criteria that would warrant stopping fesoterodine include: - inability to tolerate common side effects, including dry mouth, dry eyes, and constipation - lack of satisfactory urinary symptom control on the highest dose of fesoterodine - immediate withdrawal in case of life-threatening side effects (uncommon, including angina, angioedema, diverticulitis, gastroenteritis, heat prostration, hypersensitivity reactions, irritable bowel syndrome, QT prolongation) Once withdrawn from fesoterodine, managing physicians would use their clinical judgment to switch the patient to another anti-cholinergic medication or switch to another class of medication (beta 3 agonist, or mirabegron). These patients would continue to be followed until after the 8 week follow-up visit, as the statistical plan will involve intention-to-treat analysis. The patients will continue to participate in the 8 week follow-up visit (including questionnaires and SPPB), regardless of whether or not they were switched to another medication. All adults will receive printed educational material on fluid modification, behavioral strategies, and Kegel exercises. 8 week follow up visit: One week prior, the study coordinator will once again provide subjects with accelerometers and instructions for wearing the accelerometer. At the 8 week visit, the patient will again complete self-administered physical activity, urinary symptoms, adherence, pill count, and neurocognitive instruments and tests with the oversight of a trained investigator (see Instrument and Testing Schedule below). The monitor will be retrieved from the patient by a study coordinator or investigator at the 8 week follow up visit. Instrument and Testing Schedule BASELINE VISIT: Urinary questionnaires (OABq-SF, UDI-6) Preference: Belief in Medication Questionnaire (BMQ), Bidirectional Visual Analogue Preference scale Physical activity:

Accelerometer (gold standard), Self-reported questionnaires (IPAQ, CHAMPS) Neurocognitive measures: Questionnaires (Mini Cog, Falls risk), Short Physical Performance Battery Quality of Life: SF-12 Bowels: Birmingham 8 WEEK FOLLOW-UP VISIT: Physical activity: Accelerometer (gold standard), Self-reported questionnaires (IPAQ, CHAMPS) Neurocognitive measures: Questionnaires (Mini Cog, Falls risk follow up), Short Physical Performance Battery Quality of Life: SF-12 Urinary: Questionnaires (OABq-SF, UDI-6) Adherence: Questionnaires (Belief in Medication follow up questionnaire, MASRI), pill count Patient Global Index of Improvement (PGI-I) form Bowels: Birmingham Qaseem A, Dallas P, Forciea MA, Starkey M, Denberg TD, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Nonsurgical management of urinary incontinence in women: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2014 Sep 16;161(6):429-40. Ellsworth PI. The pharmacologic management of idiopathic overactive bladder in primary care. J Fam Pract. 2014 Feb;63(2 Suppl):S38-45. Review. Association of Reproductive Health Professionals. A Quick Reference Guide for Clinicians: Diagnosis and Management of Overactive Bladder. https://www.arhp.org/uploadDocs/OABQRG.pdf. Assessed 6.5.2015

Study duration

Penn Urogynecology has an established track record of successfully recruiting adults with OAB into cohort studies and randomized control trials. We plan to recruit 13 to 14 patients per month to reach target enrollment of 80 patients by 6 months. As in most clinical trials of OAB, we anticipate that two-thirds of recruited subjects will be female. Patients will be followed for a total of 8 weeks (see Design). Ideally, we would start subject recruitment in March 2016, and subject recruitment and data collection would be finished in September of 2016.

Resources necessary for human research protection

Describe research staff and justify that the staff are adequate in number and qualifications to conduct the research. Describe how you will ensure that all staff assisting with the research are adequately informed about the protocol and their research related duties. Please allow adequate time for the researchers to conduct and complete the research. Please confirm that there are adequate facilities for the research.

INSTITUTIONAL PLANS Facilities Available at the Sponsoring Institution The University of Pennsylvania has a long history of multidisciplinary clinical and translational research in womens health. The proposed clinical study is a multi-disciplinary collaboration between the Divisions of Urogynecology (OB/GYN), Urology (Surgery), Geriatrics and the Exercise Physiology Unit. Dr. Arya will recruit patients from three sites, including: the Divisions of Urogynecology (OB/GYN) the Division of Urology (Surgery) the Division of Geriatrics (Internal Medicine) There is a long track record of collaboration between Urogynecology, Urology and Geriatrics for recruiting patients for clinical trials through the Pelvic Floor Disorder Network (U-10, NIH) under Dr. Arya (PI) and Dr. Smith (co-PI), and Dr. Johnson (co-investigator).The University of Pennsylvania Health System (UPHS) is an academic tertiary care referral center that draws patients from a wide geographic area. Patients represent a diverse racial and socioeconomic distribution, including inner city and suburban populations. The Division of Urogynecology cares for the full spectrum of urinary incontinence and related disorders and has four clinics at Hospital of University of Pennsylvania, Pennsylvania Hosptial, Chestnut Hill Hospital and Radnor. The Continence Center of the Division of Urology (Director: Ariana Smith, MD) has female urology clinics at both the Hospital of the University of Pennsylvania and Pennsylvania Hospital. The clinical and research infrastructure of these two hospitals are completely integrated with electronic inpatient and outpatient medical records, shared clinical responsibilities, on-call schedule, and research nurses and study coordinators. The Division of Geriatrics (Internal Medicine) has over 20 academic and research faculty who offer consultative services to departments conducting clinical trials and/or translation research, including extensive expertise in research in older adults. The Womens Health Clinical Research Center (WHCRC) of the Department of OB/GYN provides infrastructure to assist experienced as well as new investigators in the implementation and conduct of clinical research including assistance in IRB, continuing renewals, amendments and adverse event reporting and assistance in setting up a study binder and study monitoring. Exercise Medicine Unit, The Center for Clinical and Translational Research Center (CTRC), Director Katie Schmitz, Ph.D. (co-mentor, letter of support): The Exercise Medicine Unit (5,884 square feet) offers exercise training and testing services for clinical research studies. The exercise training room contains treadmills, arc trainer, recumbent bike, functional trainer, adjustable bench, and a power block area. It is staffed by a full-time, certified exercise trainer who can help design exercise training protocols and administer them to clinical research study participants. Dr. Schmitz will provide mentorship in biostatistics and with

implementing the physical activity monitors and analysis of the accelerometer data. The Clinical Center for Epidemiology and Biostatistics (CCEB) provides a Clinical Research Certificate Program for clinicians associated with the university and provides a foundation in biostatistics, research methodology, epidemiology and grant writing to allow those completing to coursework to have the tools to pursue a career as an independent researcher. The CCEB will provide biostatistics support for this project. The CCEB has been actively involved in clinically- and pharmacologically-oriented research since 1978. As a Type II Center, it is the primary home for epidemiology and biostatistics at the University of Pennsylvania. It is an interdisciplinary and interdepartmental program of more than 275 individuals and includes clinical and non-clinical faculty, fellows, research staff, biostatisticians, and clerical staff. Many studies in the CCEB have focused exclusively on women's health issues. Fellow research facilities of the Division of Urogynecology are located in close proximity to all patient activity. Fellows have their own dedicated desk stations and a state-of-the-art computer and printer. The PC has word-processing, spreadsheet, and statistical database analysis programs (STATA). The fellows have full access to secretarial support, information services, slide preparation and poster presentations assistance, and videotaping/editing services. Each fellows computer is connected to the main hospital network, which allows for easy and rapid retrieval of inpatient data, biomedical library access, and free access to the Internet. Literature searches may be conducted from the fellows office through these means. Additionally, the Biomedical Library is in close proximity and has extensive facilities for literature searches, journals, and inter-library loan. The library periodically holds courses on updated methods of database searches, and experienced medical librarians are always on staff. Funding and Technical Assistance: Funding support will be provided by the Pfizer/Urology Care Foundation Urologic Research Training Award Program for medications and support staff (project coordinator). Penn will support the infrastructure needed for recruiting patients for the study (from Urogynecology, Urology, Geriatrics), technical assistance with physical activity monitoring and analysis of accelerometer data (Exercise Physiology Unit, Dr. Schmitz), and creation of database in REDCap and statistical support (CCEB, Dr. Schmitz). The WHCRC of the Department of OB/GYN will provide assistance with IRB, adverse event reporting, storage and dispensing of drug, setting up study binder and study monitoring.

Characteristics of the Study Population

Target population
Adult subjects aged 65 or older with overactive bladder undergoing treatment with medication

Subjects enrolled by Penn Researchers
80

Subjects enrolled by Collaborating Researchers
0

Accrual
Recruitment/Retention Experience: The urogynecology/urology clinics of the Hospital of University of Pennsylvania are high volume referral clinics staffed by four urogynecologists and one urologist. We see 125 female and 50 male patients with OAB per month with eligibility:participation ratio of 1.5:1 in clinical trials. In recent trials, 50% of recruited adults were Caucasian and 45% African-American. We anticipate that the female:male ratio will be 2:1. Sample Size: Specific Aim 1: A sample size of 68 evaluable subjects will provide 90% power to detect a correlation coefficient of 0.72 or greater, assuming a correlation coefficient of 0.5 or less between the physical activity questionnaires and the criterion standard (accelerometer) is undesirable (null hypothesis). Assuming a 15% loss to follow-up, we plan to enroll 80 patients to ensure an adequate sample of at least 68 subjects with complete datasets. Specific Aim 2: We have conservatively assumed that 50% subjects will express preference for medication. Prior Penn studies show 56% adherence at 8 weeks in unselected subjects. Assuming that adherence will be 80% in subjects expressing preference for medication, a sample size of 80 subjects will provide 90% power to demonstrate a 30% difference in adherence rates in subjects who do or do not have preference for medication. Specific Aim 3: Assuming two-tailed alpha of 0.05, a sample size of 80 subjects will provide 90% power to show a 30% difference in physical activity in the proportion of subjects expressing preference for medication versus those without preference.

Key inclusion criteria
Inclusion Criteria: adults aged 65 or older, urinary urgency of quite a bit severity or more on the Overactive Bladder Questionnaire-Short Form (OABq-SF),50 who are eligible for pharmacologic therapy for overactive bladder

Key exclusion criteria
Exclusion Criteria: predominant stress incontinence (on UDI-6), current/recent use (6 m) or contraindication to anti-cholinergic medication, severe voiding difficulties, men on 5-alpha reductase inhibitors, severe neurologic disease, recent anti-incontinence or prolapse surgery, other urinary tract conditions such as calculus or recurrent UTI.

Vulnerable Populations

	Children Form
	Pregnant women (if the study procedures may affect the condition of the pregnant woman or fetus) Form
	Fetuses and/or Neonates Form
	Prisoners Form
	Other
x	**None of the above populations are included in the research study**

The following documents are currently attached to this item:

There are no documents attached for this item.

Populations vulnerable to undue influence or coercion
All patients will be advised that participation in the study is completely voluntary. Financial reimbursement is minimal ($50), and is only for covering transpotation/parking costs, which will minimize the risk of coercion for the economically disadvantaged. Patients will also be assured that their participation will not affect their care or treatment. Also, each person will be provided the opportunity to decline or participate in the study through the process of thorough informed consent. Penn employees and students who may be approached during their evaluation in the urogynecology clinics will be told that their decision to participate will not impact their standing with the University.

Subject recruitment
Dr. Chu and other study investigators will recruit patients from physician offices/clinics from three clinical divisions, including: the Divisions of Urogynecology (OB/GYN) the Division of Urology (Surgery) the Division of Geriatrics (Internal Medicine) There is a long track record of collaboration between Urogynecology, Urology and Geriatrics for recruiting patients for clinical trials through the Pelvic Floor Disorder Network (U-10, NIH) under Dr. Arya (PI) and Dr. Smith (co-PI), and Dr. Johnson (co-investigator).The University of Pennsylvania Health System (UPHS) is an academic tertiary care referral center that draws patients from a wide geographic area. Patients represent a diverse racial and socioeconomic distribution, including inner city and suburban populations. The Division of Urogynecology cares for the full spectrum of urinary incontinence and related disorders and has four clinics at Hospital of University of Pennsylvania, Pennsylvania Hosptial, Chestnut Hill Hospital and Radnor. The Continence Center of the Division of Urology (Director: Ariana Smith, MD) has female urology clinics at both the Hospital of the University of Pennsylvania and Pennsylvania Hospital. The clinical and research infrastructure of these two hospitals are completely integrated with electronic inpatient and outpatient medical records, shared clinical responsibilities, on-call schedule, and research nurses and study coordinators. The Division of Geriatrics (Internal Medicine) has over 20 academic and research faculty who offer consultative services to departments conducting clinical trials and/or translation research, including extensive expertise in research in older adults. Potential subjects will be identified either by clinical providers during routine visits to the recruitment offices, or by the research staff using Epic. Potentially eligible subjects may be identified by reviewing the EMR of patients scheduled for visits. The study staff will then either send a message to the provider reminding them to discuss the study with the subject when they come for their visit, OR will contact the subject via phone in advance to introduce the study. Potential subjects may also be identified via Epic after they have completed their clinical visit. Patients who have had clinical appointments in recent years may be identified as potential subjects via review of Epic or request from the PennData Store. If they were not

offered study participation in the office, they will be contacted by phone or mail regarding their interest in participation. Potential subjects also have the option of self-referring, if they see study recruitment materials and are interested in participation, and their medical records are available for review and confirmation of eligibility.

Will the recruitment plan propose to use any Penn media services (communications, marketing, etc.) for outreach via social media avenues (examples include: Facebook, Twitter, blogging, texting, etc.) or does the study team plan to directly use social media to recruit for the research?
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Subject compensation*
Will subjects be financially compensated for their participation?
Yes

The following documents are currently attached to this item:

There are no documents attached for this item.

If there is subject compensation, provide the schedule for compensation per study visit or session and total amount for entire participation, either as text or separate document

Patients will be reimbursed a total of $50 for their time. This will be provided in $25 increments: once at the baseline visit, and once at the follow-up 8 week visit. Subjects will be paid using ClinCards.

Study Procedures

Suicidal Ideation and Behavior
Does this research qualify as a clinical investigation that will utilize a test article (ie- drug or biological) which may carry a potential for central nervous system (CNS) effect(s)?
No

Procedures
Study visits will typically occur in the subjects home, unless they prefer to come to the office. 1. Recruitment and Enrollment: Following a routine office visit, or upon self-referral and review of records, the patient will be scheduled for a baseline visit with the coordinator, if eligible. Additional pre-screening may occur with the subject via phone. 2. Baseline visit: The study coordinator will finish confirming eligibility via pre-screening questions (if not already completed prior to the visit). Once eligibility is confirmed, subjects will provide consent. Additionally, the subjects will fill out the following questionnaires: Preference: Belief in Medication Questionnaire (BMQ, gold standard), Bidirectional Visual Analogue Preference scale Physical activity: Accelerometer (gold standard), Self-reported questionnaires (IPAQ, CHAMPS) Neurocognitive measures: Questionnaires (Minicog, Falls risk) Urinary: Questionnaires (OABq-SF, UDI-6) Quality of Life: SF-12 Bowels: Questionnaires (Birmingham) Short Physical Performance Testing will be performed with oversight from trained personnel. The study coordinator will provide subjects with accelerometers and instructions for wearing the accelerometer. The monitor will be retrieved from the patient by a study coordinator or investigator a week later. 3. Intervention: All subjects will receive a 90-day supply of open label fesoterodine 4 mg per day, which they will start 1 week after the baseline visit. After 2 weeks, dose may be increased to 8 mg over the telephone based on symptom report. Change of prescription to another anti-cholinergic may occur during the study period, if determined necessary by the physician. See full criteria in previous intervention section above. 4. 8 week follow up visit: At this visit, the patient will complete the following self-administered physical activity, urinary symptoms, adherence, pill count, and neurocognitive instruments and tests: Physical activity: Accelerometer (gold standard), Self-reported questionnaires (IPAQ, CHAMPS) Neurocognitive measures: Questionnaires (Minicog, Falls

risk), Short Physical Performance Battery Urinary: Questionnaires (OABq-SF, UDI-6) Bowels: Questionnaires (Birmingham) Quality of Life: SF-12 Adherence: Questionnaires (BMQ follow up, MASRI), pill count Patient Global Index of Improvement (PGI-I) form The study coordinator will again provide subjects with accelerometers and instructions for wearing the accelerometer, one week prior to the 8 week visit. The monitor will be retrieved from the patient by a study coordinator or investigator at the 8 week visit. Instrument and Testing Schedule BASELINE VISIT: Preference: Belief in Medication Questionnaire (BMQ, gold standard), Bidirectional Visual Analogue Preference scale Physical activity: Accelerometer (gold standard), Self-reported questionnaires (IPAQ, CHAMPS) Neurocognitive measures: Questionnaires (Mini cog, Falls risk), Short Physical Performance Testing Urinary: Questionnaires (OABq-SF, UDI-6) Quality of Life: SF-12 Bowels: Questionnaires (Birmingham) 8 WEEK FOLLOW-UP VISIT: Physical activity: Accelerometer (gold standard), Self-reported questionnaires (IPAQ, CHAMPS) Neurocognitive measures: Questionnaires (Mini Cog, Falls risk), Short Physical Performance Testing Urinary: Questionnaires (OABq-SF, UDI-6) Bowels: Questionnaires (Birmingham) Quality of Life: SF-12 Adherence: Questionnaires (BMQ follow up, MASRI), pill count Patient Global Index of Improvement (PGI-I) form

The following documents are currently attached to this item:

There are no documents attached for this item.

Deception
Does your project use deception?
No

International Research
Are you conducting research outside of the United States?
No

Analysis Plan
Analysis Plan Specific Aim 1 and 2: We will evaluate physical activity, adherence, and neurocognitive function before and after treatment to examine changes from baseline to 8 weeks in subjects with and without preference for medication. Concurrent validity, the relationship of the instrument to other similar evaluations, will be measured by comparing IPAQ, and CHAMPS scores to accelerometer data at baseline using the Spearman correlation coefficient and the intraclass correlation coefficient. Specifically, we will compare energy expenditure in MET*min/week (IPAQ) or MET*hour/week (CHAMPS) to that measured by the Actigraph accelerometer over the course of a week. For preference, we will compare subjects scores as indicated on the bidirectional scale to their necessity-harm differential as calculated by the Belief Screen of the BMQ using Spearman correlation coefficient. Contingency analyses tables will be used to determine the sensitivity and specificity of the bidirectional preference scale and the necessity-harm differential (as calculated on the Belief Screen) that best discriminates between those with preference for medication and those without. Discriminant validity, the ability to distinguish between populations, will be determined by comparing mean differences in energy expenditure for each physical activity instrument between responders and non-responders to anticholinergic medication as defined by the PGI-I. We will compare total MET*min/week (IPAQ) or MET*hour/week (CHAMPS), as well as energy spent in sedentary and moderate-to-vigorous physical activities (CHAMPS) between responders and non-responders using Wilcoxon rank sum test. For preference, we will compare the BMQ Belief necessity-harm differential and bidirectional preference scale score using Wilcoxon rank sum test. Responsiveness, the ability of the instruments to detect clinically meaningful change, will be assessed. First, pretreatment energy expenditure and preference will be compared with post-treatment activity and preference scores, respectively, using the t-test. Next, effect size (change in mean score/SD of baseline) and standardized response mean (change in mean score/SD of the change) will be assessed. For both, values of 0.50.7 will be considered moderate responsiveness; 0.81, good; and 1, excellent. We will measure minimum clinically important difference (MCID); specifically, the smallest change in physical activity associated with clinically meaningful change in global rating scale (mean change in energy expenditure in subjects indicating a little better or greater in the global rating scale). Specific Aim 3: We will compare within subject change in physical activity from baseline to 8 weeks using the paired t-test. Improvement in physical activity will be defined as 15% increase in energy expenditure as compared to baseline. The effect of age, co-morbidities, baseline activity, severity of cognitive impairment, BMI on physical activity will be examined using regression analysis. We will also compare change in activity, proportion of subjects

showing improvement in activity, adherence (80% or greater, as measured by pill count and MASRI), response to medication (PGI-I), overall quality of life (SF-12), neurocognitive and balance function (MMSE and Berg Balance Scale scores, respectively), and urinary symptoms (OABq-SF score) in adults expressing preference for medication to those expressing no preference. The effect of preference will be measured using regression analysis, with adjustment for baseline physical activity, Charlson co-morbitidy index, age, and BMI.

The following documents are currently attached to this item:

There are no documents attached for this item.

Data confidentiality

x **Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.**

x **Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.**

Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.

x **Wherever feasible, identifiers will be removed from study-related information.**

A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.

Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.

Subject Confidentiality
Extensive efforts will be made to ensure and maintain participant confidentiality. Data from patients will be recorded on data collection forms, which will be associated with a Subject ID number only. The patient name, medical record numbers, or other identifiers will not be present on the data collection forms themselves. The Subject ID number will be composed by the sequential ordering of participants. A log book will be kept in for data management purposes to match Subject ID number with patient medical record numbers if chart review is needed for missing data. This will also be maintained in a secure and locked filing system at all times. Any additional source documentation that may associate the patient and PHI to data (such as consent forms) will also be kept in a secure and locked filing system at all times. Additionally, any data collection forms will also be kept in a separate secure and locked filing system at all times. All data will a REDCap database using their assigned Subject ID number. This is protected by a secure system requiring log-in and password. The data from the accelerometers is downloaded using the secure software that comes with the Actigraph device, known as Actilife. This data is then analyzed by the software, and converted into Excel files. These Excel files will be password-protected.

Sensitive Research Information*
Does this research involve collection of sensitive information about the subjects that should be excluded from the electronic medical record?
No

Subject Privacy
Privacy refers to the person's desire to control access of others to themselves. Privacy concerns people, whereas confidentiality concerns data. Describe the strategies to protect privacy giving consideration to the following: The degree to which privacy can be expected in the proposed research and the safeguards that will be put into place to respect those boundaries. The methods used to identify and contact potential participants. The settings in which an individual will be interacting with an investigator. The

privacy guidelines developed by relevant professions, professional associations and scholarly disciplines (e.g., psychiatry, genetic counseling, oral history, anthropology, psychology).
Study visits will typically occur in subjects' homes, allowing for complete privacy. Any telephone calls required to contact patients will be performed in a private manner.

Data Disclosure
Will the data be disclosed to anyone who is not listed under Personnel?
No.

*Data Protection**

- x **Name**
- x **Street address, city, county, precinct, zip code, and equivalent geocodes**
- x **All elements of dates (except year) for dates directly related to an individual and all ages over 89**
- x **Telephone and fax number**
- x **Electronic mail addresses**
- x **Social security numbers**
- x **Medical record numbers**
- **Health plan ID numbers**
- **Account numbers**
- **Certificate/license numbers**
- **Vehicle identifiers and serial numbers, including license plate numbers**
- **Device identifiers/serial numbers**
- **Web addresses (URLs)**
- **Internet IP addresses**
- **Biometric identifiers, incl. finger and voice prints**
- **Full face photographic images and any comparable images**
- **Any other unique identifying number, characteristic, or code**
- **None**

Does your research request both a waiver of HIPAA authorization for collection of patient information and involve providing Protected Health Information ("PHI") that is classified as a "limited data set" (city/town/state/zip code, dates except year, ages less than 90 or aggregate report for over 90) to a recipient outside of the University of Pennsylvania covered entity?
No

Tissue Specimens Obtained as Part of Research*
Are Tissue Specimens being obtained for research?
No

Tissue Specimens - Collected during regular care*
Will tissue specimens be collected during regulator clinical care (for treatment or diagnosis)?
No

Tissue Specimens - otherwise discarded*
Would specimens otherwise be discarded?
No

Tissue Specimens - publicly available*
Will tissue specimens be publicly available?
No

Tissue Specimens - Collected as part of research protocol*
Will tissue specimens be collected as part of the research protocol?
No

Tissue Specimens - Banking of blood, tissue etc. for future use*
Does research involve banking of blood, tissue, etc. for future use?
No

Genetic testing
If genetic testing is involved, describe the nature of the tests, including if the testing is predicative or exploratory in nature. If predictive, please describe plan for disclosing results to subjects and provision of genetic counseling. Describe how subject confidentiality will be protected Note: If no genetic testing is to be obtained, write: "Not applicable."
Not applicable

Consent

1. Consent Process

Overview
Informed consent will be obtained by the study coordinator after the patient is identified as a potential recruit for the study. The subjects will have as much time as needed to consider participation between informing the prospective participant and obtaining consent. The patient may also choose to withdraw from the study at any time. Investigators will emphasize that participation (or lack of participation) in the study: 1) not influence their evaluation, care, or treatment 2) is completely voluntary 3) does not involve any financial compensation 4) may be terminated at any time. Layman terms will be used by those obtaining the consent. The consent will be written at a 6th grade reading level. All questions will be answered to the patient's satisfaction and understanding before informed consent is obtained.

Children and Adolescents
Not applicable

Adult Subjects Not Competent to Give Consent
All adult subjects must be competent to give informed consent to be eligible for inclusion into this study.

2. Waiver of Consent

Waiver or Alteration of Informed Consent*
No Waiver Requested

Minimal Risk*

Impact on Subject Rights and Welfare*

Waiver Essential to Research*

Additional Information to Subjects

Written Statement of Research*
No

If no written statement will be provided, please provide justificiation

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit

Potential Study Risks

Physical Risks: Because this is a trial involving the use of fesoterodine, there are possible physical risks to the patients secondary to the medication in use and the clinical outcome. However, this is minimal since fesoterodine is 1) a FDA-approved medication available in the United States and regularly used for treatment of overactive bladder, and 2) has relatively few and mild side effects. Risks include: 10%: Gastrointestinal: Xerostomia (19% to 35%; dose related) 1% to 10%: - Central nervous system: Insomnia (1%) - Dermatological: Rash (1%) - Gastrointestinal: Constipation (4% to 6%), dyspepsia (2%), nausea (1% to 2%), abdominal pain (1%) - Genitourinary: Urinary tract infection (3% to 4%), dysuria (1% to 2%), urinary retention (1%) - Hepatic: ALT increased (1%), GGT increased (1%) - Neuromuscular & skeletal: Back pain (1% to 2%) - Ocular: Dry eyes (1% to 4%) - Respiratory: Upper respiratory tract infection (2% to 3%), cough (1% to 2%), dry throat (1% to 2%) - Miscellaneous: Peripheral edema (1%) - 1% (Limited to important or life-threatening): Angina, angioedema, diverticulitis, gastroenteritis, heat prostration, hypersensitivity reactions, irritable bowel syndrome, QTc prolongation Additionally, we will be starting with the lowest dose of fesoterodine available and monitoring all adverse effects. In a meta-analysis of randomized controlled trials with fesoterodine, any adverse effects were usually categorized as mild to moderate, and was most commonly associated with dry mouth and constipation (mild adverse effects).(Wyndaele 2014) Additionally, amongst elderly patients taking fesoterodine, no trials have shown changes in mean MMSE score, computer-based cognitive test battery (CogState), or Rey Auditory Verbal Learning Test scores, even in the vulnerable elderly (patients at high risk for functional decline or death within 2 years).(Chapple 2015) There is a potential for falls during the SPPB testing, but this will be conducted with the oversight of trained personnel, and subjects are encouraged to vocalize concerns and stop if there are any potential for falling during the course of the testing. Loss of confidentiality: Any study in which personal health information (PHI) is collected has the potential risk of loss of confidentiality. However, extensive efforts will be made to ensure and maintain security of PHI and maintain participant confidentiality. Patients will be identified and screened by physician investigators at each site involved in patient care in their offices. The patient will be brought into a private room before discussing the study and enrollment with the patient in the privacy of a private room. During the study, interactions with patients will involve questionnaires and tests which will be conducted in private rooms in physicians' offices. Data from patients will be recorded on data collection forms, which will be associated with a Subject ID number only. The patient name, medical record numbers, or other identifiers will not be present on the data collection forms themselves. The Subject ID number will be composed by the sequential ordering of participants. A log book will be kept in for data management purposes to match Subject ID number with patient medical record numbers if chart review is needed for missing data. This will also be maintained in a secure and locked filing system at all times. Any additional source documentation that may associate the patient and PHI to data (such as consent forms) will also be kept in a secure and locked filing system at all times. Additionally, any data collection forms will also be kept in a separate secure and locked filing system at all times. One year after the study has been completed, any forms with patient identifiers (such as logs and consents) will be destroyed. All data will be logged into a REDCap database using their assigned Subject ID number. This is secure and password protected. The data from the accelerometers is downloaded using the secure software that comes with the Actigraph device, known as Actilife. This data is then analyzed by the software, and converted into Excel files. These Excel files will be password-protected. There are no psychological, social, economic, monetary, or legal risks to this study. Wyndaele JJ, Schneider T, MacDiarmid S, Scholfield D, Arumi D. Flexible dosing with fesoterodine 4 and 8 mg: a systematic review of data from clinical trials. Int J Clin Pract. 2014 Jul;68(7):830-40. doi: 10.1111/ijcp.12425. Chapple C, Oelke M, Kaplan SA, Scholfield D, Arumi D, Wagg AS. Fesoterodine Clinical Efficacy and Safety for the Treatment of Overactive Bladder in Relation to Patient Profiles: A Systematic Review. Curr Med Res Opin. 2015 Mar 23:1-78.[Epub ahead of print]

Potential Study Benefits

Potential benefits to the individual subject include improvement of overactive bladder symptoms from fesoterodine use. Additionally, by validating and measuring responsiveness in physical activity, neurocognitive, and balance instruments, we will be able to increase generalizability of these instruments and validate them for use in future clinical trials. Lastly, this will provide preliminary data on the impact of treatment preference and anti-cholinergic medications on physical activity and falls risk in older adults with overactive bladder, potentially improving quality of life and decreasing life-

threatening consequences of falls in the elderly.

Alternatives to Participation (optional)
Patients are not required to participate in the study. Alternatives would include trying other medical and surgical treatments for overactive bladder without questionnaires, measurements of daily activity with an activity monitor, or other testing.

Data and Safety Monitoring
The Principal Investigator will be responsible to monitoring safety, privacy, and data integrity. This study contains low risks, as fesoterodine is a first-line drug already used in daily in clinical practice for treatment of overactive bladder. Study progress will also be reviewed by the PI. Review of the rate of subject accrual, adherence to inclusion/exclusion criteria will occur to assure that participants meet the eligibility criteria. There will be ongoing collection of data on adverse events and compliance to the treatment protocol throughout the study by research staff.

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit Assessment
The benefits of this treatment outweigh the risks. As discussed before, there is the potential for risk of physical harm and loss of confidentiality as part of participation in this study. However, the risk of physical harm is minimal secondary to the minor adverse effects of fesoterodine, and minimization of the dose administered in this study. Additionally, these medications are already being used as first-line medication in the treatment of overactive bladder in the urogynecology/urology fields. The loss of confidentiality will be minimized by careful and secure management of all paper and electronic documentation of patient data. Additionally, participation in questionnaires and neurocognitive/balance testing could help clinicians discover patients at risk of falls and refer subjects for other medical evaluation as needed. Participation in this study could potentially benefit the patient by decreasing overactive bladder symptoms and improving quality of life. If this trial is successful, benefits to elderly patients could result in improved quality of life, decreased urinary symptoms, increased safety, and decreased risk of the morbidity and mortality associated with falls.

General Attachments

The following documents are currently attached to this item:

There are no documents attached for this item.