Nutrition and Incontinence: ~ contributing factors?

CW McGrother - public health
MMK Donaldson - epidemiology

1. Review scientific evidence
   ~ Leicestershire MRC Studies
   ~ Boston Area Study
   ~ Weight loss studies

2. Further research perspectives
   ~ Disease model evaluation
   ~ Clinical trials

Background

Prevalence:
- Incontinence: 25-45% women; 5-25% men
- Storage symptoms: 20% people >40 want help

Storage syndromes:
- overactive bladder (OAB)
- stress urinary incontinence (SUI)

Pathogenic processes:
- OAB ~ diabetes, ischaemia, neuromuscular
- SUI ~ obesity, parity, mechanical load

Leics MRC Study: aims

To evaluate the associations of modifiable factors with urinary storage syndromes:
- healthy diet and lifestyle predictors
- nutrient predictors
- comorbid factors
- socio-economic indicators

Leics MRC Study: methods

- Prospective cohort data
- 7000 women & 5500 men aged 40 or more
- Baseline and 3 annual follow-ups (postal)
- Exposures – EPIC food frequency questionnaire
- Outcomes - OAB / SUI incidence
- Analysis – logistic regression

Leics MRC Study: diet and lifestyle

<table>
<thead>
<tr>
<th></th>
<th>OAB</th>
<th>SUI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/day v 0-3/day</td>
<td>0.69 (0.48-0.98) *</td>
<td>-</td>
</tr>
<tr>
<td>Chicken</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2+weeks v &lt;1week</td>
<td>0.64 (0.48-0.87) **</td>
<td>-</td>
</tr>
<tr>
<td>Bread</td>
<td></td>
<td></td>
</tr>
<tr>
<td>daily v weekly</td>
<td>0.68 (0.55-0.86) ***</td>
<td>0.76 (0.61-0.96) *</td>
</tr>
<tr>
<td>Fizzy drinks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>daily v weekly</td>
<td>1.41 (1.02-1.98) *</td>
<td>1.62 (1.18-2.22) *</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>current v never-smoker</td>
<td>1.44 (1.19-1.76) *</td>
<td>-</td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>obese v acceptable</td>
<td>1.46 (1.07-1.99) *</td>
<td>1.54 (1.11-2.12) **</td>
</tr>
</tbody>
</table>

* P < 0.05, ** P < 0.01, *** P < 0.001
multivariate adjusted for age and physical functioning, exercise and OAB or SUI
Leics MRC Study: nutrients

**Women**

<table>
<thead>
<tr>
<th>OAB</th>
<th>OR* (p value)</th>
<th>SUI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium</td>
<td>0.60 (0.05)</td>
<td>Carbohydrate</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>0.51 (0.008)</td>
<td>Total fat</td>
</tr>
<tr>
<td>Protein</td>
<td>0.56 (0.06)</td>
<td>Saturated fats</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>0.52 (0.08)</td>
<td>Cholesterol</td>
</tr>
<tr>
<td>Zinc</td>
<td>1.84 (0.03)</td>
<td></td>
</tr>
</tbody>
</table>

*Lowest / highest quintile; univariate adjusted for age, energy intake and SUI or OAB.

**Leics MRC Study: diet and lifestyle**

**Men**

<table>
<thead>
<tr>
<th>OAB</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beer</td>
<td>never / rarely</td>
</tr>
<tr>
<td>Potatoes</td>
<td>0-5/week</td>
</tr>
</tbody>
</table>

| | 1.00 *** | 0.69 (0.46-0.98) | 0.69 (0.49-1.00) | 0.32 (0.19-0.54) |
| | 1.00 * | 1.08 (0.73-1.60) | 1.48 (1.05-2.07) |

*P values *p < 0.05, **p < 0.01, ***p < 0.001

Multivariate adjusted for age and physical functioning, exercise and fluid intake.

**Leics MRC Study: nutrients**

**Men**

<table>
<thead>
<tr>
<th>OAB</th>
<th>OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiamine</td>
<td>Quintile 1</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

*Lowest / highest quintile; univariate adjusted for age and energy intake.

**Boston Area Study: nutrients**

**Women**

<table>
<thead>
<tr>
<th>Urinary Incontinence</th>
<th>OR (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High energy intake</td>
<td>2.86 (0.0001)</td>
</tr>
<tr>
<td>High SFA:PUFA* ratio</td>
<td>2.48 (0.005)</td>
</tr>
</tbody>
</table>

**Men**

<table>
<thead>
<tr>
<th>Storage Symptoms</th>
<th>OR (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High energy intake</td>
<td>1.88 (0.01)</td>
</tr>
<tr>
<td>High PUFAs</td>
<td>1.44 (0.006)</td>
</tr>
<tr>
<td>High energy + sodium</td>
<td>1.85 (0.0001)</td>
</tr>
<tr>
<td>Severity : Low MUFA + PUFA</td>
<td>1.76 (0.0001)</td>
</tr>
</tbody>
</table>

Estimate: diet prevents 70% cases

Multivariate adjusted for age, race, waist circumference, physical activity, smoking, diabetes, CVD, and fats adjusted for other types of fat.

SFA: saturated fat; PUFAs: polyunsaturated fat; MUFA: monounsaturated fat.

**Weight Loss Studies: women**

Clinical trials - 3 controlled trials have demonstrated that weight loss (ie energy, low SFA, exercise) reduces incontinence:

- Subak 2002 (SUI + UUI syndromes)
- Brown 2006 (incontinence: SUI> UUI)
- Wing 2010 (incontinence: UUI> SUI)

Surgical - 4 case series have demonstrated that bariatric surgery reduces incontinence:

- Deitel 1988 (SUI only)
- Bump 1992 (SUI only)
- Sugerman 2003 (SUI + UUI)
- Ahroni 2005 (incontinence only)

**Further Research**

1. Disease models?
2. Clinical trials?
Diabetic Ischaemic Neurogenic Psychogenic Myogenic other

**Disease Models**

**Diabetes and Obesity Model**

Research questions:

1. Do lifestyle factors implicated in diabetes and obesity contribute to the onset of OAB and SUI

2. Which main predictors and pathways are involved?

**Hypothetical Causal Chain**

<table>
<thead>
<tr>
<th>Immutables</th>
<th>Lifestyle</th>
<th>Intermediates</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>high glycemic index</td>
<td>low activity</td>
<td>diabetes</td>
</tr>
<tr>
<td>parity</td>
<td>energy intake</td>
<td>diabetes</td>
<td>SUI</td>
</tr>
</tbody>
</table>

**Results: literature review**

![Causal Chain Diagram]

- Key: Cross-sectional associations; Predictive associations
- All lines represent associations based on published evidence

**Results: OAB data 1**

![Data 1 Diagram]

**Results: OAB data 2**

![Data 2 Diagram]

- Key: Cross-sectional associations; Predictive associations
- Literature-based factors Confounding factors
Conclusions

1. Obesity:
   - probable causal factor

2. Poor quality diet:
   (sub-optimal nutrition + high energy intake)
   - likely contributing factors

General Health Factors

<table>
<thead>
<tr>
<th>General factors</th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Health:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent / V good</td>
<td>1.0 ***</td>
<td>1.0 ***</td>
</tr>
<tr>
<td>Good</td>
<td>1.6 (1.3,2.0)</td>
<td>1.5 (1.3,1.8)</td>
</tr>
<tr>
<td>Fair</td>
<td>3.2 (2.6,3.9)</td>
<td>2.1 (1.7,2.5)</td>
</tr>
<tr>
<td>Poor</td>
<td>6.3 (4.8,8.3)</td>
<td>2.0 (1.4,2.8)</td>
</tr>
</tbody>
</table>

Women - cross sectional univariate, age adjusted. * p<0.05   ** p<0.01    *** p<0.001

Healthy diets

Diabetes Prevention Program (DPP & Finnish DPP)
- Weight reduction, reduced SFA and trans fats, high in fibre
- Blood pressure (DASH)
- Rich in fruits, vegetables, and low-fat dairy foods, and reduced in red meat, fats, and cholesterol
- Cardiovascular disease (BHF)
- Replacement of dietary saturated fat with monounsaturated fats and low glycaemic index carbohydrates, 5 fruit and veg/day, reduce salt intake and limit alcohol consumption
- Depression (MHF)
- Less refined high sugar foods, more wholegrain cereals, nuts, beans, lentils, fruit and vegetables
- General Health (Mediterranean diet)
- Use olive oil as main fat, increase fruit and vegetable intake, pasta, rice and whole grain, unprocessed food, eat fish every day (ie, yoghurt and cheese (fermented products), red meat in moderation (in place of doused), lots of fish (including oily fish), eggs in moderation, fresh fruit instead of pastries cakes etc, wine in moderation with meals, exercise every day

Healthy Diet Principles

- Optimize fats (eg SFA, oily fish, olive oil)
- Optimize carbohydrates (eg low GI, whole grain)
- Optimize proteins (eg low red meat, moderate milk)
- Optimize minerals (eg potassium, zinc, salt)
- Maximize vitamins B and D (eg pulses, oily fish)
- Maximize vegetable intake to tolerance
- Maximize nutrient density
- Maximize bio-availability (eg phytates, yoghurt)
- Minimize some drinks (eg fizzy, alcohol, coffee)
- Minimize calorie intake
- Minimize processed foods
- Optimize fluid intake
**References**

Leicestershire MRC Study

BACH Study
- Marescaux N, Giovannucci E, McVey KT, McSherry CW, Birkby J. Dietary macronutrients and dietary factors in women with overactive bladder. BJU Int 2001;87:79-85.

Weight loss

**NICE Levels of Evidence**

<table>
<thead>
<tr>
<th>Level</th>
<th>Source of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++</td>
<td>High quality meta-analyses, systematic reviews of RCTs or RCTs with a very low risk of bias</td>
</tr>
<tr>
<td>1+</td>
<td>Well-conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias</td>
</tr>
<tr>
<td>1</td>
<td>Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias</td>
</tr>
<tr>
<td>2++</td>
<td>High quality systematic reviews of case-control or cohort studies; high-quality case-control or cohort studies with very low risk of confounding, bias or chance and a high probability that the relationship is causal</td>
</tr>
<tr>
<td>2+</td>
<td>High quality case-control or cohort studies with low risk of confounding, bias or chance and a moderate probability that the relationship is causal</td>
</tr>
<tr>
<td>2</td>
<td>Case-control or cohort studies with a high risk of confounding, bias or chance and a moderate probability that the relationship is causal</td>
</tr>
<tr>
<td>3</td>
<td>Observational studies or other types of studies</td>
</tr>
<tr>
<td>4</td>
<td>Expert opinion, formal consensus</td>
</tr>
</tbody>
</table>

NICE = National Institute for Health and Clinical Excellence

**Pathogenesis**

- **Adipose tissue**
  - Previously viewed as inert
  - Acts as an endocrine gland
  - Secrete adipokines
- **Thought to regulate**
  - Metabolism
  - Vascular haemostasis
  - Inflammatory processes

**Excess visceral adipose tissue associated with:**
- Levels of inflammatory cytokines
  - TNF-alpha
  - Interleukin 6, leptin
- Levels of adiponectin

**Leading to:**
- Dyslipidaemia
- Reduced glucose metabolism
- Decreased insulin sensitivity
- Increased inflammation and accelerated atherosclerosis
### Methods: source of data

**Prospective cohort**: 7000+ women aged 40 or more
5816 responded to 1 year follow-up

**Baseline**:
- Physical activity
- Diet (EPIC)
- Glycaemic index (Brand-Miller)
- Diabetes, BMI (reported)
- Confounders - age, parity, SEG etc

**1 year outcome**: Onset of OAB; onset of SUI

*Leicestershire MRC Incontinence Study*

### Analysis

- **Analyses**
  - Predictive between blocks
  - Cross-sectional within blocks

- **MIM modelling software**
  - Log linear modelling
  - Backwards stepwise (saturated)
  - Model of best fit (AIC)
  - Parsimonious approach

- **Statistics**
  - STATA for odds ratios using formulae from MIM

### Other studies

#### Weight loss

<table>
<thead>
<tr>
<th>Surgical</th>
<th>4 case series have demonstrated that bariatric surgery reduces incontinence:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 studies SUI only 1, 2</td>
</tr>
<tr>
<td></td>
<td>1 study SUI + UUI 3</td>
</tr>
<tr>
<td></td>
<td>1 study UI 4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diet</th>
<th>A waiting list study used a 3 month liquid diet for weight reduction, after 3 months the waiting list control group went on the same diet. Authors concluded that weight loss of 5-10% had similar efficacy to other nonsurgical treatments (60% intervention group vs 15% control group reductions) for weekly episodes of incontinence, both SUI and UUI</th>
</tr>
</thead>
</table>

### Methods: literature review

**Outcomes**: OAB / SUI in elderly group

**Threshold**: 3 prospective studies / RCTs (interblock)
3 cross-sectional studies (intrablock)

**Conflicts**: assessment of the weight of evidence

Note: threshold ~ 3 studies sufficient to support a link and include recently identified factors

### Other studies

#### Weight loss

**Lifestyle RCTs**

- **Diabetes Prevention Programme** - an RCT of overweight pre-diabetic women using an intensive weight loss and exercise programme vs control.
  - A secondary analysis of these results showed lower prevalence of total UI in the lifestyle group vs placebo group (38% vs 46%)
  - Differences were greatest for SUI (31% vs 37%). Change in weight accounted for most of the change (35%) while exercise explained 5%

- **PRIDE** - an RCT designed to investigate weight loss on UI in overweight/obese women with 10+ UI episodes/week. Intervention (modelled on DPP) was intensive weight loss, weight maintenance and exercise.
  - Total UI, SUI and UUI all had significantly fewer episodes/week in treatment group, but most effective in UUI group

1: Brown 2006; 2: Wing & Subak 2010

### Methods: graphical chain modelling

- Clarifies the hypothesis and hidden assumptions about confounding
- Handles potentially complex inter-relationships between factors
- Displays the model and all pathways as a picture
- Orders the variables within a temporal sequence
- Controls for potential reverse causality between blocks by building model block by block
- Distinguishes linked contributing factors from isolated non-contributing factors