

olds fixed as, for close in space, less than 5 km, and for close in time, less than 1 year apart.<sup>7</sup> The Knox test regards a pair of cases as being in “close proximity” if they are both born at addresses that are simultaneously close in space and time. The number of case pairs observed ( $O$ ) and expected ( $E$ ) to be in close proximity was obtained and the magnitude of the excess estimated by  $S = [(O - E)/E] \times 100$ . To adjust for the effect of varying population density, tests were repeated replacing fixed geographic distances with nearest neighbor thresholds. This approach also provides a better metric for space-time clustering that might arise from person-to-person transmission rather than from fixed spatial sources.

An underlying problem with the Knox test is the arbitrary choice of thresholds. We used a simplification of a second-order procedure based on  $K$  functions to partly overcome this limitation.<sup>8</sup> Fixed geographic distance and NN thresholds were both used in the  $K$  function analyses.

The study included 1144 boys diagnosed with cryptorchidism and 537 boys diagnosed with hypospadias (14 had both conditions), who were born during 1993–2000, identified from a population-based register that covered the Northern Region of England. Oper-

ations were performed for 1056 cases of cryptorchidism and 447 cases of hypospadias. Overall, there was statistically significant space-time clustering for cases of cryptorchidism and hypospadias. Further analysis showed that clustering was restricted to cases of hypospadias with no evidence of clustering for cryptorchidism (Table 1).

If cryptorchidism, hypospadias, and testicular cancer constitute the “testicular dysgenesis syndrome,” then there may be etiologic factors that are common to all 3 conditions.<sup>1</sup> The findings from the present study, together with tentative results from a study of space-time clustering of testicular cancer,<sup>5</sup> suggest that there may be an environmental component to the etiology of hypospadias and testicular cancer, at least for some cases.

The occurrence of space-time clustering is consistent with an etiologic agent that displays a temporary occurrence at a number of different locations. Infections would be a highly plausible candidate. It is not suggested that the condition itself would arise from person-to-person transmission. Rather, the infection may precipitate the condition in a small number of individuals. The infection may act in combination with other environmental exposures and genetic predisposition.

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## ERRATUM

**Steenland K, Armstrong B. An overview of methods for calculating the burden of disease due to specific risk factors. *Epidemiology*. 2006;17:512–519**

On page 513, just above the heading “Attributable Fraction in the Presence of Confounding or Effect Modification,” the formula should read:  $I = p_p(RR)I_o + (I - p_p)I_o$