International Urogynecology Journal
https://doi.org/10.1007/s00192-019-04058-w

REVIEW ARTICLE

Urinary incontinence and cardiovascular disease: a narrative review

Gregor John [1,2]

Received: 14 March 2019 / Accepted: 16 July 2019

Abstract

Introduction and hypothesis Urinary incontinence (UI) has recently been associated with increased mortality. This observation deserves consideration, since UI is a frequent condition. Shared risk with cardiovascular disease and UI could offer part of the explanation.

Methods In this narrative review, we explore the association between UI and some cardiovascular risk factors: obesity, diabetes, high blood pressure, tobacco smoking, alcohol, and caffeine intake. We also review the benefit of cardiovascular risk management on bladder health.

Results Bladder function is affected by many cardiovascular risk factors. They can be protective or detrimental. Obesity, diabetes, and, to a lesser extent, high blood pressure and cigarette smoking have been associated with UI in different settings, precede new onset UI in longitudinal studies, have a dose effect, and have a biologic mechanism linked with UI. Thus, UI could be considered a possible consequence of metabolic syndrome. Furthermore, prevention programs aimed at decreasing weight, quitting smoking, healthy diet, and increasing physical activity have resulted in a decreased incidence, prevalence, and severity of UI.

Conclusions Knowing the association among UI, cardiovascular risk factors, and mortality should encourage UI screening in the population as well as cardiovascular risk factor screening among patients with UI. The secondary benefit for UI could be an important motivator for increasing adherence to cardiovascular prevention programs.

Keywords Cardiovascular risk factor · Mortality · Urinary incontinence

Introduction

Urinary incontinence (UI) is frequent, estimated to affect 423 million individuals worldwide in 2018 [1]. Incontinent patients have a poorer quality of life, lower work productivity, and higher risk of suffering from major depressive disorder [2, 3]. They have a higher risk of being institutionalized and utilize medical services at a higher rate than patients not suffering from UI [4, 5]. Thus, UI has a considerable impact on everyday life and places a burden on caregivers and healthcare systems.

Since 1950, UI has been pointed out as a possible marker of poor outcome and death [6]. Godfarb first observed that in an institutionalized geriatric population, only 3% of the incontinent patients were still alive at the end of the study compared with 25% in the control group. He concluded that UI is one of the indicators of high mortality [6]. This unexpected association has been recently confirmed in two meta-analyses: after a new-onset stroke [7] and in the general population [8]. Although caution must be taken with meta-analyses of observational studies, repeated observation in different settings, a large effect that persists in pool analysis adjusted for confounders, and a dose-response effect (mortality increasing with the severity of UI) support a real association. However, a fundamental point must be resolved: How could urine leakage be associated with death?

Many components of metabolic syndrome may impact the continence mechanism. Gacci et al. found that men with lower urinary tract symptoms (including UI) have 68% higher odds of suffering from major adverse cardiac events [9]. Thus, the apparent high mortality among patients suffering from UI may be concealed by its association with cardiovascular diseases. This hypothesis deserves to be explored since it could potentially impact public health strategies. In this narrative review, we aim at summarizing the available evidence on the association between UI and each cardiovascular risk factor as well as alcohol and caffeine intake. We also review the benefit of cardiovascular risk management on bladder health.

✉ Gregor John
gregor.john@h-ne.ch

[1] Department of Internal Medicine, Hôpital neuchâtelois, Rue de la Maladière 45, 2000 Neuchâtel, Switzerland

[2] Department of Internal Medicine, Geneva University Hospitals (HUG), Gabrielle-Perret-Gentil 4, CH-1205 Geneva, Switzerland

Published online: 26 July 2019

Methods

Studies of interest were searched in MEDLINE, using Medical Subject Headings keywords "urinary incontinence" AND "risk factors" AND "*any individual risk factor*" (smoking, high blood pressure OR hypertension, obesity OR overweight, cholesterol, caffeine, alcohol) without year limitation. To give a general idea of the available evidence, a semiquantitative summary of the number of positive longitudinal and cross-sectional studies was built for each factor. The cross-sectional studies were arbitrarily separated based on the number of included patients (< 1000, 1000–5000, and > 5000 patients). As indirect information, the association between UI and comorbid conditions classically associated with cardiovascular risk factors [heart disease, chronic obstructive pulmonary disease (or cough), stroke, and dementia] was also noted.

Results

Association between cardiovascular risk factors and urinary incontinence

Body weight

Obesity is a universally acknowledged risk factor for UI [urge UI (UUI), stress UI (SUI), and mixed UI (MUI)] (Table 1). Obesity increases abdominal pressure and thus results in supplementary stress on the bladder closure system [10]. Other mechanisms, such as insulin resistance or oxidative stress, may also play a role in impairing the pelvic floor and detrusor muscles by causing vascular damage [11].

Compared with patients with a normal body mass index (BMI < 25), overweight patients (BMI 25–30) are more likely to report UI, and this risk is greatest for obese patients (BMI > 30) [11]. In large population-representative samples (e.g., NHANES [12], Nurses Health Study [13, 14], EPINCONT [15]), obesity increases the odds of suffering from UI by 50% to 350%, and the association persists in analyses that control for potential confounding factors [11].

In prospective studies, patients continent for urine at baseline are at increased risk for developing new-onset UI if they increase their BMI or waist circumference in the follow-up evaluations [10, 16, 17]. Similarly, patients already suffering from UI are more prone to progression of their UI with increasing weight/BMI [10, 16, 17].

Diabetes

Type II diabetes mellitus (DM) has a growing epidemiology that parallels obesity. Many cross-sectional studies in various populations have found high prevalence of UI in diabetic patients (Table 1). Similarly, compared with normal glucose tolerance, pre-diabetic states have been shown to increase the risk of UI [18]. The odds ratio for reporting UI in large sample studies ranges between 1.1 and 2.3 [61, 60]. Furthermore,

Table 1 Semiquantitative summary of published evidence for the association between urinary incontinence (UI) and cardiovascular risk factors, some related comorbid conditions, and alcohol and caffeine consumption

Potential risk factor	Cross-sectional studies			Prospective studies	Total number of published studies and proportion of positive studies (+) *	
	< 1000 pts	1000–5000 pts	> 5000 pts			
Cardiovascular risk factors						
BMI/obesity	++++	++++	+++	+++	> 100	90%(+)
Diabetes	+++	++++	++	++	> 60	75% (+)
Smoking	++	++	++	+	> 50	50% (+)
Hypertension	++	++	+	+	> 20	50% (+)
Associated comorbid conditions						
Heart disease	++	+	+	+	> 20	50% (+)
COPD/cough	+++	+++	++	+	> 30	90% (+)
Stroke	++	++	+	++	> 20	75% (+)
Dementia	++	+	+	+	> 10	100% (+)
Alcohol and caffeine consumption						
Alcohol	+	+	+	+	> 20	50% (+)
Caffeine	+	+	+	+	> 10	50% (+)

The approximate number of positively associated cross-sectional and prospective studies is given for each factor. The total number of available studies in PubMed and the proportion with a positive association (+) is also given. Cross-sectional studies are stratified by study size. +: 1–5 publications; ++: 5–10 publications; +++: 10–20 publications; ++++: > 20 publications where the factor is associated with UI. The number of studies may include more than one publication on the individual cohort

BMI: body mass index; COPD: chronic obstructive pulmonary disease; pts.: patients; UI: urinary incontinence

incontinent diabetic patients have more frequent and heavy episodes of urine leakage compared with incontinent patients without DM [19–21].

Compared with non-diabetic patients, continent diabetic patients have a higher incidence of new onset UI over time (mostly UUI) [10, 14]. A new diagnosis of DM in the follow-up interval is associated with a 50% increased hazard of suffering from new weekly or daily incontinence [10]. In a large prospective study, gestational diabetes increased the risk of suffering from all types of post-partum UI (particularly UUI and MUI) [22].

Diabetic cystopathy affects up to 40–80% of diabetic patients and results from alteration of the detrusor muscle microarchitecture and function, secondary to microvascular damage [23]. With long-standing DM, autonomic neuropathy impairs bladder function. In addition, recurrent urinary tract infection and osmotic diuresis induced by hyperglycemia may result in urinary symptoms and UI. UUI and overactive bladder are the clinical expression of these mechanisms. Gestational diabetes increases SUI risk by increasing both the maternal risk of complications and weight of the fetus.

High blood pressure

The association between high blood pressure (HBP) and urinary incontinence is less well established than that between UI and DM or obesity (Table 1). The odds of having UI are increased by up to 50% for patients with HBP, but higher unadjusted effects have been published, for example, in a population-based survey in Taiwan (OR: 1.8; CI: 1.5–2.3) [24]. The effect persists after adjustment for many confounders [25].

In a large British population-representative cohort at the age of 68 years, HBP assessed 4 to 8 years before increased the prevalence of UUI at age 68, and the association persisted after adjusting for sex, SUI, and previous stroke [26]. However, the statistical significance was lost after adjusting for other vascular risk factors (DM, smoking). Baseline HBP increased the odds of suffering from new-onset UUI in the Nurses Health Study [10] and, for pregnant women, of suffering from postpartum incontinence [22]. No studies explored a dose-response effect for blood pressure.

Smoking and high blood cholesterol

The association between tobacco smoking and urinary incontinence is very weak (Table 1). According to cross-sectional studies, tobacco could have a large impact on UI prevalence [27], play no role [28], or even have a protective effect [10]. Smoking at baseline was not associated with incident UI in most longitudinal studies, except in three small studies [29–31]. However, in the EPINCONT study [15], the authors found a dose-response effect when comparing heavy (> 20 cigarettes per day) other smokers (< 20 cigarettes per day). The effect on the prevalence of UI (SUI, UUI, and MUI) was seen among current and former smokers, but was more evident for severe UI, and was independent of potential confounding factors (age, parity, coughing, or dyspnea). The increased risk for former smokers compared with never smokers, also seen in the Nurses Health Study II, could highlight a remaining effect after quitting smoking or could be explained by the fact that incontinent patients are more prone to quit smoking [14, 15].

Blood pressure and smoking impact the lower urinary system by altering the vascular/microvascular supply to the bladder and pelvic muscle. HBP has been associated with some bladder receptor dysfunction [32]. Tobacco has an anti-estrogenic effect and impairs collagen synthesis [33]. Smoking can also increase abdominal pressure secondary to pulmonary-related disease and/or coughing (Table 1). Blood lipids have not been extensively studied, but may play a role in prostatic inflammation resulting in hyperplasia and urologic symptoms [9].

Alcohol consumption

Alcohol is a diuretic and might increase detrusor instability. Earlier in vivo and in vitro animal studies in rats showed that ethanol impairs detrusor contractility with a dose-dependant effect [34]. However, another animal study found decreased oxidative stress among diabetic rats exposed to moderate alcohol consumption [35] and ethanol-mediated relaxation of smooth muscle of the bladder that adapts to alcohol-induced diuresis [36]. Thus, alcohol could have beneficial and detrimental effects on the bladder.

The association between alcohol consumption and UI is unsolved. A rapid search of the scientific literature reveals equivalent numbers of studies with and without an effect of alcohol on UI (Table 1). In the LookAHEAD study, the OR of any UI increased by 1.06 (CI: 1.00–1.12; $p < 0.05$) for any increase in the number of drinks per week in adjusted analysis [37]. Kincade et al. found greater urine loss for those participants who drink alcohol [38]. Nevertheless, the association between UI and alcohol consumption was lost after adjusting for confounders in other studies [39]. Furthermore, a protective effect of moderate alcohol drinking was seen in a small cross-sectional study among men [40]. Similarly, results from Bortolotti et al. suggest an unadjusted trend of decreasing prevalence of UI with an increasing number of alcoholic drinks per week and for a large range of alcoholic consumption, but the tests did not reach the statistical threshold [41].

In a longitudinal study, alcohol consumption was associated with a decreased likelihood of resolving UI [17]. Alcohol consumption at baseline was associated with post partum UI for pregnant women, but the association disappeared in adjusted analysis [42].

Alcohol has a J-shaped association with mortality; 1–2 drinks per day has the greatest impact on reduction of cardiovascular and all-cause mortality, but higher intake increases the risk of death [43]. The risk of dying for patients suffering from alcohol use disorders is three- to fourfold that of the general population [44].

Caffeine consumption

Caffeine has diuretic properties, and low doses can cause transient contraction of the detrusor muscle, which might favor UI episodes [45]. A few cross-sectional and three prospective studies explored the association between caffeine consumption and UI (Table 1). Consumption of two daily cups of coffee or more (250 mg per day) is associated with an increased risk of suffering from moderate to severe UI [28]. In the large prospective NHS II, among 65,176 women continent for urine, the risk of developing UI was only seen when comparing women with the highest (450 mg) to the women with the lowest consumption of caffeine [46]. The association was obvious for UUI, but not for SUI or MUI. The quantity of caffeine drunk correlates with the volume of urine loss and the number of episodes of leakage [38]. However, the evidence is sparse, and studies show conflicting results. Caffeine could even have a protective effect on UI [47].

In a dose-response meta-analysis of prospective studies, the association between mortality and caffeine consumption had a non-linear association. Consumption of three cups per day offered the largest risk reduction for cardiovascular mortality (21%, CI: 16–26%) [48].

How management of cardiovascular risk factors impacts bladder health

Isolated intervention

Weight loss has a protective effect on the risk of developing UI [49]. A decrease in BMI (≥ 5%) over a 3-year period is associated with a lower risk of persistent or new SUI [50]. Furthermore, weight loss can improve symptoms for patients suffering from UI. In a meta-analysis of randomized studies of UI in obese or overweight patients, the intervention group (weight loss) achieved a greater proportion of cure or improvement [45]. However, considering the cure rate alone, the analysis did not reach the statistical threshold. In one study among obese patients, bariatric surgery resulted in an effective weight loss at 1 year and a dramatic decrease in UI prevalence for women (49.3% before and 18.3% after surgery) and men (21.8% before and 9.8% after surgery) [51]. The differences were still significant after 3 years.

Tight control of glycemia might prevent incident UI by its beneficial impact on microvascular and neurologic complications of diabetes [52]. In a prospective study of women with type I DM, in a multivariable logistic regression adjusted for age, BMI, daily insulin dose, parity, hysterectomy, autonomic neuropathy, and infection, long-term poor glycemic control was associated with an increased risk of UI (OR: 1.03; CI: 1.01–1.06) per mmol/mol increase in HbA1c) [52]. For type II DM, the beneficial effect of tight glycemic control is less evident, possibly blurred by the frequent comorbid conditions that influence the risk of UI (obesity, HBP, etc.). Links between HbA1c and UI were suspected in small cross-sectional studies [53]. However, many larger and prospective reports failed to highlight any single biochemical determinant of diabetes that could be clearly associated with the risk of UI (duration of DM, drugs used, HbA1c) [21, 54]. In the National Health and Nutrition Examination Survey (NHANES), among women with intermediate-range HbA1c (HbA1c 6.5–8.5%) and after adjusting for age and BMI, each 1% increase in HbA1c was associated with a 13% increase in the risk of any incontinence (CI: 1.03–1.25) and a 34% (CI: 1.06–1.69) increase in the risk of stress incontinence [18]. This was not found for poorly controlled diabetes (HbA1c > 8.5%). In a second analysis of the same population, biochemical markers of type II DM, plasma glucose, and HbA1c were all associated with SUI and UUI [12]. However, the association was confounded by BMI and was not statistically significant after adjustment. Nevertheless, diabetic neuropathy is a microvascular complication dependent on tight glycemic control, and macrovascular complications have all been associated with UI [20, 55, 56].

There is no trial of smoking cessation that focuses on the effect on UI. However, past smokers have a persistent risk of suffering from UI. In some studies, the prevalence is equal to or even higher than that of current smokers. Therefore, it seems unlikely that intervention on cigarette smoking could have a significant impact on UI treatment/prevention in the short term. Nevertheless, a persistent and higher prevalence of UI patients in the past smoker group may indicate that incontinent patients are more prone to quit smoking. Furthermore, cough and cigarette-related heart or pulmonary disease increases UI risk and could be prevented by quitting smoking.

Three studies assessed the effect of caffeine intake reduction on UI, and all showed no statistically significant changes in the number of UI episodes [45]. No studies to date have explored an intervention to reduce alcoholic beverage intake with a focus on UI as an outcome.

Integrated intervention

In a randomized controlled study of prediabetic obese women, intensive lifestyle modification (healthy diet, increased exercise, quitting smoking, losing weight) resulted in a lower risk of suffering from any UI compared with the metformin treatment group or the placebo group [49]. The number needed to treat was 12 to prevent one SUI over 3 years and 20 to prevent

one UUI. Weight loss, increased exercise, and less incident diabetes explained 35% of the effect, which was mostly driven by decreased BMI [49].

In a randomized controlled study of diabetic obese men, intensive lifestyle modification (aimed at losing weight, healthy, low calorie diet, and increased exercise) resulted in a lower risk of suffering from any UI compared with the support and education alone group [57]. After 1 year, the prevalence of UI in the intervention group dropped from 11.3% to 9.0%. Compared with controls, UI participants in the intervention group had a greater chance of resolving their UI (OR: 1.9; CI: 1.0–3.6).

Finally, for 380 older men continent for urine, self-identified as sedentary, and enrolled in a physical activity trial, the increase in physical performance was independently associated with a lower risk of incident UI at 1 year [29].

Discussion

Bladder function is affected by cardiovascular risk and lifestyle. These factors can be protective or can precipitate/exacerbate bladder conditions. Obesity, diabetes, and, to a lesser extent, HBP and cigarette smoking have been associated with UI in different settings (constituency), precede new onset UI in longitudinal studies (temporality), have a dose effect (biologic gradient), and have a biologic mechanism linked with UI (plausibility), facts arguing for causality [58]. Thus, UI should be considered a possible consequence of metabolic syndrome, as obstructive sleep apnea and polycystic ovary syndrome are.

In the previously mentioned meta-analysis, pooled analysis of models adjusting for cardiovascular factors revealed a persistent but attenuated effect of UI on mortality. Although this could translate into the presence of other potential hypotheses linking UI and death, under-adjustment is plausible. A prospective study should account for a dose effect between some factors and the risk of UI and between the factors and mortality (e.g., BMI, HbA1c, smoking, alcohol consumption).

Knowing the link among UI, cardiovascular disease, and death could have three potential public health benefits. First, cardiovascular risk screening and risk management should be offered to all UI patients. In many instances, intervention for bladder health (weight loss programs, exercise) will also result in an indirect decrease in mortality. Second, UI is a frequently overlooked condition. Health providers recognize limited competence, and few are aware of the possible dramatic consequences of UI. Patients are reluctant to talk about UI. Dedicated information centered on UI's unfavorable outcomes that parallel cardiovascular disease would help patients recognize UI as a health problem that needs to be solved and might change priorities for care providers. Finally, prevention programs aimed at decreasing weight, quitting smoking, healthy diet, and increasing physical activity have all resulted in a decreased incidence, prevalence, and severity of UI. Such an impact on bladder health will certainly add to motivation of patients to adhere to "unpopular" lifestyle modification programs (mainstay of cardiovascular preventive medicine). Indeed, aiming at a possible control of urinary leaks is probably easier to appreciate for patients than aiming at a controlled blood pressure or lipid profile (although it has important health issues). Besides, patients with UI have been shown to better benefit from some interventions to prevent important health burdens, like in the case of the fall prevention program [59].

This article has many limitations. First, although it tried to give a realistic picture of the available evidence to link cardiovascular factors and UI, this work is not a systematic review. It explored only one database, without strict criteria for data extraction or study quality rating. Second, most studies included in this review used a cross-sectional design, where the sequential relationship between the supposed risks factor and UI cannot be made, and thus can only suggest a possible association. Furthermore, studies generally included mostly women. Thus, an association between risk factors and UI in men is less well established. Finally, some studies explored only risk factors for a specific subtype of UI: urge UI (UUI), stress UI (SUI), or mixed UI (MUI). Furthermore, the definition used varied across studies.

The observation of a higher cardiovascular disease and mortality risk among patients with UI should raise awareness among patients and care providers in order to better identify urinary complaints and offer treatment.

Acknowledgements I gratefully acknowledge Simone Madigan for her correction of the English manuscript.

Compliance with ethical standards

Conflicts of interest None.

References

1. Irwin DE, Kopp ZS, Agatep B, Milsom I, Abrams P. Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. BJU Int. 2011;108:1132–8.
2. Sexton CC, Coyne KS, Vats V, Kopp ZS, Irwin DE, Wagner TH. Impact of overactive bladder on work productivity in the United States: results from EpiLUTS. Am J Manag Care. 2009;15:S98–S107.
3. Abrams P, Kelleher CJ, Kerr LA, Rogers RG. Overactive bladder significantly affects quality of life. Am J Manag Care. 2000;6:S580–90.
4. Luppa M, Luck T, Weyerer S, Konig HH, Brahler E, Riedel-Heller SG. Prediction of institutionalization in the elderly. A systematic review. Age Ageing. 2010;39:31–8.

5. Yang E, Lisha NE, Walter L, Obedin-Maliver J, Huang AJ. Urinary incontinence in a national cohort of older women: implications for caregiving and care dependence. J Women's Health (Larchmt). 2018;27:1097–103.
6. Goldfarb AI. Predicting mortality in the institutionalized aged: A seven-year follow-up. Arch Gen Psychiatry. 1969;21:172–6.
7. John G, Bardini C, Megevand P, Combescure C, Dallenbach P. Urinary incontinence as a predictor of death after new-onset stroke: a meta-analysis. Eur J Neurol. 2016;23:1548–55.
8. John G, Bardini C, Combescure C, Dallenbach P. Urinary incontinence as a predictor of death: a systematic review and meta-analysis. PLoS One. 2016. https://doi.org/10.1371/journal.pone.0158992 **eCollection 2016**.
9. Gacci M, Corona G, Sebastianelli A, Serni S, De Nunzio C, Maggi M, et al. Male lower urinary tract symptoms and cardiovascular events: a systematic review and meta-analysis. Eur Urol. 2016;70:788–96.
10. Waetjen LE, Ye J, Feng WY, Johnson WO, Greendale GA, Sampselle CM, et al. Association between menopausal transition stages and developing urinary incontinence. Obstet Gynecol. 2009;114(5):989–98.
11. Khullar V, Sexton CC, Thompson CL, Milsom I, Bitoun CE, Coyne KS. The relationship between BMI and urinary incontinence subgroups: results from EpiLUTS. Neurourol Urodyn. 2014;33:392–9.
12. Weinberg AE, Leppert JT, Elliott CS. Biochemical measures of diabetes are not independent predictors of urinary incontinence in women. J Urol. 2015;194(6):1668–74.
13. Matthews CA, Whitehead WE, Townsend MK, Grodstein F. Risk factors for urinary, fecal, or dual incontinence in the Nurses' Health Study. Obstet Gynecol. 2013;122:539–45.
14. Danforth KN, Townsend MK, Lifford K, Curhan GC, Resnick NM, Grodstein F. Risk factors for urinary incontinence among middle-aged women. Am J Obstet Gynecol. 2006;194:339–45.
15. Hannestad YS, Rortveit G, Daltveit AK, Hunskaar S. Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. BJOG. 2003;110:247–54.
16. Thom DH, Haan MN, Van Den Eeden SK. Medically recognized urinary incontinence and risks of hospitalization, nursing home admission and mortality. Age Ageing. 1997;26:367–74.
17. Maserejian NN, Minassian VA, Chen S, Hall SA, McKinlay JB, Tennstedt SL. Treatment status and risk factors for incidence and persistence of urinary incontinence in women. Int Urogynecol J. 2014;25:775–82.
18. Wang R, Lefevre R, Hacker MR, Golen TH. Diabetes, glycemic control, and urinary incontinence in women. Female Pelvic Med Reconstr Surg. 2015;21:293–7.
19. Doshi AM, Van Den Eeden SK, Morrill MY, Schembri M, Thom DH, Brown JS. Women with diabetes: understanding urinary incontinence and help seeking behavior. J Urol. 2010;184:1402–7.
20. Devore EE, Townsend MK, Resnick NM, Grodstein F. The epidemiology of urinary incontinence in women with type 2 diabetes. J Urol. 2012;188:1816–21.
21. Lee SJ, Karter AJ, Thai JN, Van Den Eeden SK, Huang ES. Glycemic control and urinary incontinence in women with diabetes mellitus. J Women's Health (Larchmt). 2013;22:1049–55.
22. Chuang CM, Lin IF, Horng HC, Hsiao YH, Shyu IL, Chou P. The impact of gestational diabetes mellitus on postpartum urinary incontinence: a longitudinal cohort study on singleton pregnancies. BJOG. 2012;119:1334–43.
23. Abdel-Fattah M, Rizk DE. Diabetes mellitus and female urinary incontinence: a time for change. Int Urogynecol J. 2012;23:1481–2.
24. Chang KM, Hsieh CH, Chiang HS, Lee TS. Risk factors for urinary incontinence among women aged 60 or over with hypertension in Taiwan. Taiwan J Obstet Gynecol. 2014;53:183–6.
25. Townsend MK, Lajous M, Medina-Campos RH, Catzin-Kuhlmann A, Lopez-Ridaura R, Rice MS. Risk factors for urinary incontinence among postmenopausal Mexican women. Int Urogynecol J. 2017;28:769–76.
26. Tsui A, Kuh D, Cardozo L, Davis D. Vascular risk factors for male and female urgency urinary incontinence at age 68 years from a British birth cohort study. BJU Int. 2018. https://doi.org/10.1111/bju.14137.
27. Van Oyen H, Van Oyen P. Urinary incontinence in Belgium; prevalence, correlates and psychosocial consequences. Acta Clin Belg. 2002;57:207–18.
28. Davis NJ, Vaughan CP, Johnson TM 2nd, Goode PS, Burgio KL, Redden DT, et al. Caffeine intake and its association with urinary incontinence in United States men: results from National Health and Nutrition Examination Surveys 2005-2006 and 2007-2008. J Urol. 2013;189:2170–4.
29. Morrisroe SN, Rodriguez LV, Wang PC, Smith AL, Trejo L, Sarkisian CA. Correlates of 1-year incidence of urinary incontinence in older Latino adults enrolled in a community-based physical activity trial. J Am Geriatr Soc. 2014;62:740–6.
30. Kim H, Yoshida H, Hu X, Yukawa H, Shinkai S, Kumagai S, et al. Risk factors associated with onset of urinary incontinence in a community-dwelling elderly population: a 4-year follow-up study. Nihon Koshu Eisei Zasshi. 2004;51:612–22.
31. Miller YD, Brown WJ, Russell A, Chiarelli P. Urinary incontinence across the lifespan. Neurourol Urodyn. 2003;22:550–7.
32. Frazier EP, Schneider T, Michel MC. Effects of gender, age and hypertension on beta-adrenergic receptor function in rat urinary bladder. Naunyn Schmiedeberg's Arch Pharmacol. 2006;373:300–9.
33. Bump RC, McClish DK. Cigarette smoking and urinary incontinence in women. Am J Obstet Gynecol. 1992;167:1213–8.
34. Yokoi K, Ohmura M, Kondo A, Miyake K, Saito M. Effects of ethanol on in vivo cystometry and in vitro whole bladder contractility in the rat. J Urol. 1996;156:1489–91.
35. Bae WJ, Choi YS, Kim SJ, Cho HJ, Hong SH, Kim SW, et al. Effects of moderate alcohol intake in the bladder of the Otsuka Long Evans Tokushima Fatty diabetic rats. J Korean Med Sci. 2015;30:1313–20.
36. Malysz J, Afeli SA, Provence A, Petkov GV. Ethanol-mediated relaxation of guinea pig urinary bladder smooth muscle: involvement of BK and L-type Ca2+ channels. Am J Phys Cell Phys. 2014;306:C45–58.
37. Phelan S, Kanaya AM, Subak LL, Hogan PE, Espeland MA, Wing RR, et al. Prevalence and risk factors for urinary incontinence in overweight and obese diabetic women: action for health in diabetes (look ahead) study. Diabetes Care. 2009;32:1391–7.
38. Kincade JE, Dougherty MC, Carlson JR, Wells EC, Hunter GS, Busby-Whitehead J. Factors related to urinary incontinence in community-dwelling women. Urol Nurs. 2007;27:307–17.
39. 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;87:715–21.
40. Lee AH, Hirayama F. Is alcohol consumption associated with male urinary incontinence? Low Urin Tract Symptoms. 2011;3:19–24.
41. Bortolotti A, Bernardini B, Colli E, Di Benedetto P, Giocoli Nacci G, Landoni M, et al. Prevalence and risk factors for urinary incontinence in Italy. Eur Urol. 2000;37:30–5.
42. Zhu L, Li L, Lang JH, Xu T. Prevalence and risk factors for peri- and postpartum urinary incontinence in primiparous women in China: a prospective longitudinal study. Int Urogynecol J. 2012;23:563–72.
43. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular

disease outcomes: a systematic review and meta-analysis. BMJ. 2011;342:d671.
44. Roerecke M, Rehm J. Alcohol use disorders and mortality: a systematic review and meta-analysis. Addiction. 2013;108:1562–78.
45. Imamura M, Williams K, Wells M, McGrother C. Lifestyle interventions for the treatment of urinary incontinence in adults. Cochrane Database Syst Rev. 2015. https://doi.org/10.1002/14651858.CD003505.pub5.
46. Jura YH, Townsend MK, Curhan GC, Resnick NM, Grodstein F. Caffeine intake, and the risk of stress, urgency and mixed urinary incontinence. J Urol. 2011;185:1775–80.
47. Tettamanti G, Altman D, Pedersen NL, Bellocco R, Milsom I, Iliadou AN. Effects of coffee and tea consumption on urinary incontinence in female twins. BJOG. 2011;118:806–13.
48. Crippa A, Discacciati A, Larsson SC, Wolk A, Orsini N. Coffee consumption and mortality from all causes, cardiovascular disease, and cancer: a dose-response meta-analysis. Am J Epidemiol. 2014;180:763–75.
49. Brown JS, Wing R, Barrett-Connor E, Nyberg LM, Kusek JW, Orchard TJ, et al. Lifestyle intervention is associated with lower prevalence of urinary incontinence: the Diabetes Prevention Program. Diabetes Care. 2006;29:385–90.
50. Suskind AM, Cawthon PM, Nakagawa S, Subak LL, Reinders I, Satterfield S, et al. Urinary incontinence in older women: the role of body composition and muscle strength: from the Health, Aging, and Body Composition Study. J Am Geriatr Soc. 2017;65:42–50.
51. Subak LL, King WC, Belle SH, Chen JY, Courcoulas AP, Ebel FE, et al. Urinary incontinence before and after bariatric surgery. JAMA Intern Med. 2015;175:1378–87.
52. Lenherr SM, Clemens JQ, Braffett BH, Dunn RL, Cleary PA, Kim C, et al. Glycaemic control and risk of incident urinary incontinence in women with type 1 diabetes: results from the Diabetes Control and Complications Trial and Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study. Diabet Med. 2016;33:1528–35.
53. Chiu AF, Huang MH, Wang CC, Kuo HC. Higher glycosylated hemoglobin levels increase the risk of overactive bladder syndrome in patients with type 2 diabetes mellitus. Int J Urol. 2012;19:995–1001.
54. Ebbesen MH, Hunskaar S, Rortveit G, Hannestad YS. Prevalence, incidence and remission of urinary incontinence in women: longitudinal data from the Norwegian HUNT study (EPINCONT). BMC Urol. 2013;13:27.
55. Jackson SL, Scholes D, Boyko EJ, Abraham L, Fihn SD. Predictors of urinary incontinence in a prospective cohort of postmenopausal women. Obstet Gynecol. 2006;108:855–62.
56. Ebbesen MH, Hannestad YS, Midthjell K, Hunskaar S. Diabetes related risk factors did not explain the increased risk for urinary incontinence among women with diabetes: The Norwegian HUNT/EPINCONT study. BMC Urol. 2009;9:11.
57. Breyer BN, Phelan S, Hogan PE, Rosen RC, Kitabchi AE, Wing RR, et al. Intensive lifestyle intervention reduces urinary incontinence in overweight/obese men with type 2 diabetes: results from the Look AHEAD trial. J Urol. 2014;192:144–9.
58. Hill AB. The environment and disease: association or causation? Proc R Soc Med. 1965;58:295–300.
59. Rapp K, Lamb SE, Buchele G, Lall R, Lindemann U, Becker C. Prevention of falls in nursing homes: subgroup analyses of a randomized fall prevention trial. J Am Geriatr Soc. 2008;56:1092–7.
60. Chiarelli P, Brown W, McElduff P. Leaking urine: prevalence and associated factors in Australian women. Neurourol Urodyn. 1999;18:567–77.
61. Lewis CM, Schrader R, Many A, Mackay M, Rogers RG. Diabetes and urinary incontinence in 50- to 90-year-old women: a cross-sectional population-based study. Am J Obstet Gynecol. 2005;193:2154–8.