

## GENETIC AND ENVIRONMENTAL INFLUENCES ON STRESS URINARY INCONTINENCE: RESULTS OF A LARGE POPULATION-BASED CLASSICAL TWIN STUDY

### Hypothesis / aims of study

Whereas prior studies have hypothesized that SUI is multifactorial in nature and explained by both environmental and genetic factors, the aim of this study is to use a classical twin analyses to explore the extent to which genetic and environmental factors influence the development of stress urinary incontinence (SUI) in a large community based sample of monozygotic (MZ) and dizygotic (DZ) twins. Twin studies provide the most rigorous statistical model for determining whether disease states are due to hereditary or environmental factors.

### Study design, materials and methods

Structural equation models (SEM) were fitted to data obtained from surveys collected from 751 twin sister pairs (n=1502) with 652 MZ pairs and 99 DZ pairs, obtained from the world's largest annual gathering of twins held at the Twins Days Festival in Twinsburg, Ohio from 2003-2007. SEM, also known as covariance modeling, is a general approach for the analysis of variance, correlations and heritability. MX software was utilized for this analyses.<sup>(1)</sup> Stress urinary incontinence was elicited by an affirmative answer to the question, "Do you leak urine with coughing, straining, laughing, physical activity or exercise?" SEM were configured with three latent variables which model possible effects of: additive genes (A), shared environment (C), and individual-specific environment (E). We used a sequential modeling technique to assess the model fit, by using -2 log likelihood ratio test and Akaike Information Criterion.<sup>(2)</sup> Heritability can be estimated from the most parsimonious model that includes an additive genetic effect.

### Results

There were 638 MZ and 99 DZ twin sister pairs with complete data pertaining to SUI. The mean age was  $41.7 \pm 16.1$  years (range 18 – 85), and the mean body mass index (BMI) was  $26.1 \pm 6.4$  (range 13.5 – 55.8), with race comprised of 89.5% white, 6.0% Black, 2.0% Hispanic, and 2% of other ethnicities. There was no difference in general demographics: age, race, parity, BMI, menopausal status, mode of delivery or prior surgery between MZ and DZ twins. The overall prevalence of SUI was 42.3% and 49% in MZ and DZ twins respectively. The tetrachoric correlation was 0.789 in MZ, and 0.748 in DZ twins. Both correlations were significant indicating a high concordance of SUI amongst MZ and DZ twins. The concordance was not found to be significantly higher in MZ versus DZ twins – with MZ correlation nearly equaling DZ correlation, and largely overlapping 95% confidence intervals (MZ: 0.721-0.845; DZ: 0.536-0.882) both indicating that genetic effects were not contributory. Univariate model-fitting procedures supported this finding. Sequential structural equation modeling of the categorical data revealed that the CE model including shared environmental and unique environmental effects provided the best fit (Table 2). The heritability of SUI in the ACE model was 8.26% (95%CI: 0%-52%) which was not statistically significant. Shared environmental factors contributed to approximately 70.63% (95%CI: 27.95-83.50) of the variance among twins compared to unique environmental factors which contributed 21.1% (95%CI: 15.5-27.84), both of which were significant.

Table 2. Best-Fitting Model to Assess Variation of Genetic and Environmental Components for Stress Urinary Incontinence

Model	-2lnL	df	Δdf	X <sup>2</sup>	probability
ACE	1779.790	1483			
AE	1788.696	1484	1	8.906	0.003
<b>CE</b>	<b>1780.003</b>	<b>1484</b>	<b>1</b>	<b>0.213</b>	<b>0.644</b>
E	2033.578	1485	1	253.575	<0.001

NOTE: Model in bold type indicates the most suitable model according to the principle of parsimony.

Abbreviations: df: degrees of freedom

### Interpretation of results

The results of this study indicate that there was no increased risk for SUI among MZ twins when compared with DZ twins suggesting that there is no genetic component of heritability. These results contradict prior epidemiological studies which have reported familial clustering for SUI thereby, suggesting a genetic predisposition.<sup>(3)</sup> The results from this large population-based sample suggests that SUI is explained by shared and unique environmental factors and not inherited as has previously been suggested by other studies.

### Concluding message

This classical twin study, analyzing over 1500 predominantly Caucasian twins, strongly suggests that SUI is explained by environmental factors and is not inherited or determined by genetics as has been previously hypothesized. Stress incontinence, in other words, is for these women a product of '*nurture*' rather than '*nature*'. Future studies will be focused on applying this model to a more racially diverse sample. In the meantime, these findings should reinforce the need to focus efforts squarely on preventable environmental risk factors – such as traumatic childbirth – and to abandon the notion that SUI represents a woman's predetermined genetic fate.

### References

1. Mx: Statistical modeling, 7<sup>th</sup> ed. Richmond, VA: Virginia Commonwealth University, 2006.
2. Methodology for Genetic Studies of Twins and Families. Dordrecht, The Netherlands: Kluwer Academic Publishers, 1992.
3. Acta Obstet Gynecol Scand (2004); 83: 912-916.

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<b>Is this a clinical trial?</b>	No
<b>What were the subjects in the study?</b>	HUMAN
<b>Was this study approved by an ethics committee?</b>	Yes

<b>Specify Name of Ethics Committee</b>	Evanston Internal Review Board
<b>Was the Declaration of Helsinki followed?</b>	Yes
<b>Was informed consent obtained from the patients?</b>	Yes