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#### ENVIRONMENTAL FACTORS VERSUS GENETICS IN WOMEN WITH FECAL **INCONTINENCE: A CLASSICAL TWIN STUDY OF IDENTICAL AND NON-IDENTICAL TWINS**

### Hypothesis / aims of study

Fecal incontinence (FI) is a distressing prevalent condition associated with significant morbidity, impaired quality of life and financial burden. Little is known regarding the role heritability plays in the development of this condition versus environmental etiologies. The aim of this study is to determine the relative contribution of genetic and environmental factors to fecal incontinence using a classical twin model in a large community based sample of identical and non-identical twins.

## Study design, materials and methods

This is a population-based cross sectional classical twin study of 778 identical twin sister pairs (n=1556) and 117 (n=234) nonidentical pairs. A multi-item epidemiologic survey was administered to volunteer participating twin sister pairs recruited at the annual Twins Days Festivals in Twinsburg, Ohio from 2003-2008. Fecal incontinence was elicited by an affirmative response to the question, "Do you lose control of stool before reaching the bathroom?" Concordance and correlation rates were calculated and structural equation models (SEM) were used to estimate heritability. SEM, also known as covariance modeling, is a general approach for the analysis of variance and heritability. It considers the variance of fecal incontinence in a population to be the sum of both genetic and environmental variance components. SEM was configured with three latent variables which models possible effects of: additive genes (A), shared environment (C), and random error (E). We used a sequential modeling technique to assess the model fit, by using -2 log likelihood ratio test and Akaike Information Criterion (AIC).<sup>(1)</sup> Heritability can be estimated from the most parsimonious model that includes the lowest AIC value. MX software was utilized for this analyses.

### Results

There were 752 identical and 113 non-identical twin sister pairs with complete data pertaining to FI. The mean age was 41.2±16.2 years (range 18 – 85), and the mean body mass index (BMI) was  $26.2 \pm 6.6$  (range 15.0 - 57.1), race comprised of 90.0% white, 6.1% Black, 1.7% Hispanic, and 1.3% of other ethnicities. There was no difference in general demographics: age, race, parity. BMI, menopausal status, mode of delivery or prior surgery between identical and non-identical twins. The overall prevalence of FI was 8.56% and 7.83% in identical and non-identical twins, respectively. The concordance rates were not significantly different between identical and non-identical twins (88.96% vs. 90.27%, p=0.386) thereby, indicating that genetic effects were not contributory. Similarly, the sequential structural equation modeling of the categorical data revealed that the CE model including shared and random environmental effects provided the best fit to the data with shared environmental factors contributing to approximately 59.12% (95%CI: 0.0%-71.06%) of the variance among twins. The heritability (proportion of variation contributed by genetic factors) was 0.0% (95%CI: 0.0%-69.14%) for FI.

### Interpretation of results

This study suggests the relative importance of environmental factors over genetic ones in explaining the differences in FI observed between identical and non-identical twins. The confidence interval of the mean variance of 59.12% contributed by common environmental effects is wide, largely due to the disparity in the number of non-identical (n=113) vs. identical twin pairs (n=752). Nevertheless, our results are consistent with prior epidemiological studies, which have demonstrated the impact of environmental factors, such as age, menopause and parity as risk factors for FI.<sup>(</sup>

### Concluding message

This classical twin study, analyzing over 1700 predominantly Caucasian twins, suggests that fecal incontinence is determined by environmental factors and less likely by genetics. These findings underscore the need to focus efforts on preventing environmental risk factors, such as those known to lead to pelvic floor trauma which would predispose women for fecal incontinence. Future studies will be focused on applying this model to a more racially diverse sample, as well as increasing size of the nonidentical twin cohort.

#### References

- Mx: Statistical modeling, 7th ed. Richmond, VA: Virginia Commonwealth University, 2006 1.
- Methodology for Genetic Studies of Twins and Families. Dordrecht, The Netherlands: Kluwer Academic Publishers, 1992 2.

Specify source of funding or grant	None
Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes
Specify Name of Ethics Committee	Evanston Internal Review Board
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	No