2. STUDY PROTOCOL

2.1 Introduction

The Boston Area Community Health Survey is an observational study of a range of urologic symptoms in a population-based, random-sample of Hispanic, non-Hispanic African American, and non-Hispanic Caucasian men and women aged 30 to 79 years residing in Boston, Massachusetts.

2.2 Background and Significance

The BACH study will provide valuable baseline data regarding the prevalence of urological conditions among African-American, Caucasian and Hispanic populations. It will also provide the necessary first step in designing and anchoring the interpretation of data for any future longitudinal study.

Several limitations are common to the prior studies of each condition discussed above. Foremost is the lack of population-based data in general, and the glaring absence of data regarding minority populations. Because a substantial proportion of people affected by these conditions do not seek medical treatment or screening, studies of clinic-based samples are limited and not generalizable. Reliable estimates of these conditions cannot be derived from large surveys of the U.S. population such as NHANES III. Existing studies are limited by the lack of standardized assessment tools with established reliability and validity. Finally, health care access and utilization behavior and the impact of medical care on the conditions of interest has not been well studied.

2.2.1 Benign Prostatic Hyperplasia

Benign prostatic hyperplasia (BPH), a non-malignant enlargement of the periurethral tissue of the prostate gland, is a very common condition in aging men, characterized clinically by urinary obstruction (Stimson, 1990). The spectrum of presentation ranges from asymptomatic prostate enlargement to bothersome symptoms, and may lead to life-threatening conditions such as acute urinary retention, sepsis, and renal failure. An estimated 50% to 70% of men over age 50 experience symptomatic BPH (Boyle, 1994). BPH causes considerable morbidity in men aged 65 and older, with an estimated 1.2 million visits to urologists in the U.S. in 1989 and 188,000 transurethral prostatectomy (TURP) procedures performed in 1995 (Graves, 1997).

Much current knowledge about the prevalence of BPH is derived from selected clinic or autopsy series. This knowledge is limited because only about half of BPH is symptomatic, and many symptomatic men do not seek treatment because of reluctance to discuss the problem or an assumption that the symptoms are inevitable with aging (Boyle, 1994). Autopsy data show a strong association of BPH with age, although these data are not useful for establishing population prevalence. BPH is nonexistent in men under age 30 but can be found in 88% of autopsied men over age 80 (Berry, 1984).

Population-based prevalence estimates of symptomatic BPH are often based on samples of white men; a comparison of age-specific prevalence of clinical BPH in different racial populations has

not been done (Lepor, 1996). The prevalence of BPH in white men in Olmstead County, MN was estimated at 17% of men 50-59 years, 27% of men 60-69 years, and 35% of men 70-79 years (Jacobsen, 1995). The generalizability of this estimate is limited because of the subjects' uniformly high socioeconomic status (SES) and access to high-quality health care. Only one study has compared the incidence of BPH between African-American and white men (Sidney, 1991). No difference in the age-adjusted risk for BPH between African-Americans and whites was found, but this study was limited to surgically treated BPH, and prostatectomy rate is not a reliable predictor of clinical BPH (Lepor, 1996).

Despite its high prevalence and impact on public health, there is little knowledge concerning the natural history of BPH or risk factors for the condition. Risk factor studies are limited to men undergoing surgery for BPH, so do not represent all men with the condition. Currently, the only established risk factors for BPH are increasing age and testicular androgens (the disease is absent in men castrated before puberty). Circulating androgens seem less important (Gann, 1995). Possible lifestyle factors for BPH include cigarette smoking, obesity, alcohol consumption (and cirrhosis), coffee drinking, and exercise. Demographic correlates of BPH are never-married status, low SES, and Jewish religion (Morrison, 1992; Gann, 1995; Guess, 1992). Improved knowledge of BPH risk factors is crucial for planning appropriate treatment and prevention strategies.

There is still no standard operational definition of BPH for use in epidemiologic investigations (Guess, 1995). Assessment of BPH in research studies has included measurement of prostate size, determination of urinary flow rate, identification of symptom complexes, or various combinations of these. With age, symptoms of BPH increase and urinary flow rate decreases, but these changes are not directly related to prostate size (Rittmaster, 1994; Simpson, 1996). The American Urological Association (AUA) symptom index, a validated 7-question, self-administered scale developed in 1992 (Barry, 1992a), is a recommended standard assessment tool for BPH symptoms (McConnell, 1994 Krongrad, 1997), and is one of a number of existing instruments used in planning the BACH Survey.

2.2.2 Prostatitis

Prostatitis is very common but still poorly understood, especially in comparison to other prostate conditions like prostate cancer and BPH (NIH-NIDDK, 1995). Although prostatitis is responsible for almost 2 million physician visits annually in the U.S. (McNaughton Collins, 1998b), reliable prevalence estimates are lacking because of definitional inconsistencies. Chronic prostatitis, the most common subtype, can cause considerable morbidity from the associated clinical symptoms of pelvic area pain, urinary or voiding complaints, and sexual dysfunction. Unlike BPH and prostate cancer, which occur primarily in older men, chronic prostatitis affects adult men of all ages (McNaughton Collins, 1998a). The age-specific incidence of chronic prostatitis appears to remain low until the fifth decade (Roberts, 1998). Whether the prevalence increases with age as with BPH is not clear, partly because physicians appear more likely to assign a diagnosis of BPH than prostatitis for older men than for younger men who present with similar symptoms (McNaughton Collins, 1998a). Very little is known about variation in chronic prostatitis by race or ethnicity. It was recently found that blacks were

more likely to visit a physician for prostatitis than whites, but the difference was not statistically significant (McNaughton Collins, 1998b).

Major gaps in the current knowledge of the epidemiology of chronic prostatitis are due mostly to the fact that diagnosis is based on clinical symptoms rather than standard diagnostic tests, resulting in a lack of standard operational definition usable for research purposes (McNaugton Collins, 1998a). Confusion also stems from the traditional application of the nonspecific term 'prostatitis' to describe all types of the condition. To address this deficiency, the following classification scheme was recently devised at an NIH/NIDDK sponsored conference: (1) acute bacterial prostatitis, (2) chronic bacterial prostatitis, (3) chronic nonbacterial prostatitis/chronic pelvic pain syndrome, and (4) asymptomatic inflammatory prostatitis (NIH-NIDDK, 1995). This same workshop strongly recommended that a population-based symptom index be developed and that survey research be initiated to further define the epidemiology of chronic prostatitis, especially the distribution of the disease in minority populations (NIH-NIDDK, 1995).

The Chronic Prostatitis Collaborative Research Network (NIH/NIDDK DK-97-008), a multi-center 5-year study, was initiated in 1997 to examine the natural history, epidemiology, etiology, diagnosis and treatment of chronic prostatitis in clinic populations. A major part of this study was to develop and validate a chronic prostatitis symptom score and a prostatitis-specific health-related quality-of-life scale for use in clinic populations. This instrument is known as The National Institutes of Health Chronic Prostatitis Symptom Index (Litwin, 1999).

2.2.3 Hypogonadism

Male hypogonadism, a deficiency in testosterone secretion by the testes, may be caused by: (1) insufficient gonadotropin secretion by the pituitary (hypogonadotropic); or (2) pathology in the testes (hypergonadotropic) (McTierney, 1995). Hypogonadism may be congenital or acquired. Acquired hypergonadotropic hypogonadism is most often seen in elderly men and is the syndrome of interest in the proposed study. The defining features of hypogonadism are reduced serum testosterone levels, with associated symptoms such as decreased libido and erectile function and maintenance of secondary sexual characteristics (Plymate, 1994). The unresolved questions are: (1) whether a hypogonadal syndrome exists in aging men with declining testosterone levels (Tenover 1994); (2) whether a symptom complex related to low testosterone levels can be defined; (3) whether there is a threshold level of testosterone below which symptoms become clinically apparent; and (4) what the prevalence of this condition is in aging men.

2.2.4 Erectile Dysfunction/Sexual Dysfunction

Erectile dysfunction (ED), defined as the consistent inability to sustain an erection sufficient for sexual performance (NIH, 1993), is estimated to affect millions of American men (Feldman, 1994a) and to be increasing rapidly worldwide (Aytaç, 1999). Although not a life-threatening condition, ED has a profound effect on the well-being of aging men (Krane, 1989). The National Ambulatory Medical Care Survey reported 1.3 million office visits for treatment of ED in the U.S. in 1996, more than twice the rate in 1985 (CDC, 1998; NIDDK, 1995). Despite the estimated magnitude of this problem, little is known regarding the basic epidemiology of this

disorder in minority populations, and epidemiologic studies of this highly prevalent condition have been identified as an urgent priority (NIH, 1993). Reliable measures of the prevalence of ED in the U.S. are lacking, and estimates vary widely with the definitions used. Most prior research has been based upon clinic samples of men referred for treatment and/or has focused on Caucasian men. These men represent only a fraction (probably less than 10 percent) of all that are affected. Thus, the generalizability of prior studies is quite limited, and very little is known about racial/ethnic differences (Shabsigh, 1996; Slag, 1983; Perez, 1993).

In the fifty years since the Kinsey survey (1948), understanding of the mechanisms of ED and treatment strategies have changed dramatically, leading to increased interest and awareness in both the scientific community and the general population (Krane, 1989; Shabsigh, 1996; NIH, 1993). The most recent estimates from a large population-based study are from the National Health and Social Life Survey (a U.S. probability sample) (Laumann, 1999) and from the Massachusetts Male Aging Study (MMAS) (McKinlay, 1998). These data suggest that 10-20 million men in the U.S. may be affected, with up to 30 million affected if men with partial ED are included (Feldman, 1994a; NIH, 1993). Both studies document a strong correlation between ED and increasing age. Because these estimates are based on predominantly white populations, virtually no data exist regarding the variability of age-specific ED prevalence across racial/ethnic groups.

Racial/ethnic variations in the perceptions and expectations for normal sexual functioning may affect prevalence estimates, through cultural variation in symptom reporting, perceived impact on quality of life, and likelihood of seeking medical care. Although in the past ED was often accepted as an inevitable consequence of aging, men increasingly seek care for ED expecting to regain function (Jonler, 1995; NIH, 1993; Perez, 1993; Shabsigh, 1996), particularly since the introduction of oral sildenafil (Goldstein, 1998). Slag (1983) reported that among men in a medical clinic, those who chose further evaluation for ED were older and using more medications. In another clinic-based study, Perez (1993) reported that age and non-white racial status were inversely associated with interest in evaluation for ED. Despite this trend, few data exist regarding knowledge and perceptions of ED and health care utilization for ED in the general population, particularly with respect to racial/ethnic variability. The few studies available are based on small samples or were not designed to address ED specifically (Perez, 1993; Jonler, 1995; Keil, 1992).

As recently as 20 years ago, it was commonly thought that most cases of ED ("90%") were psychogenic (Spark, 1980). In current practice it is accepted that ED is often attributable to organic causes (Plaud, 1996; Rosen, 1995). Damage to arteries, smooth muscle, and fibrous tissue resulting in altered blood flow to and from the penis are the most common causes of ED (Krane, 1989; NIDDK, 1995). This is often the result of chronic disease, such as diabetes, kidney disease, atherosclerosis, and vascular disease (NIDDK, 1995). ED is common among diabetic men, with up to 50 percent of diabetic men affected (Benet, 1995). The MMAS reported an association between heart disease and ED, with complete ED present in 39% of men treated for heart disease compared with 9.6% of all other men sampled (Feldman, 1994a). In the follow-up phase of MMAS, incident ED was predicted by baseline coronary risk factors including overweight and dietary fat (Feldman, 2000). Michal (1982) documented an association between ED and peripheral vascular disease symptoms. ED has also been associated with

history of myocardial infarction (Diokno, 1990; Wabrek, 1980), coronary artery bypass surgery (Gundle, 1980), and stroke (Agarwal, 1989). Several commonly prescribed medications have been associated with increased rates of ED, including antihistamines, antihypertensive agents, antidepressants, tranquilizers, appetite suppressants, and cimetidine (Goldstein, 1983; Krane, 1989; Wein, 1988).

Endocrine disorders that are often associated with ED are hypogonadism and hyperprolactinemia (Krane, 1989). Nevertheless, the effect of androgens on ED remains unclear (Maatman, 1986; Bancroft, 1983; Korenman, 1990). In clinic-based studies, the relationship of endocrine levels to ED may be confounded by referral biases in the study population (Kaiser, 1988). Lifestyle factors have also been associated with ED. In the follow-up phase of MMAS, incident ED was associated with dietary intake (Feldman, 2000). Chronic alcoholism has been associated with ED in some studies, but not consistently (Diokno, 1990; Feldman, 1994a; Kosch, 1988; Morley, 1986; Slag, 1983). Obesity and sedentary behavior may be related to ED via effects on hormone concentration and metabolism, although few studies have addressed this issue, and the relationship remains unclear (Kosch, 1988). The relation of cigarette smoking to ED has particularly profound implications for public health, as the prospect of ED might be considered a strong deterrent to initiation of smoking in young men as well as a compelling reason for smoking cessation (Katscher, 1994). In the baseline MMAS study, cigarette smoking exacerbated the association between heart disease and ED (Feldman, 1994a). In the follow-up phase of MMAS, incident ED was associated with both active and passive cigarette smoking (Feldman, 2000). Cigarette smoking has been linked to atherosclerosis in the hypogastric-cavernous arterial bed (Rosen, 1991).

Racial differences in prevalence of the chronic conditions, pharmacological therapies, and health behavior suspected to be associated with ED have been documented. Whether these variations explain racial/ethnic variation in ED prevalence is not clear. In addition, the impact of these differences on the relative influence of these risk factors on ED among minority groups has not been studied.

Epidemiologic studies of ED have also been limited by inconsistencies in assessment tools and definitions used to identify ED. While there is a consensus that a subjective report of ED is preferable to "objective" clinical measures of ED (NIH 1993), there is no single, generally accepted subjective measure. The available questionnaires, now widely used, were developed in clinical settings for self-selected populations of men seeking treatment and have not been standardized in large population-based samples (Rosen, 1997; O'Leary, 1995).

Our prior work in the MMAS has indicated that these clinical assessment tools are not applicable to general population samples. The proportion of men who leave items unanswered, or for whom questions are not applicable, is quite high when these methods are applied in a population-based sample of older men (Derby, 2000). For this reason, the MMAS has developed and validated two related methods for assessing ED in population based samples. These are based on a definition of ED that is consistent with that recommended by the NIH consensus conference (1993). The first measure uses a single question self-rating of ED status (Derby, 2000), and the second uses a group-weighted approach to create a summary classification based on the

responses to 9 specific questions related to aspects of erectile function (Feldman 1994b; Kleinman, 2000).

2.2.5 Interstitial Cystitis

Interstitial cystitis is a severe and debilitating chronic pain syndrome of unknown etiology that is characterized by recurring discomfort, pressure, or pain of suprapubic or perineal origin and with no evidence of overt infection (Messing, 1992; Propert, 2000; Parsons, 2000). The symptoms of IC vary from mild to intense and include urinary urgency and frequency as well as pain. Little is known about its epidemiology, although it is estimated to affect more than 700,000 Americans (IC Association, 2001) with a major impact on quality of life (Michael, 2000). Particularly lacking are population-based data on prevalence, incidence, and risk factors. Prevalence estimates have varied widely, ranging from 8 to 870 per 100,000 population (Bade, 1995; Jones, 1997). IC appears to affect primarily women, with a female to male ratio of 10:1 (Parsons, 2000). The mean age of onset is 42-53 years, with an average duration of symptoms of 3-5 years between onset and diagnosis (Parsons, 2000). Prior studies have suggested a positive association with allergic or autoimmune conditions and hysterectomy, and an inverse association with diabetes (Koziol, 1994). The prevalence and natural history of IC in minorities is virtually unknown. Although reports have suggested that the prevalence among African-Americans is lower than that in Caucasians, this difference is likely to be due to factors related to referral patterns, care seeking behaviors, and access to health care (Sant, 1993; Parsons, 2000).

A major reason for the lack of consistent prevalence estimates is that most studies have not been population-based (Held, 1990; Bade, 1995; Oravisto, 1975). Furthermore, case-ascertainment instruments suitable for use in epidemiologic studies do not exist. Although the NIH has established strict criteria for defining IC (Gillenwater, 1988), these are not readily applied to population-based studies, and it has been suggested that they exclude large numbers of patients with mild to moderate symptoms (Parsons, 2000). The existing instruments have been designed primarily for use in clinical settings to monitor response to treatment rather than for the purpose of case-ascertainment (e.g. the O'Leary-Sant IC Symptom Index) (Lubeck, 2001; Goin, 1998; O'Leary, 1997; Koziol, 1993, Keller, 1994). Thus, in order to advance knowledge of the epidemiology of IC, there is a need to develop and validate a standardized instrument for use in population-based epidemiologic studies and for the application of this instrument in a large, multi-ethnic population.

2.2.6 Chronic Pelvic Pain of Bladder Origin

Chronic pelvic pain (CPP) is a common and debilitating disorder with significant negative impact on the lives of women and men. Study of CPP is complicated by the involvement of multiple organ systems that make diagnosis and estimation of prevalence difficult. CPP is usually defined as pain in the pelvic area severe enough to cause functional disability of at least 3 months duration (Reiter 1998; Scialli 1999). One survey of U.S. women estimated the prevalence of CPP to be about 15% of women aged 18 to 50 years (Mathias, 1996). While endometriosis is the most common cause of CPP in women, gastrointestinal, urologic, musculoskeletal, and

psychological factors also can play a role (Scialli, 1999). Less information is available for CPP in men, and there are no reliable published prevalence estimates for male CPP.

One under-researched source of CPP is chronic pelvic pain of bladder origin (CPPB). This is a symptom complex that, while not gender- or age-specific, is poorly defined and may be diagnosed as interstitial cystitis in women and chronic abacterial prostatitis or prostatodynia in men. Indeed, pain symptoms have been identified as the most prominent manifestation of chronic prostatitis, with pain in the suprapubic area that could represent CPPB reported to occur in 6% to 60% of men with chronic prostatitis (Krieger, 1996; Berghuis, 1996). Wenninger (1996) found that chronic prostatitis patients exhibited a mean sickness impact profile similar to that reported for myocardial infarction, angina or Crohn's disease, with pain being the significant contributing factor. It has been suggested that chronic abacterial prostatitis be considered a urologic chronic pain syndrome (Egan, 1997).

Epidemiologic data on CPPB are sparse due to the lack of a standardized definition and the lack of reliable and valid instruments to identify the syndrome in population samples. Risk factors for CPPB are unknown and may be difficult to identify without longitudinal data because the time from symptom appearance to clinical diagnosis may be long. The identification of symptoms of CPPB in population-based samples would contribute greatly since prior research has concentrated mostly on individuals affected with IC. The prevalence and burden of CPPB may be underestimated because IC is only one form of CPPB.

2.2.7 Urinary Incontinence

Urinary incontinence is a highly prevalent and costly health problem. A 1994 estimate of the direct costs of care for UI was $11.2 billion annually in the community and $5.2 billion in nursing homes (Hu, 1994). This cost estimate was 60% higher than one just four years earlier

Table 1. Estimated prevalence of CPPB, IC, and UI in U.S. men and women (All ages/adults).

	UI	IC	CPPB
Females	10-40/100 [1]	865/100,000 [3]	------ [5]
Males	19/100 [2]	96/100,000 [4]	------ [5]

Sources :
[1] Bump and Norton, 1998; Herzog, et al., 1990
[2] Herzog, et al., 1990b
[3] Jones and Nyberg, 1997
[4] Jones and Nyberg, 1997, based on 501 cases/100,000 US men and women.
[5] Reliable population estimates are unavailable.

(Hu, 1990). UI is estimated to affect 30%-40% of older American women (Bump, 1998; Herzog, 1990a) and almost 20% of men (Herzog, 1990b). The prevalence of UI increases with age in both genders (Thom, 1998; Temml, 2000). While duration and frequency of UI were comparable in women and men, gender differences were reported in type of UI in a European study (Temml, 2000). Stress urinary incontinence was significantly more prevalent in women (92% of incontinent individuals) than in men (29.5%), while the prevalence of urge incontinence was similar in both genders.

The vast majority of data on UI come from studies of Caucasians. This may be due to sample and design limitations or to an underreporting of UI by African-American women and other ethnic groups because acceptance of UI as a normal consequence of aging deters minority women from seeking diagnosis and treatment (Fultz, 1999; Brown, 1999; Thom, 1997; Burgio, 1996).

UI has significant social, psychological, physical, and emotional consequences for individuals (Grimby, 1993; Ashworth, 1993; Wyman, 1987; Ory, 1986). Gender differences in the impact of UI on quality of life have been reported, with stress UI being more bothersome for women than men (Temml, 2000). However, as with prevalence data, information concerning racial/ethnic differences in the impact of UI on quality of life is not available.

Gender-specific risk factors for UI have been identified, but once again in primarily Caucasian samples. In addition to age, in women, reproductive risk factors such as parity and hysterectomy have been associated with UI (Thomas, 1980; Jolleys, 1988; Sommer, 1990; Burgio, 1996; Yarnell, 1982; Foldspang, 1992). Other potential risk factors include menopausal and estrogen status (Burgio, 1991; Rekers, 1992; Jolleys, 1988), obesity and higher BMI (Brown, 1999; Mommsen, 1994; Burgio 1991; Yarnell 1982), current medications (Montella, 1996), smoking, collagen defects, chronic respiratory disease, and occupation-related strain on the pelvic floor. UI in men has been correlated with a history and symptoms of cardiovascular disease and vision problems (Diokno, 1990). Whether these risk factors are the same or different for other racial/ethnic groups has yet to be determined.

2.3 Specific Aims

Despite the fact that minority individuals are thought to be at elevated risk for several urologic disorders, white populations have been the focus of most research to date, including our own Massachusetts Male Aging Study (MMAS, AG-04673, DK-44995, DK-51345). Although not life-threatening, these conditions have a profound effect on quality of life and are estimated to affect many millions of people.

Three independent variables will be investigated: age, sex, and race/ethnicity. The dependent variables are BPH, prostatitis, hypogonadism, ED/sexual dysfunction, IC, CPPB symptom complexes, and UI. Intervening variables to be measured include health status (e.g., co-morbid medical conditions, medication use, reproductive history) and health care utilization, lifestyle (e.g., smoking, alcohol consumption), sociodemographics (e.g., occupation, marital status), and body composition (e.g., body mass index). The relationships between the independent and dependent variables will be explored to ascertain the presence of independent effects, effect modification, and/or confounded effects attributable in some part to the intervening variables.

The study will have two parts: 1) a cross-sectional or baseline component and 2) a longitudinal component (provided funding is obtained). The BACH Survey is designed to stand alone as a cross-sectional survey and will provide valuable descriptive information, currently lacking, regarding the epidemiology of urologic conditions in different racial/ethnic groups. An

additional benefit of the study is that it has the unique potential to serve as a foundation for the future collection of prospective data regarding the natural history of urologic disorders in minority populations. Population-based longitudinal data are currently not available for the variety of conditions assessed in the BACH Survey.

2.3.1 Cross-Sectional Aims

1. To estimate and compare the age-specific prevalence of common urologic disorders, namely benign prostatic hyperplasia, erectile dysfunction, chronic prostatitis and hypogonadism in a population-based sample of Hispanic, Black (non-Hispanic), and white (non-Hispanic) men 30 to 79 years of age.

2. To estimate the sex-, age-, and race/ethnicity-specific prevalence of interstitial cystitis, chronic pain of pelvic origin and urinary incontinence in a population-based sample of Hispanic, Black (non-Hispanic), and white (non-Hispanic) men and women 30 to 79 years of age.

3. To measure the relative contribution of factors suspected and known to be associated with these urologic disorders ("risk factors for prevalence") within each minority sample, including physiological factors (e.g., hormone levels, anthropometrics, underlying chronic diseases, and medications), and lifestyle factors (e.g., smoking, alcohol consumption, sexual behavior, and physical activity).

4. To determine whether variation in associated physiological, lifestyle, socioeconomic and behavioral factors can account for any racial/ethnic variation in the prevalence of urologic disorders.

5. To examine access, help-seeking and utilization behavior specific to the urologic disorders of interest. Knowledge levels, perceptions, barriers, triggers, patient trust specific to urologic conditions and their variability by sex, age and race/ethnicity will be examined.

2.3.2 Longitudinal Aims

1. Estimate the sex-, age-, and race/ethnicity-specific incidence of the same urological disorders in members of the population-based sample not identified as symptomatic during the prevalence survey.

2. Identify risk factors (including age, reproductive history, co-morbid medical conditions, body mass, alcohol consumption, nutrition, medication use, smoking) for urological disorders and determine whether risk factors vary with sex, and/or race/ethnicity (effect modification).

3. Assess health resource utilization of women and men with urological disorders compared to members of the cohort who are unaffected.

4. Assess quality of life and functional status, including role of co-morbid medical conditions, for women and men with urological disorders.

2.4 Methods

2.4.1 Study Design and Sampling

Overall Approach

BACH is a population-based, random-sample survey designed to provide normative data on prevalent urologic conditions in men and women of diverse race/ethnicity. The study involves an in-home baseline assessment of 6,000 randomly sampled Boston-area Hispanic, Black (non-Hispanic), and white (non-Hispanic) women and men. Given our objectives, the sample had to be of sufficient size and diversity to permit robust group estimates. Therefore, we are recruiting 6,000 Boston women and men. Approximately 2,000 will be Hispanic, 2,000 will be African American (non-Hispanic), and 2,000 will be Caucasian (non-Hispanic). As the prevalence of certain urological symptoms varies by age, with some tending to show up earlier in life and others later in life, we allocated our sample relatively uniformly over the age range of interest so that there are 250 subjects per gender/race cell for each age decade (30-39, 40-49, 50-59, 60-79). These are idealized cell-size targets. We are not quota sampling; we are using a sampling design that may mean that we recruit slightly more or slightly fewer people in certain groups.

Using 2000 Census data, the first part of our sampling design involved grouping the 16 major Boston neighborhoods into manageable, racially and ethnically homogeneous geographic sub-areas. Next, we classified each Census block within the 4 major sub-areas as low-density minority, high-density African American, or high-density Hispanic. This has allowed us to concentrate on geographic areas with the largest expected yield of the most difficult to reach persons. This classification scheme yielded 12 strata in which we are sampling 10% of the low-density blocks in all 4 geographic areas, 10% of the high-density African American blocks, and 70% of the high-density Hispanic blocks in all 4 geographic areas. These stratum sampling fractions were chosen because they allow the average design factor to be no more than 1.5 and the design factor within each stratum to be no more than 2, while also bringing us close to our target sample distribution. The overall design factor is estimated to be 1.27.

The final aspect of our sampling design is that we sub-sample households and individuals. For example, we are taking 20% of eligible and willing Caucasian persons residing in households where the oldest household member is between 30 and 39 years of age. Further, we are taking 100% of eligible and willing minority persons residing in households where the oldest household member is between 60 and 79 years of age.

We are implementing our sampling design in "batches". Batches are defined as successive random sub-samples of Census blocks across the 12 strata. We have 6 batches for this study, with approximately 1000 participants expected in each. Approximately $1/6^{th}$ of the total number of blocks sampled from each stratum will be included in each batch. So, if we expect to sample a

total of 1,788 blocks in Boston, then each batch will involve going to 132 blocks distributed among our 12 strata. Other large-scale epidemiologic studies have used this approach with success, such as the Pawtucket Heart Health Program (Feldman, 1996). An advantage to this batch approach is the ability to iteratively alter proportions to ensure adequate numbers and accommodate NIDDK research priorities.

The longitudinal study component would include follow-up measurements at intervals to be decided. This component could coincide with the baseline data collection because of the batch approach we are using.

Baseline Interview

After screening and enlisting eligible and willing Respondents (including people in the enumeration sub-study), the BACH Survey sends a Food Frequency Questionnaire to each Respondent, to be completed prior to the interview. The interview then takes place in the home or at another location (such as NERI) and includes obtaining informed consent, the taking of physiologic measures, venipuncture, administration of the Interviewer-Administered Questionnaire, and administration or collection of the Self-Administered Questionnaire.

2.4.2 Measurements

Race/Ethnicity

Race/ethnicity will be determined according to modifications to the federal standard recently instituted by the U.S. Office of Management and Budget (Wallman, 1998) involving a two-step self-identification process. As part of the initial screening, conducted either in-person or by a telephone interview, subjects will be asked first if they consider themselves at least partly Hispanic; then if they consider themselves at least partly Black or African-American (non-Hispanic black); then if they consider themselves at least partly White or Caucasian (non-Hispanic white). A more detailed question will determine primary self-identification with an ethnic/racial group follows. This multi-step procedure is least threatening during initial screening, has the least adverse effect on response rates, and provides reliable self-identification of racial/ethnic grouping. It has been implemented successfully on other multi-ethnic studies at NERI and elsewhere. For this study, the major aim of which is to examine racial/ethnic differences in urologic disorders, we will only recruit men who self-identify primarily with a single ethnic/racial group (Hispanic, non-Hispanic black, or non-Hispanic white). Inclusion of men identifying with more than one category would result in racial/ethnic subgroups that could not be combined in a straightforward way and would be too small for separate analysis.

Urological Symptoms

As the survey instrument developed, the BACH Survey team repeatedly discussed options for improving the assessment of the urological symptoms that we are studying. One option

considered was to use pre-existing, validated symptom inventories designed, in many cases, for use in clinical settings. Many of these inventories were recommended by the BACH Survey's Scientific Advisory Committee (SAC) during our first meeting in September 2002. Initially, we included the pre-existing symptom inventories in the instrument as systematically as possible. That is, we kept all items in an inventory together (e.g., items from the American Urological Association on BPH were grouped in sequence). We also grouped together all symptom inventories referring to similar time frames to minimize confusion during administration. As the instrument evolved, however, we encountered several problems with this option. These problems included:

1. Redundancy across symptom inventories (as noted by the SAC and pilot team)
2. Complex skip patterns that made the instrument difficult and awkward to administer, despite the use of transitions
3. Length of the instrument
4. Some questions were 'off the mark'
5. Some instruments may be appropriate in clinical settings, where diagnosis is possible, but less appropriate in epidemiological research
6. The variation in time frame (e.g., from one month to one week) and response categories among inventories was frustrating and somewhat confusing for respondents (as noted by the pilot team)

In addition, we were concerned that reliance on the clinical instruments might limit our ability to break new ground on the epidemiology of particular symptom profiles and illness definitions. Therefore, we adopted an alternative that involved using questions from symptom inventories that were recommended by the SAC and using them in a way that avoids the problems detailed above. Specifically, we did the following:

1. <u>Included one question per symptom</u>
   Given the substantial overlap across symptoms inventories (especially those for IC, BPH, and prostatitis), we did not include all questions from all symptom inventories *as they were published;* however, we will still have assessment of *all* relevant symptoms.

2. <u>Used the same time frame throughout</u>
   With the exception of the UI questions, which ask about the last 12 months and then the last 7 days, the majority of questions in the instrument now ask about the *last month*.

3. <u>Included a question about chronicity for each symptom or category of symptoms</u>
   For each IC, BPH, and prostatitis question, we included a follow-up question about the *duration of each symptom*, to address chronicity. We included only one question about chronicity for UI.

4. <u>Used the same response categories for all of the questions on IC, prostatitis, BPH, and CPPB</u>

These questions now ask the respondents to respond that (a) they do not have the symptom or that they have it (b) rarely, (c) a few times, (d) fairly often, (e) usually, or (f) almost always have the symptom.

There are multiple advantages to this approach. Specifically, the questionnaire is shorter, there are substantially fewer skip patterns, the time referent and response categories for many of the symptoms are consistent and will facilitate the construction of scales, and the elimination of redundant questions meant we could add questions from scales that were previously omitted

The following sections describe the measurement of specific conditions and the pre-existing scales that pertain to them (if any).

Benign Prostatic Hyperplasia

Questions were taken from the American Urological Association's (AUA) Symptom Index for BPH, a 7-item self-administered questionnaire that rates BPH symptoms quantitatively as mild (0-7), moderate (8-19), or severe (20-35) (Barry, 1992). The AUA index is recommended by the Agency for Health Care and Policy Research of the U.S. Department of Health and Human Services as the preferred instrument for BPH symptom assessment (McConnell, 1994) and is reliable, valid, and practical for use both in clinical practice and in population-based epidemiological research (Barry, 1992a,b). We added questions from Epstein et al.'s (1992) Quality of Life Questionnaire for BPH, called the BPH-QOL, to assess how BPH might impact Respondents' activities and feelings of well-being.

Chronic Prostatitis

Currently there is no standard instrument for assessment of chronic prostatitis, so we used questions from an instrument developed as part of the Chronic Prostatitis Collaborative Research Network (NIH/NIDDK DK-97-008) (called the NIH's Chronic Prostatitis Symptom Index). Our Scientific Advisory Committee recommended this instrument.

Hypogonadism

Serum level of testosterone (T) below 250 ng/dl is used to define hypogonadism. We also measure free and bound fractions of serum T. Because the syndrome by clinical consensus involves symptoms accompanying low T, we also collect information on fracture history, muscle strength, shaving frequency, and libido. We also measure serum luteinizing hormone (LH) to discriminate between primary (hyperpituitary) and secondary (hypopituitary) hypogonadism. Additionally, we include questions from the questionnaire for Androgen Deficiency in Aging Males ADAM (Morley et al., 2000), which ask Respondents to report on symptoms characterizing hypogonadism (e.g., fatigue, loss of height over time, etc.).

Erectile Dysfunction/Sexual Dysfunction

Building on our earlier work in MMAS (Feldman, 1994b), we have developed a multi-item scale for assessing ED based on responses to the MMAS sexual activity questionnaire (Kleinman, 2000). This scale correlates well with a single-question self-assessment of ED and with published clinical assessments (Rosen, 1997; O'Leary, 1995). We have included a single direct question asking the subject to describe his erectile function status, which our prior work suggests may be practical for assessing ED in a population sample, in the self-administered medical questionnaire (Derby, 2000). The single question is consistent with the NIH consensus conference definition of ED (NIH, 1993) and correlates well ($r>0.70$) with two published measures developed for clinical settings (Rosen, 1997; O'Leary, 1995). Data from the follow-up phase of MMAS showed that on the sensitive topic of ED, a single question had the advantage of considerably reducing the rate of missing data: only 9% were not classified because of missing response to the single question, as compared to 18% with the 6-item Rosen scale and 11% on the multi-item MMAS scale.

Inclusion of both the single question and the multi-item scale will allow for internal comparisons and further refinement of the measures. Although these assessments have been developed and validated in the population-based MMAS sample, they have not been applied to an ethnically diverse population. Should one method prove to be culturally unacceptable, or to suffer from differences in interpretation, the inclusion of a second assessment will maximize the proportion of men classified.

Chronic Pelvic Pain of Bladder Origin and Interstitial Cystitis

For the measurement of chronic pelvic pain of bladder origin and interstitial cystitis, we include questions from symptom inventories designed specifically for these conditions as well as questions from symptom inventories designed for other urological conditions, but applicable to IC and chronic pelvic pain nonetheless. For example, some questions are from the NIH's Chronic Prostatitis Symptom Index (CPSI), Sandvik et al.'s severity index for epidemiological surveys for urinary incontinence (Sandvik 2000), and/or the American Urological Association's Symptom Index for BPH (AUA). The symptom inventories specific to interstitial cystitis include the Interstitial Cystitis Problem Index (ICPI) and the Interstitial Cystitis Data Base. Many of these questions focus on whether Respondents have experienced certain types of pain (e.g., pain in the urethra, pain upon filling of the urinary bladder, etc.), urinary frequency, and urgency, among other things.

Urinary Incontinence

The measures of incontinence status, severity of UI, and type of UI are those recommended by Dr. Jeanette Brown, who is a member of the BACH Survey SAC. According to Dr. Brown (personal correspondences, 2001 and 2002), these questions are based on previously validated questions for the diagnosis of incontinence by type (Hannestad 2000; Sandvik 1995; Lagro-Janssen 1991). Similar questions were tested for reproducibility in 450 women participating in a trial for the Heart and Estrogen/Progestin Replacement Study (HERS) (Grady 2002; Brown 1999).

Dr. Brown has used these urinary incontinence self-report questions in the Study of Osteoporotic Fractures (Brown 1996; Brown 2000), Healthy ABC, Heart and Estrogen/Progestin Replacement Study (HERS) (Grady 2002; Brown 1999), Diabetes prevention program, Action for Health in Diabetes (Look AHEAD), Epidemiology of Diabetes Interventions and Complications (EDIC) Study, and the NHANES 2001-2003. These questions have been pre-tested for comprehension and consistency in a wide variety of study participants. Similar questions have been used in the Epidemiology of Incontinence in County of Nord-Trondelag (EPINCONT) (Hannestad 2000) studies. The data from the BACH Survey will be comparable with these studies.

To assess severity of UI, we are using the Sandvik severity index (Sandvik 2000). Quality of life of persons with UI is being measured with the Incontinence Impact Questionnaire (IIQ). The IIQ assesses the impact of UI on various activities, roles and emotional states. Validity and reliability of the instruments are strong and have been reported in women (Shumaker, 1994) and men (Dugan, 1998). The specific measures, therefore, include the following: whether respondents leak urine and if so, how often, how much, and for how long it has been occurring (e.g., less than 3 months, 3 to less than 6 months, etc.). For respondents who leak urine, the measures also address whether leakage occurred during the performance of certain activities, type of protection used (if any) and the number of pads used in a 24-hour period if the respondent uses pads for protection. The measures also assess whether respondents who leak urine have sought health care treatment and the type of actions they are currently taking for their leakage (e.g., exercises, medication, etc.).

Due to the breadth and depth of symptoms included in these inventories and subsequently in the BACH Survey, BACH data will allow us to break new ground on the epidemiology of particular symptom profiles and of illness definitions.

Physical Measurements

Height is measured with a carpenter's rule, weight with a portable battery-operated scale, and blood pressure with a standard sphygmomanometer according to protocols developed for large-scale epidemiologic field work (McKinlay, 1984). Pulse rate, hip circumference, and waist circumference are also measured.

Blood Measurements

Blood samples are obtained within two hours of awakening to obtain basal levels and control for diurnal variability (Bremner, 1983). Two samples are drawn from the antecubital space 25 minutes apart and pooled at the time of assay to smooth out episodic secretions (Brambilla, 1996). Medication usage is noted. Samples are transported from the interview site (home, office, etc.) to NERI in portable coolers and stored in freezers until transport to the laboratory. Serum will be stored at NERI in 5-ml scintillation vials at −20°C, shipped to the laboratory on dry ice, and stored at −70°C until the time of assay.

All laboratory work will performed by the CDC-certified Laboratory for Clinical Investigation, directed by Dr. Nader Rifai, located at Children's Hospital Medical Center, Boston, and affiliated with Harvard Medical School. The use of this single nearby facility for all assays will

facilitate prompt, efficient transfer of samples and information and regular monitoring by NERI staff for quality control. Assays to be performed include steroid hormones, LH, lipids, and apoproteins.

Health Status

Health status and history are determined by a general medical questionnaire. Medications are inventoried by the interviewer and later coded according to the American Hospital Formulary System.

Health Care Utilization and Quality of Life

BACH will provide information on knowledge of symptoms and risks, major triggers to health action, barriers (perceived and objective) to primary and urologic care, and psychosocial factors (e.g., stigma/embarrassment) concerning urological conditions. Questions concerning medical provider visits and insurance coverage were selected from the Medical Expenditure Panel Survey (Cohen, 1996, Lefkowitz, 1991, Monheit, 1997, Weinick, 1997, 1998a, 1998b) and adapted and field-tested so as to be appropriate and specific to the conditions of interest and to the specific health care options in Boston, MA (e.g. "free care" community health centers, etc.).

Sociodemographics and Lifestyle Variables

The in-home interview includes questions on age, employment, occupation, marital status, living arrangement, education, and income, mostly drawn from the instruments of Cornoni-Huntley (1983) and Ostfeld (1985). It also includes questions about active and passive smoking, alcohol consumption, physical activity, diet, and sexual activity (McKinlay, 1997).

Alcohol and Tobacco Use

Alcohol consumption over the previous 30 days is assessed in detail at the BACH interview. The frequency and quantity of consumption of beer, wine and hard liquor is recorded, allowing for quantification of ethanol consumption for each beverage type and overall. Additional questions address binge drinking. Consumption of the same beverage types over the previous year is assessed in the Block Food Frequency Questionnaire (Block, 1986).

Questions asked at the baseline interview will allow assessment of never/former/current cigarette and cigar smoking status, duration of smoking for former and current smokers, and number of cigarettes and cigars for current smokers. Other questions address exposure to passive smoking at home and outside the home. In addition, serum cotinine, although it has a relatively short half-life, is useful for detecting passive exposure to cigarette smoke as well as corroborating self-report of smoking. The CG/MS method to be used by Dr. Rifai is sound, simple, and inexpensive.

Physical Activity

Physical activity is assessed with the PASE (Physical Activity Scale for the Elderly), an instrument that was developed and validated by investigators at NERI (Washburn, 1993). It

includes questions about activities done during the previous week including walking; light, moderate and strenuous sports and recreational activities; household work; and job-related physical activities. The physical activity score that is calculated with this instrument has been shown to correlate with physiologic indicators of fitness including heart rate and measures of muscle strength (Washburn, 1993).

Dietary Assessment

Average dietary intakes over the previous year are assessed with the 1/2002 version of the modified Block Food Frequency Questionnaire (Block, 1986). This instrument, available in both English and Spanish, has been used extensively in epidemiologic studies and validated in a nationally representative sample (Subar, 2001). It assesses the frequency of consumption and serving size of over a hundred individual or grouped food and beverage items and also includes questions about the use of dietary supplements, fortified foods, and specific dietary fats. The questionnaire is designed to be self-administered. It is mailed to the participants' homes prior to their BACH baseline interview. Instructions are included in the mailing as well as a photograph that illustrates serving size choices. At the BACH interview, the data collector checks the questionnaire to make sure that it has been completely filled out and, if not, asks the participant to complete it at that time. If this is not possible, the participant is given a postage-paid envelope in which to return the completed questionnaire. The completed questionnaires are sent to Block Dietary Data Systems (Berkeley, CA) for processing. Food values (i.e. frequency consumed and serving size for each food item) as well as nutrient values (i.e. total consumption of each micro- and macronutrient) are provided electronically for addition to the NERI database. The inclusion of food values allows for the examination of dietary patterns as defined in many different ways.

Psychosocial Variables

Included as part of the in-home interview will be published scales measuring quality of life (QOL) and depressive symptoms, two related but distinct variables. QOL will be measured with the Medical Outcomes Study Short-Form 12 (SF-12) Item Health Survey (Ware, 1992). This instrument is probably the most widely used to assess QOL. It has demonstrated acceptable psychometric properties in all three proposed ethnic groups, including samples of African American patients (Johnson, 1995) and Hispanic men with BPH (Arocho, 1998a; Arocho, 1998b) and is valid and reliable in Spanish form (Ayuso-Mateos, 1999). Depressive symptoms, as measured by the Center for Epidemiological Studies-Depression (CES-D) scale, has figured prominently as a risk factor for ED in the MMAS. There is also literature to suggest that depressive symptoms are associated with the remaining urologic conditions. The CES-D has demonstrated good psychometrics as a screening tool for depressive symptoms in diverse racial/ethnic groups, including persons of white (Radloff, 1977), African American (Blazer, 1998; Roberts, 1998), and Hispanic (Falcon, 2000; Gonzalez, 1995; Mahard, 1988) race/ethnicity. Furthermore, the CES-D is both valid and reliable in Spanish speaking populations (Gonzalez, 1995).

2.5 Data Collection

Data collection for the BACH Survey consists of 2 major phases, screening and the baseline interview.

2.5.1 Eligibility Criteria

Men and women must meet the following criteria to participate in the Baseline Interview:

- Primary residence of the following communities within the city of Boston, Massachusetts:
  Allston, Back Bay, Beacon Hill, Brighton, Central Boston, Charlestown, Chinatown, Dorchester, Downtown, East Boston, Fenway/Kenmore, Hyde Park, Jamaica Plain, Mattapan, Mission Hill, North End, Roslindale, Roxbury, South Boston, South End, West Roxbury
- Able to speak and read English or Spanish
- Age 30-79 YEARS at time of first contact (not CAPS for years)
  - For preselected contact, first contact is the Household screener
  - For other household members, first contact is the Individual Screener
- Cognitively able to provide verbal consent
- Self-identified as Hispanic regardless of racial self identification
- Self-identified race in the following areas
  - Respondent considers him/herself exclusively African-American
  - Respodent considers him/herself African-American, multi-racial
  - Respondent considers him/herself exclusively White

2.5.2 Screening for Eligible Subjects

At the beginning of each batch, we used the Boston Resident List to prepare for screening. The state of MA requires that each city compile a listing of residents annually, and these lists have the added benefit of including some basic socio-demographic identifiers such as date of birth and the names of residents at each address. We used date of birth information (if recorded) to apply sampling fractions and the names on the list to address our introduction letters sent to each potential Respondents' household.

Currently we have four versions of the introduction letter: 1) no phone listed for household, English; 2) no phone listed for household, Spanish; 3) phone listed for household, English; 4) phone listed for household, Spanish. For those with unlisted phones, the letter asks the respondent to call NERI's toll-free number and to speak directly with project staff for screening. Households with listed numbers receive 1 introduction letter and households without listed phone numbers receive up to 3.

After sending the introduction letter, we attempt to call Respondents with a listed phone for a minimum of 10 attempts. If these attempts do not yield a contact, we then field trace these

households by knocking on their doors. Furthermore, we field trace ALL households that do not have telephone numbers listed. In this way, we expect better coverage than reliance on a single recruitment method (phone or field) would provide.

To maximize yield, field staff conduct these visits at different times of the day and on different days of the week including weekends. If no one answers the door, staff will leave project materials (introductory letters, project brochures) and attempt to gather the household enumeration information from neighbors. If the resident's name is listed on the mailbox, door, or apartment building, the complete name and address is recorded at the time of the visit. If household enumeration information cannot be obtained in the field, the project office staff will use NERI's in-house system for access to the most recent CD-ROM residential telephone list, cross-referenced by street address and by last name. Further searches will be conducted if necessary on Internet databases such as www.555-1212.com; www.databaseamerica.com; www.four11.com; www.infospace.com; or www.switchboard.com.

Telephone screening occurs primarily in the first 3 months of a given batch, and field screening occurs in the last 3 months (giving a 6 month batch "window"). The overlapping of batches reduces time in the field and minimizes staff burn out.

Enumeration Sub-study

Despite the advantages of using the Boston Residents List for participant recruitment, we conducted, as a precaution, a methodological sub-study comparing it to a small-scale enumeration. Specifically, we sampled ten blocks from the four major geographic areas in Boston, including two predominantly African American, seven predominantly Hispanic, and one predominantly Caucasian block. These blocks were selected randomly from the first Batch sub-sample. Each block was split in half, with one half randomly assigned to the enumeration approach and the other to the residents list method. The enumeration method involved sending a data collector to each household in the selected areas to conduct a full count of residents, similar to the census.

The objectives of the methodological sub-study were to: assess the level of agreement between the two identification and recruitment methods; and determine and compare the costs for identifying and making appointments for baseline interviews with eligible individuals using the enumeration compared to resident list method.

Overall, 445 distinct addresses were screened by the 2 methods on the 10 blocks of this sub-study.

2.5.3 Recruitment and Retention

Procedures to Enhance Participation

Included as standard protocol in all of NERI's large community research studies are a number of measures to enhance participation and minimize subject burden. These procedures have been customized as follows to increase participation and retention of research subjects in the proposed study.

All project materials will be available in English and Spanish. Participants will receive a $100 stipend, transportation as needed, and results of selected blood tests. To assure the community of the study's legitimacy, all interviewers wear official photo ID and provide toll-free telephone numbers for access to project staff and, independently, to the NERI Institutional Review Board for any inquiry about participants' rights. Every respondent executes and receives a copy of the appropriate informed consent, receiving help if necessary to understand it. We rigorously enforce confidentiality by using respondent ID numbers rather than names on all internal records.

In all project correspondence we make an effort to be personal rather than institutional, by having senior project staff hand-sign all letters; printing names and addresses directly on every envelope rather than on labels; using postage stamps rather than metering mail; and including the project name and logo. We schedule appointments through an efficient centralized computer system; verify and send advance postal reminders for all appointments; conduct interviews at the most comfortable or convenient locale, such as home, workplace, church, or health center; and reschedule cancelled interviews up to three times.

Community Outreach and Publicity

For successful recruitment of community-based samples, particularly of minority populations, intensive community publicity and outreach efforts prior to beginning data collection are essential (Demark-Wahnefried, 1995; Paskett, 1996). The goals of publicity are (1) to increase awareness of the importance of health issues facing aging men; (2) to reinforce the credibility of NERI as a research organization in the targeted communities; and (3) to increase participation. Publicity efforts will begin at the inception of the study. Recruitment phase activities are designed to increase participation. Outreach efforts for cohort retention, such as public service information and educational activities, will continue throughout the study to maintain contacts and provide services to the community. We will work with a well-known Boston-based image development and multi-media company whose staff have strong ties to community leaders in minority neighborhoods in the greater Boston area and extensive experience in public and media relations. Publicity and outreach activities will include obtaining support from community leaders, developing informational brochures, placing articles in local newspapers, broadcasting on radio and television, placing billboard and poster advertisements, holding press conferences, and establishing contact with local health centers and churches. We will form community advisory boards, made up of members of the target population, to advise on recruitment activities.

An extremely important strategy in increasing minority participation in studies is to give something back to the community (Paskett, 1996). This study provides participants the results of their blood pressure and serum lipid measurements, a cash incentive for participation, and transportation to the interview. In addition, we will offer ongoing educational information to the community.

Recontact

One year after the baseline interview, each participant will be asked to complete a short form confirming or updating contact information. The purpose of this recontact is to maintain close communication with the subjects to facilitate future follow-up in a potential longitudinal study.

Upon completion of the baseline visit, participants will be reminded about the follow-up to occur after one year and will be asked for the names, addresses and telephone numbers of two contacts who do not live in the participant's household. These contacts will be called in the event that the participant cannot be reached. Two weeks before the recontact date the participants will be called to remind them that they will be receiving a short form in the mail. The recontact materials will be mailed in a Federal Express package including an explanatory letter and a business reply envelope for returning the completed form. We will also include a small gift incentive in the package, such as a pre-paid telephone card activated upon receipt of the completed contact information card. NERI has successfully used Federal Express delivery as a cost-efficient and effective way to track participants in large surveys. Up to three packages will be mailed for those who do not respond to the initial mailing.

Beyond the one-year contact, additional activities will be directed at minimizing losses to follow-up, including (1) mailing postcards every six months for indicating change of address or telephone number; (2) establishing a birthday card list so that all subjects receive a card from the study on their birthday; (3) sending holiday cards; and (4) issuing an annual newsletter to report news about the study, provide health information, and remind participants of the importance of their contribution. In addition, we will work with New Image Associates to ensure that publicity and community service activities continue throughout the study. Such activities may include community events, radio and television ads, billboards in the local communities, development of a study web site on the Internet, and provision of educational programs at local health centers and/or churches.

2.5.4 Translation

NERI will assume responsibility for completing the translation of all project materials into "generic" U.S. Spanish; a back-translation into English; and a third-party reconciliation. The first two steps will be completed by an outside firm (contracted by NERI) that will employ two different individuals to perform these tasks. NERI will receive a form signed by the firm's principal to this effect. At that point, bilingual (Spanish-English) NERI staff members will review the translation and resolve any identified discrepancies. Final resolutions will be made by NERI staff (with input from the outside firm that conducted the original translation), under the direction of the Principal Investigator, Dr. McKinlay.

2.6 Data Management and Quality Control

Quality-control activities that are standard at NERI will be incorporated into the proposed project. The purpose of these activities is to ensure accuracy and completion of the data collected; to ensure standard implementation of data collection protocols; and to provide feedback to project staff to maintain high standards of data collection performance. Specific quality-control activities planned for this project include the following:

- Standard research protocols documented in a data collectors manual
- Training field technicians to conduct non-biased research interviews, and perform phlebotomy and other physical measurements according to standard research protocols
- A two-stage data editing procedure, technician observation, and tape recorded interviews
- Periodic observation of field work by Field Supervisor
- Respondent call-backs
- Measurement drift monitoring
- Daily field logs; and
- Regular field staff meetings and debriefings.

2.7 Statistical Considerations

2.7.1 Precision and Power

The following calculations of precision and power are based on the projected sample size of the parent study, 1,000 men and 1,000 women in each of 3 racial/ethnic groups. Because the targeted endpoints vary in prevalence from relatively rare (IC, CPPB) to relatively common (UI), we consider base rates between 0.01 to 0.25. The lower-prevalence calculations apply as well to the measurement of incidence, because (a) assessment of incidence is formally equivalent to assessment of prevalence in a cohort known to have been free of the condition at baseline, and (b) the at-risk cohort will be roughly the same size as the original cross-sectional sample (on the square-root-dependent scale of power calculations) because of likely prevalence of the conditions and short follow-up.

The precision with which we can estimate an underlying prevalence *P*, *a*s given by the standard error of estimate for a binomial proportion, is displayed in Table 3 (following page) for the full sample (3N) and for one racial/ethnic stratum (N). The higher prevalences can be estimated with 3-5% precision in the full sample and 5-10% in a single stratum. The lower prevalences can be estimated with 10-20% precision in the full sample and 15-30% precision in a single stratum.

For comparing two groups or subgroups, the detectable difference in prevalence, as given by the asymptotic formula of Fleiss (1981), is displayed in Table 3. For higher-prevalence conditions the detectable difference between strata is 9-15% of the base rate; for lower-prevalence conditions, the strata would have to differ by 20-50%. Subgroup comparisons within strata would require severe differences to be detectable.

For detecting the influence of continuous predictors on prevalence or incidence, we used the formula of Hsieh (1989), modified for two-tailed inference, to tabulate the least detectable increase in odds of a condition per standard deviation of predictor (Table 3) and the power to detect the effect of a 1-sd increase in predictor (Fig. 3). For higher-prevalence conditions, the detectable odds ratio (OR) in the full sample would be 1.2, depending on whether the predictor is evaluated alone or controlled for other, partially correlated predictors (e.g., potential confounders). Within one racial/ethnic stratum, the detectable OR would be 1.3-1.4. For lower-prevalence conditions, the detectable OR is 1.3-1.8 in the full sample and 1.5-2.7 in a single stratum.

2.7.2 Statistical Analyses

Cross-Sectional Aims

For validation of case-ascertainment instruments, we will use standard methods to characterize and optimize the instruments. These include Cronbach's alpha to measure internal consistency and factor-analytic procedures to determine dimensionality and inter-item relations. If a "gold-standard" clinical assessment of the condition is available, we will use it to establish criterion validity and estimate the conventional decision-analytic parameters including sensitivity, specificity, and positive predictive value. If no "gold standard" is available, then we will use logistic regression, canonical correlation, and ROC analysis to relate the instrument to a collection of consensus variables related to the condition and determine an optimal cutoff score for defining the condition (An example of this approach appears in Smith, 2000).

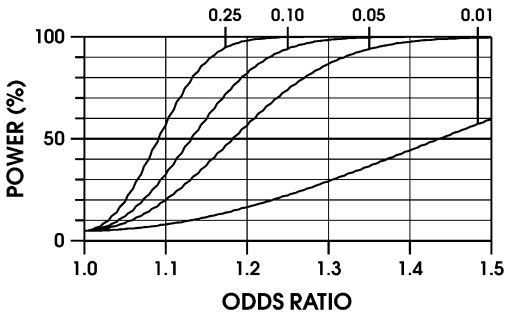

Fig. 2. Power to detect odds ratio attributable to 1-sd increase in predictor by simple logistic regression in combined sample (N=3000). Each curve represents one level of base prevalence.

Estimation of prevalence in strata of sex, age, and race/ethnicity, is straightforward. Aim 3 is to correlate each condition with demographic, physiological, and behavioral variables. This will be accomplished by logistic regression on single predictors, followed by multiple regression to identify patterns of confounding and interaction, particularly with race/ethnicity.

Longitudinal Aims

Longitudinal Aim 1 is to estimate incidence of the conditions over a 3-year period. Although we plan a fixed follow-up interval, the most precise estimate is obtained by counting events per person-year at risk. Aim 2 is to identify risk factors for incidence. Poisson regression will be employed to evaluate each predictor of incident events, controlling for length of follow-up interval and testing for confounding and interaction with other predictors, particularly race/ethnicity. Time-to-event ("survival") methods such as Cox regression will be used to assess the impact of censoring. Aims 3 and 4, concerning health resource utilization, quality of life, and functional status, are formally similar to Aim 2 and will be addressed with the same methods.

2.8 Human Subjects

2.8.1 Recruitment

Those subjects who are selected will be contacted, and participation will be strictly voluntary. Field instructions will clearly specify that no interview (by telephone or in person) is to be pursued if:

- The respondent is ill or just recovering from major surgery or other treatment;

- The respondent expresses reluctance because of a current family crisis, such as a close family member being terminally ill or having just died, or respondent being in the midst of divorce or separation proceedings;

- The respondent is unable to complete the questionnaire or interview because of disability, such as lack of hearing or sight, mental retardation, or major speech defect, or

- The subject is institutionalized in a nursing home, acute-care hospital, or comparable facility.

- In these circumstances, not only are responses likely to be distorted or atypical, but also the risk of psychological stress caused by the interview may be high. If the problem is temporary, an interview may be rescheduled at the discretion of the Field Supervisor in consultation with the P.I., provided the respondent consents verbally to a later recontact.

2.8.2 Informed Consent

The venipuncture procedure will be explained fully to the respondent by the Field Technician. The minimal risk of infection from this procedure will be noted, and any questions from the respondent will be fully answered. When the respondent is comfortable with the procedure, he will be asked to sign the consent form.

Only two attempts will be made by the Field Technician to insert the needle into a vein in the antecubital space. The first attempt will be made following written consent. The second attempt will be made only with further, verbal consent of the respondent. If both attempts are unsuccessful (veins difficult to locate, veins collapsing) and the respondent still wishes the blood sample to be drawn (anticipated in 3-5% of cases), the Field Supervisor or a Nurse Field Assistant will make a repeat visit (if necessary) to obtain the samples using other appropriate veins. An abbreviated interview will obtain current information on variables likely to affect hormone levels, e.g., medications or nutrition.

Experience of our Field Supervisors with venipuncture in the home has been very successful, with no untoward incident in thousands of cases. Appropriate procedures will be instituted for immediate reporting and follow-up of any field incidents. Clinic referrals will be coordinated by the senior medical staff at Boston Medical Center.

2.8.3 Protection of Confidentiality

Confidentiality among research staff will be maintained by using the following system.

Once the sample list has been constructed, it will be kept in a locked file for which only the Principal Investigator and Project Directors will have access.

All subsequent use of the list for mailings and identification of the respondents will be under the direct supervision of one of the aforementioned staff members.

For further protection of individual respondent histories, a master list containing the names and addresses of respondents and the identification numbers will be kept in the locked, limited-access file with no duplicates in the office. For safety, the Principal Investigator will arrange for one duplicate file to be secured elsewhere while remaining accessible for updating, e.g., in a safe-deposit box.

All questionnaires and interview schedules will contain only an identification number. Field logs will have names and addresses detached as soon as they are no longer required.

For full security, all completed interviews and questionnaires will be kept in a separate set of files also locked when not being used by project staff. No instruments will be allowed outside the office, except in carefully monitored batches for keypunching.

Similar security procedures will be used for computer data tapes. Sign-out procedures for all removals from the data files will be strictly enforced.

These security procedures have been used successfully on the MMAS and other projects for which the investigators have been responsible. All NERI employees are required to sign annually an Oath of Confidentiality.

2.8.4 Benefits and Risks

The immediate benefit to respondents will be the availability of a report summarizing their hormone and lipid profiles. This otherwise expensive set of laboratory tests will be made available to respondents free of charge as well as to their physicians, if requested. An indirect benefit will be the increased knowledge concerning erectile dysfunction and other common urologic disorders.

The only risk to respondents is the negligible one from blood drawing. No problem arose from the thousands of samples drawn in the two waves of MMAS. Safety will be maximized through

the use of a tightly controlled protocol, and any incident reports will be filed using a standard procedure.

2.9 Literature Cited

Agarwal A, Jain DC. Male sexual dysfunction after stroke. J Assoc Physicians India 1989; 37:505.

Arocho R, McMillan CA, Sutton-Wallace P. Construct validation of the USA-Spanish version of the SF-36 health survey in a Cuban-American population with benign prostatic hyperplasia. Qual Life Res 1998a;7:121–6.

Arocho R, McMillan CA. Discriminant and criterion validation of the US-Spanish version of the SF-36 Health Survey in a Cuban-American population with benign prostatic hyperplasia. Med Care 1998b;36:766–72.

Ascherio A, Stampfer MJ, Colditz GA, Willett WC, McKinlay JB. Nutrient intakes and blood pressure in normotensive men. Int J Epidemiol 1991; 20:886-91.

Ashworth PD, Hagan MT. The meaning of incontinence: a qualitative study of non-geriatric urinary incontinence sufferers. J Adv Nurs 1993;18:1415-23.

Aytaç IA, McKinlay JB, Krane RJ. The likely worldwide increase in erectile dysfunction between 1995 and 2025 and some possible policy consequences. Br J Urol Int 1999; 84:50-56.

Ayuso-Mateos JL, Lasa L, Vazquez-Barquero JL. Internal and external validity of the Spanish version of SF-36. Med Clin (Barc) 1999;113:37.

Bade JJ, Rijeken B, Mensink HJ. Interstitial cystitis in the Netherlands: Prevalence, diagnostic criteria, and therapeutic preferences. J Urol 1995;154:2035-2037.

Bancroft J, Wu FCW. Changes in erectile responsiveness during androgen replacement therapy. Arch Sex Beh 1983; 12:59.

Barry MJ, Fowler FJ, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, Cockett ATK, Measurement Committee of Am Urol Assoc. The American Urological Association Symptom Index for benign prostatic hyperplasia. J Urol 1992a; 148:1549-1557.

Barry MJ, Fowler FJ, O'Leary MP, Bruskewitz RC, Holtgrewe Hl, Mebust WK, Measurement Committee of Am Urol Assoc. Correlation of the American Urologic Association Symptom Index with self-administered versions of the Madsen-Iversen, Boyarsky, and the Maine Medical Assessment Program Symptom Indices. J Urol 1992b; 148:1558-1563.

Barry MJ, Mohr BA, Yurgalevitch SM, McKinlay JB. False positive rate of prostate-specific antigen (PSA) levels in a community based population: results from the Massachusetts Male Aging Study. Eur Urol 1998; 33(S1):41.

Benet A, Melman A. The epidemiology of erectile dysfunction. Urol Clin N Am 1995;22:699-709.

Berghuis JP, Heiman JR, Rothman I, Berger RE. Psychological and physical factors involved in chronic idiopathic prostates. Journal of Psychosomatic Research, 1996 41(4):313-25.

Berry SJ, Coffey DS, Walsh PC, Ewing LL. The development of human benign prostatic hyperplasia with age. J Urol 1984; 132:474.

Blazer DG, Landerman LR, Hays JC, Simonsick EM, Saunders WB. Symptoms of depression among community-dwelling elderly African-American and white older adults. Psychol Med 1998;28:1311–20.

Block G; Hartman AM; Dresser CM; Carroll MD; Gannon J; Gardner LA data-based approach to diet questionnaire design and testing. Am J Epidemiol 1986;124:453-69

Boyle P. Epidemiology of benign prostatic hyperplasia: risk factors and concomitance with hypertension. Br J Clin Prac 1994; Suppl 74:18-22.

Brambilla DJ, McKinlay SM, McKinlay JB, Weiss SR, Johannes CB, Crawford SL, Longcope C. Does collecting repeated blood samples from each subject improve the precision of estimated steroid hormone levels? J Clin Epidemiol 1996; 49:345-50.

Bremner WJ, Vitiello MV, Prinz RN. Loss of circadian rhythm in blood testosterone levels with aging in normal men. J Clin Endocrinol Metab 1983; 56:1278-1281.

Brown JS, Seeley DG, Fong J, Black DM, Ensrud KE, Grady D. Urinary incontinence in older women: who is at risk? Study of Osteoporotic Fractures Research Group. Obstet Gynecol. 1996 May;87(5 Pt 1):715-21.

Brown JS, Grady D, Ouslander JG, Herzog AR, Varner RE, Posner SF. Prevalence of urinary incontinence and associated risk factors in postmenopausal women. Heart & Estrogen/Progestin Replacement Study (HERS) Research Group. Obstet Gynecol 1999;94:66-70.

Brown JS, Vittinghoff E, Wyman JF, Stone KL, Nevitt MC, Ensrud KE, Grady D. Urinary incontinence: does it increase risk for falls and fractures? Study of Osteoporotic Fractures Research Group. J Am Geriatr Soc. 2000 Jul;48(7):721-5.

Bump RC, Norton PA. Epidemiology and natural history of pelvic floor dysfunction. Obstet Gynecol Clin North Am 1998;25:723-46.

Burgio KL, Ives DG, Locher JL, Arena VC, Kuller LH. Treatment seeking for urinary incontinence in older adults. J Am Geriatr Soc 1994;42:208-12.

Burgio KL, Locher JL, Zyczynski H, Hardin JM, Singh K. Urinary incontinence during pregnancy in a racially mixed sample: characteristics and predisposing factors. Int Urogynecol J Pelvic Floor Dysfunct 1996;7:69-73.

Burgio KL, Matthews KA, Engel BT. Prevalence, incidence and correlates of urinary incontinence in healthy, middle-aged women. J Urol 1991;146:1255-9.

Centers for Disease Control and Prevention. 1996 National Ambulatory Medical Care Survey. CD-ROM Series 13, No. 14, SETS Version 2.0 (Beta). Hyattsville, MD: U.S. Dept. Health and Human Services, National Center for Health Statistics, 1998.

Cohen JW, Monheit AC, Beauregard KM, Cohen SB, Lefkowitz DC, Potter DE, Sommers JP, Taylor AK, Arnett RH 3rd (1996). The Medical Expenditure Panel Survey: A National Health Information Resource Inquiry 1996/1997 Winter;33:373–389. AHCPR Pub. No. 97-R043.

Cornoni-Huntley J, Barbano HE, Brody JA, Cohen B, Feldman JJ, Kleinman JC, Madans J. National Health and Nutrition Examination I: epidemiologic followup survey. Public Health Rep 1983; 98:245-251.

Crawford SL, McGraw SA, Smith KW, McKinlay JB, Pierson JE. Do blacks and whites differ in their use of health care for symptoms of coronary heart disease? Am J Public Health 1994; 84:957-964.

Demark-Wahnefried W, Strigo T, Catoe K, Conaway M, Brunetti M, Rimer BK, Robertson CN. Knowledge, beliefs, and prior screening behavior among blacks and whites reporting for prostate cancer screening. Urology 1995; 46(3):346-51.

Derby CA, Araujo AB, Johannes CB, Feldman HA, McKinlay JB. Measurement of erectile dysfunction in population-based studies: the use of a single question self-assessment in the Massachusetts Male Aging Study. Int J Impot Res 2000;12(4):197-204.

Diokno AC, Brown MB, Herzog AR. Sexual function in the elderly. Arch Internal Med 1990; 150:197-200.

Diokno AC, Brock BM, Herzogar J. Medical Correlates of urinary incontinence in the elderly. Urol 1990; 36:129-138.

Dugan E, Cohen SJ, Rodinson D et al. The quality of life of older adults with urinary incontinence : Determining generic and condition-specific predictors, Quality Life Res 1998 ;7 :337-344.

Egan KJ, Krieger JL. Chronic abacterial prostatitis – a urological chronic pain syndrome? Pain 1997;69:213-218.

Falcon LM, Tucker KL. Prevalence and correlates of depressive symptoms among Hispanic elders in Massachusetts. J Gerontol B Psychol Sci Soc Sci 2000;55:S108–16.

Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol 1994a; 151:54-61.

Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Construction of a surrogate variable for impotence in Massachusetts Male Aging Study. J Clin Epidemiol 1994b; 47:457-467.

Feldman HA, Johannes CB, Derby CA, Kleinman KP, Mohr BA, Araujo AB, McKinlay JB. Erectile dysfunction and coronary risk factors: prospective results from the Massachusetts male aging study. Prev Med. 2000 Apr;30(4):328-38.

Feldman HA, McKinlay SM, Niknian M. Batch sampling to improve power in a community trial: experience from the Pawtucket Heart Health Program. Eval Rev 1996 Jun;20(3):244-74

Fleiss JL. Statistical Methods for Rates and Proportions, 2nd ed. New York: Wiley, 1981, pp. 39-45.

Foldspang A, Mommsen S, Lam GW, Elving L. Parity as a correlate of adult female urinary incontinence prevalence. J Epidemiol Community Health 1992;46:595-600.

Fultz NH, Herzog AR, Raghunathan TE, Wallace RB, Diokno AC. Prevalence and severity of urinary incontinence in older African American and Caucasian women. J Gerontol A Biol Sci Med Sci 1999;54:M299-303.

Gann PH, Hennekens CH, Longcope C, Verhoek-Oftedahl W, Grodstein F, Stampfer MJ. A prospective study of plasma hormone levels, nonhormonal factors, and development of benign prostatic hyperplasia. Prostate 1995; 26:40-49.

Gillenwater JY, Wein AJ. Summary of the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases workshop on interstitial cystitis, National Institutes of Health, Bethesda, Maryland, August 28-29, 1987. J Urol 1988;140:203-206.

Goin JE, Olaleye D, Peters KM, Steinert B, Habicht K, Wynant G. Psychometric analysis of the University of Wisconsin Interstitial Cystitis Scale: implications for use in randomized clinical trials. J Urol 1998;159:1085-90.

Goldstein I, Krane RJ. Drug-induced sexual dysfunction. World J Urol 1983; 1:239-243.

Goldstein I, Lue TF, Padma-Nathan H, Rosen RC, Steers WD, Wicker PA, for the Sildenafil Study Group. Oral sildenafil in the treatment of erectile dysfunction. N Engl J Med 1998; 338:1397-1404.

Gonzalez VM, Stewart A, Ritter PL, Lorig K. Translation and validation of arthritis outcome measures into Spanish. Arthritis Rheum 1995;38:1429–46.

Grady D, Herrington D, Bittner V, Blumenthal R, Davidson M, Hlatky M, Hsia J, Hulley S, Herd A, Khan S, Newby LK, Waters D, Vittinghoff E, Wenger N. Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II). JAMA. 2002 Jul 3;288(1):49-57.

Graves EJ, Gillum BS. Detailed diagnoses and procedures, National Hospital Discharge Survey, 1994. National Center for Health Statistics. Vital Health Stat 13 (127), 1997.

Grimby A, Milsom I, Molander U, Wiklund I, Ekelund P. The influence of urinary incontinence on the quality of life of elderly women. Age Ageing 1993;22:82-9.

Guess HA, Jacobsen SJ, Girman DJ, Oesterling JE, Chute CG, Panse LA, Lieber MM. The role of community-based longitudinal studies in evaluating treatment effects. Example:benign prostatic hyperplasia. Medical Care 1995; 33 (Suppl):AS26-AS35.

Guess HA. Benign prostatic hyperplasia: antecedents and natural history. Epidemiol Rev 1992;14:131-153.

Gundle MJ, Reeves BR, Tate S, Raft D, McLaurin LP. Psychosocial outcome after aortocoronary artery surgery. Am J Psychiat 1980; 137:1591.

Hannestad YS, Rortveit G, Sandvik H, Hunskaar S. A community-based epidemiological survey of female urinary incontinence: the Norwegian EPINCONT study. Epidemiology of Incontinence in the County of Nord-Trondelag. J Clin Epidemiol. 2000 Nov;53(11):1150-7.

Herzog AR, Fultz NH. Prevalence and incidence of urinary incontinence in community-dwelling populations. J Am Geriatr Soc 1990a; 38:273-281.

Herzog, AR, Diokno AC, Brown MB, Normolle, DP, and Brock BM. Two year incidence, remission, and change patterns of urinary incontinence in noninstitutionalized older adults. J Gerontol: Med Sci 1990b;45:M67-M74.

Held P, Hanno P, Wein A, Pauly M, Cahn M: Epidemiology of interstitial cystitis: 2. In: Interstitial cystitis. P. Hanno, D. Staskin, R. Krane and A. Wein (eds) New York: Springer Verlag, 1990, p.29.

Hsieh FY. Sample size tables for logistic regression. Stat Med 1989; 8:795-802.

Hu TW. Impact of urinary incontinence on health-care costs. J Am Geriatr Soc 1990;38:292-5.

Hu TW. The cost impact of urinary incontinence on health care services, Nation Multi-Specilty Nursing Conference on Uriniary Continence, Phoenix, AZ, 1994.

Interstitial Cystitis Association. Rockville, MD. www.ichelp.org, 2001.

Jacobsen SJ, Girman CJ, Guess HA, Oesterling JE, Lieber MM. New diagnostic and treatment guidelines for benign prostatic hyperplasia. Potential impact in the United States. Arch Intern Med 1995; 155:477-481.

Johnson PA, Goldman L, Orav EJ, Garcia T, Pearson SD, Lee TH. Comparison of the Medical Outcomes Study Short-Form 36-Item Health Survey in black patients and white patients with acute chest pain. Med Care 1995;33:145–60.

Jolleys JV. Reported prevalence of urinary incontinence in women in a general practice. Br Med J (Clin Res Ed) 1988;296:1300-2.

Jonler M, Moon T, Stone NN, Heisey D, Bruskewitz RC. The effect of age, ethnicity and geographical location on impotence and quality of life. Br J Urol 1995; 75:651-655.

Jones CA, Nyberg L. Epidemiology of interstitial cystitis. Urology 1997;49:2-9.

Kaiser FE, Viosca SP, Morley JE, Mooradian AD, Davis SS, Korenman SG. Impotence and aging: clinical and hormonal factors. J Am Geriat Soc 1988; 36:511-519.

Katscher F. The human costs of tobacco use (letter). NEJM 1994; 331:618.

Keil JE, Sutherland SE, Knapp RG, Waid LR, Gazes PC. Self-reported sexual functioning in elderly blacks and whites: The Charleston Heart Study Experience. J Aging Health 1992; 4:112-125.

Keller ML, McCarthy DO, Neider RS. Measurement of symptoms of interstitial cystitis: A pilot study. Urol Clin North Am 1994;21:67-71.

Khavari KA, Farber PD. A profile instrument for the quantification and assessment of alcohol consumption. J Stud Alc 1978; 39:1525-39.

Kinsey AC, Pomeroy WB, Martin CE. Sexual behavior in the human male. Phila.delphia: Saunders, 1948.

Kleinman KP, Feldman HA, Johannes CB, Derby CA, McKinlay JB. A new surrogate variable for erectile dysfunction status in the Massachusetts male aging study. J Clin Epidemiol. 2000 Jan;53(1):71-8.

Korenman SG, Morley JE, Mooradian AD, Davis SS, Kaiser FE, Silver AJ, Viosca AP, Garza D. Secondary hypogonadism in older men: Its relation to impotence. J Clin Endocrinol Metab 1990; 71:963-969.

Kosch SG, Curry RW, Kuritzky L. Evaluation and treatment of impotence: a pragmatic approach addressing organic and psychogenic components. Fam Pract Res J 1988; 7:162.

Koziol JA, Clark DC, Gittes RF, Tan EM. The natural history of interstitial cystitis: a survey of 374 patients. J Urol 1993;149:465-469.

Koziol JA. Epidemiology of interstitial cystitis. Urol Clin North Am 1994;21:7-20.

Krane RJ, Goldstein I, de Tejada IS. Impotence. N Engl J Med 1989;321:1648-1659.

Krieger JN, Egan KJ, Ross SO, Jacobs R, Berger RE. Chronic pelvic pains represent the most prominent urogenital symptoms of "chronic prostatitis." Urology 1996;48:715-722.

Krongrad A, Perczek RE, Burke MA, Granville LJ, Lai H, Lai S. Reliability of Spanish translations of select urological quality of life instruments. J Urol 1997; 158:493-496.

Lagro-Janssen TL, Debruyne FM, Smits AJ, van Weel C. Controlled trial of pelvic floor exercises in the treatment of urinary stress incontinence in general practice. Br J Gen Pract. 1991 Nov;41(352):445-9.

Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. JAMA 1999; 281:537-544.

Lefkowitz D, Monheit AC. Health insurance, use of health services, and health care expenditures. Rockville (MD): Agency for Health Care Policy and Research; 1991. National Medical Expenditure Survey Research Findings 14. AHCPR Pub. No. 92-0017.

Lepor H, Shapiro E, Wang B, Liang YC. Comparison of the cellular composition of benign prostatic hyperplasia in Chinese and Caucasian-American men. Urol 1996; 47:38-42.

Litwin MS, McNaughton-Collins M, Fowler FJ Jr, Nickel JC, Calhoun EA, Pontari MA, Alexander RB, Farrar JT, O'Leary MP. The National Institutes of Health chronic prostatitis symptom index: development and validation of a new outcome measure. Chronic Prostatitis Collaborative Research Network. J Urol 1999;162:369–75.

Lubeck DP, Whitmore K, Sant GR, Alvarez-Horine S, Lai C. Psychometric validation of the O'leary-Sant interstitial cystitis symptom index in a clinical trial of pentosan polysulfate sodium. Urology. 2001 Jun;57(6 Suppl 1):62-6.

Maatman TJ, Montague DK. Routine endocrine screening in impotence. Urol 1986; 27:499-502.

Mahard RE. The CES-D as a measure of depressive mood in the elderly Puerto Rican population. J Gerontol 1988;43:P24–5.

Mathias SD, Kuppermann M, Liberman RF, Lipschutz RC, Steege JF. Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. Obstet Gynecol 1996;87:321-7.

McConnell JD, Barry MJ, Bruskewitz RC, et al. Benign Prostatic Hyperplasia: Diagnosis and Treatment. Quick Reference Guide for Physicians. Rockville, MD: Agency for Health Care Policy and Research, U.S. Dept. Health and Human Services, publication AHFCR 94-0582, 1994.

McConnell JD. The pathopysiology of benign prostatic hyperplasia. J Androl 1991; 12:356-363.

McKinlay JB, Feldman HA, Durante R, Goldstein I, Longcope C. Sex hormones, cardiovascular disease, and erectile dysfunction. Am J Epidemiol 1997; 145(11):S1.

McKinlay SM, Kipp DM, Johnson P, Downey K, Carelton RA. A field approach for obtaining physiological measures in surveys of general populations: response rates, reliability and costs. In: Proceedings of the Fourth Conference on Health Survey Research Methods. Washington, DC: U.S. Dept. Health and Human Services Publication PHS 84-3346, 1984.

McNaughton Collins M, Barry MJ. Controversies in prostate cancer screening. JAMA 1996; 276:1976-1979.

McNaughton Collins M, Barry MJ. Epidemiology of prostatitis. In: J Curtis Nickel, (ed). Prostatitis. Oxford: Isis Medical Media Ltd., 1998a.

McNaughton Collins M, Stafford R, O'Leary M, Barry M. How common is prostatitis? A national survey of physician visits. J Urol 1998b; 159; 1224-1228.

McNaughton Collins M, Kleinman KP, Barry MJ, Meigs JB, Yurgalevitch SM, McKinlay JB. Prostate-specific antigen (PSA) levels: effect of sexual activity. Prostate J 1999; 1:82-87.

McTierney LM, McPhee SJ, Papadakis MA, eds. Current Medical Diagnosis & Treatment 1995. Norwalk: Appleton & Lange, 1995, p. 994.

Messing E. Interstitial cystitis and related syndromes. In: Campbell's Urology. Edited by P.C. Walsh, A.B. Retik, T.A. Stamley and E.D. Vaughn, Jr. Philadelphia: W.B. Saunders Co. 1992 p.982.

Michael YI, Kawachi I, Stampfer MJ, Colditz GA, Curhan GC. Quality of life among women with interstitial cystitis. J Urol 2000;164:423-427.
Michal V. Arterial disease as a cause of impotence. Clin Endocrinol Metab 1982; 11:725.
Mommsen S, Foldspang A. Body mass index and adult female urinary incontinence. World J Urol 1994;12:319-22.
Monheit AC, Vistnes JP. Health insurance status of workers and their families: 1996. Rockville (MD): Agency for Health Care Policy Research: 1997. MEPS Research Findings No. 2 AHCPR Pub no. 97-0065.
Montella AJ, Wordwell CJ. The effects of drugs on the lower urinary tract. In: Ostergard D, Bent A (eds): Urogynecology and urodynamics. Baltimore: Williams and Wilkins, 1996.
Montie RA Jr. Review of the role of androgenic hormones in the epidemiology of benign prostatic hyperplasia and prostate cancer. Urol 1994; 43:6:892-9.
Morley JE. Impotence. Am J Med 1986; 80:897-905.
Morrison AS. Risk factors for surgery for prostatic hypertrophy. Am J Epidemiol 1992; 135:974-980.
National Institute of Diabetes and Digestive and Kidney Diseases. National Kidney and Urologic Diseases Information Clearinghouse, NIH publication 95-3923, 1995.
National Institutes of Health Consensus Development Panel. Impotence. JAMA 1993; 270:83-90.
National Institutes of Health. National Institute of Diabetes and Digestive and Kidney Diseases Workshop on Chronic Prostatitis: summary statement. Bethesda, MD: U.S. Dept. Health and Human Services, 1995.
O'Leary MP, Lenderking WR, Barber B, Sagnier PP, Guess HA, Barry MJ. A brief male sexual function inventory for urology. Urol 1995; 46:697-706.
O'Leary MP, Sant GR, Fowler FJ Jr, Whitmore KE, Spolarich-Kroll J. The interstitial cystitis symptom index and problem index. Urology 1997;49(5A Suppl):58-63.
Oravisto K. Epidemiology of interstitial cystitis. Ann Chir Gynaec Fenniae 1975:64:75-7.
Ory MG, Wyman JF, Yu L. Psychosocial factors in urinary incontinence. Clin Geriatr Med 1986;2:657-71.
Ostfeld AM, Eaker E. Measuring psychosocial variables in epidemiological studies of cardiovascular disease. Arteriosclerosis 1985; 5:116-118.
Parsons CL, Kamarei M, Monga M. Interstitial Cystitis. In: Women and Health, edited by MB Goldman, MC Hatch. Academic Press, 2000: p 1110.
Paskett ED, DeGraffinreid C, Tatum CM, Margiticse. The recruitment of African-Americans to cancer prevention and control studies. Prev Med 1996; 25:547-553.
Perez ED, Mulligan T, Wan T. Why men are interested in an evaluation for a sexual problem. J Am Geriat Soc 1993; 41:233-237.
Plaud JJ, Dubbert PM, Holm J, Wittrock D, Smith P, Edison J, McAnulty R, Caddell J, Summerville M. Erectile dysfunction in men with chronic medical illness. J Beh Ther Exp Psychiat 1996; 27:11-19.
Plymate S. Hypogonadism. Endocrinol Metab Clin North Am 1994; 23:749-72.
Propert KJ, Schaeffer AJ, Brensinger CM, Kusek JW, Nyberg LM, Landis JR, and the Interstitial Cystitis Data Base Study Group. J Urol 2000;163:1434-1439.
Radloff L. The CES-D scale: a self-report depression scale for research in the general population. Appl Psych Meas 1977; 1:385-401.

Reiter RC. Evidence-based management of chronic pelvic pain. Clin Obstet Gynecol 1998;41:422-435.

Rekers H, Drogendijk AC, Valkenburg HA, Riphagen F. The Menopause, urinary incontinence and other symptoms of the genito-urinary tract. Maturitas 1992; 15:101-111.

Rittmaster RS. Finasteride. N Engl J Med 1994; 330:120-125.

Roberts R, Lieber M, Rhodes T, Girman C, Bostwick D, Jacobsen S. Prevalence of a physician-assigned diagnosis of prostatitis: the Olmstead County Study of urinary symptoms and health status among men. Urology 1998; 51:578-584.

Rosen MP, Greenfield AJ, Walker TG, Grant P, Dubrow J, Bettmenn MA, Fried LE, Goldstein I. Cigarette smoking: an independent risk factor for atherosclerosis in the hypogastric-cavernous arterial bed of men with arteriogenic impotence. J Urol 1991; 145:759-763.

Rosen RC, Leiblum SR. Treatment of sexual disorders in the 1990s: an integrated approach. J Consult Clin Psychol 1995; 877-890.

Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile Function (IIEF): A multidmensional scale for assessment of erectile dysfunction. Urol 1997; 49:822-830.

Safran DG, Kosinski M, Tarlov AR, Rogers WH, Taira DH, Lieberman N, Ware JE. The Primary Care Assessment Survey: tests of data quality and measurement performance. Med Care 1998;36:728–39.

Sandvik H, Hunskaar S, Vanvik A, Bratt H, Seim A, Hermstad R. Diagnostic classification of female urinary incontinence: an epidemiological survey corrected for validity. J Clin Epidemiol. 1995 Mar;48(3):339-43.

Sandvik H, Seim A, Vanvik A, Hunskaar S. A severity index for epidemiological surveys of female urinary incontinence: comparison with 48-hour pad-weighing tests. Neurourol Urodyn. 2000;19(2):137-45.

Sant GR. Interstitial cystitis in minority women. J Assoc Academic Minority Physicians 1993;4:89-92.

Scialli AR, for the Pelvic Pain Expert Working Group. Evaluating Chronic Pelvic Pain. A Consensus Recommandation. J Reprod Med 1999;44:945-952.

Shabsigh R. Impotence on the rise as a urological subspecialty (editorial). J Urol 1996; 155:924-925.

Shumaker SA, Wyman JF, Uebersax D, McClish JA, Fanti for the Continence Program in Women (CPW) Research Group. Health-related quality of life measures for women with urinary incontinence: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Quality of Life Research 1994 3:291-306.

Sidney S, Quesenberry CP, Sadler MC, Guess JA, Lydick EG, Cattolica EV. Incidence of surgically treated benign prostatic hypertrophy and of prostate cancer among blacks and whites in a prepaid health care plan. Am J Epidemiol 1991; 134:825-829.

Simpson RJ, Fisher W, Lee AJ, Russell EB, Garraway M. Benign prostatic hyperplasia in an unselected community-based population: a survey of urinary symptoms, bothersomeness and prostatic enlargement. Br J Urol 1996; 77:186-191.

Slag MF, Morley JE, Elson MK, Trence DL, Nelson C, Nelson A, Kinlaw WB, Beyer S, Nuttall FQ, Shafer RB. Impotence in medical clinic outpatients. JAMA 1983; 249:1736-1740.

Smith KW, Feldman HA, McKinlay JB. Construction and field validation of a self-administered screener for testosterone deficiency (hypogonadism) in aging men. Clin Endocrinol (Oxf) 2000;53:703–711.

Sommer P, Bauer T, Nielsen KK, Kristensen ES, Hermann GG, Steven K, Nordling J. Voiding patterns and prevalence of incontinence in women. A questionnaire survey. Br J Urol 1990;66:12-5.

Spark RF, White RA, Connolly PB. Impotence is not always psychogenic: Newer insights into hypothalmic-pituitary-gonadal dysfunction. JAMA 1980; 243:750-755.

Stimson JB, Fihn SD. Benign prostatic hyperplasia and its treatment. J Gen Internal Med 1990; 5:153-165.

Subar AF et al. Comparative validation of the Block, Willett, and National Cancer Institute Food Frequency Questionnaires. Am J Epidemiol 2001;154:1089-1099.

Temml C, Haidinger G, Schmidbauer J, Schatzl G, Madersbacher S. Urinary incontinence in both sexes: prevalence rates and impact on quality of life and sexual life. Neurourol Urodyn 2000;19-259-71.

Tenover JS. Androgen administration to aging men. Clin Androl 1994; 23:877-892.

Thom D. Variation in estimates of urinary inconinence prevalence in the communityL effects of differences in definition, population characteristics, and study type. J Am Geriatr Soc 1998;46:473-80.

Thom DH, van den Eeden SK, Brown JS. Evaluation of parturition and other reproductive variables as risk factors for urinary incontinence in later life. Obstet Gynecol 1997;90:983-9.

Thomas TM, Plymat KR, Blannin J, Meade TW. Prevalence of urinary incontinence. Br Med J 1980;281:1243-5.

Wabrek AJ, Burchell RC. Male sexual dysfunction associated with coronary heart disease. Arch Sex Beh 1980; 9:69-75.

Wallman KK. Data on race and ethnicity: Revising the federal standard. Am Stat 1998; 52:31-35.

Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473–83.

Washburn RA, Smith KW, Jette AM, Janney CA. The physical activity scale for the elderly (PASE): development and evaluation. J Clin Epidemiol 1993; 46:153-162.

Wein AJ, Van Arsdalen KN. Drug-induced male sexual dysfunction. Urol Clin N Am 1988; 15:23-30.

Weinick RM, Drilea SK. Usual Sources of Health Care and Barriers to Care, 1996. Statistical Bulletin Jan-Mar 1998a; 79:11–17. AHCPR Pub. No. 98-R024.

Weinick RM, Weigers ME, Cohen, JW. Children's Health Insurance, Access to Care, and Health Status: New Findings. Health Affairs March/April 1998b; 17:127–136. AHCPR Pub. No.98-R035.

Weinick RM, Zuvekas SH, Drilea SK . Access to Health Care-Sources and Barriers, 1996. Rockville (MD): Agency for Health Care Policy and Research; 1997. MEPS Research Findings No. 3 AHCPR Pub. No. 98-0001.

Wenninger K, Heiman JR, Rothman I, Berghuis JP, Berger RE. Sickness impact of chronic nonbacterial prostatitis and its correlates. J Urol 1996;155:965-8.

Wyman JF, Harkins SW, Choi SC, Taylor JR, Fantl JA. Psychosocial impact of urinary incontinence in women. Obstet Gynecol 1987;70:378-81.

Yarnell JW, Voyle GJ, Sweetnam PM, Milbank J, Richards CJ, Stephenson TP. Factors associated with urinary incontinence in women. J Epidemiol Community Health 1982;36:58-63.