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Urinary storage symptoms and comorbidities: a prospective population cohort study in middle-aged and older women

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Abstract

Objective: to identify predictive morbidities for urinary storage syndromes including indicators for neurological, musculoskeletal, cardiovascular, immune, lower bowel and psychological systems. This is the first study to test prior hypotheses, based on a literature review.
Design: this was a prospective cohort study involving 12,570 female respondents aged 40 or more registered with general practitioners and living at home in Leicestershire. Postal questionnaires were used at baseline and 1-year follow-up (response rates 65 and 79%, respectively).
Measures: pure stress urinary incontinence (SUI) and overactive bladder syndrome (OAB) were defined using standardised symptom indicators. Specific morbidities included reported medical diagnoses, standardised symptoms and general health indicators. Associations were identified using logistic regression, adjusting for age and physical impairment, with separate models for general and specific morbidities.
Results: multivariate morbidities consistently associated (i.e. both longitudinally and cross-sectionally) were SUI—cystitis and obesity; and OAB—bowel urgency, osteoporosis, imbalance, ankle swelling, cystitis, poor health and old age. Other independent predictors were SUI—multiple sclerosis and joint pain; and OAB—deep vein thrombosis and diabetes. Con-

sistent univariate indicators supported neurological, musculoskeletal, cardiovascular, immunological and psychological connections with both types of storage disorder plus an association with lower bowel problems for OAB.
Conclusions: abnormal urinary storage symptoms were predicted by obesity and poor general health, involving a range of systems of the body. OAB showed more extensive links than SUI with specific morbidities, including more medically diagnosed as opposed to symptom-based conditions. These findings were independent of problems with physical impairment.

Keywords: *urinary disorders, comorbidities, epidemiology, incontinence, aetiology, elderly*

Background

Urinary incontinence has been seen mainly as a functional consequence of disabling diseases such as dementia or as a direct consequence of childbirth and other trauma. However, the bladder forms part of a sensitive and complex system of the body that operates largely autonomously but remains under voluntary control [1]. As such, it is vulnerable to general disease processes related to ageing. Thus, associations with poor health and obesity [2] could represent pathogenic as well as functional involvement of the bladder. A distinction between urge and stress incontinence is now well recognised. Urge incontinence is consistently linked with urinary urgency and, usually with frequency and nocturia, in the syndrome of overactive bladder syndrome (OAB). Stress incontinence represents a syndrome on its own. These symptomatic diagnoses show positive but limited association with urodynamically defined detrusor overactivity and stress incontinence [3]. The prevalence of urge incontinence increases with age. Stress incontinence by comparison shows a peak around age 45–59 more so than in old age [4, 5]. Most previous comorbidity studies have considered incontinence as a whole [6] or urge and stress inclusive of those with mixed symptoms [2, 7]. Consequently, differences in the sample age group translate into differences in case mix, making it difficult to identify consistent comorbid relationships.

The main clinically recognised comorbidities involve neurodegenerative diseases, e.g. dementia [8], Parkinson's disease, multiple sclerosis (MS) and spinal injury. Allied to these conditions, relationships with osteoporotic fracture [9] balance and falls [10] suggest a wider connection with the musculoskeletal system, although they have been attributed to urgency plus incontinence [11, 12]. Arthritis is also commonly associated with incontinence, but the mechanism for this is usually assumed to be functional rather than a disease process [8, 13]. Links with stroke [14] may reflect neurological damage but also wider atherosclerosis in addition to physical impairment. Episodes of cystitis have been linked to separately occurring incontinence [15]. Links with depression [11, 13] are usually assumed to be reactive. Links with faecal incontinence are also recognised [11, 16] usually in relation to childbirth trauma, cognitive impairment and faecal impaction.

In addition to neurological damage [1], OAB has been pathophysiologically associated with partial denervation leading to bladder irritability and decreased contractility [17] possibly due to ischaemia [18]. Stress incontinence has been associated with a decline in function of the urethral sphincter, pudendal nerve and pelvic floor muscles [19], possibly related to ageing [20] and constitutional susceptibility of connective tissue [21] as well as to the traumatic and metabolic effects of childbirth and pregnancy [22].

Theoretically, related morbidities could occur together, either simultaneously or in sequence. Knowledge of the specific nature and sequence of development would improve understanding of the aetiological process and thereby the potential for prediction and prevention. The aim of this epidemiological study was to identify consistent and coherent general health and specific comorbidities implicated in disease processes, leading to the onset of pure forms of OAB and stress urinary incontinence (SUI) in women in the general population. The choice of comorbidities was informed by review of available literature [7].

Methods

This was a prospective cohort study within the MRC Incontinence programme, designed to provide an evidence base for developing services in the UK. A random sample of 20,247 women aged 40 or more was drawn from the Leicestershire Health Authority lists of 108 general practices (i.e. 71% of all practices), of which 19,241 proved eligible. People living in residential and nursing homes were excluded. Postal questionnaires, including two reminders, were used at baseline and at 1-year follow-up. Structured information was collected on all lower urinary tract symptoms, general health, selected comorbidities, activities of daily living (ADL) and reproductive history. Potential biases were explored in a related study of non-responders at baseline [23]. Baseline cases and non-cases were also compared for dropout rate at 1-year follow-up. The numbers of cases identified were: at baseline—pure SUI 837, pure OAB 824 and mixed 1281; and at follow-up—pure SUI 239, pure OAB 317 and mixed 422.

Definitions

Urinary storage symptoms definitions were consistent with recommended standards and validated against pad test and diary [3, 24]. SUI was defined as leakage on laughing, coughing or exercise occurring monthly or more. OAB was defined as 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. Pure OAB and pure SUI were mutually exclusive. These symptoms were the most specific, independent and consistent markers identified from: (i) a regression analysis of the same symptoms associated with urodynamic diagnoses of detrusor overactivity and stress incontinence among 490 participants in a treatment trial within the same

programme [25]; and (ii) a review of similar studies [26–30] from which the current approach provided the most accurate results [28].

Specific comorbidity indicators were formulated for a range of diseases previously identified or hypothesised within the neurological, musculoskeletal, cardiovascular, immunological, psychological systems and the lower bowel. These included the following diagnoses apparently reported by a doctor: Parkinson's disease, MS, epilepsy, spinal cord injury, dementia or Alzheimer's disease, osteoporosis, hypertension, angina, heart attack, blocked leg arteries, deep-vein thrombosis, Raynaud's disease, diabetes, rheumatoid arthritis and depression. The level of agreement between self-reported and physician-reported chronic conditions has been shown to be very good for well-recognised diseases [31–33]. Those with well-established diagnostic criteria, e.g. diabetes, ischaemic heart disease and hypertension, tend to show better agreement than conditions such as arthritis and atherosclerosis.

Whilst medical diagnoses may be relatively accurate, this approach may be insensitive in detecting comorbid conditions. Many patients with symptoms of arthritis, for example, remain undiagnosed. Therefore, symptom indicators were formulated, using standardised questions for the following: joint pain/stiffness, breathlessness, ankle swelling, balance/dizziness, falls, hearing problems, difficulty remembering recent events and vision problems not fully corrected by wearing glasses, suggesting possibly cataract, diabetes, glaucoma or neuritis [34]. Self-reported conditions were also preferred for stroke, minimal trauma fracture, cystitis or urinary infection, bowel symptoms including soiling, urgency and straining, hay fever, dermatitis or eczema, asthma and 'allergy' to food, medication or elastoplast, the last representing a cell-mediated reaction.

Indicators for general health, as distinct from specific disease, included physical impairment in terms of ADL [35] and standard questions for general health and long-term health problems [36]. Self-reported height at age 20 and current weight were used to calculate a body mass index (BMI) which was categorised as underweight (<20), acceptable (20–25), overweight (>25–30) and obese (>30) [37].

Analysis

Cross-sectional and longitudinal data were analysed separately throughout using logistic regression models. Likelihood ratio tests were used to determine the significance for each morbidity ($P<0.05$). All results were adjusted for age, and all analyses were repeated adjusting for age and ADL. Separate multivariate models were developed for general health and specific morbidity indicators to avoid distortion of both patterns of association. Parity was also included in the model for specific comorbidities, as a potential confounder.

Multivariate modelling was carried out for specific morbidities in two stages. First, potentially related morbidities were categorised into the following groups: neurological, musculoskeletal, cardiovascular, 'allergy' and lower bowel. All significant related morbidities from the univariate analysis were entered into a multivariate model using backward stepwise techniques to build a final model for each group. Second, all the significant morbidities from each group together with cystitis, depression and parity (where univariately significant) were entered into a final model using similar techniques.

Cross-sectional analyses used prevalent cases of pure syndrome in the baseline survey. Longitudinal analyses used incident cases of pure syndrome at 1-year follow-up in people free from the relevant syndromes at baseline. These cases were regressed against baseline comorbidity reports in all analyses. Associations identified both longitudinally and cross-sectionally are described in the results as consistent comorbidities. Univariate associations across a range of similar system indicators were also considered to represent potential aetiological pointers. Bonferroni adjustments were not appropriate because morbidities were selected following literature review [38].

Results

The age distribution of the sample aged 40 and over (range 40–98; median 58.0; mean 59.5; and SD 13.0) was similar to that for the UK. The response at baseline was 65.3%. Responders were slightly older than non-responders (median age 58 and 56 years) but included a slightly lower proportion (59.6%) of women aged 80 or more. The in-depth non-responders study suggested that 7% were unable to cooperate due to illness and frailty [23]. Response at follow-up was 79.7%. There was no difference in the dropout rate between cases and non-cases of urinary storage disorder at baseline. Baseline prevalences of pure SUI, pure OAB and mixed syndromes were 7.7, 7.7 and 12.7%, respectively. The incidence rates over 1 year were 3.6, 5.4 and 4.5%, respectively. Baseline prevalences for general health factors showed poor health affected 5.9%, long-term health problem 33.6% and obesity 19.5%, in line with other similar studies in women [36].

Overactive bladder syndrome

General health

There were consistent longitudinal and cross-sectional univariate associations with all the general health indicators (Table 1). The strongest associations were with poor health and physical impairment. There was evidence of a significant cross-sectional link with both underweight and obesity. In the multivariate analysis, only poor health was consistently associated (Table 2). Physical impairment and long-term illness appeared to accompany rather than precede OAB, amid evidence of an association with old age.

Specific morbidity

There were consistent univariate links with the bowel (soiling, urgency and straining), neurological (spinal injury, poor vision, imbalance and memory), musculoskeletal (osteoporosis, falls, non-rheumatoid joint pain and fracture), cardiovascular (breathlessness, ankle swelling, ischaemic heart disease and diabetes), immunological (cystitis and medicine 'allergy') and psychological (depression) systems (Table 3). In the multivariate analysis, only bowel urgency, cystitis, imbalance, osteoporosis and ankle swelling were consistently associated

Table 1. General health factors associated with storage syndromes: univariate analyses in women[a]

		Stress incontinence		Overactive bladder	
General factors	Prevalence (%)	Longitudinal OR (95% CI)	Cross-sectional OR (95% CI)	Longitudinal OR (95% CI)	Cross-sectional OR (95% CI)
General health					
Excellent/very good	35.7	1.0*	1.0***	1.0***	1.0***
Good	36.9	1.5 (1.0, 2.0)	1.5 (1.3, 1.8)	1.3 (0.9, 1.6)	1.6 (1.3, 2.0)
Fair	21.6	1.5 (1.0, 2.2)	2.1 (1.7, 2.5)	2.3 (1.7, 3.1)	3.2 (2.6, 3.9)
Poor	5.9	2.3 (1.2, 4.3)	2.0 (1.4, 2.8)	4.0 (2.5, 6.3)	6.3 (4.8, 8.3)
Long-term illness	33.6	1.0 (0.7, 1.4)	1.4 (1.2, 1.7)***	1.7 (1.3, 2.2)***	2.8 (2.4, 3.3)***
ADL					
Best 1	18.2	1.0*	1.0***	1.0***	1.0***
2	14.6	0.8 (0.5, 1.4)	1.6 (1.3, 2.1)	1.1 (0.7, 1.7)	1.4 (1.0, 2.0)
3	36.4	1.4 (0.9, 2.0)	2.2 (1.8, 2.8)	1.4 (0.9, 2.0)	2.1 (1.6, 2.8)
Worst 4	30.8	1.6 (1.0, 2.4)	2.4 (1.9, 3.2)	2.7 (1.8, 4.0)	4.9 (3.7, 6.6)
BMI					
Underweight	3.2	0.7 (0.2, 2.4)	0.9 (0.5, 1.6)	1.2 (0.5, 2.5)	2.0 (1.4, 2.9)
Acceptable	38.7	1.0***	1.0***	1.0*	1.0 ***
Overweight	38.6	1.4 (0.9, 1.9)	1.4 (1.1, 1.6)	1.3 (1.0, 1.8)	1.2 (0.97, 1.4)
Obese	19.5	2.3 (1.5, 3.3)	2.0 (1.7, 2.5)	1.6 (1.1, 2.2)	1.5 (1.2, 1.8)

[a]Age adjusted. *$P \leq 0.05$, **$P < 0.01$, ***$P < 0.001$. ADL, activities of daily living; BMI, body mass index.

Table 2. General health factors associated with storage syndromes: multivariate analyses

	Stress incontinence		Overactive bladder	
General factors	Longitudinal OR (95% CI)	Cross-sectional OR (95% CI)	Longitudinal OR (95% CI)	Cross-sectional OR (95% CI)
General health				
Excellent/very good	1.0	1.0***	1.0***	1.0***
Good	1.3 (0.9, 1.8)	1.4 (1.1, 1.7)	1.3 (0.9, 1.6)	1.5 (1.2, 1.8)
Fair	1.2 (0.7, 1.9)	1.8 (1.4, 2.3)	2.3 (1.7, 3.1)	1.9 (1.5, 2.5)
Poor	2.0 (0.9, 4.2)	2.0 (1.3, 3.1)	4.0 (2.5, 6.3)	3.2 (2.3, 4.5)
Long-term illness	0.6 (0.3, 1.0)	1.0 (0.8, 1.3)	1.2 (0.8, 1.7)	1.6 (1.2, 2.0)***
ADL				
Best 1	1.0	1.0***	1.0	1.0***
2	0.8 (0.4, 1.3)	1.6 (1.2, 2.1)	1.0 (0.6, 1.6)	1.3 (0.9, 1.8)
3	1.1 (0.7, 1.7)	1.8 (1.4, 2.3)	1.0 (0.6, 1.6)	1.6 (1.1, 2.1)
Worst 4	1.0 (0.5, 1.8)	1.4 (1.0, 2.0)	1.3 (0.7, 2.3)	2.1 (1.5, 3.0)
BMI				
Underweight	0.7 (0.2, 2.4)	0.9 (0.5, 1.5)	0.9 (0.4, 2.1)	1.5 (0.9, 2.3)
Acceptable	1.0***	1.0***	1.0	1.0
Overweight	1.4 (0.9, 1.9)	1.2 (1.0, 1.5)	1.3 (1.0, 1.8)	1.1 (0.9, 1.3)
Obese	2.3 (1.6, 3.3)	1.7 (1.4, 2.1)	1.2 (0.9, 1.9)	1.1 (0.8, 1.4)
Age (10-year increase)	0.9 (0.7, 1.0)	0.8 (0.7, 0.8)***	1.2 (1.1, 1.3)**	1.1 (1.0, 1.2)*

*$P \leq 0.05$, **$P < 0.01$, ***$P < 0.001$. ADL, activities of daily living; BMI, body mass index.

(Table 4). Diabetes and DVT were additional independent predictors whereas MS, memory and vision problems, rheumatoid arthritis and other joint pain plus faecal soiling and straining appeared to accompany rather than precede OAB. Parity was not associated with OAB.

Stress incontinence

General health

There were consistent longitudinal and cross-sectional univariate associations with obesity, poor health and physical impairment (Table 1). In the multivariate analysis, only obesity was consistently associated (Table 2). Poor health and physical impairment appeared to accompany rather than precede SUI amid evidence of an association with young age.

Specific morbidity

There were consistent univariate links with the immunological (cystitis and food 'allergy'), cardiovascular (breathlessness, ankle swelling and hypertension), neuromusculoskeletal (poor hearing and non-rheumatoid joint pain) and psychological

Table 3. Specific morbidity factors associated with storage syndromes: univariate analyses[a]

Specific factors	Prevalence %	Stress incontinence		Overactive bladder	
		Longitudinal OR (95% CI)	Cross-sectional OR (95% CI)	Longitudinal OR (95% CI)	Cross sectional OR (95% CI)
Depression	20.2	1.4 (1.0, 2.0)*	1.8 (1.5, 2.1)***	1.4 (1.0, 1.9)*	2.0 (1.7, 2.4)***
Dementia	0.5	No cases	No cases	4.0 (0.8, 19.5)	2.9 (1.3, 6.7)*
Poor memory	39.6	1.2 (0.9, 1.6)	1.8 (1.6, 2.1)***	1.5 (1.1, 1.8)***	2.0 (1.8, 2.4)***
Parkinson's	0.4	No cases	No cases	2.9 (0.8, 10.3)	2.2 (0.9, 5.0)
Epilepsy	1.2	1.9 (0.5, 6.1)	0.9 (0.4, 1.9)	0.8 (0.1, 3.4)	2.2 (1.2, 3.9)*
Multiple sclerosis	2.7	1.1 (0.1, 8.4)	1.0 (0.4, 2.9)	1.0 (0.1, 7.6)	7.6 (4.1, 13.9)***
Spinal injury	1.2	0.7 (0.2, 2.1)	1.1 (0.7, 1.8)	2.1 (1.1, 3.8)*	2.5 (1.8, 3.6)***
Poor vision	20.2	1.5 (1.0, 2.0)*	1.1 (0.9, 1.3)	1.5 (1.1, 2.0)**	2.2 (1.8, 2.5)***
Poor hearing	29.0	1.4 (1.0, 1.9)*	1.5 (1.3, 1.7)***	1.3 (0.9, 1.6)	1.6 (1.3, 1.8)***
Poor balance	34.1	1.3 (0.9, 1.7)	1.5 (1.3, 1.8)***	1.9 (1.5, 2.4)***	2.4 (2.1, 2.8)***
Falls	26.9	1.3 (0.9, 1.8)	1.1 (0.9, 1.3)	1.4 (1.0, 1.7)*	1.9 (1.7, 2.3)***
Osteoporosis	6.7	0.9 (0.4, 1.7)	1.5 (1.1, 2.0)*	1.9 (1.3, 2.8)**	2.1 (1.6, 2.7)***
Fracture	15.0	1.1 (0.7, 1.6)	1.1 (0.8, 1.3)	1.4 (1.0, 1.8)*	1.3 (1.1, 1.5)*
Rheumatoid arthritis (RA)	15.6	1.1 (0.7, 1.7)	1.1 (0.8, 1.3)	1.3 (0.9, 1.8)	1.9 (1.5, 2.2)***
Joint pain (non-RA)	38.6	1.5 (1.1, 2.0)*	1.4 (1.2, 1.7)***	1.3 (1.0, 1.6)*	1.5 (1.3, 1.8)***
Diabetes	5.4	1.6 (0.8, 2.8)	1.1 (0.7, 1.6)	2.0 (1.2, 3.1)**	1.4 (1.1, 2.0)*
Stroke	3.6	1.9 (0.9, 3.5)	1.1 (0.7, 1.7)	1.7 (1.0, 2.8)	2.0 (1.5, 2.7)***
Heart attack /angina	7.5	1.2 (0.6, 2.2)	1.7 (1.2, 2.3)**	1.6 (1.0, 2.4)*	2.1 (1.7, 2.7)***
Blocked arteries	3.7	1.0 (0.4, 2.6)	0.8 (0.5, 1.4)	1.5 (0.8, 2.7)	1.7 (1.2, 2.4)**
Hypertension	27.9	1.5 (1.1, 2.0)*	1.3 (1.1, 1.5)**	1.2 (0.9, 1.5)	1.4 (1.2, 1.6)***
Raynaud's	1.9	1.3 (0.5, 3.2)	1.0 (0.6, 1.8)	0.9 (0.3, 2.3)	2.0 (1.2, 3.1)**
DVT	2.5	0.5 (0.1, 2.2)	1.1 (0.7, 1.9)	2.7 (1.5, 4.7)**	1.2 (0.8, 2.0)
Ankle swelling	39.2	1.5 (1.1, 1.9)**	1.5 (1.3, 1.7)***	1.7 (1.4, 2.2)***	1.9 (1.7, 2.2)***
Breathlessness	32.3	1.6 (1.2, 2.1)**	1.9 (1.7, 2.3)***	1.9 (1.5, 2.3)***	2.1 (1.8, 2.5)***
Asthma	10.6	1.2 (0.7, 1.9)	1.9 (1.6, 2.4)***	1.0 (0.7, 1.5)	1.2 (0.9, 1.5)
Hay fever	15.6	1.1 (0.7, 1.6)	1.4 (1.1, 1.6)**	1.1 (0.8, 1.5)	1.0 (0.8, 1.3)
Dermatitis/eczema	12.0	0.8 (0.4, 1.2)	1.1 (0.9, 1.3)*	1.4 (0.9, 1.9)	1.3 (1.1, 1.6)*
Food allergy	9.0	1.6 (1.0, 2.4)*	1.3 (1.0, 1.7)*	1.4 (0.9, 2.0)	1.4 (1.1, 1.8)**
Medicine allergy	17.4	1.1 (0.8, 1.6)	1.5 (1.2, 1.8)***	1.6 (1.2, 2.1)**	1.4 (1.2, 1.7)**
Elastoplast allergy	10.1	1.4 (0.9, 2.1)	1.4 (1.1, 1.7)**	1.6 (1.1, 2.3)**	1.2 (0.9, 1.5)
Cystitis	14.4	2.0 (1.5, 2.8)***	1.9 (1.6, 2.3)***	1.6 (1.1, 2.2)**	2.6 (2.2, 3.1)***
Bowel					
Soiling	2.0	2.0 (0.9, 4.6)	1.8 (1.2, 2.7)*	4.0 (2.3, 6.9)***	5.3 (3.9, 7.2)***
Urgency	8.2	1.4 (0.8, 2.2)	1.8 (1.4, 2.3)***	2.6 (1.7, 3.7)***	4.2 (3.4, 5.2)***
Straining	14.8	1.3 (0.8, 1.8)	1.8 (1.5, 2.2)***	1.7 (1.2, 2.2)**	2.4 (2.0, 2.8)***
Parity					
0	12.8	1.0	1.0***	1.0	1.0
1	14.3	1.3 (0.7, 2.2)	1.3 (0.9, 1.7)	1.0 (0.6, 1.5)	1.2 (0.9, 1.6)
2	38.5	1.5 (0.9, 2.4)	1.7 (1.3, 2.2)	0.9 (0.6, 1.3)	1.1 (0.8, 1.4)
3+	34.5	1.7 (1.0, 2.8)	1.9 (1.5, 2.5)	1.1 (0.8, 1.6)	1.2 (0.9, 1.5)

[a]Age adjusted. *$P \leq 0.05$, **$P < 0.01$, ***$P < 0.001$.

(depression) systems (Table 3). In the multivariate analysis, only cystitis was consistently associated (Table 4). MS and joint pain were additional predictors, whereas depression, memory problems, poor hearing, breathlessness, asthma and bowel straining appeared to accompany rather than precede SUI. The independent cross-sectional association between parity and prevalent rather than incident cases of SUI probably reflects the distant effects of childbirth in this age group.

Mixed incontinence showed almost all the elements of both SUI and OAB but usually more strongly than either of the pure forms (results not shown).

Discussion

Pure OAB was independently predicted by poor health rather than by poor physical impairment. The association with old age, although consistent with other studies [2, 39], disappeared after controlling for a full range of specific comorbidities, suggesting that the condition is age related rather than age dependent. The independent specific predictors included bowel urgency, imbalance, osteoporosis, ankle swelling, diabetes, DVT and cystitis. Diabetes has been associated previously with urge incontinence [2]. Other studies involving older people, in whom OAB predominates, have also shown a relationship with

Table 4. Specific morbidity factors associated with storage syndromes: multivariate analyses

		Stress incontinence		Overactive bladder	
Specific factors		Longitudinal OR (95% CI)	Cross-sectional OR (95% CI)	Longitudinal OR (95% CI)	Cross sectional OR (95% CI)
Depression			1.4 (1.1, 1.7)***		
Memory			1.4 (1.1, 1.7)***		1.2 (1.0, 1.5)*
Multiple sclerosis		1.5 (1.0, 2.1)*			3.0 (1.2, 7.8)*
Vision					1.3 (1.0, 1.6)*
Hearing			1.2 (1.0, 1.5)*		
Balance				1.4 (1.0, 1.9)**	1.4 (1.1, 1.7)***
Osteoporosis				**1.8 (1.1, 2.9)***	**1.5 (1.0, 2.1)***
Rheumatoid arthritis					1.5 (1.0, 2.0)*
Joint pain		1.4 (1.0, 1.9)*			1.4 (1.1, 1.8)**
Diabetes				2.2 (1.3, 3.6)**	
DVT				2.5 (1.3, 4.6)**	
Ankle swelling				**1.4 (1.0, 1.9)****	**1.2 (0.9, 1.5)***
Breathlessness			1.4 (1.1, 1.8)***		
Asthma			1.5 (1.1, 1.9)**		
Cystitis		**1.9 (1.3, 2.7)*****	**1.5 (1.2, 1.9)*****	**1.6 (1.1, 2.3)****	**2.1 (1.6, 2.6)*****
Bowel					
Soiling					1.8 (1.1, 2.9)*
Urgency				**2.2 (1.5, 3.4)****	**2.8 (2.1, 3.7)*****
Straining			1.5 (1.2, 1.9)***		1.4 (1.0, 1.8)**
Parity					
0			1.0***		
1			1.2 (0.8, 1.7)		
2			1.6 (1.2, 2.2)		
3+			1.7 (1.2, 2.3)		
Age (10-year increase)		**0.8 (0.6, 0.9)****	**0.7 (0.6, 0.8)*****		
ADL					
Best	1		1.0***		1.0***
Worst	2		1.4 (1.0, 1.8)		1.1 (0.7, 1.6)
	3		1.7 (1.3, 2.2)		1.3 (0.9, 1.9)
	4		1.3 (0.9, 1.8)		2.0 (1.3, 3.0)

*$P \leq 0.05$, **$P < 0.01$, ***$P < 0.001$. Consistent factors in bold. ADL, activities of daily living.

diabetes [11, 40, 41] and similarly for osteoporosis [9], dementia [42], faecal incontinence [11, 43], imbalance [10] cardio-pulmonary [6, 9, 11, 40], cardiovascular [13, 44] and poor health [42]. However, connections between OAB and DVT or ankle swelling have not been demonstrated before. DVT has been linked with diabetes and other predisposing factors including varicose veins, use of hormone replacement therapy (HRT) and thrombophilic states [45].

The diversity of comorbidity and system indicators for OAB suggests the existence of several subgroups of OAB and/or a common underlying problem involving multiple organs. Possible mechanisms undermining multiple systems could include suboptimal nutrition (particularly for people with vulnerable constitutions including diabetes). The relatively prominent association with bowel urgency, soiling and straining may implicate bowel dysfunction. Artificially induced diabetic neuropathy provides a mechanism for one of the main animal models for OAB [17]. Diabetes is also consistent with the proposed model of denervation probably related to ischaemia [18], triggering increased excitability of the smooth bladder muscle.

Osteoporosis has been proposed as a long-latency deficiency disorder and related to suboptimal vitamin D status [46, 47]. Vitamin D is associated with physical dysfunction and balance problems [48], both of which independently accompanied OAB. Calcium absorption and metabolism are also dependent on vitamin D and are important for smooth muscle tone and contractility. Links with vitamin D deficiency have also been observed for diabetes [49].

Pure SUI was predicted by obesity and not by physical impairment. The association with young age remained after controlling for potential specific comorbidities. The independent specific predictors were confined to cystitis, MS and joint pain with parity also implicated. Relationships with obesity [50, 51] and childbirth [52, 53] have consistently been shown for SUI [2, 22, 54–61] more so than urge incontinence [2]. An inverse association with age is also a consistent finding [58] and has been related to a disappearance of the effect of parity with age [55]. Association with joint problems [13] has been reported for incontinence in older women, but a connection between MS and SUI has not. Links with asthma may suggest an element of immune dysfunction.

SUI has been associated with pelvic floor weakness, prolapse and bladder neck hypermobility [19]. The underlying mechanism proposed for this is a constitutional variation in collagen and its remodelling via enzymes susceptible to steroid hormones [21]. In this model, obesity may exert a direct mechanical load on the pelvic floor plus an indirect effect via oestrogen generated from adipose tissue [62]. It is interesting in this respect that SUI is observed to peak around age 45–59

and dip thereafter [58], perhaps in line with hormonal and obesity patterns. Obesity and laxity of joints are also associated with osteoarthritis for which potential systemic risk factors include HRT, poor nutrition and genetic factors [63].

Cystitis is commonly linked with incontinence [41, 44, 64, 65], and the potential for misinterpretation of symptoms is considerable. However, in a careful clinical study, although both stress and urge were related to cystitis during acute episodes, the relationship was confined to stress incontinence. In the same study, cystitis was associated with urogynaecological surgery, and the suggested underlying mechanisms involved predisposition to such surgery and a degree of susceptibility to infection [15]. Acute episodes of cystitis involve urgency and incontinence, but it has also been suggested that at other times, the urothelium may detect noxious chemicals and bacteria and transmit signals to induce emptying [1], thereby perpetuating a link with urge incontinence.

Depression was consistently associated with both OAB and SUI univariately. This is consistent with other studies of incontinence as a whole [11, 13, 66]. In the current study, the association between OAB and depression appeared to depend largely on the presence of the physical morbidities. However, there was evidence to suggest that depression may accompany the onset of SUI independently.

The less-than-expected associations with dementia [13, 42], stroke [11, 13, 14, 40, 42] and Parkinson's disease [9, 13, 67] could be because of under-representation of these groups within the present study. The sample excluded those in residential and nursing homes where prevalences are particularly high. There was also a small element of non-response bias in relation to the postal questionnaire for those unable to cooperate because of poor health. Problems with random measurement error, inherent to the method of relying on reported conditions, are likely to reduce the strength of observed associations. Thus, this approach may be prone to missing genuine connections, particularly for very disabling conditions, but it has the advantage of providing a population perspective.

Certain conditions were not predictive, yet were associated cross-sectionally. This may be because of a greater power provided by the larger number of prevalent compared to incident cases, particularly for relatively rare morbidities. For more common conditions, the pattern of association is likely to reflect the sequence of the disease process. Parity may not register as a predictor for SUI in this study because its effect in generating new cases occurred at an earlier age. Most morbidities related to newly incident cases also appeared to be associated with prevalent cases of incontinence, but some were confined to incidence, including DVT and diabetes for OAB and MS and joint pain for SUI. Morbidities with high-incident and low-prevalent effects may be recent in onset, remittent or responsive to treatment. In the multivariate analyses, it is also possible that the separate cross-sectional and longitudinal models selected different indicators for statistical reasons despite being based on exactly the same range of indicators.

Methodologically, the current study was relatively large scale and wide ranging compared to previous studies, providing good power to detect specific associations, subject to the usual chance effects. Using mutually exclusive symptom syndromes maximises diagnostic accuracy and minimises heterogeneity because of mixed forms. Extensive misclassification would tend to undermine rather than re-enforce the distinctive comorbidity patterns observed for OAB and SUI. Our objective was to identify potential morbid associations rather than any form of predictor. Therefore, we allowed adjustment for age and physical impairment but deliberately did not adjust for lifestyle, socioeconomic, physical measurement or quality of life factors likely to be involved in the same chain of events and thereby distorting or reducing the chances of detecting morbid associations. We recognise potential relationships with drugs and surgery used to treat the morbidities and lifestyle factors but consider these to be beyond the scope of the current article. Clinical confirmation of these findings is needed.

Key points

- This prospective study confirmed previously identified specific associations between SUI and obesity, parity and cystitis.
- New independent predictors for SUI identified were MS and joint pain (i.e. non-rheumatoid arthritis).
- Previously identified associations with incontinence in older people were confirmed prospectively in relation to OAB for poor health, diabetes, cystitis and bowel urgency problems.
- New independent predictors for OAB identified were osteoporosis, DVT, ankle swelling and imbalance.
- Physical impairment as an independent factor appeared to accompany rather than precede the development of storage symptoms.

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Conflicts of interest

There were no conflicts of interest for any of the authors.

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