

**CAN TWIN STUDIES BE USED TO INFER CAUSATION?**Hopper J. L.,<sup>1</sup> Byrnes G. B.,<sup>1</sup> Gurrin L. C.,<sup>1</sup> Dite G. S.,<sup>1</sup> Scurrah K. J.,<sup>1,2</sup> and Seeman E.<sup>3</sup><sup>1</sup> Centre for Molecular, Environmental, Genetic and Analytic (MEGA) Epidemiology, School of Population Health, University of Melbourne, Australia<sup>2</sup> Department of Physiology, University of Melbourne, Australia<sup>3</sup> Department of Medicine (Austin Hospital), University of Melbourne, Australia

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Consider pairs of traits X and Y measured for twin pairs. If X causes Y, and if X is correlated in twin pairs, there will be a marginal correlation between Y in one twin and X in the co-twin (cross-trait cross-twin correlation) that will reduce or disappear once allowance is made for (i.e., we condition on) the X value of the twin. If Y and X are correlated due only to familial factors for Y and for X that overlap, then the cross-trait cross-twin association may be altered by conditioning on the X value of the twin, but probably to a lesser extent than in the first scenario. If the relationship between X and Y is due to within-person confounding alone, there will be no marginal cross-trait cross-twin association. By analyzing relationships between Y and X using data from twins or relatives it might be possible to distinguish situations in which a relationship between the 2 variables is more or less likely to be causal. Note that the X variable could represent a measured genotype. We present a general regression framework to analyze these scenarios, and a series of examples with continuous outcomes variables (Y = blood pressure, X = body mass index; Y = bone area, X = muscle area; Y = mammographic density, X = number of live births, age at menarche, and height) that illustrate the different results from application of the regression model. We also discuss the plausibility of the competing models. Twin studies may therefore be important to help identify associations that may have a causal component and therefore be worthy of investigation by intervention studies, and help rule out associations most likely and/or mostly due to confounding. It could also help identify genetic associations in which the measured variant is of functional significance. Care needs to be taken in making these judgements and ancillary information would help in any decision making. This paradigm could help relaunch twin studies as a tool for medical and scientific research.

**A SUCCESSFUL MODEL OF A NORTH-SOUTH COLLABORATION**

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This presentation will describe the process of setting up a population-based twin study in Sri Lanka, funded by Wellcome Trust, and representing a collaboration between the Sri Lankan Twin Registry and the Institute of Psychiatry, King's College London. This study has recruited nearly 2000 twin pairs, and 2000 singletons sampled from an identical sampling frame, and has collected data on common mental disorders, substance misuse, post-traumatic stress disorder and somatic symptoms. The main issues in developing such a collaboration will be described and include: (a) gaining funding; (b) developing relations of trust; (c) developing research which is culturally appropriate; (d) learning to communicate from a distance; (e) having robust research governance; and (f) ensuring the project adds value for both parties.

**EMERGENCE OF PRIMARY INCISORS IN AUSTRALIAN TWINS**Hughes T.,<sup>1</sup> Townsend G.,<sup>1</sup> Seow K.,<sup>2</sup> Gotjamanos T.,<sup>3</sup> Gully N.,<sup>1</sup> Bockmann M.,<sup>1</sup> and Richards L.<sup>1</sup><sup>1</sup> School of Dentistry, University of Adelaide, Australia<sup>2</sup> School of Dentistry, University of Queensland, Brisbane, Australia<sup>3</sup> College of Medicine, University of Notre Dame Australia, Fremantle, Australia

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The biological basis of human tooth eruption is still not completely understood and very few studies have explored how genetic factors contribute to this process. Model-fitting methods were applied to tooth emergence data for 98 twin pairs aged between 1 and 3 years who are enrolled in a continuing longitudinal study of Australian twins. The contributions of genetic and environmental factors to variation in timing of emergence of human primary incisors were quantified. Comparisons of means and variances for timing of tooth emergence did not reveal any systematic differences between zygosity groups or between sexes. Emergence times of maxillary centrals and mandibular laterals were less variable than those of maxillary laterals and mandibular centrals. The only antimeric pair to display significant directional asymmetry was the maxillary laterals, with the left side tending to emerge earlier than the right. Estimates of narrow-sense heritability were high, ranging from 82 to 94% in males and 71 to 96% in females. Variation in timing of emergence of the primary incisors in this

twin cohort was under strong genetic control, with a small but significant contribution from the external environment.

**TWIN REGISTERS IN ASIA AND AFRICA**

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Recently, the number of twin registries has increased sharply in Asian countries. To foster collaborations among twin researchers in Asia and other countries in the world, the Asian Society for Twin Studies (ASTS) was developed. This paper presents an overview of existing twin registers in Asia and recent activities of the ASTS. Additionally, a plan on the development of a population-based twin registry in South Africa will be discussed.

**INFLUENCE OF CHORIONICITY ON HERITABILITY ESTIMATES OF HEIGHT, WEIGHT, AND BODY MASS INDEX IN SOUTH KOREAN TWIN CHILDREN**Hur Y.-M.<sup>1</sup> and Shin J.-S.<sup>2</sup><sup>1</sup> Medical Research Center, Seoul National University, Seoul, South Korea<sup>2</sup> Department of Obstetrics and Gynecology, College of Medicine, Pochon Cha University, Seoul, South Korea

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The aim of the present study was to assess whether the heritability of body size (height, weight, and body mass index) among preschoolers, measured from maternal reports, differs according to the chorionicity of the monozygotic (MZ) twins. The twin sample was drawn from the South Korean Twin Registry, in which chorionicity data were collected at birth. Twin correlations were calculated and model-fitting analyses were carried out. Heritability estimates of body size do not differ significantly according to the chorionicity of the MZ twins.

**EFFECTS OF CHORION TYPE ON PERSONALITY IN SOUTH KOREAN PRESCHOOL TWINS**Hur Y.-M.<sup>1</sup> and Yoon S. I.<sup>2</sup><sup>1</sup> Seoul National University, Seoul, South Korea<sup>2</sup> Sook Myung Women's University, Seoul, South Korea

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Prenatal influences on children's personality development are still largely unknown. The present study investigated effects of chorionicity, and genetic and environmental factors on personality in preschool twins. The sample included 64 pairs of monozygotic (MZ) and 37 pairs of dizygotic (DZ) monozygotic (MZ) and 376 dizygotic (DZ) twins. Parents (mostly mothers) rated emotionality, activity, and sociability of these twins. Twin correlations were computed and model-fitting analyses were carried out. Chorionicity effects were significant and substantial only for emotionality. These findings were contrasted to results from the Riese study (1999) where chorion type was not related to co-twin similarity on any of the personality traits.

**GENETIC SUSCEPTIBILITY TO HERPES VIRUS INFECTION: TWIN CONCORDANCE OF INFECTIOUS MONONUCLEOSIS AND HERPES ZOSTER**

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Herpes viruses typically cause a more severe infection when acquired relatively late in life (adolescence or adulthood). For example, primary infection with Epstein-Bar virus during early childhood is generally asymptomatic but delayed primary infection during adolescence/adulthood results in clinical syndrome of infectious mononucleosis (IM). The viruses in the Herpes family also share the characteristic of reactivation after primary infection. Herpes zoster (shingles) is the reactivated infection associated with varicella zoster virus after a primary chickenpox infection. Higher concordance rate of disease among monozygotic (MZ) compared to dizygotic (DZ) twins suggest that genetic and/or early childhood risk factors may play an etiological role. We used twins registered in California Twin Program at University of Southern California, a twin registry of native Californians composed of 51,609 who have completed a 16-page questionnaire to examine whether genetic factors may be involved in susceptibility of IM and shingles. We used self-reported information from double-responding twins of whom at least one twin reported history of IM (699 pairs) and shingles (357 pairs) to calculate pair-wise concordance. Our analysis showed that concordance rate for IM was higher in MZ (12.11%) than DZ (6.07%). The concordance rate for shingles did not differ between MZ and DZ twins (MZ = 4.38, DZ = 4.48).