

1 **Overweight and obesity as major, modifiable risk factors for urinary**
2 **incontinence in young to mid-aged women: A systematic review and**
3 **meta-analysis**

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Abstract

The purpose of this review and meta-analysis was to evaluate overweight and obesity as risk factors for urinary incontinence in young to mid-aged women. Understanding these relationships during this life stage is important as early onset may develop into severe and persistent incontinence at an older age. A systematic search resulted in 497 citations, 14 of which were retained for review. Data were analysed separately by overweight and obesity, and by subtype of urinary incontinence – Stress, Urge, Mixed, and Severe. When compared with women in the normal BMI range, overweight was associated with a one third increase in risk of urinary incontinence (relative risk [RR] = 1.35, 95% confidence interval [CI] = 1.20-1.53), while the risk was doubled in women with obesity (RR = 1.95, 95% CI = 1.58-2.42). Compared with healthy weight, the risk of each urinary incontinence subtype doubled with overweight/obesity. Overweight and obesity are strong predictors of urinary incontinence, with a significantly greater risk observed for obesity. Clinical advice to young women at risk of, or presenting with, obesity should not be limited to metabolic health only, but should emphasise the role of excess weight on pelvic floor weakening and subsequent risk of incontinence.

1 Introduction

2 Urinary incontinence (UI) is defined as the complaint of involuntary loss of urine (1). It is a highly
3 prevalent condition among women, with estimates ranging from 10-40% (2). In the past, parity and older age
4 were considered the most likely causes of UI in women (3), however recent research has demonstrated an
5 increasing prevalence in both younger women (4) and nulliparous women (5). This highlights the need to
6 explore risk factors that contribute to UI other than parity and ageing. Recent research indicates that overweight
7 and obesity increase the risk of UI in women (6). The proposed mechanism underpinning this observation is a
8 chronic increase in intra-abdominal pressure (IAP), which increases intravesical pressure, while
9 simultaneously affecting urethral mobility (7).

10 In 2017, a review of the prevalence of UI and its determinants in young, nulliparous women (4)
11 reported that women with a high BMI had an increased risk of UI. The researchers did not, however,
12 differentiate between overweight and obesity, or incontinence subtype. There are two main subtypes of UI:
13 stress urinary incontinence and urge urinary incontinence, and women may experience symptoms of either
14 one, or a combination (i.e., mixed urinary incontinence). There is evidence to suggest that overweight and
15 obesity affect these subtypes of UI differently (6), however these relationships are not yet fully understood.

16 A comprehensive systematic review in 2008 assessed the evidence for overweight and obesity as risk
17 factors and targets for clinical intervention in women of all ages with UI (6). It was concluded that the
18 association between excess weight and UI is important and warrants further investigation. However, given the
19 heterogeneity of studies included in that review and the high variability of the relative risk estimates of UI (RR
20 ranged from 1.03 to 6.10), a meta-analysis may bring the scientific community closer to a consensus on the
21 relative importance of obesity as a risk factor of UI.

22 Given the current generation of young adult women is heavier and appears to be gaining weight at a
23 faster rate than previous generations (8, 9), the premise that excess weight is a prominent risk factor for
24 developing UI is concerning. Data from the Australian Longitudinal Study on Women's Health show that the
25 proportion of 18-23 year old women in the overweight or obese BMI categories increased from 20% among
26 18-23 year olds in 1996 to 33% among women in the same age range in 2013 (8, 10). Notably, the proportion
27 of young women in the obese category more than doubled. There is evidence to suggest that women who
28 develop obesity at a young age are significantly more likely to develop UI than women who develop obesity
29 later in life. This is especially true for persistent and frequent UI (11-14). For this reason, focusing research on

1 young to mid-aged women may be particularly helpful for developing primary and secondary prevention
2 strategies.

3 In the context of increasing weight from one generation to the next and indications of increasing UI
4 prevalence from a young age, the overall aim of this systematic review and meta-analysis was to determine
5 the relative importance of excess weight on UI in young to mid-aged women. The objectives were: 1) to explore
6 the associations between overweight, obesity and UI in young to mid-aged women; and 2) to explore the effect
7 of excess weight on each subtype of UI.

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10 **Methods**

11 *Search strategy*

12 An advanced, systematic search of online medical databases PubMed, EMBASE, and CINAHL was
13 conducted for papers published up until September 2017 and was limited to articles written in English. The
14 search terms were selected in consultation with an experienced librarian and included a combination of the
15 following key words: “urinary incontinence”, “body mass index”, “BMI”, “overweight”, “obesity”, “women
16 OR woman OR females OR female”, “longitudinal”, “prospective”, “cohort”, “determinants”,
17 “epidemiology”, and “risk factors”. Different combinations were used in an attempt to balance the sensitivity
18 and specificity of the literature search (search strategy available on request). To maximise search output, we
19 included specific tools available in each database; namely, MeSH terms (PubMed), Emtree phrases
20 (EMBASE), or CINAHL headings (CINAHL). Following the database search, duplicates were removed using
21 EndNote software and all remaining citations were screened using titles and abstracts for eligibility. Full-texts
22 were then retrieved for those articles deemed eligible, of which only those meeting the inclusion criteria were
23 included in the analysis. If there was uncertainty about whether a study should be included based on the
24 title/abstract, the full text was obtained, screened and resolved through discussion by two reviewers. The
25 reference lists of the included studies were manually scanned to identify any additional relevant studies not
26 identified by the search strategy. Figure 1 shows the search protocol following the PRISMA statement (15).

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1 *Eligibility criteria*

2 Inclusion parameters were predefined according to the aims of the current study. These parameters were
3 chosen to ensure the included studies were relevant to the research questions. The following criteria were used
4 when screening the citations for eligibility:

- 5 • Include a relative risk (RR) estimate (i.e., odds ratio (OR) or hazard ratio (HR) and 95% confidence
6 interval) of the association between excess weight and urinary incontinence (UI) in women. Studies
7 that reported the appropriate information for calculating the RR estimate were also included.
- 8 • Excess weight was measured by BMI, waist circumference, and/or weight (lb/kg). This was self-
9 reported or objectively measured. Studies were excluded if the baseline exposure measurement was
10 taken during pregnancy, as this may have confounded the results.
- 11 • Urinary incontinence (UI) was diagnosed based on an objective measurement (e.g., pad test), medical
12 records, or patient's self-report. Definitions of UI were consistent with those of the International
13 Continence Society (i.e., any involuntary loss of urine)(1).
- 14 • Mean age of the cohort at baseline was less than 55 years, as there are different risk factors of UI for
15 older women (2).
- 16 • Study design was limited to prospective follow-up or longitudinal cohort design. These study designs
17 provide some evidence of a temporal relationship.
- 18 • Follow up from baseline was longer than 2 years. This parameter was included to control for the
19 influence of transient factors that increase the risk of developing UI, specifically pregnancy.
- 20 • If more than one paper reported the *same* data from a cohort/or similar outcomes for the same cohort,
21 the more recent publication was included.
- 22 • Papers were excluded if it was not possible to separately extract young to mid-age women outcomes
23 from the total sample (i.e., samples including older women) to be in-line with our aims.

24

25 *Data extraction*

26 Data were extracted by the first author and checked for consistency by an independent reviewer using
27 a standardised extraction sheet. The following information was extracted: (a) age of sample; (b) study site; (c)
28 sample size; (d) follow up period of cohort; (e) exposure; (f) exposure measure; (g) outcome type; and, (h)

1 outcome measure. For each study, estimates of risk were extracted, which included unadjusted and adjusted
2 odds ratios (OR) and hazard ratios (HR) for UI. Values from the most conservative model (i.e., fully adjusted)
3 took precedence. For studies that reported more than one OR/HR, the estimate which represented overall UI
4 was extracted to avoid overlap and overestimation of the pooled effects. Strategies used to determine the
5 ‘overall UI estimate’ are described later. For studies that reported risk of developing UI according to subtype,
6 a risk estimate of each subtype was included, if the categories were mutually exclusive.

7

8 *Statistical analysis*

9 Studies were included in the meta-analysis if the exposure was reported as a BMI category of
10 overweight and/or obesity. Analyses were conducted to determine the effect of overweight and obesity on 1)
11 any UI; and 2) UI subtypes – Stress, Mixed, Urge, and Severe. Risk estimates were used to calculate the pooled
12 effect-sizes (ES) using random-effects modelling, and I-squared tests to assess heterogeneity. Further, we
13 conducted sensitivity analyses to assess the robustness of the estimated pooled ES and explore potential
14 sources of heterogeneity. For this, a univariate meta-regression was conducted. All analyses were conducted
15 using STATA v12.1 (StataCorp). 2012. Stata Statistical Software: Release 12. College Station, TX, USA).

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17 *Objective 1: Overweight and obesity and overall urinary incontinence*

18 Overweight was defined as BMI 25-30 and obesity was defined as BMI ≥ 30 . Risk estimates were all
19 relative to normal weight (BMI < 25) counterparts. Where studies reported risk estimates of overweight and
20 obesity, both were extracted, as the first objective was to determine any difference in risk of UI in overweight
21 or obesity. If the study reported more than one outcome, only one risk estimate was extracted for this ‘overall’
22 analysis, as follows: if an overall estimate of any urinary leakage (i.e., ‘Any UI’) was reported, this estimate
23 was included in the analysis; if not (i.e., in studies that reported risk estimates by UI subtype only), the estimate
24 for Mixed UI was included; if Mixed UI was not reported, then the estimate for Stress UI was used. Mixed UI
25 and Stress UI tend to be the most common subtypes in this demographic group (16-18), and therefore were
26 considered more representative than Urge and Severe UI. The risk estimates were then pooled and reported
27 as overall risk of developing UI by (1) overweight (BMI 25-30) and (2) obesity (BMI > 30).

28

29 *Objective 2: Overweight and obesity and subtypes of urinary incontinence*

1 Estimates of overweight and obesity were pooled according to UI outcome – Stress, Mixed, Urge, and
2 Severe. The definitions were considered equivalent between papers, as all are consistent with those of the
3 International Continence Society (1). For clarity, in the current review, subtypes were defined as:

- 4 • Stress UI - involuntary leakage associated with effort or exertion (e.g., coughing, sneezing, jumping)
- 5 • Urge UI – involuntary leakage associated with, or immediately preceded by, urgency
- 6 • Mixed UI – a combination of Stress UI and Urge UI symptoms
- 7 • Severe UI – frequency and amount of leaking urine (>a few drops)

8 For those papers reporting more than one subtype of UI, estimates for each of these were extracted, if the
9 categories were mutually exclusive.

10

11 *Unit increase in weight*

12 As an adjunct to the meta-analyses, studies including risk estimates of weight gain by unit were
13 included as part of the systematic review, provided they met the eligibility criteria. They were however
14 excluded from meta-analysis, as the ‘units’ were too heterogeneous. In the included papers, unit increase was
15 defined as waist circumference per 1cm increase, weight gain per 1 kg, weight gain per 1 pound, or BMI per
16 1-unit increase. While these categories are not equivalent, the intention of presenting these data was to ascertain
17 relationships between any indicator of weight-related increase and risk estimates. As above, the most
18 representative estimates were extracted from each of the studies. The same rules were applied to this data set;
19 that is, ‘Any’ UI was the preferred outcome. One study did not report an estimate for Any UI, but reported a
20 BMI per unit increase for Stress UI and Urge UI (14). It was decided to include both OR estimates as these
21 were derived from different women within the cohort.

22

23 *Risk of bias*

24 The Newcastle-Ottawa scale (NOS)(15) was used to assess the risk of bias in each of the included
25 observational cohort studies (S1). The checklist considers three different categories of potential risk of bias –
26 Selection, Comparability, and Outcome – and 8 criteria, with a study scoring 1 star for each of criteria
27 presenting low risk of bias (except “Comparability of cohorts on the basis of design or analysis”, which allows
28 2 stars). The categories of bias risk were as follows: low risk, 7-9 stars; moderate risk, 4-6 stars; and high risk,

1 1-3 stars. However, studies were not excluded based on their risk of bias. An extensive systematic review of
2 tools for assessing quality and susceptibility in observational studies indicated the NOS was appropriate for
3 future use (19). Critiques of the scale were noted and balanced prior to assessment, and it was decided there
4 was sufficient support for the use of the tool (20). Publication bias were explored using Egger's test and funnel
5 plots.

6

7 *Sub-group analyses*

8 Heterogeneity was measured with I^2 statistics, and a sub-group analysis was conducted to determine
9 the potential sources of heterogeneity. The following variables were included: whether the participants were
10 all parous or not, age (<35 years or >36 years), exposure measure (self-report or objective measure), follow
11 up period (<6 years or >7 years), adjusted or unadjusted model, and sample size (<1000 participants or >1001
12 participants; Table 3).

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14 **Results**

15 *Search results*

16 The search process is illustrated by the PRISMA flow chart (15) in Figure 1. The search produced a
17 total of 593 articles, of which 562 were excluded after review of titles and abstracts (and removing duplicates
18 using EndNote; $n = 6$). For the remaining 31, full-texts were retrieved and reviewed, leading to a total of 14
19 articles that met the eligibility criteria. The reasons for excluding full-texts were: follow up period less than 2
20 years, cross-sectional design, experimental design, weight-related exposure (e.g., BMI) not measured or
21 reported in isolation from other variables, or the mean age of the cohort was >55.

22

23 *Study characteristics*

24 A detailed summary of the included studies is given in Table 1. The 14 studies included data from
25 women in eight countries – Australia, France, America, Denmark, England, Scotland, Wales, and Netherlands.
26 The pooled sample size was 47,293 women; however, one study the majority of women were from a single
27 study with a sample size of 30,982 (21). Four studies had relatively small sample sizes (<506 women) (22-25),
28 five studies had moderate sample sizes (1000 to 1800 women) (14, 26-29), and the rest included over 2700

1 women (21, 30-33). In six studies, the mean age of the cohort was under 36 at baseline, five had cohorts with
2 a mean age in the 40s, and one study reported a mean age of 53 years.

3 Most studies explored urinary incontinence (UI) in young to mid-aged women in a *general* population,
4 however five studies were based on more specific populations (23, 24, 28, 29, 34). One included women from
5 the Diabetes Prevention Programme, with an inclusion criterion of BMI >24 (29), and the rest included only
6 parous women . Several self-report measures were used to measure UI. Most studies used a short questionnaire
7 (<3 items) to define UI. These definitions were all consistent with those suggested by Abrams et al. (2002).

8 Most studies used self-report to measure BMI; however, five studies measured BMI objectively (14,
9 27, 29, 31, 33). The confounding variables that were most commonly included were reproductive factors (e.g.,
10 parity, menopausal status, oral contraceptive use), sociodemographic factors (e.g., age, education,
11 socioeconomic status), and other health-related factors (e.g., diabetes, smoking, childhood enuresis).

12

1 *Objective 1: Effect of overweight and obesity on overall urinary incontinence*

2 The relative risk of developing UI in women who were overweight or obese at baseline,
3 compared with normal weight women (BMI <25), is shown in Figure 2. The pooled risk estimates were
4 1.35 (95% CI 1.20-1.53) for overweight and 1.95 (95% CI 1.58-2.42) for obesity. Overall, the pooled
5 estimate of the risk of developing UI because of excess weight exposure (overweight + obesity) was
6 1.68 (95% CI 1.47-1.92).

7
8 *Objective 2: Effect of overweight and obesity on subtypes of urinary incontinence*

9 Five studies reported separate risk estimates according to UI subtype (see Figure 3). The pooled
10 risk estimates were 1.83 (95% CI 1.47-2.28) for Stress UI, 2.45 (95% CI 1.77-3.38) for Mixed UI, 1.90
11 (95% CI 1.38-2.62) for Urge UI, and 2.28 (95% CI 1.59-3.26) for Severe UI. When considering all
12 subtypes together in an overall estimate, being overweight or obese doubled the risk of developing any
13 UI subtype (ES 2.00, 95% CI 1.74-2.31).

14
15 *Effect of unit increase in weight on urinary incontinence*

16 Seven studies included an exposure measure which reported a per unit increase in waist
17 circumference (cm), weight (kg and lb), or BMI (see Table 2). The relative risk estimates ranged from
18 1.01 to 1.10. Of those studies that use a “per unit” exposure measure, the majority reported <4% increase
19 in risk of UI per one-unit increase; while three studies reported this risk to be $\geq 5\%$.

20
21 *Risk of bias*

22 According to predefined classifications of low, moderate, and high risk of bias, none of the
23 included studies were classified as high risk. Studies ranged in scores from 4 to 7 out of a maximum
24 score of 9 (lowest risk) on the Newcastle-Ottawa scale. Nine studies had a moderate risk of bias, and
25 five studies had a low risk of bias (Table S2). Of the eight studies included in the meta-analyses, seven
26 studies were moderate risk, and one was low risk. Funnel plots showed no obvious publication bias
27 (Fig. S3).

28

1 *Subgroup analysis*

2 The overall heterogeneity in both models was relatively high (85.1%, and 75.7%, respectively; see
3 Figures 2 & 3). The results of the stratified subgroup analysis for Model 1 are shown in Table 3. Three
4 variables appear to partially explain the heterogeneity in the pooled analysis: whether the study included
5 only parous women, or not (42.36%); the follow up period (12.70%); and, sample size (48.60%). Only
6 sample size was significant in partially explaining the heterogeneity the results of the stratified subgroup
7 analysis for Model 2 are shown in Table 4. Five variables explained part of the heterogeneity in the
8 pooled analysis: whether the sample was parous (7.10%), age (1.31%), measurement of BMI (28.49%),
9 whether the model was adjusted or not (13.78), and sample size ($r^2 = 15.42$). None of these variables
10 were statistically significant in explaining the heterogeneity.

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Discussion

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To our knowledge, this is the first meta-analysis of prospective cohort studies to assess the relationship between overweight/obesity and the risk of urinary incontinence (UI) in young and mid-aged women. We observed a substantial risk increase (68%) of urinary incontinence (UI) with any excess weight in young to mid aged women. When this was broken down into BMI categories, the risk of developing UI increased by about a third in women in the overweight category (35%), and nearly doubled in women with obesity (95%). This supports the assumption that greater excess weight increases the risk of developing UI. These associations may be explained by the increased intra-abdominal pressure which results from carrying excess weight. The chronically increased pressure on the bladder caused by abdominal obesity can be greater than urethral closure pressure, leading to urine leakage (35).

The risk for all subtypes of UI was doubled in young to mid-aged women with excess weight; however, no significant differences were observed between subtypes of incontinence (i.e., Stress, Urge, Mixed, Severe). Previous research has suggested there may be differences in the aetiology of each subtype of UI, and that excess weight is more strongly associated with Stress UI and Mixed UI, than Urge UI (36). However, the results from the second meta-analysis suggest that, at least at this life stage, excess weight appears to be equally important for increasing risk across all subtypes.

Leaking urine has been overlooked in the past as a significant negative outcome of overweight and obesity, but UI can have significant impact on women's wellbeing. Negative health outcomes associated with UI include: physical discomfort, odour, and embarrassment. These can affect participation in, and perspectives on, physical activity, sexual activity, sleep, and personal relationships – all of which play a role in social, physical and emotional wellbeing (37). Furthermore, as leaking urine is one of the primary reasons that older adults lose their independence and are referred to assisted living facilities (2), most continence management strategies have focused on UI in older adults. However, some continence promotion projects have been developed for people with disabilities, and for pregnant and parous women (38). The evidence reported here suggests there is a need to address UI in young and mid-aged women as well. This is important because women who report any past UI history

1 (even mild symptoms) when they are young – are significantly more likely to have more bothersome
2 UI, than women without past UI history (13).

3 Data from the 1946 British Birth Cohort study, show that women who were overweight or obese
4 by age 20-26 were at a much higher risk of developing UI, especially Severe UI, by the time they were
5 age 50 than women who became overweight or obese at an older age. The longer women are
6 overweight, the higher the risk of developing UI. In the current study, there was no difference in risk
7 between younger (<36 years) and older women (36-53 years). This result points to the importance of
8 excess weight, above and beyond age-related risk. In light of these findings, it may be that younger
9 women who are, or are at risk of becoming, overweight or obese should be targeted for strategies to
10 achieve or maintain a healthy weight as a means of preventing UI.

11 A main strength of this review and meta-analysis was the inclusion of prospective cohort
12 studies, which provide more convincing evidence for a temporal relationship between exposure and
13 outcome than cross-sectional data. Furthermore, there was no significant evidence of publication bias
14 observed in the current review, likely due to the comprehensiveness of the search terms used. The use
15 of a tool to assess the risk of bias of each study is considered a strength. The meta-analysis also provides
16 stronger support for the results demonstrated by each individual study and corroborates the importance
17 of maintaining a healthy weight to improve health outcomes.

18 A limitation of the study was that only five of the included studies adjusted for parity. We could
19 not therefore be certain that our risk estimates were completely independent of parity, even though we
20 restricted our analyses to data from studies with a >2-year follow-up, to account for potential transitory
21 UI during and following pregnancy. Therefore, the estimated risks of overweight and obesity on
22 developing UI may be somewhat overestimated. Future studies should adjust for parity, given the
23 relationship between parity and UI is well-established.

24 Given that the increase in UI risk was significantly greater in women with obesity than in
25 overweight women, our meta-analysis would have been strengthened by a sub-analysis of data from
26 women with severe or extreme obesity . However, none of the studies presented sub-categories of
27 obesity. Future studies should explore differences in the relationships between excess weight and UI
28 subtypes and severity, using as many categories of excess weight as possible. Another factor that limits

1 the generalisation of our results is that included studies were limited to those published in English and
2 to high-income western countries (e.g., Europe, US, Australia).

3 In the first meta-analysis model, the heterogeneity of the pooled effect size was high. However,
4 while sources of heterogeneity included parity, follow-up time, and sample size, only the latter showed
5 a statistical difference. That is, the risk estimates from studies with small (<600) sample sizes was
6 significantly larger than the pooled risk estimate for studies with large (>1800) sample sizes. Overall,
7 the results showed that studies with moderate sample sizes (600-1800) elicited a similar risk estimate
8 to those with large sample sizes. This may be useful for determining sample size for future observational
9 studies. There were no significant sources of heterogeneity in the second meta-analysis model. Overall,
10 the subgroup analysis revealed that while many of the studies varied in sample characteristics, data
11 collection, and statistical analysis, the discrepancies did not significantly affect the final outcome.
12 However, based on the observations from the current study, future research should adjust for parity
13 when considering the relationship between overweight and obesity and UI in younger to mid-aged
14 women. Also, where possible, data should be collected from at least moderate sized samples (>600) to
15 avoid overestimating the influence of overweight and obesity on UI incidence.

16 In summary, to our knowledge this is the first meta-analysis to date on the relationship between
17 overweight and obesity in young to mid-aged women with UI. The results showed that overweight and
18 obesity increased the risk of UI at this life stage. The increased risk persisted across subtypes of UI, and
19 the risk was exacerbated in women with a BMI above 30. As more women develop overweight or
20 obesity, and at a younger age, the prevalence of UI is likely to increase in young to mid-aged women.
21 Clinicians and researchers should therefore focus on the prevention of weight gain as a prevention
22 strategy for UI, as well as developing continence management strategies for women at this life stage
23 with obesity.

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