



## Review – Incontinence

# Dynamic Progression of Overactive Bladder and Urinary Incontinence Symptoms: A Systematic Review

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### Abstract

**Context:** Overactive bladder (OAB) and urinary incontinence (UI) are worldwide public health problems. Longitudinal epidemiologic studies that assess the natural history of OAB and UI are valuable in making accurate prognoses, determining causes and consequences, and predicting resource utilization.

**Objective:** Our aim was to assess whether the severity of OAB and UI symptoms progress dynamically over time, with the secondary aim of assessing factors that may be associated with symptom progression and regression.

**Evidence acquisition:** A systematic review of English articles published between January 1, 1990, and September 20, 2009, was conducted using PubMed and Embase. Search terms included longitudinal, natural history, overactive bladder, incontinence, progression, remission, and regression. Eligibility was assessed by Dr. Irwin with editorial assistance. Studies were required to be longitudinal and population based; meeting abstracts and conference proceedings were excluded. Results were assessed qualitatively.

**Evidence synthesis:** Overall, the 7 longitudinal studies of OAB and 14 longitudinal studies of UI reviewed reported an increase in the incidence and remission/regression of both OAB and UI symptoms over time that varied across studies (eg, OAB incidence, 3.7–8.8%; UI incidence, 0.8–19%). The studies provide evidence for a dynamic progression of OAB and UI symptoms (eg, among women with OAB without urge urinary incontinence [UUI], 28% reported OAB with UUI 16 yr later) and also show that although symptom severity progresses dynamically, for many individuals symptoms also persist over long time periods.

**Conclusions:** The results support the hypothesis that OAB and UI symptom severity progress dynamically and are also sustained over time. However, the variations in symptom definitions and methods used across studies prevent statistical determinations of overall incidence rates. The recognition of OAB and UI as progressive conditions allows for a shift from the current treatment paradigm of symptom control alone to one of symptom management.

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## 1. Introduction

Overactive bladder (OAB) and urinary incontinence (UI) are both debilitating and bothersome conditions [1–3]. Cross-sectional studies show both OAB and UI to be highly prevalent. For example, the EPIC study, based on current International Continence Society (ICS) definitions, found that approximately 11% of men and 13% of women in four European countries and Canada reported OAB symptoms [4]. The Epidemiology of Lower Urinary Tract Symptoms study, also based on ICS definitions, found that the prevalence of urge urinary incontinence (UUI) and stress urinary incontinence (SUI) is disproportionately higher in women compared with men (UUI, 13.1% vs 4.5%; SUI, 14.8% vs 0.4%) [5].

Whereas cross-sectional studies have improved the understanding of the prevalence of OAB and UI, it is important to assess the natural history and long-term outcomes of these conditions in longitudinal studies [6]. In particular, it is important to assess whether symptoms progress, remain constant, or undergo spontaneous remission over time to make accurate prognoses. This information is prerequisite to determining causes and consequences, to predicting resource utilization, and to enhancing the understanding of OAB and UI by patients and clinicians.

Although many systematic reviews of OAB and UI treatment efficacy and outcomes have appeared in the literature (eg, [7–9]), relatively few reviews have focused on the natural history of these conditions (eg, [6,10,11]), and none of these have been systematic in design. The longitudinal study design is well suited to assess the progression of OAB and UI symptoms because it allows the incidence of OAB and UI to be assessed. The primary aim of this systematic review is to assess how OAB and UI symptoms progress over time based on qualitative comparisons of progression, remission, and/or regression rates across published population-based longitudinal studies. The secondary aim of the review is to assess factors that may be associated with symptom progression and regression.

## 2. Evidence acquisition

A systematic review of longitudinal studies of OAB and UI restricted to articles published in English between January 1, 1990, and September 20, 2009, was performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement [12]. Studies were eligible for inclusion in the database if they were population based and reported the incidence, progression, remission, and regression of OAB and/or UI symptoms. Studies were excluded if they were based on clinical trials, cross-sectional design, medical diagnoses, surgical techniques, patient-reported outcomes, economic outcomes, disease management, and treatment outcomes. Also excluded were articles without abstracts, review articles, meeting abstracts and conference proceedings, and studies that were not focused primarily on OAB and/or UI.

Studies were identified by searching PubMed and Embase. The following search terms were used in each case: *overactive bladder, urinary incontinence, longitudinal, natural history,*

*prospective, population-based, incidence, progression, remission, regression* (see the Appendix A). Also included was one article by Malmsten et al. [13], which was submitted and subsequently accepted for publication during the preparation of this review. Articles were initially filtered for relevance by successive keyword searches according to the eligibility and exclusion criteria. Full-text versions of articles of interest were obtained and assessed for relevance by Dr. Irwin with editorial assistance from Simon J. Slater, PhD (see Acknowledgments). Data were extracted by Dr. Irwin with assistance from Dr. Slater with the aid of the data extraction tables shown in Tables 1 and 2. Information sought included study description; population, gender, age, source, and size; follow-up duration and interval; recall period; symptom definitions; incidence/progression; and remission/regression rates. To avoid bias in assessing how OAB and UI symptoms progress over time, the hypothesis that these symptoms progress dynamically over long time periods was specified before the searches were performed. Data were assessed qualitatively and are summarized descriptively.

## 3. Evidence synthesis

The search captured 21 randomly sampled, population-based longitudinal studies of OAB and UI (Fig. 1), among which 7 focused on OAB [13–19], 9 focused on UI, and 5 focused on UI subtypes (SUI, UUI, and mixed urinary incontinence [MUI]) [20–33] (Table 1). A PubMed search based on an identical search strategy but using MeSH terms did not capture any additional articles. Sample sizes ranged from 206 to 64 650, and most studies focused exclusively on women (16 studies) and on populations  $\geq 40$  yr of age (16 studies). Only six studies had a total duration of  $\geq 5$  yr, and only eight included multiple follow-up surveys (Table 1).

Among the studies, 14 were prospectively designed to capture the incidence of new cases of OAB or UI as well as the progression of symptom severity within a defined time period [13–15,19,21–23,25–29,31,33]. In the remaining seven studies, incident cases were inferred based on comparisons of prevalence measured in two or more separate surveys, which does not typically capture detailed information about the progression and regression/remission of symptoms.

### 3.1. Trends in overactive bladder symptom progression and regression/remission

Overall, the reported incidence rates of OAB varied across the studies (Table 2). Among the 21 studies reviewed, 4 [13,14,17,18] defined OAB according to the ICS definition as urgency, with or without urgency incontinence, usually with increased daytime frequency and nocturia [34,35]. For a population of women in the United Kingdom, a study based on ICS definitions reported a 1-yr incidence rate of OAB of 8.8% [18] compared with 5.4% reported by a study that did not use ICS definitions [16]. Another study based on ICS definitions [14] reported a 16-yr cumulative incidence of OAB of 20% (average annual incidence, 1.25%) in Swedish women (Fig. 1). A study of similar design [13] reported an

**Table 1 – Results of Medline literature survey for longitudinal studies performed between 1990 and 2009**

Study	Description	Gender	Age, yr	Country	Population source
Malmsten et al. [13]*	Cohort of men administered a prevalence survey about OAB using postal questionnaires in 1992 and 2003	M	56–103	Sweden	Population register
Wennberg et al. [14]	Prevalence of OAB and UI in women were compared in 1991 and 2007 using self-administered postal questionnaire	F	≥20	Sweden	Two cross-sectional studies performed using the same populations
Dallosso et al. [17]	Data on urinary symptoms and diet were collected from men using a postal questionnaire	M	≥40	United Kingdom	General practitioner registers
Dallosso et al. [18]	Data on urinary symptoms and diet were collected from women using a postal questionnaire	F	≥40	United Kingdom	General practitioner registers
Donaldson et al. [15]	Cohort of women administered three annual surveys about OAB symptoms and SUI using postal questionnaires	F	≥40	United Kingdom	General practitioner registers
McGrother et al. [16]	A prospective cohort study of women administered postal questionnaires at baseline and 1-yr follow-up	F	≥40	United Kingdom	General practitioner registers
Moller et al. [19]	Cohort of women were administered a postal questionnaire about lower urinary tract symptoms with 1-yr follow-up	F	40–60	Denmark	Civil registration
Holtedahl and Hunskaar [30]	UI in women was assessed using a self-administered questionnaire	F	50–74	Norway	Three municipalities in northern Norway
Byles et al. [20]	Long-term changes in the UI status of women were assessed based on postal questionnaires as part of the Australian Longitudinal Study on Women's Health Survey	F	70–75	Australia	Australian universal health insurance database
Goode et al. [23]	Prospective cohort study of a random population of men and women with UI (stratified to be 50% black, 50% men, and 50% rural) administered a structured questionnaire by trained interviewers	M/F	65–106	United States	Medicare beneficiaries
Lifford et al. [22]	Prospective study of the incidence, progression, and remission of UI in a cohort of nurses administered postal questionnaires about UI in 2000 and 2002 (Nurses Health Study)	F	54–79	United States	Nurses in 14 states
Townsend et al. [21]	Cohort of nurses administered postal questionnaires about UI in 2001 and 2003 (Nurses Health Study)	F	36–55	United States	Nurses in 14 states
Waetjen et al. [24]	Comparison of prevalent SUI, UUI, and MUI with UI that developed over 5 yr of follow-up in a racially and ethnically diverse cohort of midlife women using an interviewer- and self-administered questionnaires	F	42–52	United States	Participants in the Study of Women's Health Across the Nation (SWAN) survey
Jackson et al. [25]	Prospective study to assess risk factors associated with occurrence of UI among postmenopausal women based on data collected at clinical visits	F	55–75	United States	Group model health maintenance organization enrollees
Wehrberger et al. [26]	Women initially participated in a self-administered prevalence survey about UI and were then administered a follow-up postal questionnaire	F	20–84	Austria	Participants in voluntary health examinations in Vienna
Hagglund et al. [27]	Cohort of women were administered a postal questionnaire about UI	F	22–50	Sweden	Participants in a previous cross-sectional study in 1995
Liu and Andrews [28]	UI was assessed in a cohort of elderly men and women using a computer-assisted telephone interview	M/F	≥70	Australia	State electoral database
Samuelsson et al. [29]	UI in women was assessed using a postal questionnaire	F	20–59	Sweden	Participants in a gynecologic health examination program within a defined geographic region who met entry criterion
Nygaard and Lemke [31]	UI in women was assessed using an in-home interviewer-administered questionnaire	F	≥65	United States	Noninstitutionalized residents from two rural Iowa counties
Burgio et al. [32]	UI in women was assessed using an interviewer-administered telephone questionnaire	F	42–50	United States	Driver's license records in Pennsylvania
Herzog et al. [33]	UI in men and women was assessed using an interviewer-administered questionnaire	M/F	≥60	United States	Multistage stratified area probability sample

OAB = overactive bladder; MUI = mixed urinary incontinence; SUI = stress urinary incontinence; UI = urinary incontinence; UUI = urge urinary incontinence.

Table 2 – Symptom progression and remission

Study	Size	Follow-up duration, yr	Follow-up interval, yr	Recall period, yr	Symptom definition	Progression/incidence	Regression/remission
Malmsten et al. [13]*	3257	11	–	–	ICS definitions used	Mean annual incidence OAB: 3.7% UI: 0.8%	Only a minority of men reported regression of symptoms
Wennberg et al. [14]	1081	16	–	–	ICS definitions used	Baseline to 16-yr increase in the number of women reporting: OAB: 9% (17–26%) UI: 13% (15–28%) SUI: 7% (12–19%) UUI: 10% (2–12%) Cumulative incidence over 16 yr OAB: 20% UI: 21%	–
Dallosso et al. [17]	4887	1	–	–	ICS definitions used UUI: “Do you have such a strong desire to pass urine that you leak before reaching the toilet?” (Y/N) Urgency: “When you need to pass urine, how strong is the urge usually?” Scored on a 5-point scale (overwhelming, very strong, strong, normal, weak)	1-yr incidence of OAB, 5.3% in men	–
Dallosso et al. [18]	5816	1	–	–	ICS definitions used UUI: “Do you have such a strong desire to pass urine that you leak before reaching the toilet?” (Y/N) Urgency: “When you need to pass urine, how strong is the urge usually?” Scored on a 5-point scale (overwhelming, very strong, strong, normal, weak)	1-yr incidence of OAB, 8.8% in women	–
Donaldson et al. [15]	12 750 (baseline)	3	1	1	UUI: “Do you have such a strong desire to pass urine that you leak before reaching the toilet?” SUI: “Does any urine leak when you laugh, cough, or exercise?” Urgency: “How often is the urge to pass urine very strong making it difficult to delay urination?”	Incidence among women without OAB or SUI at baseline (number of new cases per year expressed as a proportion of noncases in the previous year) At 1 yr: OAB: 6.9%; SUI: 7.3% At 2 yr: OAB: 6.0%; SUI: 6.1% At 3 yr: OAB: 6.8%; SUI: 6.4%	Remission among women without OAB or SUI at baseline (number of remitted cases per year expressed as the proportion of cases in the previous year) At 1 yr: OAB: 38.8%; SUI: 34.9% At 2 yr: OAB: 38.9%; SUI: 34.4% At 3 yr: OAB: 36.9%; SUI: 33.7%
McGrother et al. [16]	19 241	1	–	–	SUI: Leakage on laughing, coughing, or exercise, occurring monthly or more OAB: Urgency leakage (a strong desire to pass urine resulting in leakage) or urgency (a strength of urgency that was typically very strong or overwhelming), occurring monthly or more	1-yr incidence rates in women SUI: 3.6% OAB: 5.4% Mixed syndromes: 4.5%	–
Moller et al. [19]	2284	1	–	–	Urgency: “Do you rush to the toilet because of a sudden desire to void?” UUI: “Do you leak urine if suddenly you need to rush to the toilet?” Symptoms were scored on a 4-point scale (never, sometimes, weekly or more, daily or more)	Proportion of women reporting urgency and UUI sometimes at baseline and weekly or more at 1 yr Urgency: 6.1% UUI: 2.7%	Proportion of women reporting urgency and UUI weekly or more at baseline and never at 1 yr Urgency: 29.0% UUI: 42.0%

Table 2 (Continued)

Study	Size	Follow-up duration, yr	Follow-up interval, yr	Recall period, yr	Symptom definition	Progression/incidence	Regression/remission
Holtedahl and Hunskaar [30]	489	1	–	–	UI: An objective demonstration of leakage according to 1988 ICS definitions	Incidence of regular UI in women after having no leakage at first consultation UI: 0.9%	No convincing cases of spontaneous remission in women
Byles et al. [20]	7158	9	Four study periods	1	UI frequency: “Have you experienced leaking urine either never, rarely, sometimes, or often in the last 12 months?”	Women reporting UI “sometimes” or “often” at any visit over 9 yr after reporting UI “rarely” or “never” at baseline UI: 14.6%	–
Goode et al. [23]	490 women; 496 men	3	1	0.5	“In the past 6 months, have you leaked even a small amount of urine?” (Y/N)	Women vs men reporting UI at 1 yr after reporting no UI at baseline: 15% vs 12% Women vs men reporting UI at 2 yr after reporting no UI at 1 yr: 13% vs 12% Women vs men reporting UI at 3 yr after reporting no UI at 1 and 2 yr: 8% vs 8%	3-yr remission rates for women vs men reporting UI at baseline over 3 yr: 39% vs 55%
Lifford et al. [22]	23 792	2	–	1	UI frequency: “During the past 12 mo, how often have you leaked urine or lost control of your urine?” (never, less than one per month, one per month, two to three per month, approximately one per week, approximately one per day)	2-yr incidence of UI in women: More than one UI episode per month: 18.4% One UI episode per month: 2.3% One UI episode per week: 1.9% Progression (increase from one UI episode per month to one UI episode or more per week): 32.1%	2-yr regression (decrease from one UI episode or more per week to one UI episode per month): 4.4% 2-yr remission (decrease from one UI episode or more per week to no UI episodes): 2.0%
Townsend et al. [21]	64 650	2	–	1	UI frequency: “During the last 12 months, how often have you leaked or lost control of your urine?” (never, less than one per month, one per month, two to three per month, one per week, almost everyday)	Total 2-yr incidence of leaking at least one time per month in women: UI: 13.7% UUI: 0.4% <sup>†</sup> MUI: 0.6% <sup>†</sup>	Proportion of women reporting more than one UI episode per month at baseline reporting no UI episodes by the second year: UI: 13.9%
Waetjen et al. [24]	2702	5	1	1	UI: “In the past year (or since your last study visit), have you ever leaked even a small amount of urine involuntarily?” (almost daily or daily [daily], several days per week [weekly], less than one day per week [monthly], less than once a month, or none)	Average 1-yr incidence of at least monthly incontinence in women: UI: 11.1%	–
Jackson et al. [25]	1017	2	1	1	UI: “Have you had accidental leakage of your urine during the past year?” (Y/N)	Women reporting no UI at baseline and any UI at follow-up: UI at 1 yr: 19% UI at 2 yr: 19%	Women reporting any UI at baseline and no UI at follow-up UI at 1 yr: 14% UI at 2 yr: 14%
Wehrberger et al. [26]	441	6.5 (mean)	–	0.08 (1 mo)	UI: “Have you leaked any urine at all during the past 4 weeks?” UI frequency: “How often do you leak urine?”	Incidence of UI over 6.5 yr in women: 25.6%	Remission of UI over 6.5 yr in women: 19.0%
Hagglund et al. [27]	248	4	–	–	UI assessed based on detrusor instability score	Mean annual incidence of UI in women: 4%	Mean annual remission of UI in women (remission was not defined): 4%
Liu and Andrews [28]	2087	2	1	–	UUI: “Do you have any difficulty holding your urine until you get to the toilet?” (often, occasionally, or never) SUI: “Do you accidentally pass urine?” (often, occasionally, or never)	Incidence of at least occasional UUI: UUI at 1 yr: 17.4% (men), 22.6% (women) UUI at 2 yr: 30.4% (men), 37.5% (women) SUI at 1 yr: 11.9% (men), 16.5% (women) SUI at 2 yr: 20.7% (men), 30.8% (women)	–
Samuelsson et al. [29]	382	Mean 4.7	–	–	UI: “Do you suffer from involuntary loss of urine?” (seldom, at least once per month, at least once per week, or daily)	Women reporting any UI: During follow-up period: 13.7% At least weekly: 2.4%	Remission rate of any UI in women: 27.8%

**Table 2 (Continued)**

Study	Size	Follow-up duration, yr	Follow-up interval, yr	Recall period, yr	Symptom definition	Progression/incidence	Regression/remission
Nygaard and Lemke [31]	2025	6	3	–	<p>UI: "How often do you have difficulty holding your urine until you can get to the toilet?" (never, hardly ever, some of the time, most of the time, all of the time; never and hardly ever were grouped as negative responses)</p> <p>SUI: "Do you ever leak urine when you cough, sneeze, or laugh?"</p>	<p>3-yr incidence in women:                      UI at 3 yr: 20.4%                      UI at 3–6 yr: 28.5%                      SUI at 3 yr: 24.0%                      SUI at 3–6 yr: 28.6%</p>	<p>3-yr remission in women (remission was not defined):                      UI at 3 yr: 31.7%                      UI at 3–6 yr: 22.1%                      SUI at 3 yr: 28.6%                      SUI at 3–6 yr: 25.1%</p>
Burgio et al. [32]	206	3	–	–	<p>Participants were asked whether they had ever leaked even a small amount of urine involuntarily</p>	<p>The 3-yr cumulative incidence of at least monthly UI in women: 8.0%</p>	–
Herzog et al. [33]	1956	2	1	1	<p>UI: "In the past 12 months, about how many days have you lost any urine, even a small amount, beyond your control?"</p>	<p>Incidence:                      UI from baseline to 1 yr: 22.4% (women), 9.0% (men)                      UI from 1 to 2 yr: 18.6% (women), 9.2% (men)</p>	<p>Remission (refers to no UI at 1 yr or 2 yr):                      UI from baseline to 1 yr: 11.2% (women), 26.7% (men)                      UI from 1 to 2 yr: 13.3% (women), 32.3% (men)</p>

ICS = International Continence Society; OAB = overactive bladder; SUI = stress urinary incontinence; UI = urinary incontinence; UII = urge urinary incontinence.

average annual incidence of 3.7% over 11 yr in men (Fig. 2), although this higher incidence rate might reflect the older age of the population assessed in this study (56–103 yr).

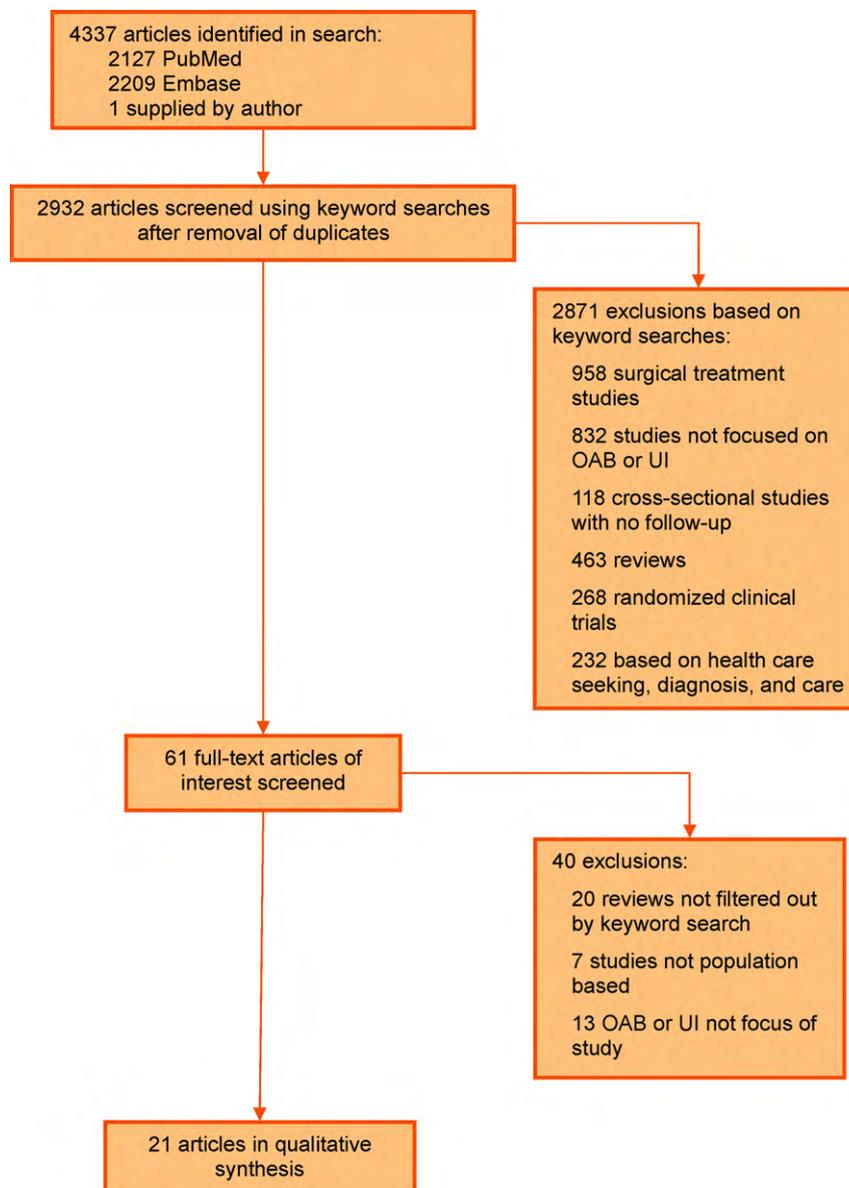
Wennburg et al provided evidence supporting a dynamic progression of OAB symptom severity over time [14]. Over a 16-yr period (1991–2007), the proportion of women with OAB without UII (OAB dry) did not differ significantly (1991, 11%; 2007, 10%; Fig. 2A); however, the number of women with OAB with UII (OAB wet) increased from 6% to 16%. Among women with OAB dry in 1991, 23% remained OAB dry and 28% reported symptom progression to OAB wet in 2007. Among women who were OAB wet in 1991, 53% remained OAB wet and 21% reported symptom regression to OAB dry in 2007. The rate of complete remission of OAB symptoms was greater for women who were OAB dry (49%) compared with those who were OAB wet (26%).

A study by Malmsten et al. [13] demonstrated a dynamic progression of OAB symptoms in men from 1992 to 2003. The proportions of men with OAB dry (1992, 13.7%; 2003, 36.9%) and OAB wet (1992, 1.9%; 2003, 7.4%; Fig. 2B) increased. Among men who were OAB dry in 1992, 49.5% remained OAB dry and 12.6% reported symptom progression to OAB wet in 2003; among men who were OAB wet in 1992, 51.1% remained OAB wet and 42.2% reported symptom regression to OAB dry in 2003. The rate of complete remission of OAB symptoms was notably greater for men who were OAB dry (37.9%) compared with those who were OAB wet (6.7%).

**3.2. Trends in the progression and regression of urinary incontinence symptoms**

The incidence rates of UI varied across the studies (Table 2), although nine of the studies of UI did not distinguish between UI subtypes. A study [30] that defined UI according to the 1988 ICS definition as an objective demonstration of leakage [36] reported that among Norwegian women with no UI at baseline, 0.9% had UI during the next year. In contrast, Wennberg et al in a study that defined UI according to the ICS definition as the complaint of any involuntary leakage of urine reported an incidence of 21% over 16 yr in Swedish women (average annual incidence: 1.3%) [14]. A similar study of Swedish men [13] reported an incidence of 9% over 11 yr (average annual incidence: 0.8%). Studies that did not use questions based on ICS definitions and had disparate methodologies including varying recall times reported variable incidence rates. For example, a study of postmenopausal women in the United States that defined UI subjectively according to the question, "Have you had accidental leakage of your urine during the past year?" reported that 19% of women who were continent at baseline reported UI within 1 yr [25]. Goode et al. [23] reported a 1-yr incidence rate of 13% in women and 12% in men, based on a yes/no response to the question, "In the past 6 months, have you leaked even a small amount of urine?" Based on the question, "Have you leaked any urine at all during the past 4 weeks?" Wehrberger et al. [26] reported a mean annual incidence of UI of 3.9% over 6.5 yr.

The severity of UI symptoms also progresses dynamically over time, although symptoms experienced at baseline also



**Fig. 1 – Flow diagram of the search results.**  
OAB = overactive bladder; UI = urinary incontinence.

persist throughout the duration of follow-up. Lifford et al. [22] reported that among men and women reporting one UI episode per month at baseline, 32.1% reported progression of UI to one or more UI episodes per week over 2 yr. Herzog et al. [33] assessed UI symptom transitioning between mild, moderate, and severe forms within 1- and 2-yr follow-up periods. Individuals who were continent at baseline and who subsequently became incontinent at 1 and 2 yr were most likely to develop mild UI; among those reporting mild or moderate UI at baseline, few became severely incontinent at 1 and 2 yr. Another study found that a report of UI at a prior follow-up visit was a strong predictor of UI (odds ratio 24.7 for any incontinence) [25]. Wennberg et al. [14] noted that most women (66%) with UI at baseline reported UI 16 yr later; there was also a considerable regression of symptoms (34%). Also examined were changes in UI

frequency among women reporting UI both at baseline and 16 yr later. Among women who experienced one or more UI episode per month at baseline, 57% reported at least weekly UI 16 yr later; among women with at least weekly UI at baseline, only 14% reported regression of their symptoms 16 yr later. In contrast with OAB, the rates of remission of UI symptoms parallel the corresponding incidence rates. For example, in a study of 64 650 women [21] a 2-yr UI incidence rate of 13.7% was accompanied by a 2-yr complete remission rate of 13.9% (Table 2). The reported regression and remission rates vary across studies. For example, Lifford et al. [22] reported that among women reporting one or more UI episode per week at baseline, 4.4% reported a regression of UI frequency to one UI episode per month, and 2.0% reported a complete remission of symptoms over 2 yr.

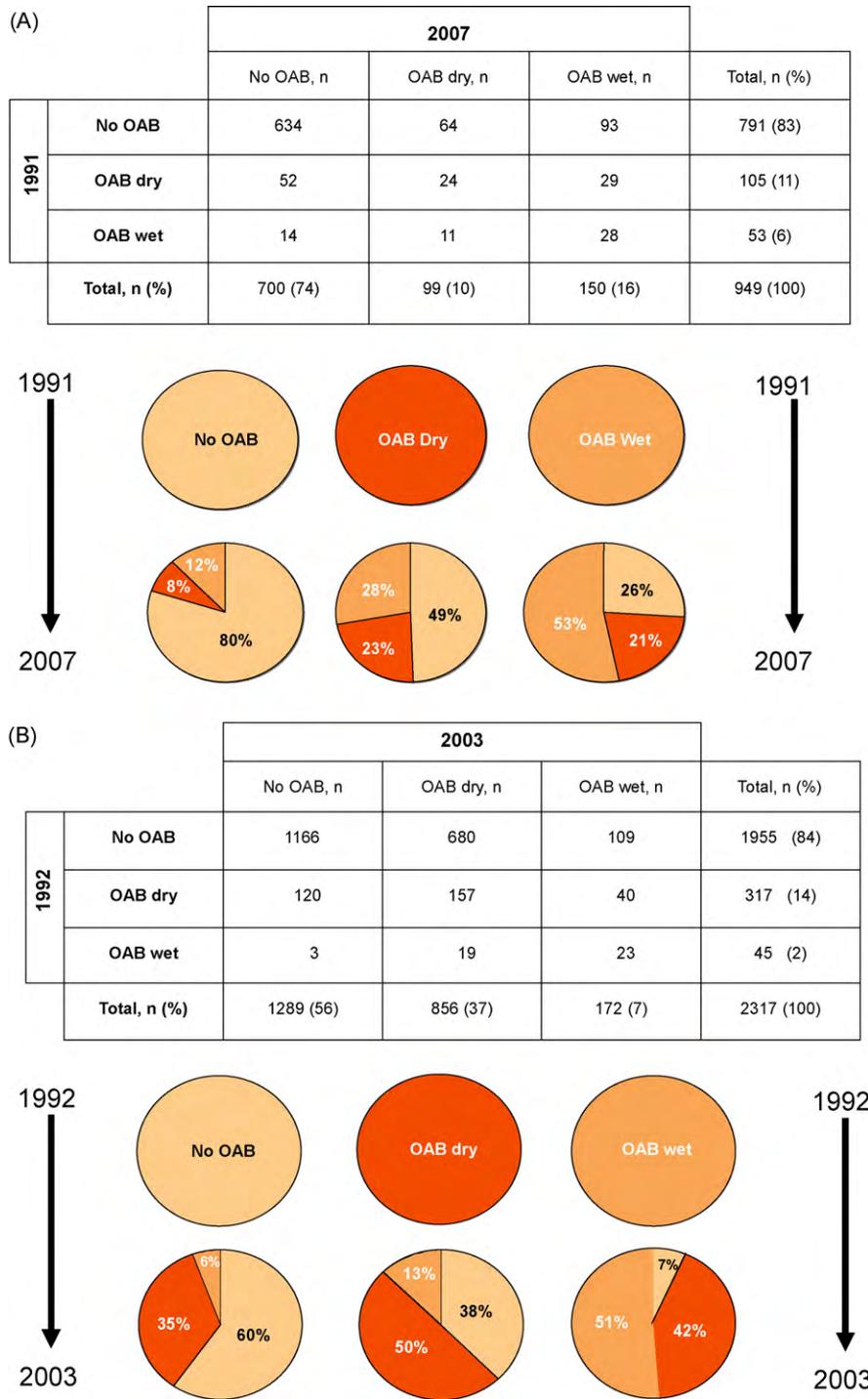


Fig. 2 – The dynamic progression of overactive bladder (OAB) symptom severity revealed by changes in the percentage distribution of individuals with no OAB symptoms (No OAB), OAB without urinary incontinence (UI) (OAB dry), and OAB with UI (OAB wet). (A) Symptom progression in the same women over a 16-yr period between 1991 and 2007. Reproduced with permission of Elsevier [14]. (B) Symptom progression in the same men over an 11-yr period between 1992 and 2003. Reproduced with permission of Elsevier [13].

3.3. Factors associated with overactive bladder and urinary incontinence progression

Based on prevalence measurements, factors associated with OAB and UI have been shown to include gender [17,18,28,33],

age [14,15,17,18,21,27,29,31], race and ethnicity [23–25], parity [20,21,24], dietary and lifestyle factors [17,18,24,29, 31], and comorbid conditions including constipation [2,20, 31], diabetes [16,20,24,25], and obesity/body mass index [16,20,24,32,37,38]. Relatively few studies have assessed risk

factors for the progression and remission/regression of symptoms; these studies have primarily focused on gender and age effects.

Cross-sectional studies reveal only small gender differences in prevalence in OAB [39,40]. None of the longitudinal studies reviewed directly address OAB symptom progression between genders in the same sample population. However, some gender-specific differences are alluded to by comparing the results of studies by Wennberg et al. [14] and Malmsten et al. [13], both of which used similar symptom definitions and methodologies to assess OAB symptom progression in women and men, respectively.

In contrast to OAB, cross-sectional studies have shown that the prevalence of all subtypes of UI (particularly SUI) is greater in women compared with men [39–42]. However, Goode et al. [23] reported a 3-yr incidence of UI in women that was only slightly higher compared with men (29% vs 24%). Herzog et al. [33] provided evidence that the patterns of progression and regression of UI symptoms differ between genders. Among women and men who reported mild UI at baseline, 51.5% and 49.2%, respectively, persisted with mild UI at 2 yr, 26.6% and 12.7% reported progression to moderate UI, and 3.6% and 3.2% reported progression to severe UI. Among women and men who reported severe UI at baseline, 52.9% and 50.0%, respectively, persisted with severe UI at 2 yr, 29.4% and 12.5% reported regression to moderate UI, 9.8% and 25.0% reported regression to mild UI, and 5.9% and 12.5% reported complete remission of UI symptoms.

Among studies addressing the effect of age on OAB symptom progression, Donaldson et al. [15], using validated symptom severity scores, reported that the severity of OAB increased with age for respondents 40–49 yr of age, reached a plateau for those 50–59 yr, increased steeply for those 60–69 yr, continued to rise for those 70–79 yr, and reached a plateau for those  $\geq 80$  yr. Hagglund et al. [27] also reported a decrease in remission rates with age (20–22 yr, 33%; 41–50 yr, 13%); however, these differences were not significant. Another study found that women reporting remission of UI were younger compared with women who remained incontinent for a period of 5 yr (mean age: 46.0 vs 50.3 yr) [29]. Townsend et al. [21] also found that among women who reported one or more UI episode per week at baseline, the complete remission of UI over 2 yr was more common in younger (36–45 yr) compared with older (46–55 yr) women (23.5% vs 15.1%); in addition, fewer younger women compared with older women persisted with one or more UI episode per week (46.9% vs 56.2%) [21].

### 3.4. Discussion

The reviewed studies clearly demonstrate an increasing incidence of OAB and UI over time, as well as a persistence of symptoms that illustrates the chronic nature of each condition. In addition, the severity of OAB and UI symptoms progresses dynamically over long time periods, as exemplified by the progression in OAB symptoms from OAB dry to OAB wet [13,14]. This is consistent with a hypothesis originally proposed by Stewart et al based on the results of

the National Overactive Bladder Evaluation (NOBLE) study that OAB dry precedes OAB wet [40]. The recognition of OAB and UI as progressive conditions allows for a shift from the current treatment paradigm of symptom control alone to one of symptom management, including measures to prevent the condition worsening. Such measures might include increasing adherence to treatment regimens and behavioral modifications including bladder training, pelvic floor muscle exercises, and lifestyle modifications [43].

The disparities in incidence rates between studies likely reflect confounders that are commonly encountered in the design of epidemiologic studies based on survey questionnaires, including study population heterogeneity, age-related variations, population sampling procedures, self-selection and attrition, analyses of nonresponders, survey methods (eg, postal vs telephone surveys), and differences in symptom definitions, assessment, and quantification [6,11]. For example, it is not clear from the methods described in many of the reviewed studies whether the same symptom definitions were used for baseline and follow-up questionnaires. Reported rates of symptom remission and regression are also likely to be affected by treatments received during the follow-up period; this information should be captured in questionnaires so that these rates can be adjusted accordingly. Taken together, these points emphasize the importance of standardizing study designs and questionnaires, as far as reasonably practicable, so that overall rates of incidence and remission and symptom progression may be determined.

It is apparent that slight variations in the phrasing of questions can lead to pronounced differences in corresponding incidence rates (Table 2). The definitions of OAB and UI were standardized by the ICS in 1998 [36] and updated in 2002 [34]; however, some studies do not adhere strictly to current ICS definitions, and some studies predate these definitions. There is also a wide variation between the studies in the definitions of UI (and UI subtypes) used as the basis of the survey questions (Table 2), which likely contributes to the apparent disparities in the incidence rates of UI. Also, there are currently no established definitions of symptom progression for OAB or UI. For OAB, this might correspond to a progression from no OAB to OAB dry or wet, OAB dry to OAB wet, and/or an increase in frequency. Objective measures based on urodynamics, bladder wall thickness, and urinary nerve growth factor (NGF) might alleviate the disparities; however, it is difficult to incorporate these into studies based on questionnaires. For example, Høltedahl et al. [30] defined UI according to the 1988 ICS definition as an objective demonstration of leakage [36], and participants were assigned objectively as continent or incontinent based on pad tests or frequency-volume charts; only 0.9% of women with no UI at the baseline reported UI during the next year. Wehrberger et al. [26] defined UI according to a subjective yes/no response to the question, “Have you leaked any urine at all during the past 4 weeks?” and reported a mean annual incidence of UI of 3.9%. Disparities between incidence rates of UI subtypes might also reflect differences in the symptom definitions and methodologies used (Table 2). For example, Donaldson et al. [15] used risk models to assess the

association of responses to postal questionnaires based on ICS definitions with urodynamic diagnosis of detrusor activity and SUI. These models were then used to define a urodynamically predictive symptom syndrome of SUI, from which a 2-yr incidence of SUI of 6.1% in women was reported. In contrast, Liu and Andrews [28] reported 2-yr incidence rate of 30.8% for SUI in women, using a computer-assisted telephone interview in which SUI was defined according to the question “Do you accidentally pass urine?” (Table 2). There are also marked variations between studies in the levels of symptom severity used to define UI. For example, some studies define UI as any loss of urine, whereas others define UI as leakage occurring monthly, weekly, or daily. It is also notable that nine of the studies of UI included in this review did not distinguish between UI subtypes, and only five studies provided data for UUI alone.

The timing of questions should be considered when designing questionnaires for long-term studies. Recall periods differed markedly among the 19 studies reviewed; because OAB and UI symptoms can vary over time, this might provide an explanation for the observed periodicity and/or fluctuations in UI and OAB prevalence. Follow-up and recall timing are also important to establish whether comorbid conditions occurred before or after the onset of OAB symptoms. Questionnaires should also garner information concerning treatment occurring between follow-up visits that might result in an underestimation of prevalence rates and an overestimation of remission rates. Also, respondents might answer questions more accurately if posed more than once [31]. In addition, individuals with symptoms are more likely to respond to surveys compared with those with no symptoms (ie, responder bias) [44]. However, individuals with UI are commonly stigmatized by their condition [45], which is likely to contribute to nonresponder rates.

The methods used for sample selection and survey administration also varied across studies. For example, some studies were based on random samples from general practitioner registers [15–18] or group model health maintenance organization enrollees [25], both of which are subject to sample bias owing to the fact that they do not entirely reflect the overall population [33]. Some sample populations may also be biased according to whether or not they include institutionalized patients. The modes of questionnaire administration used included both self-administered postal questionnaires and personal interviews that were either conducted by telephone or administered by an interviewer. Interviews commonly achieve a higher response rate compared with postal questionnaires and provide the opportunity to assess OAB and UI symptoms objectively. However, a personal interview may engender more embarrassment in participants, which may lead to the underreporting of symptoms.

Future studies of OAB and UI progression will likely be aided by lessons learned from epidemiologic studies of other diseases. Examples of archetypal studies of cardiovascular disease (CVD) include the Framingham Heart Study (FHS) [46], the Atherosclerosis Risk in Communities study [47], and the Multi-Ethnic Study of Atherosclerosis

[48]. The FHS is an ongoing longitudinal study initiated in 1948 that has provided insights into CVD progression and risk factors. This study also highlights the need to follow OAB and UI symptoms over long time periods to provide information on risk factors that are acquired at a relatively young age. Moreover, the fact that the FHS is a pan-generational study allows for genetic and familial factors associated with CVD to be investigated. Longitudinal studies such as the Swedish Twin Study [49] and the Boston Area Community Health Survey [41] should allow genetic and familial factors associated with OAB and UI to be investigated.

Cross-sectional studies, including the EPIC and NOBLE studies, demonstrate an increase in OAB and UI prevalence with age [4,39,40]. The increase in OAB and UI incidence with age may be linked to other age-related conditions, including neurologic and cerebrovascular disorders, pelvic tumors, and pelvic floor weakness [16], and it has important implications for public health and resources because the proportion of the population  $\geq 65$  yr of age will double over the next 2 decades [50]. The incidence of OAB is similar between genders. Notably, although the results indicate that men and women share similar incidences of UUI, women report an increased incidence of overall UI, which primarily reflects an increased incidence of SUI relative to men. This could result from anatomic differences, including the shorter urethra and absence of a prostate in women, which might contribute to a decreased bladder outlet resistance compared with men [51].

Whereas most of the reviewed studies indicate that symptoms reported at baseline generally continue at follow-up, evidence indicates that OAB and UI symptom severity spontaneously wax and wane over time. A study consisting of four survey periods (S1–S4) over 9 yr [20] showed that among women reporting UI sometimes or often at S1, 41% reported UI never or rarely at S2. However, among these women at S2, 26% went on to report UI sometimes or often at S3, and among these women at S3, 60% went on to report UI never or rarely once again at S4. Studies of disease progression might be aided by the use of biomarkers such as bladder wall thickness [52] and urinary NGF levels [53]. Urinary NGF levels may differ between incontinent and continent OAB patients and in patients with detrusor overactivity versus those without, and it has been suggested that urinary NGF levels might rank with bladder wall thickness as potential biomarkers for incontinent OAB [54]. Urinary levels of cytokines, chemokines, and growth factors are elevated in patients with idiopathic OAB, suggesting a role of inflammation in the pathology of OAB and that these inflammatory mediators might serve as biomarkers for the condition [55]. In this regard, it has been shown that chronic inflammation results in the chronic activation of sensory fibers that mediate the sensation of urgency and hypersensitivity. The interaction of inflammatory mediators with the parasympathetic and sensory innervations of the bladder might, at least in part, result in an altered sensation of urgency [55]. Moreover, the structural changes in the lower urinary tract induced by chronic inflammation might provide a mechanistic link between OAB

and other inflammatory diseases and suggest a novel mechanism by which OAB symptoms might progress.

#### 4. Conclusions

OAB and UI are highly prevalent and progress dynamically over time, characterized by both considerable incidence and remission rates. In general, the results support the hypothesis that OAB dry progresses to OAB wet and that the severity of UI symptoms increases over time. Although some evidence suggests differences in the progression of OAB and UI according to gender and age, further studies are needed to assess risk factors for symptom progression and regression or remission.

**Author contributions:** Debra E. Irwin had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Irwin, Milsom, Chancellor, Kopp, Guan.

**Acquisition of data:** Kopp, Guan.

**Analysis and interpretation of data:** Irwin, Milsom, Chancellor, Kopp, Guan.

**Drafting of the manuscript:** Irwin, Milsom, Chancellor, Kopp, Guan.

**Critical revision of the manuscript for important intellectual content:** Irwin, Milsom, Chancellor, Kopp, Guan.

**Statistical analysis:** Irwin, Milsom, Chancellor, Kopp, Guan.

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#### Appendix A

Search strategies were as follows:

PubMed search:

(overactive bladder[Title/Abstract] OR urinary incontinence[Title/Abstract]) AND (longitudinal[Text Word] OR natural history[Text Word] OR prospective[Text Word] OR population-based[Text Word] OR incidence[Text Word] OR remission[Text Word] OR regression[Text Word])

EMBASE search:

overactive AND bladder:ab,ti OR (urinary AND incontinence:ab,ti) AND (longitudinal OR natural AND 'history'/exp OR

prospective OR 'population based' OR 'incidence'/exp OR 'remission'/exp OR regression) AND [english]/lim AND [abstracts]/lim AND [1–1990]/sd NOT [20–9–2009]/sd yield 2209

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