

REVIEW

"Before you go"—considering genitourinary symptoms as a sentinel indicator of the presence of, or risk for, chronic disorders in men

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Abstract

Men have a significantly shorter life expectancy compared to women, with disparities further magnified among those from disadvantaged backgrounds. Non-communicable diseases (NCDs) constitute a large proportion of the health disparity between men and women. Up to 40% of the chronic disease burden in men could be mitigated through risk factor management or early intervention. This disparity is often attributed to the engagement with primary and preventive healthcare by men which is influenced by health literacy, accessibility of care and socio-economic status. The manuscript proposes that genitourinary symptoms, specifically erectile dysfunction (ED) and lower urinary tract symptoms (LUTS), are sentinel indicators of chronic diseases or their risk factors in men. LUTS and ED share risk factors with major chronic disorders like cardiovascular disease, diabetes, and obesity, and are associated with depression and obstructive sleep apnea. Both ED and LUTS are meaningful to men and can motivate seeking care, providing healthcare providers an opportunity for preventative measures and early treatment. Such an approach also ameliorates the LUTS and ED symptoms and substantially improves quality of life. We advocate for a targeted approach that uses ED and nocturia as entry points for engaging men in healthcare. This involves public health education to raise awareness about the significance of these symptoms and encouraging healthcare providers to actively inquire about them during consultations. By addressing these symptoms, healthcare practitioners can better identify and treat underlying chronic conditions early, potentially reducing morbidity and mortality among men and helping to narrow the sex related health outcome disparities between genders.

Keywords

Lower urinary tract symptoms; Nocturia; Erectile dysfunction; Cardiovascular disease; Diabetes; Sleep apnoea; Lifestyle; Metabolic syndrome; Men's health

1. Introduction

Globally, there is on average a 5-year life expectancy gap between men and women [1]. Men from disadvantaged backgrounds live ~6 years less than their more socioeconomically privileged counterparts [2]. Internationally, over 80% of male mortality is attributed to non-communicable disease and injury [3]. Up to 40% of the burden of chronic disease in men is preventable with risk factor mitigation, versus 34% for females [4–6].

One of the reasons traditionally suggested for the difference in burden of disease between men and women is that men are less likely to use primary and preventative health services [7]. Considerable evidence argues that men are however interested in their health and do engage in health services [8], particularly when there is motivation to do so, an understanding of necessity, and the services are accessible [6].

Men prefer to be asked direct rather than open-ended ques-

tions [9]. Men have shorter consults and often leave feeling that their major concerns have not been addressed [10–12]. Unfortunately, this mismatch between the male patient's needs and the care provided represents a missed opportunity to identify important symptoms, and ultimately, identify chronic disease or its risk factors.

We therefore propose an approach to connect men to primary care and enhance the care process by focusing on erectile dysfunction (ED) and lower urinary tract symptoms (LUTS), particularly nocturia. These are conditions which have meaning for men and indicate the presence of, or risk for, chronic disease.

2. Method

We conducted a literature review without restricting dates up until 31 May 2024 using databases PubMed and Scopus. Search terms included “erectile dysfunction”, “lower urinary

tract symptoms” and “chronic disease”, limited to studies either in men or reporting data in men separately. From the results generated, citations were subsequently screened and used.

3. Engaging men in healthcare

Recent Australian data have demonstrated that 79% of Australian males over the age of 15 visited a general practitioner in 2021–2022 [13], and older men with multiple comorbidities, particularly obesity, cardiovascular disease or diabetes, regularly access healthcare services. When mental health conditions are present, men are more likely to have a greater frequency of General Practitioner (GP) visits [14]. Furthermore, another Australian study demonstrated that greater than 85% of men reported seeking information for serious health concerns, with their preferred sources being GPs or specialists, pharmacists, and online searches [15]. However, approximately 70% of men leave GP encounters feeling that their most important health issues haven’t been addressed [11]. Compared with women, men generally have shorter appointments [10]. They are also less likely to raise issues peripheral to the main reason for consultation or to check that their health care provider has understood their complaint [9, 12, 16, 17]. This has been attributed to a communication style whereby men prefer to be asked questions directly [9, 18]. This communicative mismatch results in missed diagnoses, perhaps best demonstrated in men with mental health issues. Men with a high burden of depressive symptoms account for a significantly higher proportion of frequent general practice attenders (45.9%) compared to those with a low burden of depressive symptoms (29.3%). Of men who had a high burden of depressive symptoms, only half report a physician diagnosis of depression [19]. The high proportion of missed mental health diagnoses in men is likely the consequence of lower mental health literacy, men experiencing their symptoms differently to women and GPs having difficulty identifying depression in men [20–23].

Men typically, those without prior experience of a health problem, delay accessing care and tend to self-monitor their symptoms [11, 24]. In surveys men indicate this approach is in anticipation of either an unaided recovery, or that they planned to access healthcare if their symptoms reached the point of affecting their capacity to work or function [25]. Factors that drive this delayed engagement with health care include lower health literacy, suboptimal accessibility of services and a complex interplay between interpersonal, financial (cost and time away from work) and male perceptions of general practice as being unwelcoming to men and reserved for acute health issues [6]. These issues are magnified in men of lower socioeconomic status [26] migrant populations [27], and men over the age of 65, all groups with the lowest health literacy [28].

Limited health literacy affects one’s ability to navigate the healthcare system, follow age-specific screening guidelines, understand medication instructions [28] and how men interpret their symptoms and therefore seek medical attention [29]. The Men in Australia Telephone Survey (MATeS) study reported that those participants who did not seek medical attention for ED cited primarily their belief that the disorder was due to

medications, relationship difficulties, or an inability talk about erection problems [8]. Other male cohorts have identified the belief that the condition would resolve spontaneously if young, or that it was a natural part of ageing if older [30, 31]. This is in sharp contrast to the multiple metabolic conditions and risk factors associated with ED. Cultural barriers [32] and cost [6] are also limitations to care seeking. Men may also prioritize family or work responsibilities as reasons to delay accessing healthcare [6]. Others may delay seeking medical attention due to a fear that they may be judged negatively for seeking services prematurely [11, 16].

We propose that lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) are sentinel symptoms of chronic disease and its risk factors. These are sentinel symptoms that serve as identifiable prompts for men to seek care, and for primary care physicians to identify risk and provide an entry point to prevention or early treatment of chronic disease. The strength of this approach is that it is sensitive of the time constraints of general practice, cost constraints of health care delivery and patient convenience [9, 33].

4. Erectile dysfunction as a marker of chronic disease risk

ED is defined as “failure to achieve or maintain a rigid penile erection suitable for satisfactory sexual intercourse” [34]. The exact population-wide prevalence of ED varies globally by country, at ~20.7% of men in North America, 16.8–65.4% in Europe, 13.1–71.2% in Asia, 40.3–42% in Oceania and 24–58.9% in Africa, and is largely influenced by the measurement tool and ages included in a given study. In examining Australian figures, in a study of over 1500 men, a prevalence of 40.3% in men aged 20–80. By age group, the prevalence was 15.7% in 20–29 year-olds, 8.7% in 30–39s, 12.9% in 40–49s, 31.60% in 50–59s, 52.40% in 60–69s, 69.4% in 70–79s and 68.2% in >80 year-olds [35]. Regarding the relationship of ED severity with age, a Finnish study of over 3000 men aged 50–75 years demonstrated that the proportion with moderate ED rises from 10% to 20% between the age of 50 and 75, whilst the proportion of severe ED rises from less than 5% of the studied population at age 50 to 40% by 75 years [36]. However, a more recent systematic review argued there is no trend towards ED severity based on age. How ED severity is assigned depends on the questionnaire used, with the international index of erectile function 5 (IIEF-5) survey using a score based on an individual’s questionnaire responses, whereas the Massachusetts Males Ageing Study (MMAS) self-assessment asks men to self-assign a severity. Other non-validated tools are less sensitive than these assessments [35].

ED shares risk factors with and is a marker of many underlying chronic disorders [37] characterized by vascular, neurological, endocrinologic or psychological dysfunction [38]. Some chronic disease risk factors associated with ED include obesity, dyslipidemia, excessive alcohol intake, smoking and low physical activity. Chronic disease associations meanwhile include hypertension, dysglycemia, depression, obstructive sleep apnea (OSA) and cardiovascular disease [37, 39].

Being overweight or obese has been associated with an increase in the relative risk (RR) of ED, with RR 1.5 and 3.0

respectively [37]. Smokers are 1.5× more likely than non-smokers to have ED [37]. An assessment of ~2500 Spanish men also found dyslipidemia to have an odds ratio (OR) of 1.63 for ED [40]. A 2016 systematic review totaling 121,641 subjects meanwhile demonstrated that dependent on region, hypertension represented a strong risk factor for ED, with OR of 1.46 in Asia through to OR 3.35 in Africa [41]. ED severity increases with the severity of hypertension [42]. ED occurs 10–15 years earlier in men with diabetes as compared to those without but is more frequent and severe in those with poor glycemic control as well as those with macro and microvascular complications of diabetes [37]. Conversely, considering the risk of comorbidity in men with ED, approximately 40% have hypertension, 42% have dyslipidaemia and 20% have diabetes mellitus [43].

A recent study from the United Kingdom demonstrated that of men identified as having ED, over 70% had at least one chronic health condition [43]. Though age is often listed as a risk factor, its effect is likely mediated by an increased prevalence of chronic conditions and medication use, as evidenced by the considerable number of men who can retain erections into old age [39]. The frequency and severity of ED increases with increasing medical comorbidity. For example, it has been shown that the prevalence of ED was 45% in individuals with a Charlson Comorbidity Index (CCI) score of 0, increasing to 99% when the CCI score is 3 or more [44].

ED is strongly associated with cardiovascular disease [45, 46]. Up to 47% of patients with angiographically proven coronary artery disease complain of ED, with an onset 2–3 years before symptoms of coronary artery disease and 3–5 years before a cardiovascular event (myocardial infarction or stroke) [47]. Individuals with severe ED, without a prior diagnosis of cardiovascular disease, have an increased risk of hospitalization for ischemic heart disease (RR 1.60) and heart failure (RR 8) compared with those without ED [45, 48].

Risk factor and chronic disease mitigation can not only reduce an individual's incipient risk of chronic and incident disease but can also help improve or even induce remission of their ED [49]. This was demonstrated in the instance of obese men who made lifestyle changes resulting in weight loss, with over half experiencing an improvement of erectile function [49]. Low and high level of physical activity result in greater than 20% reductions in erectile dysfunction [37, 50]. The Mediterranean diet is associated with a lower incidence of ED (Hazard ratio (HR) 0.82) [51]. Improved glycemic control with agents such as Metformin, sodium-glucose like transporter 2 (SGLT2) inhibitors and glucagon-like-peptide-1 receptor agonists (GLP1RA) have been associated with improved erectile function, though this effect may be mediated variably by either weight loss or other reductions in overall cardiovascular risk [38]. Treatment of hypercholesterolemia with statins has been associated with small but statistically significant improvements in erectile function [52], and the management of hypertension with angiotensin receptor blockers (ARBs) has also been shown to positively affect erectile function [53]. Lifestyle changes including smoking cessation and abstinence from alcohol improve the prospect of returning to erectile function, with the latter resulting in almost 90% experiencing an improvement within 3 months [54, 55]. Treatment of severe

OSA with continuous positive airway pressure (CPAP) also substantially improves erectile function. The remission of ED was less likely in unemployed men, and those with central obesity, type 2 diabetes or angina [56].

Appropriate care seeking may be limited by health literacy and delivery of care limited by practitioner knowledge and attitude. In a survey of over 1400 men, ED was the fourth most important health issue for men aged over the age of 65 [57]. Data from the Men in Australia Telephone Survey (MATEs) demonstrated that ~50% of men aged 40–49 years and ~25% aged 70 years and over sought medical advice for ED [8]. In a multinational survey of over 30,000 men, 30% of those with ED sought treatment but only half of that group ultimately received treatment [58]. Men are also accessing online direct-to-consumer (DTC) ED medications. Between 2017 and 2019, traffic to DTC websites grew 1688% [59]. This is despite studies showing that this care modality overlooks substantial burdens of comorbidity [60].

Health care practitioners are reluctant to ask about ED due to time constraints, negative attitudes regarding sexual problems, deficits in communication, the perception that older people have less interest in sex and a growing gap between clinical developments in sexual medicine and practitioner knowledge and clinical skills [61, 62].

The attitudes and health literacy of men is also a barrier to seeking treatment for ED. Young men are less likely to seek treatment for ED due to the belief that it may spontaneously resolve, whilst older men may accept it as a natural part of ageing [30, 63]. Failure to seek or receive appropriate care represents a lost opportunity for prevention, diagnosis, and remediation of chronic disease.

Erectile function is important to men, and should be a critical driver for care seeking, to the extent that care is accessible and responsive. Taken together these data suggest that education targeted to men to optimize health literacy related to ED, and to healthcare practitioners encouraging them to routinely ask about erectile function and if present assess for risk factors and early evidence of associated chronic disease, we will reduce significant morbidity and improve overall health and wellbeing in men.

5. Lower urinary tract symptoms as a marker of chronic disease risk

LUTS are grouped as either storage (nocturia, urgency, frequency, urge incontinence) or voiding (poor stream, after-dribble, difficulty initiating) symptoms [64]. The prevalence of all-severity LUTS increases with age, affecting 25% of men in their 50s, rising to ~90% by their 70s [65]. The proportion of men with severe LUTS also increases with age, at least tripling in prevalence from the 5th to the 8th decade [66, 67]. Nocturia, the most common LUTS symptom, affects between 20% and 45% of men aged 20–40 years, increasing to as much as 95% of men older than age 70 years [68]. LUTS frequently occurs concomitantly with ED; 70% of men with LUTS have co-existing ED [69]. A similar proportion of men with ED have LUTS [70]. With an increasing severity of LUTS, the risk of having ED, and particularly severe ED, rises [69, 71]. However, the magnitude of effect of the co-occurrence of

LUTS and ED to predict the risk of chronic disease is unclear [71].

As with ED, many men regard the occurrence of LUTS as an inevitable consequence of increasing age and/or reflective of benign prostatic hyperplasia (BPH). LUTS is not an inevitable consequence of increasing age and frequently reflects the cumulative burden of risk factors for, and presence of, chronic disorders beyond the lower urinary tract [56, 72, 73]. It cannot be assumed that an enlarged prostate is necessarily the cause of LUTS, particularly in the absence of significant voiding symptoms. Not all men who have LUTS have BPH, and not all men with BPH have LUTS. In fact, there is a very weak relationship between prostate size and LUTS [56]. It is hypothesized that cardiometabolic disorders and their risk factors affect the function of the urothelium and smooth muscle of the bladder wall and its continuation in the capsule surrounding the prostate, reducing compliance of the bladder and distensibility of the prostatic urethra resulting in storage and voiding symptoms, respectively [74].

Risk factors and chronic disease associations for LUTS overlap with those ED. Physical inactivity increases LUTS risk (OR 2.06) even in normal weight individuals [75]. Smoking, particularly in young men (OR 2.01) [75, 76] alcohol intake of 4 or more drinks per day (OR 1.15) [77], higher total energy intake, higher sodium and lower protein intake [78] are associated with the occurrence and severity of LUTS.

Proximate chronic disease risk factors associated with LUTS include obesity, insulin resistance, hypertension and dyslipidemia [8, 56]. Obesity, especially with a body mass index (BMI) over 35 kg/m² and central obesity measured by waist circumference predict moderate to severe LUTS (ORs 1.38 and 1.50, respectively) [79, 80]. Following surgery for BPH there is an increased risk of residual overall and storage LUTS in men with a waist circumference over 102 cm (ORs 0.343 and 0.208 respectively) [81]. Hypertension has also been associated with LUTS [8, 79]. The association between hypertriglyceridemia (OR 1.48), and low high-density lipoprotein (HDL) (OR 1.56) and LUTS occurs in the context of metabolic syndrome [79].

Like ED, men with Type 2 Diabetes Mellitus (T2DM) (OR 1.32) [82], cardiovascular disease (CVD) [81], and depression [83] are more likely to have LUTS. LUTS themselves are also predictive of OSA (OR 1.64) [84], incident depression (OR 2.77) [83], T2DM in men under the age of 50 years, cardiovascular disease [81], stroke and cerebral white matter hypodensities which are themselves strongly correlated with stroke risk (RR 2.89) [85]. Men with moderate to severe LUTS have a much higher CVD risk (OR 2.38) compared to men with mild or no LUTS. This association was particularly pronounced in men with a body mass index >30 kg/m² (OR 2.32) [81], but also evident in healthy young men [86], and men with type 2 diabetes [64]. The bidirectional relationship between LUTS and depression has been linked to inflammation [83]. The presence of inflammation appears to be a common factor for a number of conditions associated with LUTS. For example, men with inflammatory bowel disease are 3.5× more likely to have LUTS, particularly if they have active perianal disease or depression [87]. Chronic periodontal disease (CPD) has been associated with urgency and weak stream [88, 89].

Severe LUTS are also associated with mobility or daily activity limitations [51].

Amelioration of the symptoms or occurrence of LUTS may be achieved by management of the risk factors and chronic disorders. For example, increased physical activity [90], weight loss [91], reduction in dyslipidaemia [92], smoking cessation [76] and treatment of OSA with continuous positive airway pressure (CPAP) resolves or substantially improves LUTS and associated quality of life [93].

Despite its prevalence and profound impact on quality of life, in one study less than 10% of men with severe LUTS sought treatment [94]. Even amongst men with moderate-to-severe LUTS, one third have not discussed this with their doctor [95].

From a patient perspective, a lack of health literacy means that the adverse health associations of LUTS may not be understood. Men may consider LUTS to be an inevitable consequence of ageing and may except the symptoms particularly if there is minimal impact on daily functioning or quality of life. Other factors that limit engagement with healthcare for LUTS include embarrassment, and the opportunity cost of seeking care [95, 96]. Men with a high degree of bother from their symptoms particularly if significant nocturia is present have been shown to be the group most likely to seek care. Nocturia is the commonest LUTS symptom, affecting 25.3% of men in the Boston Area Community Health Survey (BACH) [97], though higher proportions have been described in other populations [68]. Nocturia is also the symptom most closely associated with chronic disorders [68] and with higher all cause mortality and cardiovascular death [98]. Therefore, in accordance with the notion of time efficiency and consistent with the data, we propose that a single question relating to nocturia is sufficient. This is highly pertinent given the men most dissatisfied with their symptoms are 27 times more likely to seek care [96]. Failure to link the symptoms to chronic disease and its risk factors, even in the presence of BPH, represents a significant lost opportunity to prevent or reduce the severity of chronic disorders.

6. Conclusions

LUTS and ED are frequent, important to men, often occur together and are good predictors of both prevalent and incident disease and share risk factors with these disorders [69]. Identifying and managing underlying chronic disorders and their risk factors provide an opportunity for the prevention of and early intervention in chronic disorders, as well as amelioration of LUTS and ED symptoms. This is an approach that has considerable potential to reduce the burden of disease and substantially improve the quality of life of men [8, 99, 100]. Men care about the presence of LUTS and ED but tend not to understand the significance of these symptoms and implications for management a problem compounded, by the fact that doctors mostly fail to ask about or adequately address them.

We propose a simple, time efficient, identifiable and inexpensive approach to improving men's health whereby primary health care providers are encouraged to ask about the presence of ED and nocturia and respond accordingly together with targeted public health education as to the significance of ED

and nocturia. This would be optimally facilitated by accessible male friendly and culturally safe care.

ABBREVIATIONS

BACH, Boston area community health survey; BPH, Benign prostatic hyperplasia; CCI, Charlson comorbidity index; CPAP, Continuous positive airway pressure; CPD, Chronic periodontal disease; CVD, Cardiovascular disease; DTC, Direct to consumer; ED, Erectile dysfunction; GLP1RA, GLP-1 receptor agonist; GPs, General practitioners; IIEF-5, International index of erectile function 5; LUTS, Lower urinary tract symptoms; MATeS, Men in Australia telephone survey; MMAS, Massachusetts males ageing study; NCDs, Non-communicable diseases; OSA, Obstructive sleep apnea; SGTL2, Sodium glucose like transporter 2.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

GAW developed the concept; ST—wrote the initial manuscript; DJ, GAW—review and editing. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

None.

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