The impact of urinary incontinence on multiple health outcomes:

Review

The impact of urinary incontinence on multiple health outcomes: an umbrella review of meta-analysis of observational studies

Running Title: Urinary Incontinence and Health Outcome

Pinar Soysal[1]*, Nicola Veronese[2]*, Simona Ippoliti[3]*, Damiano Pizzol[4]*, Anne Marie Carrie[3], Simina Stefanescu[3], Guillermo F. López-Sánchez[5], Yvonne Barnett[6], Laurie Butler[6], Ai Koyanagi[7], Louis Jacob[8], Ramy Abou Ghaydya[9,10], David Sheyn[9,10], Adonis K Hijaz[9,10], Jose M Oliva-Lozano[11], Jose M Muyor[11], Mike Trott[12], Andreas Kronbichler[13], Igor Grabovac[14], Mark Tully[15], Lin Yang[16], Jimin Hwang[17], Jong Yeob Kim[18], Seoyeon Park[18], Junmin Song[19], Jae Il Shin[20], Petre-Cristian Ilie[3±], Lee Smith[11±]

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*Authors contributed equally

[±]Senior authors

1. Department of Geriatric Medicine, Faculty of Medicine, Bezmialem Vakif University, Adnan Menderes Bulvarı (Vatan Street), 34093 Fatih, İstanbul, Turkey.
2. Department of Internal Medicine, University of Palermo, Geriatrics Section, Palermo, Italy.
3. The Queen Elizabeth Hospital Foundation Trust, King's Lynn, United Kingdom.
4. Italian Agency for Development Cooperation, 33 Street, Amarat, Khartoum 79371, Sudan
5. Vision and Eye Research Institute, School of Medicine, Faculty of Health, Education, Medicine and Social Care, Anglia Ruskin University, Cambridge, United Kingdom.
6. Faculty of Science and Engineering, Anglia Ruskin University, Cambridge, UK, CB1 1PT
7. Research and Development Unit, Parc Sanitari Sant Joan de Déu, CIBERSAM, 08830, Barcelona, Spain; ICREA, Pg. Lluis Companys 23, 08010, Barcelona, Spain.

8. Faculty of Medicine, University of Versailles Saint-Quentin-en-Yvelines, 78180 Montigny-le-Bretonneux, France.
9. Department of Urology, University Hospitals Cleveland Medical Center, 11000 Euclid Avenue, Cleveland, OH, USA
10. Case Western Reserve University School of Medicine, Cleveland, OH, USA
11. Health Research Centre, University of Almeria, Almeria, Spain.
12. The Cambridge, Centre for Sport and Exercise Sciences, Anglia Ruskin University, Cambridge, UK, CB1 1PT
13. Department of Internal Medicine IV, Medical University Innsbruck, Innsbruck, Austria.
14. Department of Social and Preventive Medicine, Centre for Public Health, Medical University of Vienna,1090 Wien, Austria
15. Institute of Mental Health Sciences, School of Health Sciences, Ulster University, Newtown Abbey BT37 0QB, UK
16. Department of Cancer Epidemiology and Prevention Research, Cancer Control Alberta, Alberta Health Services, Calgary, Canada
17. Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
18. Yonsei University College of Medicine, Seoul, Republic of Korea
19. Keimyung University School of Medicine, Daegu, Republic of Korea
20. Department of Pediatrics, Yonsei University College of Medicine, Seoul, Republic of Korea

Corresponding author:

Professor Jae Il Shin, Department of Pediatrics, Yonsei University College of Medicine, Seoul 03722, Korea. (telephone: 82-2-2228-2050; FAX: 82-2-393-9118; email: SHINJI@yuhs.ac)

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Abstract

Background & Aim: We aimed to capture the breadth of health outcomes that have been associated with the presence of Urinary Incontinence (UI) and systematically assess the quality, strength, and credibility of these associations through an umbrella review and integrated meta-analyses.

Methods: We assessed meta-analyses of observational studies based on random-effect summary effect sizes and their p-values, 95% prediction intervals, heterogeneity, small-study effects, and excess significance. We graded the evidence from convincing (Class I) to weak (Class IV).

Results & Discussion: From 3172 articles returned in search of the literature, 9 systematic reviews were included with a total of 41 outcomes. Overall, 37 out of the 41 outcomes reported nominally significant summary results ($p < 0.05$), with 22 associations surviving the application of a more stringent p-value ($p < 10^{-6}$). UI was associated with worse scores than controls in female sexual function (Class II), while it was also associated with a higher prevalence of depression (odds ratio [OR]=1.815; 95% confidence interval [CI]: 1.551-2.124), and anxiety (OR=1.498; 95%CI: 1.273-1.762) (Class IV). UI was associated with poorer quality of life (QoL), higher rate of mortality (hazard ratio=2.392; 95%CI: 2.053-2.787) an increase in falls, frailty, pressure ulcers, diabetes, arthritis, and fecal incontinence (Class IV).

Conclusions: UI is associated with female sexual dysfunction, with highly suggestive evidence. However, the evidence of other adverse outcomes including depression, anxiety, poorer QoL, higher mortality, falls, pressure ulcers, diabetes, arthritis, fecal incontinence, and frailty is only weak. A multidimensional approach should be taken in managing UI in the clinical setting.

Keywords: Urinary Incontinence, Health Outcomes, Umbrella Review, Meta-analysis

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INTRODUCTION

The International Association of Urinary Incontinence (ICS) defines urinary incontinence (UI) as complaints of involuntary leakage of urine, which is recognized by the World Health Organization as an important health problem with significant social and economic burden[1, 2]. UI can be observed and may cause negative clinical consequences at any age[3, 4]. Regardless of the UI type, the prevalence among females is 17.6% between the ages of 20-39 years, 27.9% among females aged 20-49 years, while it is present in almost one out of every two females aged over 60 years[3]. Among males, UI is extremely rare before the age of 65 years; however, its prevalence is 15% among those aged 65 years and over and 25% among those aged 80 years and over[5]. Therefore, UI affects millions of people around the world, and it is important to determine what complications it can cause.

For many years, there have been an increasing number of studies investigating the mental and physical effects of UI on people of both sexes, different age groups, and in different physiologic states, such as pregnant women or institutionalized geriatric patients[6, 7]. According to their results, patients with UI have a lower quality of life (QoL), lower labor productivity, poorer sexual function, and higher risk of major depressive disorder and social isolation[8]. Especially in older adults, the risks of major adverse events are high, including falls and fractures, skin infections, functional impairment, caregiver burden, institutionalization, and mortality[9-15]. Considering both the indirect costs associated with these complications and the health expenditure required for the diagnosis and treatment of UI, the annual cost-of-illness for UI in European populations was calculated as €7 billion; in the United States, UI was estimated to cost $82.6 billion in 2020[16, 17]. These studies, published with increasing frequency, resulted in the publication of systematic reviews with meta-analyses. However, to date, most systematic reviews have focused on a single disease endpoint, and no systematic evaluation of the relationships between UI and various physical and mental health outcomes has been carried

out. A better understanding of the full spectrum of health risks associated with UI is important for clinical practice.

Therefore, this study was designed to capture the breadth of results shown in observational studies regarding UI and to systematically evaluate the quality, strength, and reliability of these relationships. We used an umbrella review with integrated meta-analyses to combine evidence from a wide range of outcomes and populations.

METHODS

This umbrella review followed a pre-planned but unpublished protocol available upon request to the corresponding author. This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) indications for reporting findings of systematic reviews and meta-analyses[18].

Data sources and searches

We conducted an umbrella review[19], searching the MEDLINE, Scopus, Embase databases, Cochrane library, CINAHL and PSYCINFO from inception until 20th July 2022 with: "(Meta-Analysis[ptyp] OR metaanaly*[tiab] OR meta-analy*[tiab] OR Systematic review [ptyp] OR "systematic review" [tiab]) AND ("urin* incontinence"[tiab] OR "bladder incontinence"[tiab] OR "urin* leakage"[tiab] OR "urine bladder incontinence"[tiab] OR "urine leakage"[tiab] OR wetting [tiab] OR incontinence)[tiab]. In addition, we hand-searched the reference lists of eligible5 articles.

Study selection

In this umbrella review, we included: (1) systematic reviews with meta-analyses that included people with UI; (2) meta-analyses of observational studies (longitudinal or case-control) that investigated the association of UI with any health-related outcome (e.g., QoL, falls, depression, mortality). Two authors (PS, LS) independently performed title and abstract screening. Disagreements were resolved through consensus with another independent author (DP). Full texts of all potentially eligible articles were then retrieved by the same three authors and any disagreement was resolved with another independent author (NV).

Data extraction

Two independent investigators (SI, MT) extracted the following information for each meta-analysis independently: first author name; publication year; the number of studies; study population; type of effect size; study design; the number of participants with (cases) and without (controls) events for each study. We also extracted the study-specific estimated relative risk for health outcomes (risk ratio, RR; odds ratio OR; hazard ratio, HR; mean difference, WMD; standardized mean difference, SMD) and 95% confidence intervals (CIs). We finally extracted the data for the Assessment of Multiple Systematic Reviews (AMSTAR)-2 tool[20]. When more than one meta-analysis on the same research question using the same study design was identified, the one with the largest number of participants was selected.

Data synthesis and analysis

For each meta-analysis, we estimated the summary effect size and its 95% CI by using a random-effects model based on the DerSirmonian-Leird method[21]. We also estimated the prediction intervals (PIs) and its 95% CI, which further accounts for between-study effects and estimates the certainty of the association if a new study may address the same association[22-

24]. Between-study inconsistency was estimated with the I^2 metric, with values $\geq$ 50% indicative of heterogeneity and values between 50-75% of moderate heterogeneity and $\geq$ 75% of high heterogeneity[25]. Then, we calculated the evidence of small-study effects (i.e. whether small studies inflated effect sizes) using the regression asymmetry test with a p-value < 0.10 being indicative of this potential bias[26].

Finally, we applied the excess of significance test (Ioannidis' test)[27]. Because of the limited statistical power of this test, a lenient significance threshold (p < 0.10) was adopted[28]. We considered the effect size of the largest study for each outcome, and based on this, we estimated the power of each constituent study with an algorithm using a non-central *t* distribution. Excess significance for each meta-analysis was considered whenever p < 0.10. All statistical analyses were conducted using Stata, version 14.0 (StataCorp).

Grading the evidence

For observational studies, using the criteria mentioned above, significant associations (i.e. p<0.05) were categorized into convincing, highly suggestive, suggestive, or weak evidence (class I to IV), following a grading scheme that has already been applied in various fields, as reported in Supplementary Table S2 [29-32]. According to credibility assessment criteria for meta-analyses of observational studies, the level of evidence was determined as follows: **Convincing (class I):** High significant association; large sample size, having the event of interest; the largest component study reporting a nominal statistically significant result; a 95% PI that excluded the null; no large heterogeneity; no evidence of small-study effect; no excess significance bias. **Highly suggestive (class II):** High significant association, large sample size having the event of interest; the largest component study reporting a statistically significant

result. **Suggestive (class III):** Significant Associations and large sample size having the event of interest. **Weak (class IV):** Remaining statistically significant associations with P < .05.

We assessed the methodological quality of the included meta-analyses of observational studies using AMSTAR-2 that ranks the quality of a meta-analysis from critically low to high according to 16 predefined items [20]. The items are about whether it contains research questions and inclusion criteria for the review; the protocol; explaining selection of the study design; using a comprehensive literature search strategy; performing study selection data extraction in duplicate; providing a list of excluded studies and justify the exclusions; describing the included studies in adequate detail; assessing the risk of bias; reporting on the sources of funding; use appropriate methods for statistical combination of results; assessing the potential impact of risk of bias on the results; accounting for bias in primary studies when interpreting/discussing the results of the review; investigation of publication bias and heterogeneity, and conflict of interest. The critical domains and non-critical domains were evaluated by using AMSTAR-2, which is shown in Table 2 in detail [20].

RESULTS

Literature review

Overall, we identified 3172 papers. After removing the duplicates (985), 2187 title/abstracts were screened with 57 eligible full-texts. Of them, 9 studies were finally included in our umbrella review (Figure 1).

Findings of the case-control and cross-sectional studies

The median number of studies of meta-analyses for each outcome was 5 (range 2-66), the median number of participants was 814 (range 388 to 321,939), and the median number of cases was 363. A total of 41 independent outcomes was finally included.

Overall, 37 out of the 41 outcomes reported nominally significant summary results ($p<0.05$) (=90.2%), with 22 associations surviving the application of a more stringent p-value ($P < 10^{-6}$), as shown in Table 1.

Heterogeneity among studies was high, with only 14 out of 41 outcomes having low heterogeneity ($I^2<50\%$). On the contrary, 10 out of 41 had moderate heterogeneity (I^2 between 50 and 75%) and the other 17 had high heterogeneity. Eight associations presented 95% PIs excluding the null value. The small-study effect was present in 10 out of 41 outcomes included, three outcomes reported an excess significance bias, and 36 out of 41 outcomes had their largest study reporting statistically significant results.

As shown in Table 1, using the criteria mentioned above, UI was associated with significantly worse scores than controls in Female Sexual Function in five studies including 436 females before and after overactive bladder treatment, as shown in Figure 2 (lubrication, orgasm, satisfaction scores supported by a class II evidence; pain and total score sustained by a class III)[33]. The evidence supporting the role of UI in Mid-Urethral Sling (MUS) surgery for SUI at 6 months post-operative in female sexual function was supported by a weak strength of evidence, similar to the evidence in MUS surgery for SUI at 12 months post-operative[34].

Regarding mental health, UI was associated with a higher prevalence of depression (OR=1.815; 95%CI: 1.551-2.124), and anxiety (OR=1.498; 95%CI: 1.273-1.762) than people without UI (Figure 3)[35, 36]. However, given the susceptibility of this evidence to excess significance bias, these outcomes should be interpreted as having a weak strength of evidence.

Moreover, UI was associated with poorer QoL[36], higher presence of Grade II+ pressure ulcer development[37], higher rate of mortality (n=66 studies, HR=2.392; 95%CI: 2.053-2.787, class IV)[38] and an increased presence of falls and frailty than their counterparts, although these were graded as class IV evidence (Figure 4)[39-41]. Finally, urgency UI was associated with an increased presence of falls and fecal incontinence (FI), arthritis, diabetes supported by class IV evidence[39], as shown in Table 1.

As reported in Supplementary Table S3, only one meta-analysis was rated "moderate", three rated "low", whilst the other meta-analyses were rated as "critically low" according to the AMSTAR-2 criteria.

DISCUSSION

This umbrella review summarized the findings of ten previous meta-analyses of the association between UI and 41 independent outcomes. Highly suggestive (i.e., class II) evidence was found for associations between UI and female sexual dysfunction. The other outcomes including higher prevalence of depression and anxiety, poorer QoL, higher mortality, falls, fecal incontinence, pressure ulcers, and frailty were found to have weak evidence.

Female Sexual Dysfunction (FSD)

In this umbrella review, it was determined that the only result, reaching the class II level of evidence among the UI-related health outcomes, was female sexual dysfunction. UI worsened the parameters of desire, arousal, lubrication, orgasm, and satisfaction scores of FSD. Overactive bladder (OAB) treatment improved both OAB-wet and sexual functions simultaneously[33]. It has been shown that placement of a MUS, performed for stress

incontinence in females, positively affects sexual function with class IV evidence level due to improvement in UI at 6^{th} and 12^{th} months follow-up[34].

UI and FSD are two common conditions that are typically underdiagnosed and undertreated. Although it seems clear that these two urogenital conditions may be interrelated, they are generally considered as two separate problems[42]. For example, one study showed that nearly three-quarters of women who attended a urology clinic for UI or other lower urinary tract symptoms were not asked about their sexual health problems[43]. Another important issue is that although UI and FSD are commonly thought to be conditions related to aging, they can be seen widely throughout life, including the premenopausal period[42]. The prevalence of FSD in females with UI was at least 25% and of women with UI who were sexually active, 23% to 56% had FSD[43]. Even without UI, FSD has negative effects on self-esteem, well-being, and the establishment of strong relationships with a partner[42]. Negative effects of UI on sexual function resulting in coital incontinence may increase the intensity of these harmful effects and cause a decrease in the frequency of sexual activity in women due to smell, embarrassment, loss of self-confidence, and fear of repetition of UI in subsequent sexual intercourse[44, 45]. Considering that sexual activity is associated with a range of benefits for psychological and physiological well-being, such as improved QoL and mental health, heart rate variability, and lower risk of certain cancers and fatal coronary events, the relationship between UI and sexual dysfunction should be further investigated[46-48].

All three UI types (stress, urgency, and mixed) worsen sexual functions[49-51]. However, the reports on the response of sexual function following the treatment of UI are conflicting[33, 34, 42]. In this umbrella review, it was found that MUS surgery applied for stress UI improves postoperative desire, arousal, orgasm, lubrication, satisfaction, and pain scores and significantly reduces coital incontinence[34]. On the other hand, urge UI (UUI, OAB-wet) was reported to be the most influencing factor on sexuality. OAB treatments showed improvement

in both OAB-wet and sexual function, and OAB therapies significantly improved OAB and reduced female sexual dysfunction[33]. Therefore, it is important to realize that UI is a treatable risk factor for FSD, which is known to be multifactorial.

Mental health

UI not only causes physical problems but can also cause mental health problems such as depression and anxiety[52]. Although it is not a life-threatening illness, those with UI may feel high levels of stress, embarrassment, and discomfort from the odor. Moreover, UI can sometimes occur so quickly and in large volumes that it can seriously affect one's socialization[53]. UI causes a decrease in performance in daily life activities owing to frequent visits to the toilet, while general health problems such as UI-related sleep loss and daytime fatigue may increase psychological and emotional distress[54, 55]. Just like FSD, urinary system problems can deter males from leaving the house and cause limitations in their social relationships[53]. For males, urinary problems are stigmatizing and can reduce their masculine identity, causing internalization of negative self-worth and low self-esteem[56]. UI can lead to a lower sense of self-control, leading to the belief that those with UI have a lower coping capacity and reduce their sense of self-efficacy[57]. Due to all these reasons, depression and anxiety can be observed frequently in those with UI.

In addition, UI is common in those with multimorbidity and frailty, and within these patients UI is highly likely to negatively affect their mental health, above that of multimorbidity, potentially resulting in the development of clinical depression or anxiety[4, 41, 58, 59]. Therefore, common factors in etiology may explain the relationship between UI and mental health. It is worth noting findings from a previous cross-sectional study that UI-related depression and anxiety did not benefit from anti-depressants[60], while another study found

299 that treatments applied to those with UI significantly improved UI, anxiety, and depression
300 with significant correlations in their symptoms[61].

301

302 ***Quality of life (QoL)***

303 Often, individuals with UI deny and hide UI, causing physical and psychosocial restrictions in
304 daily life[36]. In fact, key consequences include loss of self-esteem and social isolation, in
305 addition to other negative outcomes such as anxiety, depression, sexual impairment, and
306 decreased physical activity[36]. All these conditions are associated with poor QoL.

307 UI can be associated with poor QoL through a variety of mechanisms. First, people with UI
308 usually exhibit more co-morbidities than those without. Although several risk factors of UI
309 have been reported, the most specifically related are gender, age, dementia, and mobility[62].
310 Moreover, fluid intake, self-motility, and diuretic therapy can also affect diuresis and thus
311 UI[62]. All these factors are commonly known to be associated with poor QoL in older people.
312 Second, it is possible for people with UI to use diapers, and the use of these tools, in certain
313 circumstances, can lead to Incontinence-Associated Dermatitis (IAD)[63], defined as "skin
314 rash and edema, sometimes accompanied by blisters with serous exudate, erosion, or secondary
315 infection"[64]. IAD, like other dermatological conditions, is associated with a poor QoL[36].
316 Finally, we believe that the poor QoL in UI can be justified by the presence of shame leading
317 to a change in lifestyles and habits (i.e., reduced or suppressed physical activity) and mental
318 disorders in these people (i.e., depression and anxiety)[2, 60].

319

320 ***Mortality***

The relationship between UI and premature death is probably multifactorial. First, the risk factors that cause UI development may themselves negatively affect survival. Conditions known as risk factors for UI such as age, multimorbidity, cognitive impairment, frailty, and disability are likely to increase mortality. For example, frail and elderly patients are at the highest risk of developing UI[41]. Therefore, the mortality rate of patients suffering from UI is expected to be higher than those who do not suffer from this condition. A recent study revealing that the relationship between UI and death may be comprehended based on increased frailty in incontinent individuals supports this hypothesis[65]. Second, UI may shorten survival by increasing multiple unfavorable outcomes. For example, UI increases the risk of falls and fall-related injuries in both genders[11, 66, 67], and it is well known that hip fracture may increase the risk of low mobility by more than 4 times, the risk of rehospitalization by 2.5 times and mortality by 1.8 times, especially in the elderly[68]. On the other hand, complications such as depression, anxiety, sexual dysfunction, and decreased QoL caused by UI may indirectly lead to a shortening of survival. In addition, a recent retrospective study reported that drugs used for UI increase the risk of mortality by 50% due to their anticholinergic effects[69]. However, future studies may reveal the truth of this hypothesis.

Grade II+ pressure ulcer development

Pressure ulcers cause severe pain, physical and psychological discomfort, and limitations in activities, and also lead to a prolonged hospital stay, healthcare utilization, and mortality[37]. The skin surface microclimate includes temperature and humidity. Exposure to moisture can cause moisture-related skin damage in the sacral area as a consequence of inflammation of the epidermis and dermis. Moisture-related damage, often incorrectly classified as a type of pressure ulcer, includes sweating-related intertrigo, skin damage around the wound resulting

from wound exudate, or effluent. The most common cause of moisture-related skin damage is IAD[64]. Skin irritants from incontinence include urine, feces, double incontinence, and liquid feces[37, 64]. Moisture from incontinence increases the vulnerability of the skin and superficial tissue layers to pressure-induced blood flow reduction[70]. Moisture also attenuates the skin and makes it more exposed to the effects of pressure and shear[64, 71]. Exposure to urine and feces results in skin hyperhydration and an increase in skin pH, reducing tissue tolerance and increasing the risk of local infection by enabling microorganisms to multiply[71].

Falls

The link between urinary incontinence and falls is likely to be related to the need to rush to the toilet and the distress and anxiety related to the aftermath of not being able to get to the toilet in time[62]. This hypothesis is in line with a previous report that falls usually happen in the bathroom[72]. Furthermore, older patients with UUI may be particularly vulnerable because UI severity can increase over time, mobility decreases with age, and older individuals are more susceptible to injury from falls[11]. Cognitive demands of carrying out multiple tasks at the same time, such as rushing to the toilet quickly, focusing on controlling urine flow, and overcoming obstacles at home, can also have a harmful effect on sustaining balance in older people[73]. Therefore, the UUI rate was higher in those who reported falls (34.5%) than those who did not (19.6%) with increased urine leakage volume related to a higher risk of falling[74]. Although it is thought that controlling the UI through medication may be beneficial in preventing falls, which is an important health problem, these drugs also have the potential to increase falls[75].

Frailty

It has been demonstrated that UI leads to a wide variety of adverse effects in older people, including falls, urinary tract infections, skin complications, functional decline, psychosocial limitations, poor quality of life, and poor health perception[41]. These complications of UI may cause an accumulation of defects that are well known to create a state of frailty. Conversely, individuals with frailty frequently experience homeostatic dysregulations leading to impairments in physical functioning, mobility, gait and balance, and cognition, which might result in UI. An important distinction in UI etiology between healthy and weak older people is the presence of conditions and factors outside of the lower urinary tract - such as cognitive impairment, poor mobility, and polypharmacy - that can precipitate the loss of continence and exacerbate the main urinary symptoms[41, 76]. Furthermore, this finding justifies the need for a multidimensional approach and clinical evaluation of the UI in older people to assess the key risk factors and the etiology of the UI, with the inclusion of new components to determine frailty, and then the integral and patient-specific treatment plan[41, 76].

Diabetes, Fecal incontinence, and Arthritis

Diabetes is an independent risk factor for UI. As a matter of fact, hyperglycemia is likely to be associated with earlier and more common adverse outcomes compared to other microvascular complications such as retinopathy, neuropathy, or nephropathy[77]. A plausible cause of UI is microvascular harm to the innervations of the bladder and urethral sphincter, sphincter dysfunction, bladder instability, urinary retention, and elevated postvoid residual urine volume adding to overflow UI, chronic bacterial colonization, and urinary tract infections (UTIs)[78, 79]. Many different patient backgrounds and clinical characteristics have been recognized as risk factors for UI. Aging is an important risk factor for UI as it is associated with decreased sensation, detrusor muscle mass, elasticity, and bladder capacity[77]. Obesity also increases

the risk of UI among diabetic women because it causes increased intra-abdominal and pelvic pressure[77]. The presence of frequent UTIs and the number of normal vaginal deliveries (parity) are other important risk factors for UI[80]. Clinical variables of patients have also been specified as important risk factors for UI in epidemiological studies and include diabetes duration, hemoglobin A1c level, and the presence of diabetic long-term complications[81]. Some investigations demonstrate that up to 50% of severe incontinence could be avoided by precluding type 2 diabetes[77]. This underscores that there is an important link between both health conditions.

The lower bowel (LB) and the lower urinary tract (LUT) are closely related. Both organs originate from the embryological cloaca and have a similar function: storage and evacuation of feces and urine, respectively[82]. Peripheral innervation plays a similar role in the function of both viscera. The central processing and perception of afferent activity ensue in the same brain areas. The close relationship between the LB and the LUT also has clinical relevance as the pathology of both co-exist[82]. UI and FI are two highly prevalent pelvic floor disorders. About 20% of women with UUI symptoms may also have symptoms of FI, referred to as double incontinence[83]. Women who suffer from both diseases have greater impairment regarding their physical and psychosocial wellbeing than do women suffering from isolated UI or FI, resulting in social isolation and reduced quality of life[84]. The usefulness of the agents used in the treatment of UUI in FI may be a clear indication of the close relationship between these two conditions[85].

Arthritis may cause restricted mobility and the ability to disrobe quickly, leading to UI. Those with UUI may be more likely to have painful osteoarthritis symptoms due to increased physical demands from responding to the greater frequency of urgent urination episodes on their already pre-existing osteoarthritis. Arthritis may also limit the ability to change positions in order to prevent stress incontinence[86].

In this review, we found that the discrepancy between the results presented and the commonly reported associations between urinary incontinence and health outcomes, except for FSD. The possible reasons for this can be explained by the limitations. First, the eligible meta-analyses included studies with significantly different designs, populations, and other basic characteristics (e.g., women, men, older and middle-aged adults), which may have contributed to the large heterogeneity in some meta-analyses. However, a common estimate of heterogeneity ($I^2 < 50\%$) was used as one of the criteria for grading convincing outcomes, even if the use of the same I^2 is still discussed [87]. Second, according to AMSTAR-2, most of the reviews had low or critically low-level quality, because most of them did not report funding, or did not have a pre-registering protocol. However, to estimate if these biases can modify our outcomes is hard to hypothesize. Another factor was that they did not assess the potential impact of risk of bias in individual studies on the results of the meta-analysis or the authors did not account for bias in primary studies when interpreting/discussing the results of the reviews. Large heterogeneity and risk of bias were responsible for both grading of the evidence and low quality. Therefore, future studies should be done by eliminating them with a better research strategy.

Conclusions

UI seems to be significantly associated with several negative health outcomes, although only the association with FSD is supported by highly suggestive evidence. However, the present review does not allow firm conclusions to be made on whether UI can be considered as a risk factor for other medical conditions including depression, anxiety, poorer QoL, higher mortality, falls, pressure ulcers, diabetes, arthritis, fecal incontinence, and frailty. A multidimensional approach to clinical assessment and treatment of UI taking account of both physical and mental health symptoms is warranted.

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Ethical Approval Statement: Not applicable since this manuscript uses a methodology of umbrella review.

Informed Consent Statement: Not applicable since this manuscript is a secondary analysis.

FIGURE LEGENDS

Figure 1. PRISMA flow diagram of the literature search.

Figure 2. Summary estimates of meta-analyses regarding sexual function (desire, arousal, lubrication, orgasm, satisfaction, pain), female coital incontinence, and treatment of UI.

Figure 3. Summary estimates of meta-analyses regarding mental health (depression, anxiety, and SF-36 score) and UI.

Figure 4. Summary estimates of meta-analyses regarding quality of life and systemic disease and UI

TABLE LEGENDS

Table 1. Main findings of the case-control and cross-sectional studies

Table 2. AMSTAR-2 quality assessment of systematic reviews and meta-analysis.

SUPPLEMENTARY TABLE LEGENDS

Supplementary Table S1. PRISMA Checklist

Supplementary Table S2. Credibility assessment criteria for meta-analyses of observational studies.

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