# Is the Incidence of Hypospadias Increasing? Analysis of Finnish Hospital Discharge Data 1970–1994

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Reports suggesting an increasing incidence of male genitourinary anomalies such as hypospadias, possibly related to environmental factors such as environmental estrogen-like compounds, have recently received considerable publicity. These reports are based on birth defects registry data, and there may be variation in the completeness of the registries used. We analyzed temporal trends in the prevalence of hypospadias in Finland to assess the previously reported low overall prevalence and to detect any possible increasing tendencies during the past decade. We identified all patients who were surgically treated for hypospadias before the age of 9 years among boys born 1970–1986 in the national hospital discharge registry. We calculated the cumulative prevalence by dividing the number of patients by the number of male births, and we used Poisson regression analysis. Out of 549,176 boys born in Finland in 1970–1986, 1,543 were treated for hypospadias by the age of 8 years (28.1 surgically treated patients per 10,000 male live births; 95% confidence interval, 26.7–29.5). The prevalence of hypospadias in Finland remained constant throughout the study period and appears to have been approximately three times higher than previously reported. Changes in completeness of registration may account for a substantial proportion of the reported increases in the prevalence of hypospadias in Finland and possibly also elsewhere. *Key words*: epidemiology, Finland, hypospadias, incidence, prevalence. *Environ Health Perspect* 108:463–465 (2000). [Online 31 March 2000]
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Hypospadias is one of the most common congenital anomalies (*1*). In this condition, the urethral meatus exits proximal to the glans penis as a result of failure of the urethral fold to unite over and cover the urethral groove during the first trimester of embryonal development (*2*). The etiology of hypospadias is unknown; however, because androgens stimulate penile growth and development, endocrinologic mechanisms probably have a major role (*2*). The prevalence of hypospadias varies widely across different populations, ranging from 0.37 to 41 per 10,000 infants (*3–5*). The comparability of reported rates is poor, however, because of differences in ascertainment and diagnostic criteria (inclusion or exclusion of minor cases). Further, the quality of data in malformation registries has not been evaluated in a systematic fashion, and there may be a considerable variation in completeness over time. Increasing temporal trends in hypospadias have been suggested, but very few longitudinal studies covering the same population have been published (*5*).

A recent study based on two birth defect surveillance systems indicated a doubling in the rate of hypospadias in the United States during the 1970s and 1980s, from approximately 20 to almost 40 cases per 10,000 births (*6*). During the same period, the reported birth prevalence of hypospadias in Denmark and Norway has increased from approximately 7 to 15–20 per 10,000 births, whereas the reported prevalence in Finland has increased slightly, but remained below that in other Nordic countries, approximately 5/10,000 births (*3,7*). The most recently reported birth prevalence of hypospadias in Finland (birth year 1997) was approximately 28/10,000 male births, indicating a substantial increase from the 1980s and the beginning of the 1990s (*7*).

Reports suggesting an increasing incidence of male genitourinary anomalies such as hypospadias, cryptorchidism, and testicular cancer, as well as declining semen quality in several industrialized countries, have recently received considerable publicity (*3,5,8,9*). Because these changes have occurred over a relatively short period, environmental rather than genetic factors are likely to provide a plausible explanation (*10*). A number of environmental compounds including some drugs, tobacco, alcohol, pesticides, and heavy metals, have been shown to have estrogen-like effects, and they have been suggested as a common cause for these male reproductive organ abnormalities (*3,5,9,10*). Disruption of the endocrine and reproductive systems as a result of relatively high exposure levels has been demonstrated in laboratory experiments and in some animal populations (*9,11*).

We studied the temporal trends in the prevalence of hypospadias in Finland among boys born in 1970–1986 using data from the hospital discharge registry.

## Materials and Methods

We identified all patients treated for hypospadias [*International Classification of Diseases-Revision 8* (ICD-8 codes 752.20–752.22 and 752.29 and ICD-9 code 7526B) (*12*)] before 9 years of age among boys born in 1970–1986 from the national hospital discharge registry, which covers all public and private hospitals in Finland. We eliminated duplicate records and patients who were not born in Finland. We calculated the cumulative prevalence from birth to 8 years of age for each birth cohort by dividing the cumulative number of surgically treated patients by the number of male live births in the index year. We assessed the temporal trend using Poisson regression analysis of the cumulative prevalence (number of treated cases divided by the logarithm of the number of births) across the 17 one-year birth cohorts, with year of birth as a continuous variable. We assessed goodness of fit by comparing nested models with a likelihood ratio test.

## Results

A total of 549,176 male children were born alive in Finland between 1970 and 1986, approximately 30,000 annually (Table 1). The total number of patients treated for hypospadias in that period was 1,543. The mean cumulative prevalence of hypospadias requiring treatment by the age of 8 years was 28.1/10,000 male live births [95% confidence interval (CI), 26.7–29.5]. In the regression analysis of cumulative prevalence by birth year, we observed more heterogeneity between individual years than could be expected on the basis of chance alone ($p < 0.05$). However, there was no evidence for a linear trend across birth years. The prevalence remained constant throughout the study period (relative change 0.00/year; CI, -0.01 to +0.01) (Figure 1). Dividing the study period into 5-year periods did not improve the fit ($p > 0.5$), nor did a sinusoidal function of birth year ($p > 0.5$).

## Discussion

The prevalence of hypospadias in Finland remained constant in birth cohorts from 1970 to 1986. Based on the upper 95% confidence interval, we could exclude a relative

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increase of ≥ 12% over the 16-year study period. In addition, our results based on hospital discharge data suggest a substantially higher overall prevalence for earlier years than previously reported (Figure 2), which is comparable to other Nordic countries (*3,7*).

In Finland, all children are examined at birth by a pediatrician. After the neonatal period the national child health surveillance system, with an extensive network of child health clinics, provides medical care free of charge. All children are examined by a physician four times during the first 2 years and then once annually up to the age of 6 years. Attendance is almost 100% (*13*). All patients with an abnormality are referred to a specialist center for evaluation and treatment.

Our material included patients who were treated surgically before 9 years of age, as recorded in the hospital discharge registry. We chose the cutoff at 9 years of age because the prevalence of treated hypospadias increased until that age. However, this cutoff did not allow us to analyze more recent birth cohorts.

Because no information on outpatient visits is currently available in the hospital discharge registry, we cannot assess the small possibility of an increase in the prevalence of cases not treated with surgery. No major changes in the treatment policy have occurred that could have affected the results. Since the 1960s or earlier, even minor cases of hypospadias have been surgically treated before children reach school-age. More recently, modern operative techniques and equipment have enabled treatment at earlier ages (*14*). These new techniques have improved the results of surgery for minor forms of hypospadias; therefore, it is unlikely that an increasing number of cases would be left untreated. If there were such cases, they would have most likely occurred in the early birth cohorts, which would be reflected as an increasing prevalence over time. Thus, our findings suggesting a lack of increasing trend are not weakened by this possibility.

The diagnostic criteria for hypospadias have not been perfectly defined; in a German study of 500 "normal" men, only 55% had the urethral meatus in the distal third of the glans (*15*). This suggests that a similar prevalence of unrecognized defects could be found among children because hypospadias is a congenital anomaly and all defects exist at birth. Sensitivity to observe and report this abnormality is likely to vary, which may account, in part, for the reported differences over time and across populations.

A previous report based on malformation registry data (*3*) suggested low overall prevalence of hypospadias in Finland and a slight increasing trend during the 1970s and 1980s. A marked increase based on more recent malformation registry data seems to have occurred after the 1980s (*7*). We believe that the difference between our results and the previous reports is because cases were underreported to the malformation registry between the 1970s and the early 1990s. We consider the validity of our approach to be superior to approaches based solely on reports to national malformation registries, especially concerning long-term trends in past years. Substantial underreporting of hypospadias to these registries has previously been demonstrated in Finland and in other Nordic countries (*4,16*). Kallen et al. (*4*) estimated that, in the 1970s, approximately one-third of infants with hypospadias severe enough to require surgery were not primarily registered in Sweden; in Denmark, the corresponding figure was almost two-thirds. Until recent years in Finland, a higher number of hypospadias has been reported annually to the hospital discharge registry than to the malformation registry, which suggests more complete coverage for the hospital discharge registry (*16*). In 1996 and 1997, the prevalence of hypospadias ascertained by the Finnish Birth Defects Registry was approximately 28/10,000 male births, which is very similar to our results, but higher than the rates reported by the malformation registry for earlier years (*7*). This apparent increase, however, is explained by improved registration. During the last few years, the birth defects registry has used both the malformation registry and the hospital discharge registry in the registration of birth defects; previously only the malformation registry was used (*7*).

The link between environmental estrogens and hypospadias has been based primarily on observations among nonmammal vertebrates and experimental *in vivo* studies. Many compounds in our environment have the potential to cause changes in the normal development of genitourinary organs (*17*). Environmental factors may account for the reported geographic differences in the incidence of hypospadias and other reproductive disorders. However, etiologic evidence based on analysis of time–series data alone must be regarded as tentative, or hypothesis-generating at most. Studies adopting a vigorous analytical approach, such as valid exposure assessment at an individual level, remain rare. Recent reanalyses of sperm count data have not unequivocally confirmed a decline in sperm quality in Europe or in the United States, but have demonstrated wide geographic variation (*18,19*). A recent analysis of data on hypospadias from large birth defects registries concluded that numerous artifacts may contribute to reported increasing trends in hypospadias (*20*). Analysis based on surgically treated cases alone may underestimate the true prevalence, but the fact that we found higher rates of surgically treated cases than have been reported from the national malformation registry clearly indicates an incomplete coverage of the malformation registry for the study period.

We did not find evidence for an increasing trend in the incidence of hypospadias, based on a large group of surgically treated cases identified from a national hospital

**Table 1.** The number of male live births and the number of patients surgically treated for hypospadias annually between 1970 and 1986.

| Year | No. of males born | No. of patients with hypospadias |
|---|---|---|
| 1970 | 33,014 | 91 |
| 1971 | 31,085 | 92 |
| 1972 | 30,376 | 93 |
| 1973 | 29,300 | 91 |
| 1974 | 31,853 | 85 |
| 1975 | 33,817 | 124 |
| 1976 | 34,306 | 91 |
| 1977 | 33,624 | 85 |
| 1978 | 32,838 | 89 |
| 1979 | 32,223 | 81 |
| 1980 | 32,349 | 65 |
| 1981 | 32,453 | 86 |
| 1982 | 34,005 | 80 |
| 1983 | 34,194 | 97 |
| 1984 | 33,230 | 96 |
| 1985 | 32,012 | 93 |
| 1986 | 31,035 | 104 |

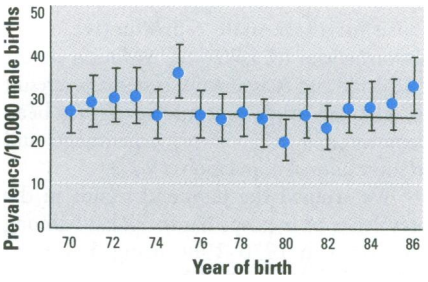


**Figure 1.** The cumulative prevalence of hypospadias before 9 years of age in Finland among birth cohorts from 1970 to 1986. Points indicate the mean prevalence among each birth cohort, the bars indicate 95% confidence intervals, and the transverse line is a regression line.

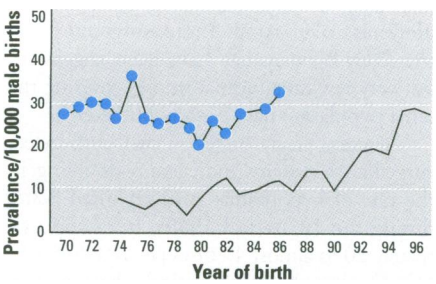


**Figure 2.** The cumulative prevalence of surgically treated hypospadias in Finland among birth cohorts from 1970 to 1986 observed in the current study (data points as compared to the prevalence reported by the Finnish Malformation Registry between 1974 and 1997 (solid line) (*7*).

discharge registry. Demonstration of the effect of an etiologic factor, such as compounds with estrogen-like effects, requires more rigorous approaches than ecologic studies and time–series analyses. Reported increases in the incidence of hypospadias may be attributable in part to improvements in registration over time.

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