

Summary

Erectile dysfunction (ED) is a common complaint among men. It is highly correlated with cardiovascular disease and other serious co-morbid conditions such as dyslipidemia, depression, renal failure, prostate cancer and benign prostatic disease. ED is often the only presenting complaint in men who have very serious cardiovascular or urologic disease. Several recent studies demonstrate that men are being diagnosed with serious co-morbid illnesses, either vascular or otherwise, following visits to physicians with a sole complaint of ED. The pursuit of dietary supplements explicitly promoted as substitutes for or alternatives to Viagra induces men to forego examination by a physician and thereby substantially impacts the public's health by potentially depriving millions of men of proper medical diagnosis and the opportunity for early detection and treatment of life-threatening diseases and conditions. Thus, these dietary supplement products represent a serious threat to the public health.

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Introduction

Erectile dysfunction (ED) is defined as "the inability to attain and/or maintain penile erection sufficient for satisfactory sexual intercourse".¹ As many as one-third to one-half of men aged 40 and older suffer from some degree of ED (Figure 1).^{2,17,19,21,24,25,34} Recent data from the Harvard Health Professionals Follow-up Study suggests that approximately 24 million men in the US age 40 and older have ED.² Erectile dysfunction may be considered a manifestation of systemic vascular disease in the majority of cases^{7,44} and the risk factors for ED are essentially the same as the risk factors for cardiovascular disease. Other serious medical conditions also associated with ED are dyslipidemia, depression, renal failure, prostate cancer and benign prostate disease.^{3,8,14,28,40,42,47}

Since the introduction of Viagra® (sildenafil citrate), an oral agent for the treatment of ED, in April 1998, the number of men seeking care for ED has increased rapidly^b (Figure 2). Although men and their physicians have shown a greater willingness to discuss erectile dysfunction, there are still millions of men with ED who have not sought treatment. ED is a very serious and distressing problem in and of itself for both men and their partners. Seeking a physician diagnosis for the treatment of ED is especially important because it has the potential to uncover other serious, often asymptomatic diseases early in the

¹ NIH Consensus Conference

² Pfizer, data on file

course of these co-morbid conditions. Avoiding medical care by obtaining dietary supplements over the Internet that purport to be “safe” and “natural” substitutes for Viagra or being induced to forego a medical examination because of claims that a dietary supplement is the herbal alternative to Viagra deprives men of the significant public health benefit conferred by early detection and treatment of these serious correlates of erectile dysfunction.

Erectile dysfunction

Sexual stimulation in the male causes nonadrenergic, noncholinergic (NANC) nerve-mediated release of nitric oxide (NO) from nerves and endothelium. NO activates guanylate cyclase and the resulting accumulation of cGMP leads to smooth muscle relaxation in the corpus cavernosum and erection.^{13,37} Impaired nitric oxide activity may play a role in the pathophysiology of both ED and cardiovascular disease.⁴⁴

The prevalence of erectile dysfunction increases monotonically with age, as does the prevalence of cardiovascular disease and cardiovascular risk (Figure 2). ED may be considered a manifestation of systemic vascular disease.^{7,44} As such, the risk factors for ED are essentially the same as the risk factors for cardiovascular disease, including hypertension, diabetes, dyslipidemia, obesity, smoking, and inactivity.^{4,6,9,10,11,17,18,19,20,23,26,27,31,32,38,43,46,47} Other serious medical conditions also associated with ED are depression, renal failure, prostate cancer and benign prostatic disease.^{3,10,14,28,29,40,42} Sociodemographic factors (age, education, income, marital status) as well as modifiable lifestyle factors such as smoking, alcohol consumption, and physical exercise are associated with ED.^{4,31,43} Approximately 28 million men in the US over the age of 40 have hypertension, 24 million have ED, and an estimated 19 million have both conditions (Figure 3). In a recent population-based prevalence study in four countries (Brazil, Italy, Malaysia and Japan), 19% of men without ED reported two or more risk factors for cardiovascular disease, while 38% of those with ED reported two or more risk factors (Figure 4).

The extent of ischemic heart disease seems to be related to the risk of ED. Greenstein reported an association between the presence of ED and the number of coronary vessels that were occluded on angiography.²² Similarly, the severity of diabetes³⁹ (measured by presence of peripheral neuropathy) and lack of glycemic control were found to correlate with the presence of ED.^{18,39}

Recent studies have also shown an association between fibrinogen and ED⁴⁵ and lipoprotein (a) levels and ED.⁴⁴

Help-seeking behavior

Prior to the availability of Viagra® (sildenafil citrate), the most common treatments for ED were intracavernosal injections, intraurethral suppositories, and prosthetic implants. Relatively few men chose to be treated due to the unpleasant nature of these treatments. Within several months following the approval of Viagra in the US, several million men presented to their physicians requesting this treatment (Pfizer, data on file). This is testament to the desire of men with ED to try a safe and effective oral drug treatment. It is even more remarkable given the reluctance of many men to visit a physician in the first place. Between the ages of 45 and 64, men visit the doctor approximately 30% less frequently than women (Figure 5). Fifteen percent of men in the US (compared to only 8% of women) have not seen a physician for one to three years, and 9 percent of men (compared to 3% of women) have not seen a doctor in more than three years according to the Centers for Disease Control. It was widely acknowledged that this influx of men to their doctors for symptomatic treatment for ED following the approval of Viagra had the potential to confer a great public health benefit if the opportunity for screening for occult cardiovascular disease was taken advantage of by the doctor.^{27,35,36}

Approximately 9 million men have filled a prescription for Viagra in the three years since approval. However, there are still approximately 15 million men with ED who have not been treated with sildenafil (Figure 5). ED is known to cause decreased satisfaction with life in general and with sexual life in particular.^{25,28} Although publicity and educational programs have increased the willingness of men and their doctors to discuss sexual problems, there are still many psychological barriers in the minds of men. It is embarrassing to men to start this discussion and men often fear that it will be embarrassing to their doctor.⁴⁸ In a recent study, forty-four percent of men seeing a urologist for problems unrelated to ED were found to have ED upon specific targeted questioning. Seventy-four percent reported that they had not discussed this with their doctor because they were embarrassed. Nine percent were unaware that urologists even dealt with erectile dysfunction.⁵ Another study reported that 68% felt that their doctor would be uncomfortable discussing a sexual problem.³⁰

ED May be an Early Marker of Serious Disease:

Many serious medical conditions are relatively asymptomatic until late in the course of the disease. Hypertension, dyslipidemia and diabetes are important examples of these. The NIH estimates that five to six million Americans have diabetes but are not aware of it. Approximately one quarter of all people with high blood pressure are not aware they have hypertension.¹² Serious end organ damage is usually present by the time these conditions become symptomatic and early medical intervention is known to prevent many of the serious outcomes of these conditions.

It has become increasingly apparent that ED may be a harbinger of serious underlying vascular disease or risk, and may, in fact, be the only presenting symptom. Deutsch reported that 12% of a group of men with ED (who had no symptoms of diabetes) were found to be diabetic by glucose tolerance tests.¹⁶ A recent study found that 4.7% of a group of consecutive patients presenting with ED had undiagnosed diabetes. An additional 12% had an abnormal fasting glucose level.⁴¹

A study of approximately 200 patients presenting to a urology clinic with the sole complaint of ED found that 15% were diagnosed with urologic malignancies upon full evaluation (7.7% had prostate cancer, 5.8% had bladder cancer and three patients were diagnosed with cancer of the kidney (2 patients) or penis (one patient)).¹⁴

Pritzker found that among 50 otherwise asymptomatic males with ED, only 15 had seen a physician within the last 2 years.³⁶ Twenty-eight of the 50 had a positive exercise stress test and 20 of the 50 patients had significant obstruction of one or more coronary arteries. Anderson reported that 16% of a small sample of patients with severe vascular ED had a positive stress test requiring further investigation.¹ Billups reported that 60% of men with ED but no other known vascular problems had abnormally high cholesterol.⁷

Studies funded by Pfizer in several health maintenance organizations (HMO) found that men were more likely to be diagnosed with serious medical conditions (diabetes, dyslipidemia, heart disease, depression) shortly after presenting for a prescription for Viagra than their peers.^{3,15} Of approximately 1 000 men newly diagnosed with ED in one HMO in the months following the launch of Viagra, 18% were diagnosed with hypertension, 16% with diabetes, 5% with ischemic heart disease and 4% with prostate cancer within a month of first visit.¹⁵ Thus, this effect is even apparent among men with easy access to health care and preventive services.

Conclusion

In many cases, ED is the only presenting complaint of men with very serious cardiovascular or urologic disease. As a result, reports of men being diagnosed with serious illness following visits to physicians with a sole complaint of ED have become increasingly common since the introduction of Viagra. Claims by makers of dietary supplements that their products are substitutes for, or alternatives to, Viagra, induce men to forego appropriate and necessary medical care and deprive them of the opportunity for detection and early treatment of life-threatening conditions.

³ Personal communication, C. Enger

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Figure 1. Approximately one-third to one-half of men over the age of 40 complain of some degree of ED (mild, moderate or complete). The prevalence of moderate and complete ED combined is approximately 10% for men in their 40's, 22% for men in their 50s and 47% for men in their 60s. These estimates are based on data from over 10,000 men in Europe, Asia, Africa and South America. Source: Pfizer, data on file.

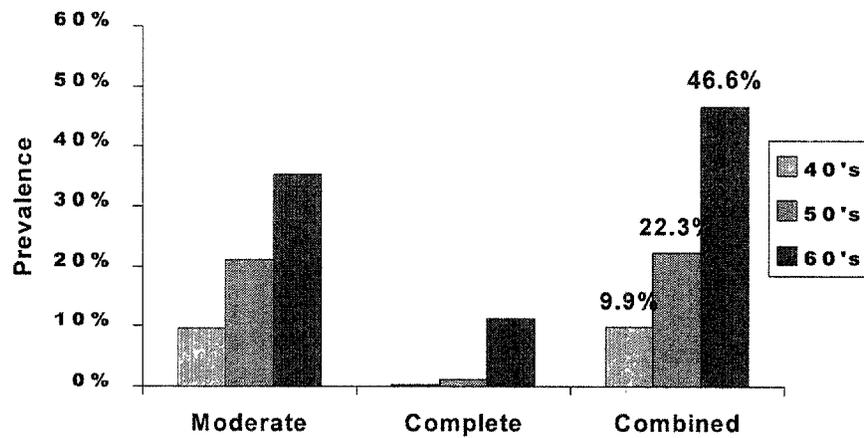


Figure 5. ED and hypertension follow a similar pattern of increasing with age.
Source: Ansong et al 2000 (ED), NHANES III (hypertension)

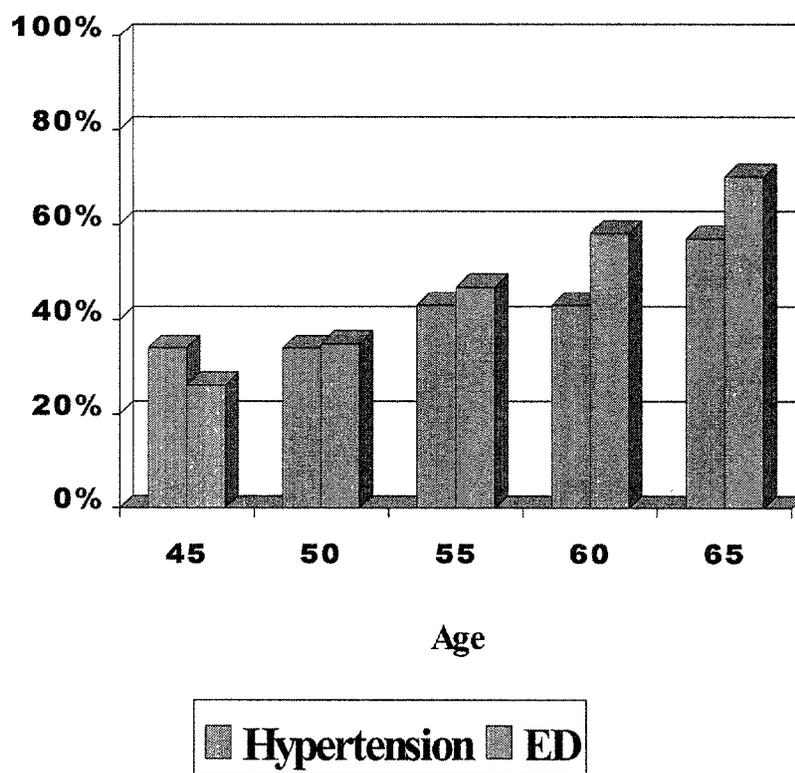


Figure 3. Estimated prevalence (in millions) of hypertension, ED, and the combination of hypertension and ED among men in the US age 40 and older. Source: NHANES (hypertension), Health Professionals Follow-Up Study unpublished data (ED)

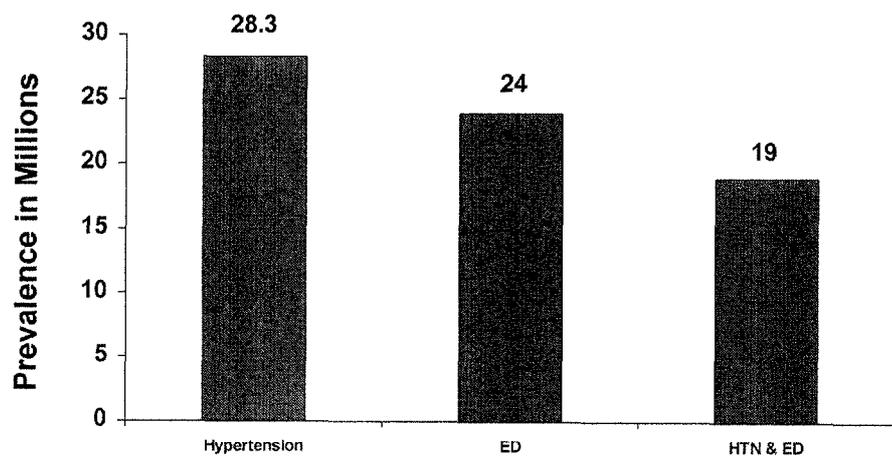
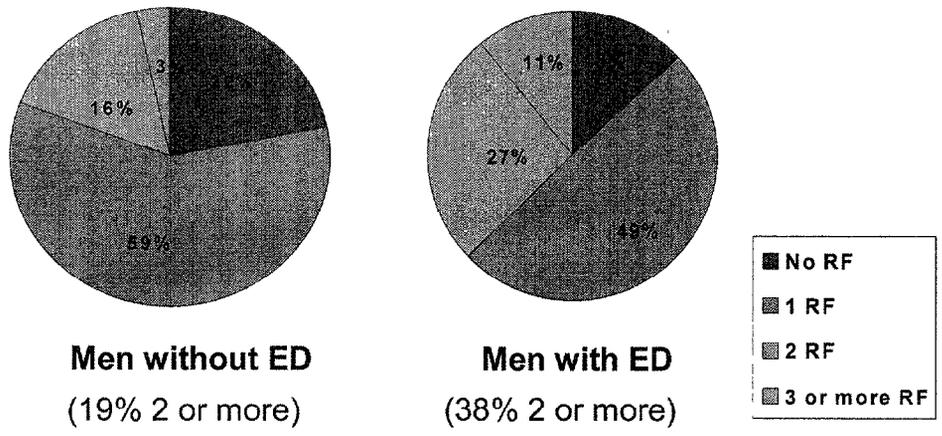


Figure 4. Number of self-reported risk factors (RF) for cardiovascular disease among men with and without ED. Source: Pfizer Cross-national Study of the Prevalence and Correlates of ED



Pfizer, data on file

Figure 5. Annual rate of visits to office-based physicians and outpatient departments by patient's age and sex: United States, 1999.

Women between the ages of 45-64 visited the physician 38% more frequently than men the same age. Source: National Health Care Survey, 1999, US National Center for Health Statistics, Centers for Disease Control

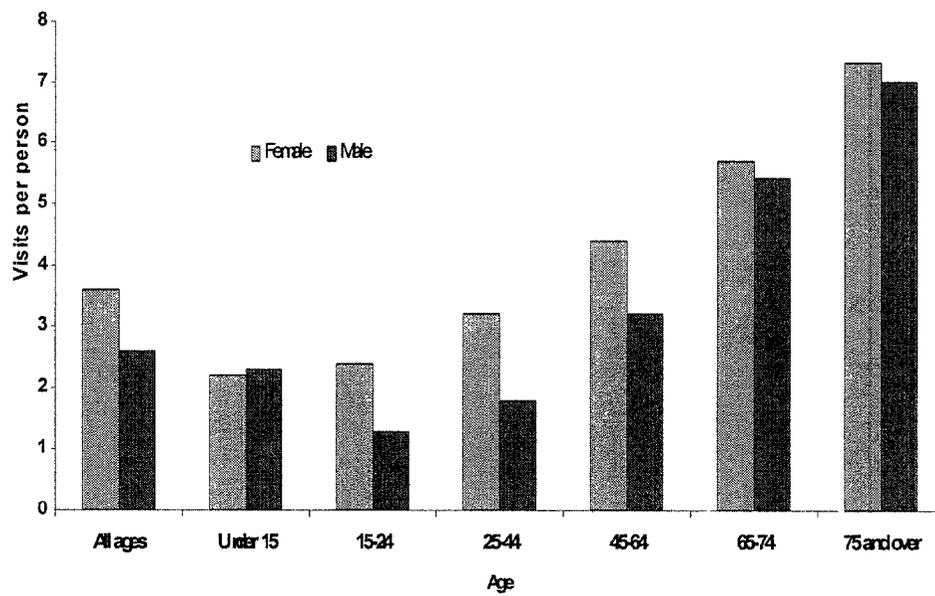


Figure 5: Of the estimated 23 million men in the US with erectile dysfunction, approximately 9 million have filled a prescription for sildenafil. Approximately 15 million men have not yet been treated with oral medication for ED (Source: Pfizer data on file)

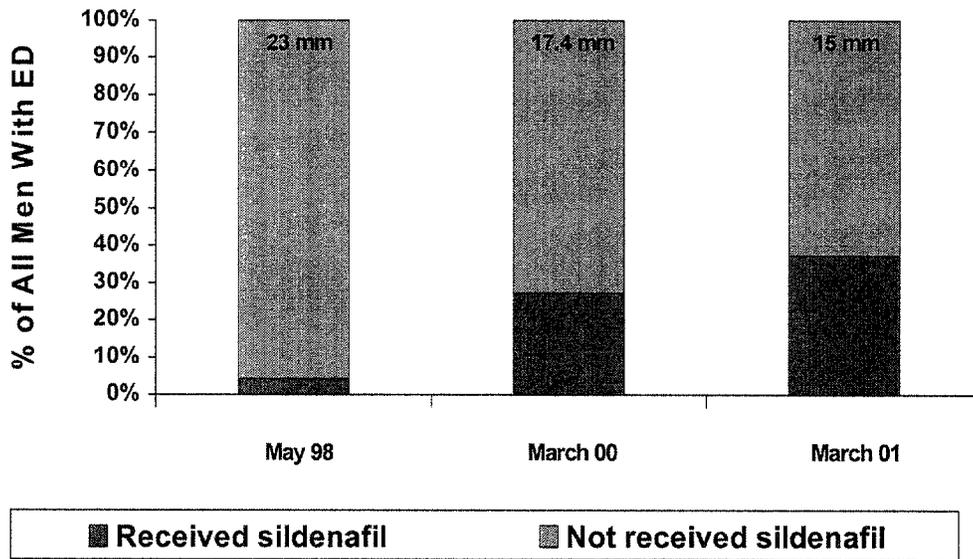


Figure 6. In a cohort of ~1000 men newly diagnosed with ED, 18% were diagnosed with hypertension, 16% with diabetes, 5% with ischemic heart disease, and 4% with prostate cancer within one month of presenting with a complaint of ED. Source: Curkendall et al, EAU 2000

