

Nutrition and Incontinence: ~ contributing factors?

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Overview

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

Women

		OAB ¹	SUI ²
Diet		OR (95% CI)	OR (95% CI)
Vegetables	4/day v 0-3/day	0.69 (0.48-0.98) *	-
Chicken	2+/week v <1/week	0.64 (0.48-0.87) **	-
Bread	daily v weekly	0.68 (0.55-0.86) ***	0.76 (0.61-0.96) *
Lifestyle			
Fizzy drinks	daily v weekly	1.41 (1.02-1.95) *	1.62 (1.18-2.22) *
Smoking	current v never smoker	1.44 (1.05-1.98) *	-
Obesity	obese v acceptable	1.46 (1.07-1.99)*	1.54 (1.11-2.12)**

P values * ≤ 0.05, ** ≤ 0.01, *** ≤ 0.001

multivariate adjusted for age and physical functioning, exercise and OAB² or SUI¹

Leics MRC Study: nutrients

Women

OAB ¹	OR* (p value)	SUI ²	OR* (p value)
Potassium	0.60 (0.05)	Carbohydrate	0.59 (0.05)
Vitamin D	0.51 (0.008)	Total fat	2.02 (0.02)
Protein	0.56 (0.06)	Saturated fats	2.02 (0.001)
Vitamin B ₆	0.62 (0.08)	Cholesterol	2.09 (0.003)
		Vitamin B ₁₂	1.84 (0.03)
		Zinc	1.89 (0.04)

*Lowest / highest quintile; univariate adjusted for age, energy intake and SUI¹ or OAB²

Leics MRC Study: diet and lifestyle

Men

OAB		OR (95% CI)	
Beer	never /rarely	1.00	***
	1-4/month	0.68 (0.46-0.98)	
	2-6/week	0.69 (0.49-1.00)	
	≥daily	0.32 (0.19-0.54)	
Potatoes	0-5/week	1.00	*
	6-7/week	1.08 (0.73-1.60)	
	≥ 8/week	1.48 (1.05-2.07)	

P values: * ≤ 0.05, ** ≤ 0.01, *** ≤ 0.001

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

Leics MRC Study: nutrients

Men

OAB		OR* (95% CI)
Thiamine	Quintile 1	1
	Quintile 2	1.26 (0.74-2.76)
	Quintile 3	1.77 (1.07-2.93)
	Quintile 4	1.82 (1.10-3.00)
	Quintile 5	1.97 (1.20-3.23)

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

Boston Area Study: nutrients

Women		Men	
Urinary Incontinence	OR (p value)	Storage Symptoms	OR (p value)
High energy intake	2.86 (0.0001)	High energy intake	1.88 (0.01)
High SFA:PUFA* ratio	2.48 (0.005)	High sodium	1.49 (0.05)
		High PUFA	1.44 (0.006)
Severity :	High SFA + energy Low MUFA + PUFA	Severity :	High energy + sodium
Estimate: diet prevent 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; PUFA: 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)

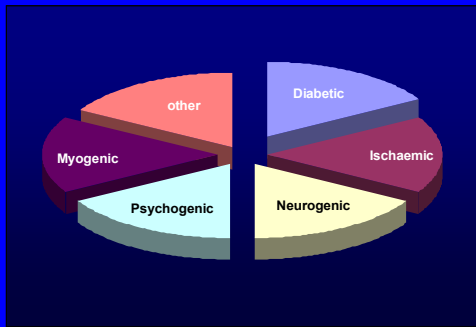
Surgical - 4 case series have demonstrated that bariatric surgery reduces incontinence:

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

Further Research

1. Disease models ?
2. Clinical trials ?

Disease Models

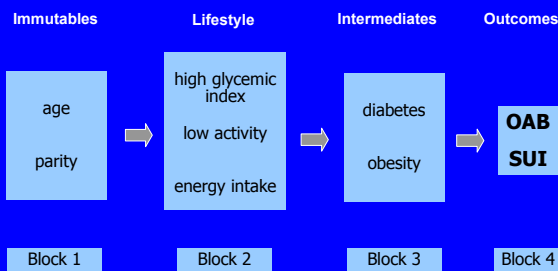


Diabetes and Obesity Model

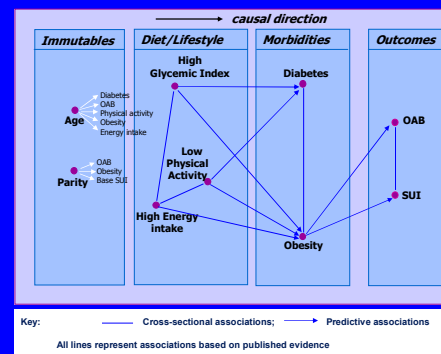
Research questions:

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?

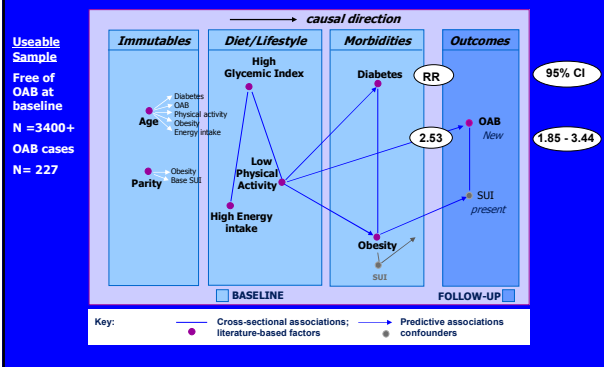
Hypothetical Causal Chain



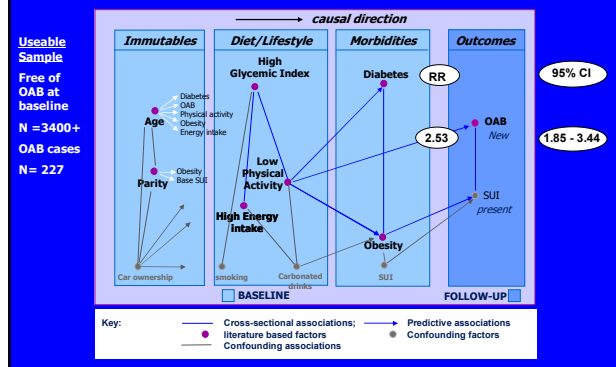
Results: literature review



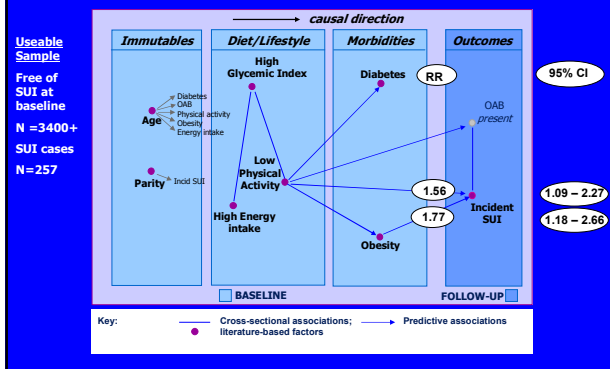
Results: OAB data 1



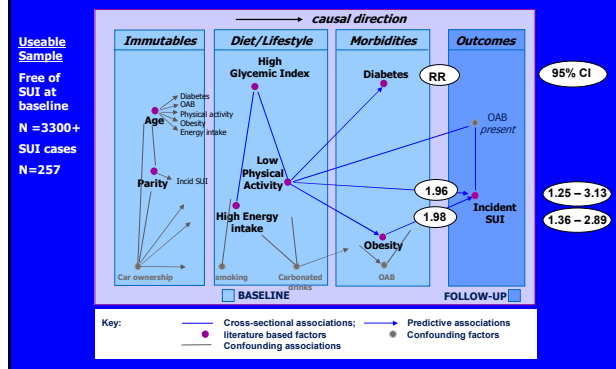
Results: OAB data 2



Results: SUI data 1



Results: SUI data 2



Conclusions

1. Obesity:
 - probable causal factor
2. Poor quality diet:
 - (sub-optimal nutrition + high energy intake)
 - likely contributing factors

General Health Factors

General factors	OR (95% CI)	OR (95% CI)
	OAB	SUI
General Health:		
Excellent / V good	1.0 ***	1.0 ***
Good	1.6 (1.3,2.0)	1.5 (1.3,1.8)
Fair	3.2 (2.6,3.9)	2.1 (1.7,2.5)
Poor	6.3 (4.8,8.3)	2.0 (1.4,2.8)

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 sweets, exercise.

Cholesterol (BHF)
Low SFA, use olive or rapeseed oil, eat oily fish regularly, eat high fibre diet, exercise.

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, no bingeing, exercise

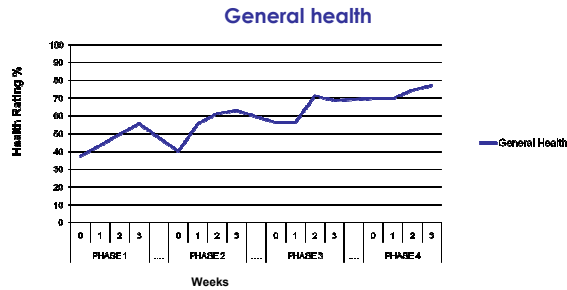
Depression (MHE)
Less refined high sugar foods, more wholegrain cereals, nuts, beans, lentils, fruit and vegetables. Eat protein at every meal. Eat a wide variety of foods to obtain all the micronutrients you need, Eat fish, especially oily fish, keep a healthy weight, limit alcohol intake, exercise

General Health (Mediterranean diet)
Use olive oil as main fat, increase fruit and vegetable intake, pasta, rice and whole grain, unprocessed food, eat dairy every day i.e. yogurt and cheese (fermented products), red meat in moderation (as part of stews), lots of fish (including oily 1+ /week), eggs in moderation, fresh fruit instead of pastries cakes etc, wine in moderation with meals, exercise every day

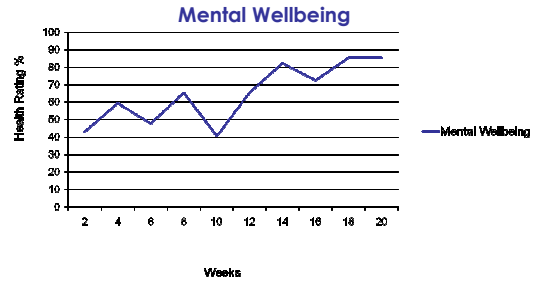
Healthy Diet Principles

- 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

Diet evaluation



Diet evaluation



References

Leicestershire MRC Study

- Dallosso HM, Matthews RJ, McGrother CW, Donaldson MMK, Shaw C. The Association of Diet and Other Lifestyle Factors With the Onset of Overactive Bladder: a Longitudinal Study in Men. *Public Health Nutrition* 2004; 7(7):885-91.
- Dallosso HM, McGrother CM, Matthew R, Donaldson MMK and the Leicestershire MRC Incontinence Study Team. Diet as a risk factor for the development of stress incontinence: a longitudinal study in women. *EJCN*, 2004;58(6):920-926
- Dallosso HM, McGrother CM, Matthew R, Donaldson MMK and the Leicestershire MRC Incontinence Study Team. Nutrient composition of the diet and the development of overactive bladder: a longitudinal study in women. *Neurourology and Urodynamics*, 2004;23(3):204-210.
- Dallosso, H.M., McGrother, C.W., Matthews R.J., Donaldson, MMK, and the Leicestershire MRC Incontinence Study Team. The association of diet and other lifestyle factors with overactive bladder and stress incontinence: a longitudinal study in women. *BJU Intl*, 2003,92:69-77

BACH Study

- Maserejian NN, Giovannucci EL, McVary KT, McGrother C, McKinlay JB. Dietary macronutrient and energy intake and urinary incontinence in women. *AJG*, 171(10):1116-25, 2010 May 15.
- Maserejian NN, Giovannucci EL, McKinlay JB. Dietary macronutrients, cholesterol, and sodium and lower urinary tract symptoms in men. *European Urology*, 55(5):1179-89, 2009 May

Weight loss

- Hunnskaar S. A systematic review of overweight and obesity as risk factors and targets for clinical intervention for urinary incontinence in women. [Review] *Neurourology & Urodynamics*, 27(8):749-57, 2008.

NICE Levels of Evidence

Level	Source of evidence
1++	High-quality meta-analysis, systematic reviews of RCTs or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies; high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2-	Case-control or cohort studies with a high risk of confounding, bias or chance and a moderate probability that the relationship is causal
3	Non-analytical studies (e.g., case reports, case series)
4	Expert opinion, formal consensus

NICE = National Institute for Health

Pathogenesis

Adipose tissue

- Previously viewed as inert
- Acts as an endocrine gland
- Secretes adipocytokines

Thought to regulate

- Metabolism
- Vascular haemostasis
- Inflammatory processes



Intra-abdominal fat surrounding the organs

Ref: Wild & Byrne 2005

Pathogenesis

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

- Surgical* 4 case series have demonstrated that bariatric surgery reduces incontinence:-
- 2 studies SUI only ^{1,2}
- 1 study SUI + UUI ³
- 1 study UI ⁴
- Diet* 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 ⁵

¹Detle1988; ²Bump 1992; ³Sugerman 2003; ⁴Ahroni 2005; ⁵Subak 2002

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%)**
- difference was greatest for SUI (31% vs 37%). Change in weight accounted for most of the change (35%) while exercise explained 5%¹**
- 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 group²**

¹Brown 2006; ²Wing & Subak 2010;

Methods: literature review

Outcomes : OAB / SUI in elderly group

Threshold : 3 prospective studies / RCTs (interblock)
3 cross-sectional studies (intra-block)

Conflict : assessment of the weight of evidence

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

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