Comorbidities and personal burden of urgency urinary incontinence: a systematic review

K. S. Coyne,1 A. Wein,2 S. Nicholson,3 M. Kvasz,4 C.-I. Chen,5 I. Milsom6

Introduction

Several subtypes of urinary incontinence (UI) have been defined by the International Continence Society, including urgency UI (UUI: involuntary loss of urine associated with urgency), stress UI (SUI: involuntary loss of urine on effort or physical exertion, or on sneezing or coughing) and mixed UI (MUI: involuntary loss of urine associated with urgency and with exertion, effort, sneezing or coughing) (1,2). UUI is one symptom of the overactive bladder (OAB) syndrome (1,2). Longitudinal studies and a systematic review of OAB and UUI suggest that these conditions are often chronic and symptom severity increases over time for many patients (3–5).

Three large-scale studies conducted in Europe and North America provide the most comprehensive data on the prevalence of UUI, with estimates ranging from 1.8% to 9.3% in men and from 3.9% to 24.4% in women (6–8); differences in these estimates are likely, at least in part, because of differences in UUI definitions, survey methods, questionnaire structure and study populations. However, all three studies demonstrate that the prevalence of UUI increases with age in both men and women (6–8). Based on data from the EPIC study (7), the ageing of the population worldwide is projected to result in an increase in the estimated number of adults affected by UUI alone from 49 million in 2008 to 55 million in 2013 (11.1% increase) and to 60 million in 2018 (22.5% increase) (9). The estimated number of adults affected by MUI (i.e. UUI with SUI) is projected to increase from 54 million in 2008 to 60 million in 2013 (11.6% increase) and to 66 million in 2018 (23.6% increase) (9).

It is well established that UI, OAB and other lower urinary tract symptoms (LUTS) are associated with numerous comorbidities (10–12). For many of these associations, it is unclear whether there is a shared aetiology, whether the relationship between conditions is causal in nature or whether treatment of one condition improves or exacerbates the other. It is also well

SUMMARY

Aims: Studies on the burden and comorbidities associated with urgency urinary incontinence (UUI) are difficult to compare, partly because of the evolution of definitions for lower urinary tract symptoms and the various instruments used to assess health-related quality of life (HRQL). This article summarises published evidence on comorbidities and the personal burden associated specifically with UUI to provide clinicians with a clear perspective on the impact of UUI on patients.

Methods: A PubMed search was conducted using the terms: (urgency urinary incontinence OR urge incontinence OR mixed incontinence OR overactive bladder) AND (burden OR quality of life OR well-being OR depression OR mental health OR sexual health OR comorbidity), with limits for English-language articles published between 1991 and 2011.

Results: Of 1364 identified articles, data from 70 retained articles indicate that UUI is a bothersome condition that has a marked negative impact on HRQL, with the severity of UUI a predictor of HRQL. UUI is significantly associated with falls in elderly individuals, depression, urinary tract infections, increased body mass index, diabetes and deaths. The burden of UUI appears to be greater than that of stress urinary incontinence or overactive bladder symptoms without UUI. UUI adversely impacts physical and mental health, sexual function and work productivity.

Conclusions: UUI is associated with numerous comorbid conditions and inflicts a substantial personal burden on many aspects of patients’ lives. Healthcare providers should discuss UUI with patients and be aware of the impact of UUI and its associated comorbidities on patients’ lives.

Message for the clinic

UUI is a common, chronic and sometimes progressive condition that impacts millions of adults worldwide. Healthcare providers should discuss it with patients and be aware of the impact of UUI and its associated comorbidities on patients’ lives.

Review criteria

A PubMed search of the literature on the comorbidities and personal burden associated with UUI was conducted, with limits for English-language articles published between 1991 and 2011. We summarise the available evidence to provide clinicians with a clear perspective on the direct impact of UUI on their patients’ daily lives.

Keywords: UUI, comorbidities, personal burden, health-related quality of life, physical and mental health, sexual function, work productivity.

Correspondence to:

Ian Milsom, Department of Obstetrics and Gynecology, Sahlgrenska Academy at Gothenburg University, Gothenburg, Sweden

Email: ian.milsom@obgyn.gu.se

Fax: +46 (31) 192940

Tel.: +46 (70) 5371602

Disclosures

Karin Coyne is an employee of United BioSource Corporation who were scientific consultants to Pfizer. Ian Milsom is a scientific consultant for Pfizer and United BioSource; has been an investigator for Pfizer and Astellas and a lecturer for Pfizer, Astellas, Recordati, SCA and Novartis; and has received grant support from Pfizer and Astellas; Sean Nicholson has been a consultant to Pfizer in connection with developing economic models of the costs associated with diabetes, cardiovascular disease, smoking and urinary incontinence; and has received grant support from Pfizer, Merck, J&J and AstraZeneca; Alan Wein consults/advises for Astellas, Allergan, Endo, Medtronic, Theravida, Pfizer, Ferring, Opko, Ethicon, Uroplasty and Merck; Marion Kvasz and Chieh-I Chen are full-time employees of Pfizer Inc.

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1Center for Health Outcomes Research, United BioSource Corporation, Bethesda, MD, USA
2Division of Urology, University of Pennsylvania School of Medicine, Philadelphia, PA, USA
3Department of Policy Analysis and Management, Cornell University, Ithaca, NY, USA
4Pfizer France, Paris, France
5Pfizer Inc, New York, NY, USA
6Department of Obstetrics and Gynecology, Sahlgrenska Academy at Gothenburg University, Gothenburg, Sweden

Systematic Review

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established that UI and OAB impart a substantial burden on affected individuals (13). However, published information on the comorbidities and personal burden associated with UUI are often based on studies of either OAB or UI, rendering it difficult to differentiate the impact of UUI from other OAB symptoms or other UI subtypes. Increased knowledge of the comorbidities and personal burden associated specifically with UUI may improve the management of this condition. In this review, we summarise the available evidence on the comorbidities and burden associated specifically with UUI to provide clinicians with a clear perspective on the direct impact of UUI on their patients’ daily lives.

**Methods**

This systematic review was conducted following the recommendations of the PRISMA statement (14). A PubMed search was conducted on 17 March 2012, and updated 6 August 2012 (Figure 1), using the following terms: (urgency urinary incontinence OR urge incontinence OR mixed incontinence OR overactive bladder) AND (burden OR quality of life OR well-being OR depression OR mental health OR sexual health OR comorbidity), with limits for English-language articles published from 1 January 1991 to 31 December 2011. Criteria for inclusion or exclusion of retrieved articles were determined prior to the literature search; article review was conducted independently by three reviewers. Articles were included if they contained comorbidity or HRQL data for the following: (i) adult subjects with UUI only, (ii) adult subjects with OAB with UUI and adults subjects with OAB without UUI or (iii) adult subjects with MUI and adults subjects with SUI only. Articles were excluded if they were as follows: (i) reviews or comment, (ii) primarily assessing neurogenic UUI, UUI prevalence or diagnosis, UUI treatment/management outcomes, pregnancy-associated UUI, surgery-associated or surgically treated UI, UUI costs or questionnaire validity, (iii) duplicate articles or (iv) updated in a more recent article. These criteria were established to include only articles that provided data specifically for UUI without confounding from other OAB symptoms, other types of UI or neurological conditions. The references cited in the included articles were scanned for additional articles. For the present review, of 1350 articles identified via the search and 14 additional articles identified from other sources, 70 articles met the eligibility criteria (Figure 1). Data were systematically reviewed. To provide evidence-based differentiation of the quality of the included articles, the data were categorised as either derived from large-scale (≥ 5000 subjects; Table 1) or smaller scale (< 5000 subjects; Table 2) studies, with reported survey response rates indicated.

**Results**

The strongest evidence on comorbidities and the personal burden associated with UUI for adults worldwide is derived from large-scale (≥ 5000 subjects)
| Study                                                                 | county                  | Sample                                                                 | Survey (response rate)                                                                                      | UUI definition                                                                                             | Outcomes assessed                                                                                           |
|----------------------------------------------------------------------|-------------------------|------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Epidemiology of Lower Urinary Tract Symptoms (EpiLUTS) (15–18)       | The United States, The United Kingdom, Sweden                         | 30,000 adults aged ≥ 40 years (14,139 men; 15,861 women)               | Population-based, cross-sectional, Internet survey in 2007–2008 (52–61%)                                 | 2002 ICS                                                                                                    | (1) UUI-associated bother among men and women with ≥ 1 OAB symptom (2) Sexual HRQL by OAB with or without UUI and gender (3) Work productivity in US adults aged 40–65 years by OAB with or without UUI, gender, county (4) Comorbidities by UUI, SUI or MUI UUI, SUI and MUI association with anxiety (HADS-A score ≥ 8) and depression (HADS-D score ≥ 8), adjusting for age, education, nocturia, BMI, parity, smoking status (5) Work productivity in UK/Ireland, functional limitations, SUI (6) Comorbidities by UI, SUI or MUI UUI, SUI and MUI association with anxiety (HADS-A score ≥ 8) and depression (HADS-D score ≥ 8), adjusting for age, education, nocturia, BMI, parity, smoking status (7) Work productivity in Austria, Belgium, Denmark, Finland, France, Germany, Greece, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, UK/Ireland (8) Predictors of moderate-severe UUI progression (multivariate logistic regression models) (9) Work productivity in the United States (10) UUI-associated bother by age and gender |
| Hordaland Health Study (HUSK) (49)                                    | Norway                  | 5321 women aged 40–44 years from Hordaland county                      | Population-based, cross-sectional, community-based mail survey (76%)                                        |                                                                                                           | UUI association with falls                                                                                   |
| Leicestershire Medical Research Council Incontinence (19)            | The United Kingdom      | 5474 men and women aged ≥ 70 years (2352 men; 3122 women)              | Cross-sectional postal survey of 23,000 community-dwelling adults selected from general practitioners lists in 1998–1999 (58%) | (1) Do you ever leak urine when you do not mean to? (2) Does any urine leak when you laugh, cough or sneeze? (SUI) (3) Do you have such a strong desire to pass urine that you leak before reaching the toilet? (UUI) | UUI association with anxiety and depression (HADS-A score ≥ 8) in multivariate logistic regression models                                                                 |
| Leicestershire Medical Research Council Incontinence (20)            | The United Kingdom      | 12,568 community-dwelling women aged ≥ 40 years selected from general practitioners lists in 1998–1999 (58%) | 3-year, prospective, longitudinal, postal survey in 1998 (65%) and 1-year follow-up in 1999 (80%)          | Do you have such a strong desire to pass urine that you leak before reaching the toilet? Response: Several times/day; several times/week; several times/month; several times/year; never/rarely; UUI = several times/month or more | UUI association with anxiety and depression (HADS-A score ≥ 8) in multivariate logistic regression models                                                                 |
| Health and Retirement Study (HRS) (35)                               | The United States       | 8603 women aged ≥ 50 years with data at baseline and 2-year follow-up   | Community-based longitudinal study in 2004–2006                                                            | Moderate-to-severe UUI: In the last month, how often did leak with an urge to urinate and could not get to the bathroom fast enough? | Predictors of moderate-severe UUI progression (multivariate logistic regression variables: age, ethnicity, comorbidities, parity, BMI, psychiatric history, functional limitations, SUI)                                                                 |
| National Family Opinion (NFO) (66)                                   | The United States       | 162,906 men and women aged ≥ 18 years matched to US census for age, geographical region, income, household size | Cross-sectional mail survey in 2005 (63%)                                                                  | UUI assessed with OAB-V8 questionnaire and 1 question on SUI (i.e. loss of urine while coughing, sneezing, laughing, lifting) | UUI-associated bother by age and gender                                                                                                                             |
| Prospective Urinary Incontinence Research (PURE) (21,22)             | Austria, Belgium, Denmark, Finland, France, Germany, Greece, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, UK/Ireland | 9487 women aged ≥ 18 years with UI and seeking or under treatment | Longitudinal, observational study in 2003–2005                                                            | Stress and Urge Incontinence Questionnaire: How many times in last 7 days have you had accidental leakage of urine onto your clothing, underwear or pad with such a sudden strong need to pass water that you could not reach the toilet in time? | (1) Symptom bother by UUI, SUI or MUI (2) Generic HRQL and disease-specific HRQL by UUI, SUI or MUI |
Table 1 Continued

| Study                                      | county         | Sample                                      | Survey (response rate)                      | UUI definition                                                                 | Outcomes assessed                                                                 |
|--------------------------------------------|----------------|---------------------------------------------|---------------------------------------------|--------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| National Overactive                        | The United States | 5204 adults aged ≥ 18 years (2469 men; 2735 women) | Population-based, cross-sectional, telephone survey in 2000–2001 (68%) and case-control study | (1) ≥ 4 urgency episodes in the last 4 weeks; (2) Either ≥ 8 micturitions/day or use of a coping strategy; (3) ≥ 3 episodes of urinary leakage in the past 4 weeks not due exclusively to SUI | (1) Generic HRQL (SF-36, MOS-Sleep) and disease-specific HRQL by UUI, SUI or MUI; (2) Mental HRQL (CES-D) in adults with OAB with or without UUI vs. matched controls; UUI association with falls/fractures |
| Fractures (SOF) (24)                       |                | 6049 community-dwelling white women aged 72–99 years from population-based listings at 4 clinical centres who provided UI information and 1 follow-up on falls | Longitudinal survey in 1994–1996             | (1) During the last 12 months, have you ever leaked or lost control of your urine? If yes: (2) How often does this leakage of urine usually occur: daily/ ≥ 1 time per week but not every day/ ≥ 1 time per month but not every week/ < once per month? (3) Under what circumstances does your leakage of urine usually occur: when I cough/sneeze/laugh/lift/stand up/ exercise, etc. (SUI); when I have the urge to urinate and cannot get to the toilet fast enough (UUI); when I am sleeping/napping/dozing (other); UUI = (1) yes and (2) ≥ weekly and (3) UUI |

CES-D, Center for Epidemiology Studies-Depression; HADS, Hospital Anxiety and Depression Scale; HRQL, health-related quality of life; ICS, International Continence Society; MUI, mixed urinary incontinence; OAB, overactive bladder; SUI, stress urinary incontinence; UUI, urgency urinary incontinence.

studies, including the Epidemiology of LUTS (EpiL-UTS) study (15–18), the Leicestershire Medical Research Council Incontinence Study (19,20), the Prospective Urinary Incontinence Research (PURE) study (21,22) and the US National Overactive Bladder Evaluation (NOBLE) Program (6,23) (Table 1). Studies that evaluated a smaller number of subjects also provide valuable information for specific patient populations and individual countries (Table 2). Data from large-scale studies, if available, are summarised first, followed by data from smaller scale studies.

UUI-associated comorbidities and mortality

Falls and fractures

The risk of falling is a concern in elderly individuals and patients with UUI, presumably because of the need to hurry to reach a toilet before leakage occurs. Elderly patients with UUI may be particularly vulnerable because UUI severity can increase over time, mobility decreases with age, and older individuals are more susceptible to injury from falls.

Numerous studies provide evidence that UUI is associated with falls and fractures, particularly among elderly people. In the Leicestershire Medical Research Council Incontinence Study of community-dwelling subjects aged ≥ 70 years, 25% (1267/5091) reported UUI and 35% (1902/5385) reported falls in the past year (19). The rate of UUI was higher in subjects who reported falling (34.5%) than in subjects who reported no falls (19.6%; p < 0.0001), with increasing volume of urine leakage associated with a greater risk of falling (p < 0.0001). In the Study of Osteoporotic Fractures (SOF), which included data from 6049 community-dwelling women aged 72–99 years, UUI occurring at least once weekly was an independent risk factor for falls [odds ratio (OR) = 1.3, 95% CI: 1.1–1.4; p < 0.001] and for non-spine non-traumatic fracture from falls [relative risk (RR) = 1.3, 95% CI: 1.1–1.7; p = 0.02] in multivariate models adjusted for known risk factors for falls (24). The risk of falls and fractures was higher among women with UUI daily compared with those with UUI weekly (24). A prospective, population-based, case–control study of 1016 Finnish, community-dwelling adults aged ≥ 70 years found that urinary urgency (RR = 1.7, 95% CI: 1.1–2.5) and UI (RR = 1.9, 95% CI: 1.3–2.9) were significant risk factors for recurrent falls over the previous 2 years in bivariate analyses; UI (OR = 1.7, 95% CI: 1.0–2.9) remained a significant risk factor in a multivariate
Table 2 Smaller scale (< 5000 subjects) studies evaluating UUI-associated comorbidities and personal burden

| Study | county | Sample | Study/survey (response rate) | UUI definition | Outcomes assessed |
|-------|--------|--------|-----------------------------|----------------|------------------|
| Vaughan et al. 2011 | Finland | Finnish National Nocturia and Overactive Bladder (FINNO) (70) | Population-based, mail survey in 2003–2004 (62.4%) | In the past 2 weeks: (1) Is the compulsion to pass urine so strong that urine starts to flow before you reach the toilet? Response: Never/rarely/often/always (2) If you cannot hold back the urine until you reach the toilet, how much is this a bother for you? Response: none/small/moderate/major | UUI bother and its impact on HRQL (generic 15D instrument) |
| Sims et al. (55) | Australia | 796 adults aged ≥ 65 years | Cross-sectional, longitudinal, interview survey in 1996 | (1) Have you ever had difficulty holding your urine until you get to the toilet? Response: often/occasionally/never (2) Do you ever leak urine when you cough, sneeze or laugh? | UUI association with depression (Depression Scale of Psychogeriatric Assessment Scales) |
| Gerst et al. (56) | The United States | 700 Mexican-American men aged ≥ 75 years from 5 Southwestern states | Follow-up survey of community-based, longitudinal, EPESE study in 2004–2005 and new cohort from area probability sampling | How often do you have difficulty holding your urine until you can get to a toilet? Response: never/hardly ever/some of the time/most of the time/all of the time; UUI = response ≥ some of the time | UUI association with depression (CES-D) |
| Wyndaele et al. (60) | Belgium | 383 women with UI at hospital urology department and 71 controls | Case-control study in 2007–2009 | UI evoked by a sudden compelling desire to void | UUI, SUI, MUI association with faecal incontinence |
| Coksuer et al. (87) | Turkey | 118 sexually active women with UUI, SUI, or MUI matched for age, parity and BMI from 3 university hospital gynaecology departments | Cross-sectional, clinic-based study | Complaint of a sudden compelling desire to pass urine that was difficult to defer | UUI, SUI and MUI impact on sexual function (Pelvic Organ Prolapse/Incontinence Sexual Function Questionnaire [PISQ-12]) OAB-wet and OAB-dry affect on sexual life |
| Heidler et al. (86) | Austria | 2365 men and women aged 19–91 years participating in health screening, including 101 men and 128 women with OAB-dry and 21 men and 79 women with OAB-wet | Health screening population study | How often do you lose urine before you got to the toilet? Response: none, once/week, 2–3 times/week, once/day, several times/day, permanent | OAB-wet and OAB-dry affect on sexual life |
| Slieker-ten Hove et al. (59) | the Netherlands | 1869 women aged 45–85 years | Population-based, mail survey (63%) | ICS Urogential Distress Inventory (UDI) | UUI association with anal incontinence |
| Worly et al. (89) | The United States | 102 women aged ≥ 18 years, sexually active, and reporting for annual gynaecological exam | Cross-sectional study conducted in 2007 (67%) | A score of ≥ 6 on Questionnaire for Urinary Incontinence Diagnosis | UUI association with depression (CES-D) and sexual function (Female Sexual Function Index [FSFI]) |
| Botlero et al. (80) | Australia | 506 community-dwelling women aged 24–80 years | Cross-sectional, recontact mail survey in 2006 (72%) | Sudden/uncomfortable urge to urinate assessed with Questionnaire for Urinary Incontinence Diagnosis (QUID) | UUI, MUI, SUI affect on well-being (Psychological General Well-being Index [PGWBI]) |
| Yagmur and Ulukoca (33) | Turkey | 600 nurses from 3 hospitals in Aydin, Turkey | Cross-sectional, interview survey in 2007 (63%) | Involuntary loss of urine linked to a strong desire to void | UUI association with recurrent UTIs and QOL |
| Study | County       | Sample                                                                 | Study/survey (response rate)                                                                 | UIU definition                                                                 | Outcomes assessed                                                                 |
|-------|--------------|------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Tsujimura et al. (58) | Japan       | 32 men aged ≥ 40 years who visited sleep clinic with complaints of sleep disturbance and were diagnosed with obstructive sleep apnoea | Clinic-based study                                                                       | 4-item OAB Symptom Score                                                        | UIU affect on sleep efficiency                                                       |
| Frick et al. (RRISK) (73) | The United States | 2109 women aged 40–69 years from Permanente Medical Care Programme of Northern California, of whom 598 reported UI | Population-based, cross-sectional, interview survey in 1999                               | During the past 12 months, on average, how often have you leaked urine, even a small amount? Women reporting at least weekly incontinence were asked to recall the number of episodes in the last 7 days occurring ‘with a physical sense of urgency’ to distinguish urge. Women were classified as having urge incontinence if more than half of incontinence episodes were associated with a sense of urgency. | UUI, MUI, SUI affect on HRQL (Incontinence Impact Questionnaire)                      |
| Aslan et al. (91) | Turkey       | 694 community-dwelling subjects (302 men; 392 women) aged ≥ 60 years from Istanbul | Cross-sectional, interview survey (63%)                                                     | Involuntary loss of urine with a sudden desire to void                            | UUI, MUI, SUI affect on QOL (KHQ)                                                    |
| Schimpf et al. (83) | The United States | 465 women (new patients presenting to hospital urogynaecology unit) aged ≥ 60 years | Clinic-based study in 2006–2007                                                             | Do you usually experience urine leakage associated with a feeling of urgency, that is, a strong sensation of need to go to the bathroom? | UUI, MUI, SUI impact on HRQL (PFIQ)                                                   |
| Tsai and Liu (43) | Taiwan       | 371 women aged ≥ 20 years without chief complaint of UI attending outpatient clinic | 371 of 551 consecutive women aged ≥ 20 years without chief complaint of UI attending outpatient clinic in 2006 (67%) | Yes response to 3 questions: (1) During the past 12 months have you ever had to urinate and then wet yourself before getting to the toilet? (2) Do you have to urinate more than 8 times in the daylight? (3) Do you have to urinate more than 3 times at night? | Comorbidities stratified by UUI, SUI or MUI (i.e. hypertension, hyperlipidaemia, osteoarthritis, allergic rhinitis, diabetes mellitus, peptic ulcer, cardiac disease, hepatic disease, sleep disorder) |
| Lasserre et al. (40) | France       | 496 women with UI aged ≥ 18 years consecutively seen by general practitioners | Cross-sectional study conducted in 2007 (496 of 584; 85%)                                   | The complaint of involuntary leakage accompanied by or immediately preceded by urgency (during previous 4 weeks) | Risk factors associated with UUI, SUI and MUI (multivariate logistic regression models with age, BMI, parity, daily activities, sexuality, QOL) |
| Markland et al. (61) | The United States | 307 women seeking treatment for UI                                       | Clinical trial baseline data                                                                 | ≥ 3 months of pure or predominant UI on the Medical, Epidemiologic, and Social Aspects of Aging Project (MESA) questionnaire, and ≥ 7 episodes on a 7-day bladder diary | UUI association with and risk factors for faecal incontinence                          |
| Izci et al. (48)     | Turkey       | 273 women with diabetes and 637 control women without diabetes (matched for age, BMI, reproductive history) aged ≥ 20 years from healthcare centres | Cross-sectional, case-control survey in 2005–2008                                          | (1) Involuntary loss of urine (yes/no) (2) Circumstance of leakage: coughing, sneezing, laughing, on effort/physical exertion, during sexual intercourse, washing hands or with a sudden and strong urge to void | UUI, MUI and SUI association with diabetes                                             |
| Study/survey (response rate) | UUI definition | Outcomes assessed |
|-----------------------------|----------------|-------------------|
| Nuotio et al. (63) | 252 (104 men; 148 women) followed in 2006 of 398 (173 men; 225 women) community-dwelling and institutionalised subjects aged ≥ 70 years in 1999–2000 | Population-based longitudinal study (92% in 2006) | Urinary leakage associated with a strong desire to void | UUI association with mortality, age, gender, comorbidities, depressive mood and functioning |
| Kemmer et al. (57) | 85-male patients (71 with obstructive sleep apnoea and 14 controls with upper airway resistance syndrome who underwent full-night in-laboratory polysomnography | Clinic-based study in 2006–2007 (100%) | Overactive Bladder Symptom score | UUI association with obstructive sleep apnoea |
| Hall et al. (36) | The United States | 1592 men and 2403 women aged ≥ 20 years | Population-based, cross-sectional, epidemiology survey of adults from Boston, MA, USA, with baseline data collected 2002–2005 | During the last 7 days, how many times did you accidentally leak urine when you had the strong feeling that you needed to empty your bladder but you could not get to the toilet fast enough? | Association of clusters of subjects based on 14 urological symptoms; including UUI, for risk factors and comorbidities |
| Cinar et al. (37) (BACH) | The United States | 2875 women aged ≥ 20 years | National, population-based, home interview survey in 2001–2002 (90% with complete UI data) | During the past 12 months, have you leaked or lost control of even a small amount of urine with an urge or pressure to urinate and you could not get to the toilet fast enough? If yes: Response: every day/a few times a week/a few times a month/a few times a year; Mild = a few times a year, Moderate = a few times a month; Severe = daily/a few times a week | UUI association with diabetes, asthma, arthritis, congestive heart failure, stroke, thyroid disease, BMI and other factors |
| Minassian et al. (47) | The United States | 975 working women aged 18–72 years (mean 48 years) | Cross-sectional study of women working at 2 retail companies (45%) | Yes response to: (1) Have you had any involuntary loss of urine? and reporting (2) Urogenital Distress Inventory (UDI-6) item: urine leakage related to the feeling of urgency | Risk factors associated with UUI, SUI or MUI (multivariate logistic regression models with age, BMI, smoking, alcohol use, exercise, parity, menopausal status, abdominal surgery) UUI, SUI and MUI affect on QOL (SF-36, KHQ), adjusted for age |
| Azuma et al. (38) | Japan | 551 women aged 16–93 years with UI presenting as new patients to tertiary care practice | Clinic-based study in 2003–2004 | Answer of ‘sometimes’ or ‘often’ on the Medical Epidemiologic and Social Aspects of Aging (MESA) urge scale | Both associated with UUI, MUI, SUI |
| Dooley et al. (71) | The United States | 293 community-dwelling women aged ≥ 80 years from primary care centre | Cross-sectional, home interview study conducted in 2003 (80%) | (1) Do you suffer from involuntary urine leakage? (2) Do you have urinary leakage associated with a sudden desire to pass urine? | Association of bacteriuria with UUI and SUI |
| Rodhe et al. (31) | Sweden | 246 women with obesity (BMI ≥ 30 kg/m²) and 379 controls (BMI < 30 kg/m²) | Case-control study from hospital obesity unit conducted 2003–2006 (62% cases; 51% controls) | Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) and Incontinence Impact Questionnaire (IIQ-7) | Proportion of obese women with UUI or SUI vs. control subjects; risk of sexual dysfunction in UUI and SUI in obese subjects and controls |
| Study                                      | Study county | Sample                              | Study/survey (response rate)                                      | UUI definition                                                                 | Outcomes assessed                        |
|-------------------------------------------|--------------|-------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------------------------|
| Choo et al. (90)                          | Korea        | 1303 women aged 40–79 years        | National, community-based, computer-assisted telephone survey conducted in 2000 (87%) | When you had an urge to urinate, did you ever lose urine before you could reach the bathroom? | UUI, SUI and MUI impact on HRQL          |
| Santaniello et al. (44)                   | Italy        | 750 women referred to urogynaecological unit in 2002–2004 for urinary or sexual conditions | Retrospective database analysis                                  | ICS criteria                                                                        | BMI classes according to UUI, SUI and MUI |
| Irwin et al. (54)                         | France, Germany, Italy, Spain, The United Kingdom | 1272 subjects with OAB symptoms from 11,521 respondents aged 40–64 years from population-based, cross-sectional survey | Population-based, cross-sectional survey                              | Positive responses to specific questions on frequency, urgency, UUI or nocturia | OAB with UUI vs. OAB without UUI on emotional well-being |
| Teo et al. (26)                           | Australia    | 782 women aged 75–86 years         | Population-based, cross-sectional study in 2002                   | Urge and stress scores calculated from Female Urinary Incontinence questionnaire | UUI association with falls               |
| Engstrom et al. (82)                      | Sweden       | 748 men aged 40–80 years           | Case-control, mail survey (74%)                                  | Danish Prostatic Symptom Score (DAN-PSS)                                        | UUI impact on HRQL (SF-36)               |
| Botros et al. (88)                        | The United States | 271 monozygotic twin pairs (542 twin sisters), including 138 sexually active twin pairs | Identical twin study with survey conducted in 2004                | Incontinence Impact Questionnaire and Pelvic Floor Distress Inventory             | UUI affect on sexual function (Pelvic Organ Prolapse/Incontinence Sexual Function Questionnaire (PSQ-12) (multivariate linear regression analysis with age, menopause, parity, BMI, tobacco use, SUI, faecal incontinence, hysterectomy) UUI, SUI and MUI affect on HRQL (Health Utilities Index) |
| Subak et al. (Diagnostic Aspects of Incontinence Study (DAISy) (77)) | The United States | 293 ambulatory women aged ≥ 40 years without a urinary tract infection, reporting ≥ 3 UI episodes/week for ≥ 3 months, and bothered enough by their UI to seek treatment | Cross-sectional study at 5 clinical sites in 2004               | UUI alone, MUI with UUI-predominant, SUI alone or MUI with SUI predominant, MUI with no predominant type, or other UI was determined by a urologist or urogynaecologist based on evaluation, including medical, surgical, reproductive and UI history, review of all medications, physical/pelvic examination, cough stress test, measurement of postvoid residual volume and participant’s 3-day voiding diary | UUI association with depression (9-item PRIME-MD Patient Health Questionnaire) Factors association with UUI, SUI and MUI (multivariate logistic regression models with age, BMI, parity, menopausal status, oestrogen replacement therapy, chronic cough, chronic constipation, alcohol use) |
| Melville et al. (50)                      | The United States | 3536 women aged 30–90 years | Random-sample survey of subjects in large health maintenance organisation | Leaking or losing urine associated with such a strong and sudden urge to urinate that one could not reach the toilet fast enough | UUI association with depression (9-item PRIME-MD Patient Health Questionnaire) |
| Bunyavejchevin et al. (42)               | Thailand     | 360 postmenopausal women (UUI, 60; SUI, 60; MUI 60; OAB, 60; controls, 120) | Case–control study conducted in 2004 | The loss of urine caused by an uncontrollable and sudden urge to urinate that occurred at least once per month and included more than just a few drops of urine | UUI association with depression (9-item PRIME-MD Patient Health Questionnaire) Factors association with UUI, SUI and MUI (multivariate logistic regression models with age, BMI, parity, menopausal status, oestrogen replacement therapy, chronic cough, chronic constipation, alcohol use) |
| Study | county | Sample | Study/survey (response rate) | UUI definition | Outcomes assessed |
|-------|--------|--------|-----------------------------|----------------|------------------|
| Kocak et al. (34) | Turkey | 1012 women aged ≥ 18 years | Community-based, cross-sectional, interview survey | Complaint of involuntary leakage accompanied by or immediately preceded by urgency | UUI association with recurrent UTIs and HRQL (Nottingham Health Profile Questionnaire) |
| Takazawa et al. (27) | Japan | 118 community-dwelling, ambulatory women aged 70-93 y using day care | Cohort study in 2001 | Involuntary urinary leakage accompanied by or immediately preceded by urgency (daily or once/week) | UUI association with falls |
| Chiaffarino et al. (74) | Italy | 1062 women with UI or OAB and 1143 age-matched controls aged ≥ 40 years at gynaecological clinic | Case-control study conducted in 2001 | Women who answered “Yes” to the following question: Have you had any involuntary urinary loss during the last month?, and/or to the 2 following questions: (1) On average do you urinate > 8 times/day and/or > 1 time during the night? and (2) Have you any urgency symptoms? If subject answered yes to the first question, she was defined as having UI; if she answered yes to the second and third question, but not to the first, she was defined as having OAB | UUI, SUI and MUI association with HRQL (SF-12) Factors associated with UI, MUI and SUI, including UTIs, diabetes, COPD, BMI (age-adjusted ORs) |
| Stach-Lempinen et al. (53) | Finland | 82 women referred to hospital OB/Gyn department for UI| Clinic-based study in 1996-1997 | Urgency Score > 7 | UUI association with depression (Hamilton Depression Scale) |
| van der Vaart et al. (85) | The Netherlands | 933 women aged 20–45 years | Population-based, cross-sectional, cohort study from population registration office of a suburban area in 1999 (67%) | Do you experience urine leakage related to the feeling of urgency? | UUI impact on HRQL (Incontinence Impact Questionnaire [IIQ]) |
| Melville et al. (51) | The United States | 218 community-dwelling women aged 18–90 years reporting urine loss ≥ 1 times/month and receiving a physician diagnosis of UI | Clinic-based study in 2000–2001 | A diagnosis of UUI was made on the basis of a negative empty supine stress test, frequent urination (> 8 micturitions/24 h), urine leakage that was related to the feeling of urgency, and the absence of UTI and stress symptoms. | UUI, MUI, SUI association with depression (9-item PRIME-MD Patient Health Questionnaire) |
| Kosimaki et al. (46) | Finland | 1963 men aged 50, 60, or 70 years from Tampere and same county | Population-based survey (62%) | Danish Prostatic Symptom Score (DAN-PSS) | The association between LUTS and other diseases (logistic regression) |
| Hagglund et al. (81) | Sweden | 787 women with UI and 787 matched controls aged 18–72 years recruited from prevalence study | Case-control, mail survey in 1996 (84%) | 10-item Detrusor Instability questionnaire (score of 8–20 indicates marked detrusor instability) | UUI impact on HRQL (SF-36) |
| Liberman et al. (72) | The United States | 483 adults with OAB (298 without UI; 185 with UUI) and 191 controls aged ≥ 18 years | Community-based, case-control, mail survey in 1997 (68%) | Incontinent OAB was defined as the accidental loss of urine caused by a sudden urge to urinate that included a minimum of ‘more than a small amount of urine’ lost once or more per month or as a ‘small amount of urine’ lost one or more times per week | OAB with UI vs. OAB without UI association with HRQL (SF-20) |
| Muscatello et al. (39) | Australia | 232 men and 262 women aged ≥ 41 years | NSWS telephone survey (1997), using urinary symptom data collected from central Sydney respondents (68%) | In the last month, how often did urine leak before you could get to the toilet during the day or night? Responses: never = 1; occasionally = 2; sometimes = 3; most of the time = 4; all of the time = 5 | Risk factors for UI, SUI and MUI (multivariate logistic regression models with age, BMI, marital status, health insurance, alcohol use, psychological distress, health status) |
regression model (25). In a cross-sectional survey of 782 community-dwelling, Australian women aged 75–86 years, UUI was an independent risk factor for falls (OR = 1.8, 95% CI: 1.3–2.4), after adjusting for age and use of central nervous system and cardiovascular drugs (26). A small study of 118 ambulatory Japanese women aged 70–93 years who used day care at a long-term care facility found that those with MUI had three times the risk of falling over the last year (OR = 3.1, 95% CI: 1.0–10.2) in a multiple regression analysis compared with those without UI, whereas UUI and SUI alone were not significantly associated with falls (27). A meta-analysis by Chiarelli and colleagues of pooled data from three of the studies described above (24–26) indicated that the odds of falls was 1.9 (95% CI: 1.3–2.8) in elderly subjects with UUI (28).

Longitudinal studies are needed to determine the causality of the association between UUI and falls, and studies on the day–night distribution of falls may determine the contribution of nocturia vs. UUI. Older individuals being evaluated for risk of falling should be questioned regarding UUI.

Urinary tract infections (UTIs)

For women in the NOBLE study, OAB with UUI was significantly more prevalent in those with doctor-diagnosed UTIs in the last 4 weeks (prevalence ratio = 2.7, 95% CI: 1.9–3.7) compared with women with no UTIs; OAB without UUI was not associated

| Study | county | Sample | Study/survey (response rate) | UUI definition | Outcomes assessed |
|-------|--------|--------|-------------------------------|----------------|------------------|
| Brown et al. (30) | The United States | 2763 postmenopausal community-dwelling women aged < 80 years with coronary heart disease and intact uterus | Baseline data from a 4-year, multi-centre, randomised, blinded trial | During the prior week, how many times, on average, have you unintentionally leaked some urine before you could get to the bathroom? | Risk factors for UUI, SUI and MUI (multivariate logistic regression models with age, race, BMI, waist-to-hip ratio, poor health, diabetes, UTIs) |
| Zorn et al. (52) | The United States | 115 new patients with UI (mean age, 58 years) seen at clinic and 80 continent controls (mean age, 49 years) | Case–control study | Urine loss following urgency and urodynamic testing demonstrating hyperactive (unstable) detrusor contractions | UUI association with depression (Beck Depression Inventory > 12 and/or depression requiring pharmacotherapy or counselling) |
| Simeonova et al. (79) | Sweden | Random sample of every 4th woman aged ≥ 20 years in a primary healthcare district of the city of Goteborg (n = 2176 respondents) | Random-sample, mail survey in 1991 (77%) | Involuntary urinary leakage that occurred at least 1/week and was considered by the woman to be a hygienic or social problem | UUI affect on HRQL (Visual Analogue Scale [VAS]) |
| Chiara et al. (92) | Italy | 94 patients aged 39–61 years referred to urogynaecology clinic | Clinic-based study conducted in 1995 (94%) | ICS definitions/uroflowmetry diagnosis | UUI, SUI and MUI association with depression (CES-D scale) |
| Grimby et al. (75) | Sweden | 120 women with UI and 313 age-matched controls aged 65–84 years in Goteborg, Sweden | Case–control survey (70%) | Involuntary urinary loss preceded by the urge to void or uncontrollable voiding with little or no warning | UUI, SUI and MUI affect on HRQL (Nottingham Health Profile Questionnaire) |
| Hunskaar et al. (76) | Norway | 36 women aged 40 to 60 years and 40 women aged ≥ 70 years who were registered at a resource centre for incontinence | Interview survey conducted in 1988 | Detrusor instability questionnaire | UUI and SUI affect on HRQL (Sickness Impact Profile [SIP]) |

BMI, body mass index; CES-D, Center for Epidemiology Studies-Depression; HRQL, health-related quality of life; ICS, International Continence Society; KHQ, King’s Health Questionnaire; MUI, mixed urinary incontinence; OAB, overactive bladder; PFIQ, seven-item Pelvic Floor Impact Questionnaire; SUI, stress urinary incontinence; UUI, urgency urinary incontinence.
with UTIs (6). In contrast, among men, UTIs in the previous 4 weeks were significantly associated with the prevalence of OAB without UUI (prevalence ratio = 2.9, 95% CI: 1.6–5.0) compared with those with no UTIs, but not with OAB with UUI (6). In a clinic-based prospective study of 2081 women aged 27–88 years with LUTS, UUI (OR = 2.2, 95% CI: 1.5–3.4; p < 0.001) was a significant predictor of UTIs in a multivariate model (29). Similar findings were reported by Brown et al. (30) in a study that identified risk factors for UUI in 2763 elderly postmenopausal women (mean age, 67 years) with coronary heart disease; the prevalence of ≥ 1 episode of UUI (OR = 2.0, 95% CI: 1.1–3.6) or MUI (OR = 2.4, 95% CI: 1.5–3.9) per week, but not SUI, was significantly associated with ≥ 2 self-reported UTIs in the last year. In community-dwelling, Swedish women aged ≥ 80 years, bacteriuria was significantly associated with UUI (adjusted OR = 3.4; 95% CI: 1.5–7.6), but not MUI (adjusted OR = 1.9; 95% CI: 0.8–4.2) or SUI (adjusted OR = 0.8; 95% CI: 0.3–2.3) after adjusting for mobility and oestrogen use (31). A case–control study conducted in Italy by Parazzini and associates reported a significant association between recurrent UTIs and UUI (adjusted OR = 2.3; 95% CI: 1.6–3.1), as well as MUI (adjusted OR = 1.9; 95% CI: 1.5–2.4) and SUI (adjusted OR = 1.3; 95% CI: 1.0–1.8), after adjusting for age (32). In a cross-sectional study of 600 nurses from hospitals in Turkey, a history of UTIs was a significant risk factor for UUI in a logistic regression analysis (OR = 3.7; 95% CI: 2.2–6.0) (33). Finally, in a cross-sectional survey of 1012 women aged ≥ 18 years from Aydn, Turkey, 43% of 61 women with UUI had recurrent UTIs (i.e. > 2 in previous year) (34).

Overall, the available evidence indicates a significant association between UUI and UTIs. Although the cause of this association is unknown, detrusor overactivity probably plays a role in these comorbid conditions.

**BMI/Obesity**

In the US community-based, longitudinal, Health and Retirement Study (HRS) of 8581 women aged ≥ 50 years, significant predictors of moderate-severe UUI development over 2 years included obesity (adjusted OR = 1.6; 95% CI: 1.2–2.1 for BMI ≥ 35 kg/m² vs. BMI < 25 kg/m²) after adjusting for age, parity, comorbidities, history of psychiatric illness, functional limitations and SUI (35). In the Boston Area Community Health (BACH) survey of 3167 community-dwelling women aged 30–79 years, symptomatic women (n = 2403) in the two most symptomatic of four clusters based on 14 urological symptoms had the highest prevalence of UUI (62–79%) and SUI (62–74%), the highest mean BMI (30–35 kg/m²), and the greatest proportion of obese (BMI ≥ 30 kg/m²) women (41–65%) (36). In a comparable cluster analysis of the 1592 symptomatic men in the BACH survey, the prevalence of UUI (52%) and SUI (32%) was highest in the most symptomatic of 5 clusters, in which men had a mean BMI of 29 kg/m² and the greatest obesity rate (43%) (37).

In the Heart and Estrogen/Progestin Replacement (HERS) Study of 2763 postmenopausal women with coronary disease in the United States, increased BMI or a higher waist-to-hip ratio was a significant risk factor for weekly UUI (adjusted OR = 1.1; 95% CI: 1.0–1.27 for 5-unit increase), but not weekly UUI (30). In a case–control study of 1062 women with UI or OAB and 1143 controls conducted in Italy, a BMI > 26.6 kg/m² was significantly associated with UUI (age-adjusted OR = 1.8; 95% CI: 1.2–2.7), MUI (age-adjusted OR = 2.5; 95% CI: 1.9–3.2) and SUI (age-adjusted OR = 1.8; 95% CI: 1.3–2.5) (32). In Japan, a cross-sectional study of 975 working women showed that a BMI ≥ 30 kg/m² was significantly associated with UUI (OR = 9.5; 95% CI: 2.3–38.1), SUI (OR = 6.0; 95% CI: 2.1–16.6) and MUI (OR = 4.7; 95% CI: 1.1–20.4) after controlling for other risk factors (38). A part of the NSW Health Survey, which included 494 Australian adults aged ≥ 41 years, found that obesity (BMI >30 kg/m²) was an independent risk factor for UUI (adjusted OR = 9.5; 95% CI: 2.1–42.6) and SUI (adjusted OR = 6.1; 95% CI: 1.4–25.7) in men, whereas obesity was a significant risk factor for UUI (adjusted OR = 3.1; 95% CI: 1.2–7.9), but not SUI, in women (39). A cross-sectional study of 600 nurses from hospitals in Turkey indicated that a BMI ≥ 25 kg/m² was not a significant risk factor for UUI in a logistic regression analysis (OR = 1.4; 95% CI: 0.9–2.1) (33).

In a cross-sectional study of 496 women aged ≥ 18 years in France, women with UUI had a comparable mean BMI (26.1 kg/m²) to women with SUI (26.2 kg/m²) or MUI (27.4 kg/m²) (40). A case–control study of 246 obese Swedish women and 379 age- and county-matched control women demonstrated that UUI was significantly more common in obese (56%) vs. control (25%) subjects (41). In another case–control study conducted in Thailand, UUI, SUI and MUI were not significantly associated with BMI in 360 postmenopausal women (42). Among 371 women aged ≥ 20 years in Taiwan, the prevalence of obesity (BMI > 27 kg/m²) was lower among women with UUI (18%) than with SUI (38%) or MUI (43%), but higher than among women without UI (12%) (43). Among 750 Italian women referred for urogynaecological problems, the prevalence of UUI and MUI increased significantly with increasing
Comorbidities and personal burden of urgency urinary incontinence

BMI, whereas the prevalence of SUI decreased with increasing BMI (44).

Overall, the available evidence suggests an association between UUI and BMI/obesity, and UUI severity and ethnicity may be contributing factors. Additional research is needed to identify the cause of this association and other possibly confounding variables.

Diabetes

Studies evaluating the association between UUI and diabetes have reported mixed results. A significant association between UUI and diabetes treated with insulin was found for 1584 elderly women aged 70–79 years in The Health, Ageing and Body Composition Study (adjusted OR = 3.5; 95% CI: 1.6–7.9) vs. women with no UI (45). Cluster analyses based on 3205 randomly selected community-dwelling women aged 30–79 years in the BACH survey demonstrated that two clusters with a high prevalence of UUI (62–79%) or SUI (62–74%) had a higher prevalence of diabetes (12–23%) than women without urological symptoms (5%) (36). In a population-based survey of 2198 Finnish men aged 50, 60 or 70 years, UUI was significantly associated with diabetes (adjusted OR = 2.0; 95% CI: 1.4–3.1) after controlling for age (46).

In contrast, National Health and Nutrition Examination Survey (NHANES) data on UI from 2001 to 2002 for 2577 US women indicated that diabetes was not a significant risk factor for women with either mild, moderate or severe UUI frequency after adjusting for 12 other factors in a multivariate model (47). In addition, a case–control study of 1062 Italian women with UI or OAB and 1143 control women conducted by Parazzini and associates found that diabetes was not significantly associated with UUI (age-adjusted OR = 1.3; 95% CI: 0.8–2.0), MUI (age-adjusted OR = 1.9; 95% CI: 0.8–1.6) or SUI (age-adjusted OR = 0.9; 95% CI: 0.6–1.5) (32). Another case–control study conducted in Turkey by Izci et al. also did not demonstrate an association between UUI and diabetes (UUI prevalence: 4% in 273 diabetic subjects; 6% in 637 matched controls), although data on diabetes duration were not collected (48).

Based on the overall evidence, additional studies are needed to determine whether an association exists between UUI and diabetes, together with identifying variables that may affect this possible association (e.g. disease duration, severity or treatment).

Anxiety and depression

Baseline data from the Leicestershire MRC Incontinence Study of 12,568 women aged ≥40 years in the United Kingdom indicated that UUI was a significant risk factor for anxiety (OR = 1.4; 95% CI: 1.2–1.6) and depression (OR = 1.4; 95% CI: 1.2–1.7) in a multivariate logistic regression analysis that adjusted for age, long-term illness, SUI, urgency and frequency (20). Interestingly, based on 1-year follow-up data, the incidence of new cases of anxiety (OR = 1.5; 95% CI: 1.2–2.0) or depression (OR = 1.6; 95% CI: 1.2–2.1) was significantly predicted by UUI at baseline, whereas new cases of UUI were significantly predicted by anxiety at baseline (OR = 1.4; 95% CI: 1.1–1.6), but not depression at baseline. These data suggest that anxiety is both a risk factor for and a consequence of UUI but depression may only be a consequence of UUI (20).

Among 14,140 men in the EpiLUTS study from Sweden, the United Kingdom and the United States, the rate of clinically relevant anxiety [Hospital Anxiety and Depression (HADS)-A scale score ≥ 8] was 47% for men with MUI, 39% for men with UUI plus other UI and 17% for men with UUI only, compared with 13% for SUI only (15). Among the 15,860 women in EpiLUTS, the rates of clinically relevant anxiety were 49%, 41% and 30% in those with MUI, UUI plus other UI and UUI only, respectively, vs. 30% for women with SUI only (15). For men in EpiLUTS, the rates of clinically relevant depression (HADS-D scale score ≥ 8) were 42% for men with MUI, 34% for those with UUI plus other UI and 15% for men with UUI only vs. 15% for men with SUI (15). The rates of clinically relevant depression in women in EpiLUTS were 35% for women with MUI, 29% for women with UUI plus other UI and 18% for those with UUI only compared with 17% for women with SUI only (15).

In the Hordaland Health Study (HUSK), a study of 5321 women aged 40–44 years from Norway, UUI was a significant risk factor for anxiety (HADS-A score ≥ 8; adjusted OR = 1.7; 95% CI: 1.1–2.6), but not depression (HADS-D score ≥ 8; adjusted OR = 1.7; 95% CI: 0.9–2.9), in a multivariate model that adjusted for age, education, nocturia, parity, BMI and smoking (49). With increasing UUI severity, the association with anxiety and depression strengthened (49). In the NOBLE study, scores on the Center for Epidemiology Studies-Depression (CES-D) scale were significantly worse for men, but not women, with OAB with UUI (mean score = 16.7) vs. OAB without UUI (mean score = 13.0) (6).

The results of smaller scale studies support the association between UUI and depression. In an age-stratified postal survey of 2536 women aged 30–90 years, depression (assessed with Primary Care Evaluation of Mental Disorders Patient Health Questionnaire) was more common in women with UUI (UUI alone or MUI; 6.6%) than in those with SUI (4.7%) or women without UI (2.2%) (50). In a sur-
vey of 1584 elderly (aged 70–79 years) white and black women, 21% reported UI at least weekly; of these women, 42% reported UUI (45). Depressive symptoms (CES-D scale score ≥ 16) were significantly associated with UUI (adjusted OR = 2.7, 95% CI: 1.4–5.3; p = 0.004) compared with continent women, whereas SUI was not (adjusted OR = 2.0, 95% CI: 0.92–4.3; p = 0.08) (45). Among 218 community-dwelling women with UI aged 18–90 years, the rate of depression (assessed with Primary Care Evaluation of Mental Disorders Patient Health Questionnaire) was significantly higher for women with UUI (21%) than those with SUI (3%; p = 0.002) (51). Depression was significantly more likely to occur in women with UUI (adjusted OR = 9.2, 95% CI: 1.8–48.0; p = 0.008) and MUI (adjusted OR = 13.5, 95% CI: 3.0–61.5; p = 0.001) than in women with SUI (51). A case–control study of 115 patients with UI and 80 controls showed that UUI was a significant risk factor for depression (Beck Depression Inventory score > 12; adjusted OR = 3.3; 95% CI: 1.6–6.7) after adjusting for age and gender (52). In a prospective study of 82 women with UI, major depression (Hamilton Depression Scale score ≥ 16) was more common in women with UUI or MUI (44%) than in women with SUI only (18%; OR = 3.7, 95% CI: 1.3–10.5; p = 0.026) (53).

In a survey of 1272 adults aged 40–64 years from 6 European countries who reported OAB symptoms, significantly more men and women with OAB with UUI (40%) reported feeling depressed compared with those without UUI (23%; p < 0.05) (54). A longitudinal study of 796 elderly (aged ≥ 65 years) Australian adults found that UUI occasionally or often (n = 220) was significantly (p < 0.01) associated with depression (score ≥ 3 on Depression Scale of Psychogeriatric Assessment Scales), with greater UUI frequency associated with an increased likelihood of depression in women only (55). Additionally, clinical depression (CES-D score ≥ 16) was significantly associated with UUI (adjusted OR = 2.9; 95% CI: 1.7–4.9) for Mexican-American men aged ≥ 75 years in the community-based Hispanic Established Population for the Epidemiological Study of the Elderly (Hispanic EPESE), based on a multivariate model (56).

Thus, the evidence indicates that UUI, either alone or in conjunction with SUI, is significantly associated with anxiety and depression. Although the underlying aetiology of these associations remains unclear, the serotonergic and noradrenergic pathways that are involved in both voiding and anxiety/depression may be the common link. Additional research is needed to determine whether these associations increase with UUI severity. Clinician awareness of the relationship between UUI and anxiety/depression may lead to earlier diagnosis of these conditions.

### Other conditions

In men, but not women, in the NOBLE study, those with OAB with UUI demonstrated significantly worse scores on the Medical Outcomes Study (MOS)-Sleep scale (mean score = 32.9) than those with OAB without UUI (mean score = 27.5) (6). In 171 adults with OAB with UI from the NOBLE case–control study, subjects with OAB with UUI demonstrated a significantly increased likelihood of sleep disturbances on the OAB-q Sleep domain scale, but not the MOS-Sleep scale, than those with OAB plus SUI (23). In a prospective questionnaire study of 85 men with obstructive sleep apnoea and controls, the prevalence of UUI was significantly higher in patients with severe obstructive sleep apnoea than in controls or in patients with mild sleep apnoea (p < 0.05) (57). However, in 32 men with diagnosed obstructive sleep apnoea, UUI was not significantly associated with sleep efficiency after controlling for nocturia, frequency and urgency (58). Longitudinal studies are needed to establish the causality of any association between sleep disorders and UUI.

Among 371 women aged ≥ 20 years in Taiwan, osteoarthritis was more prevalent in women with UUI (22%) than in women without any UI (15%), but less prevalent than in women with SUI (28%) or MUI (39%) (43). Among 1584 elderly women (aged 70–79 years) participating in the Health, Ageing and Body Composition Study, UUI showed a significant association with arthritis (adjusted OR = 1.7; 95% CI: 1.1–2.6) compared with no UI (45). NHANES data on UI from 2001 to 2002 for 2577 US women demonstrated that, after adjusting for 12 other variables, arthritis was a significant risk factor for UUI daily or a few times/week (adjusted OR = 2.3; 95% CI: 1.2–4.6), but not UUI a few times/month or a few times/year (47). The association between arthritis and UUI may result, in part, from the mobility problems experienced by patients with arthritis.

In a population-based survey of 2198 Finnish men aged 50, 60 or 70 years, UUI was significantly associated with arthritis (adjusted OR = 1.8; 95% CI: 1.4–2.4) and faecal incontinence (adjusted OR = 17; 95% CI: 7.5–40), after controlling for age (46). Flatal, liquid stool and solid stool incontinence (adjusted OR = 5.8; 95% CI: 1.8–18.2) was also significantly associated with UUI vs. no UI in women aged 45–85 years from the Netherlands (59). Wyndaele et al. found that UUI was significantly associated with faecal incontinence (adjusted OR = 2.4; 95% CI: 1.0–5.9) and difficulty postponing defecation (adjusted OR = 0.5; 95% CI: 0.3–1.0) compared with
SUI, based on a multivariate model (60). A study of 307 women with UUI only or UUI-predominant MUI reported that 56 (18%) also reported faecal incontinence, with the odds of monthly faecal incontinence increasing significantly with greater UUI frequency (OR = 1.2; 95% CI: 1.0–1.3) (61). It is likely that a common neurological or systemic mechanism contributes to the association between UUI and faecal incontinence.

**Mortality**
In a prospective Finnish study, 1052 adults aged 60–89 years were followed up for 10 years, by which time 541 subjects had died (62). Among subjects with UUI during the day or night, the 10-year mortality rate was 89% in men and 68% in women. After adjusting for age, chronic diseases and disability in daily activities, UUI was a significant risk factor for death in men (RR = 2.0; 95% CI: 1.3–3.1), but not women (62). Six-year follow-up data from the Tampere Longitudinal Study of Aging indicated that frequent UUI was significantly associated with total mortality after adjusting for age and gender (hazard ratio = 2.2; 95% CI: 1.4–3.6), whereas occasional UUI was not associated with mortality (63). Additional research is needed to further characterise the association between UUI and mortality.

**Personal burden of UUI**
Evidence indicates that UUI has a detrimental effect on an individual’s HRQL (physical, mental, social well-being and sexual function) and work productivity. In focus groups of adults aged > 60 years with UUI, DuBeau et al. conducted qualitative research that identified 32 patient-reported UUI-associated HRQL items that focused mainly on coping strategies, interruption of daily activities and emotional well-being (64). The majority of HRQL items identified by patients were different from those identified by investigators, with investigators focusing on the functional outcomes and patients focusing on subjective aspects of daily living (64). Clinicians also underestimate the symptom bother and impact on HRQL of UUI and other LUTS (65). Unfortunately, many individuals with UUI do not bring their symptoms to the attention of a healthcare provider because of embarrassment or a lack of awareness of effective treatment options (66–68). In a large-scale (n = 162,906) national survey conducted in the United States, only 46% of adults who reported OAB symptoms, including UUI, discussed their symptoms with a healthcare provider, with only 29% of those who had a discussion with their healthcare provider receiving prescription treatment within the last year (66). UUI was a significant predictor of consulting a healthcare provider (adjusted OR = 1.1, 95% CI: 1.1–1.2) in a multivariate analysis; adults with bothersome UUI had a higher treatment-seeking rate (39%) than those with UUI without bother (14%) (66).

**Symptom bother and HRQL**
In the Norwegian EPINCONT study that surveyed 27,936 women aged ≥ 20 years, 36% of women with UUI, 24% of women with SUI and 47% of women with MUI reported that their condition was bothersome (p < 0.001 for between-group differences) (69). For UK and Swedish adults in the EpilUTS study, UUI was a significant risk factor for OAB-associated bother in both men (OR = 1.8; 95% CI: 1.5–2.1) and women (OR = 1.9; 95% CI: 1.7–2.1), based on a multivariate logistic regression analysis (16). In the PURE study, UI subtype was a significant (p < 0.0001) predictor of reporting moderate-to-extreme bother (vs. not at all-to-somewhat bother); the adjusted OR (95% CI) for MUI was 1.17 (0.99–1.39) and for SUI was 0.72 (0.60–0.86), with UUI as the reference (OR = 1.0) (21). These studies indicate that greater bother generally is associated with UUI or MUI than with SUI.

In the PURE study, UI subtype was also a significant predictor of the mean EQ-5D VAS score (p < 0.0005) and the disease-specific Incontinence Quality of Life (I-QOL) questionnaire score (p < 0.0001) (21). The adjusted mean total I-QOL score was 54 for MUI, 60 for UUI and 63 for SUI, with lower scores indicating worse HRQL (21). Furthermore, secondary analyses from EpilUTS of HRQL outcomes by UI subtype (15) indicated that men and women with MUI and those with UUI plus other UI had worse generic HRQL scores on the SF-12 than those with other UI subtypes (Figure 2A). Mean scores on the Overactive Bladder Questionnaire (OAB-q) Short Form were lowest (worst HRQL) for men with MUI, followed by those with UUI plus other UI, SUI plus other UI, UUI only, other UI and SUI only (Figure 2A). The mean OAB-q Short Form scores for women according to UI subtype showed a similar pattern (Figure 2A) (15).

Data from the National Family Opinion (NFO) study demonstrated that the degree of UUI-associated bother tends to increase with age, with women bothered more than men in all age categories up to 85 years (66). In the NOBLE study, UUI had a more severe impact than SUI on OAB-q Symptom Bother, total HRQL and Sleep domain scores (Figure 2B) (23), and respondents with OAB with UUI had significantly worse SF-36 physical and mental component summary scores and MOS-Sleep scores than asymptomatic controls (6).
Smaller scale studies (Table 2) generally support the findings from large-scale studies. For the Finnish National Nocturia and Overactive Bladder (FINNO) study of 3535 men and women, as the frequency of UUI increased from rarely to always the rate of at least moderate UUI-associated bother increased from 20% to 100% (70). In subjects with OAB that occurred often and UUI that occurred often, HRQL was significantly and clinically meaningfully decreased compared with subjects with OAB that occurred often and no/rare UUI (70). Dooley et al. found that US women with MUI reported significantly greater bother, as assessed with the Urinary Distress Inventory, and symptom frequency compared with women with UUI or SUI (71). In a survey of 4896 US adults, 483 subjects with OAB symptoms, including 185 with UUI (without SUI), and 191 controls without OAB, UUI was associated with poorer scores on all MOS SF-20 domains vs. controls and poorer scores than for subjects with continent OAB (72). In the RRISK study that identified 598 women with weekly UI, MUI had a significantly greater negative impact than SUI (adjusted OR = 2.5; 95% CI: 1.4–4.3) on total HRQL, measured with the Incontinence Impact Questionnaire (73). Other county-based studies also found that UUI had a negative impact on HRQL, as assessed with various patient-reported outcome instruments (38,74–85).

Thus, UUI is a bothersome condition that has a marked negative impact on HRQL. Overall, the evidence indicates that UUI has a greater negative impact on HRQL than SUI, likely because urgency as the trigger of leakage is difficult to anticipate and control, whereas the physical activity that can trigger SUI often can be avoided.

Sexual health

An analysis of data from the EpiLUTS study also evaluated sexual health in 6326 men and 8085 women aged ≥ 40 years with OAB with UUI, OAB without UUI or no/minimal urinary symptoms (17). When compared with no/minimal symptoms in multivariate logistic regression models, OAB with UUI was associated with a greater likelihood of decreased sexual activity (men: OR = 9.3; women: OR = 11.2)
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and decreased sexual enjoyment (men: OR = 9.1; women: OR = 8.9) than OAB without UUI (decreased sexual activity, men: OR = 7.0; women: OR = 8.6; decreased sexual enjoyment, men: OR = 7.2; women: OR = 6.8). OAB with UUI also was identified as a significant predictor of erectile dysfunction (OR = 2.2) and ejaculatory dysfunction (OR = 2.1) (17).

Additional evidence on the detrimental impact of UUI on sexual health was found in smaller county-based studies. Based on data for 2365 men and women aged 19–99 years from Austria, the rate of decreased sexual activity was significantly higher in subjects with OAB with UUI (25% of 100 subjects) than in those with OAB without UUI (14% of 229 subjects; p < 0.005) (86). In a cross-sectional study of 118 sexually active women with UUI, SUI or MUI, who were matched for age, parity and BMI, those with MUI reported significantly worse sexual function [19.6 mean score on the 12-item Pelvic Organ Prolapse/Incontinence Sexual Function Questionnaire (PISQ-12); score range 0–48] than those with UUI or SUI (mean score 24.9 and 22.3, respectively; each p < 0.001 vs. MUI) (87). In the United States, a survey of 276 sexually active identical twin sisters demonstrated that UUI (p = 0.009) and parity (p < 0.001) were the only independent variables that significantly predicted sexual dysfunction based on a multivariate logistic regression analysis after controlling for seven other possible risk factors (88).

In a case–control study of 279 obese (BMI ≥ 30 kg/m²), women from a hospital obesity unit and 430 age-, gender- and county-matched controls conducted in 2003–2007 in Sweden, UUI was an independent risk factor for sexual dysfunction, as assessed with the PISQ-12, in obese women (adjusted OR = 2.0; 95% CI: 1.3–3.1) relative to obese women without UUI and controls after adjusting for age, BMI, parity, comorbidity, menopause, hormone therapy and depression (41). A study of 102 US women aged ≥ 18 years who were sexually active demonstrated that UUI (adjusted OR = 2.1; 95% CI: 1.2–8.7) was independently associated with sexual dysfunction, as assessed with the Female Sexual Function Index, after controlling for depression, sleeping problems and polypharmacy (89). A multivariate analysis of data from a study of 2005 Korean adults aged 40–89 years indicated that UUI was a significant risk factor for a negative impact on the sex life of men (adjusted OR = 4.4; 95% CI: 1.7–10.9; p = 0.002) but not of women (OR = 2.0; 95% CI: 0.8–4.7; p = 0.113) (90).

In summary, the results of the EpiLUTS study and smaller scale studies indicate that UUI is associated with decreased sexual function in men and women.

Although more information is needed on the strength of this association according to UUI severity and the mechanism underlying it, the sexual health of individuals with UUI should be assessed and vice versa.

Work productivity

Only a limited number of studies provide insights on the effect of UUI on work productivity. For US participants in the EpiLUTS study, work productivity was significantly impacted by OAB, especially OAB with UUI, in terms of constant worry about interruptions on the job, changes in work (including termination or early retirement) and decisions about job location and work hours (all p < 0.0001 for both men and women) (18). Among European men and women responding to a population-based survey, OAB with UUI had a greater impact on work productivity than OAB without UUI, and men were significantly more likely than women to report that OAB with UUI had a negative impact on daily work life (54). Additional studies that specifically evaluate the impact of UUI on work productivity of men and women are needed.

Discussion

Evidence from this comprehensive review provides a new perspective on UUI and its substantial personal burden to patients. We included only articles that differentiated between UUI and other OAB symptoms or other types of UI. Thus, this review is uniquely specific regarding comorbidities and burden associated with UUI and should be a useful resource for clinicians managing patients with this condition. UUI is associated with a number of comorbidities and has a negative impact on the lives of affected individuals. The nature of the relationship between UUI and associated comorbidities is complex and in many cases poorly understood, but these comorbidities likely contribute to the burden of UUI, regardless of the nature of the causal relationship. Diagnosis and management of UUI may play an important role in the management of some comorbid conditions and vice versa. Subjects with UUI report high rates of falls, UTIs, anxiety, depression and fecal incontinence, with elderly subjects with UUI often particularly vulnerable. At present, data demonstrating that UUI improvement over time leads to an improvement in these associated comorbidities are limited or lacking. UUI also impairs many aspects of HRQOL in millions of men and women worldwide, including psychological and emotional well-being, daily activities, sexual function and work productivity. The negative impact of UUI has been demonstrated using a wide variety of validated
insurers. Although the use of different instruments makes it difficult to compare results across studies, consistent findings with different instruments confirm the negative effect of UUI on HRQL. The majority of studies suggest that UUI has a greater detrimental effect on HRQL than does SUI. Long-term studies are needed to evaluate the effect of different treatments for UUI on various aspects of HRQL, including mental health, sexual function and work productivity.

The findings of this literature review, indicating a significant association between UUI and comorbid conditions, will have an even greater importance in the future because UUI prevalence increases with age and life expectancy is increasing in many countries. Further, only a small percentage of individuals with UUI receive treatment (66–68), suggesting a need to raise awareness of UUI among clinicians to facilitate early diagnosis and treatment of patients with bothersome and frequent UUI episodes. Greater understanding of the comorbidities associated with UUI, as well as the nature of these relationships, may aid in the diagnosis and management of both UUI and comorbid conditions. Possible limitations of the present review are that the search was limited to the PubMed database and English-language articles. Furthermore, many of the studies relied on subject-reported UUI and may not have adjusted for all possible confounding factors when assessing the impact of UUI on an outcome variable.

In conclusion, the available evidence demonstrates that UUI inflicts a substantial personal burden on patients. Additional research, including longitudinal studies, is needed to better understand the causality of the association between UUI and various comorbid conditions. Patients should be encouraged to discuss their UUI symptoms with a clinician. Patient-clinician discussions may help clinicians gain a better appreciation of the aspects of HRQL that are a concern to individual patients with UUI.

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Author Contributions

All authors contributed to the design of this systematic review, extraction and summarisation of the data, and drafting and critical review of the manuscript.

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