ORIGINAL RESEARCH

Night shift work undertaken by women and fertility treatment interact to increase prevalence of urogenital anomalies in children

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ABSTRACT

Objective To investigate the role of maternal night shift work in occurrence of urogenital anomalies in offspring, considering a possible interaction with mode of conception.

Methods A population-based cohort comprising births in South Australia (1986–2002) was produced via linkage of fertility clinic records, perinatal and birth defects data. This study concerned first births to women in paid employment (n=98103). Potential exposure to night shift was imputed by applying a job-exposure matrix to recorded occupation. Associations were examined using logistic regression, first for nurses and other night shift workers separately, then combined. An interaction term for night shift work and mode of conception was included in all models, while adjusting for covariates.

Results Associations were similar for nurses and other night shift workers, although only statistically significant for the former when considered separately. A multiplicative interaction was supported: for natural conceptions, maternal night shift work was not associated with offspring urogenital anomalies (OR=0.99, 95% CI 0.84 to 1.15); where a birth arose from fertility treatment, urogenital anomalies were significantly higher among births to all night shift workers compared with day workers (OR=2.07, 95% CI 1.20 to 3.55). This was not due to differences in the type of fertility treatment received.

Conclusions Women in occupations that probably involved night shift did not have offspring with increased prevalence of urogenital anomalies if they conceived naturally. When night shift workers conceived with fertility treatment, the prevalence of urogenital anomalies was elevated. Possibly these women had the greatest exposure to night shift work, or least tolerance for this work schedule, or heightened sensitivity to hormonal aspects of fertility treatment.

INTRODUCTION

Night and rotating shift work involving nights, hereafter referred to as ‘night shift work’, result in exposure to light at night, known to affect circadian rhythms, producing a cascade of perturbations in the endocrine system. This could have consequences for the reproductive health of women and for the development of a fetus in the womb.

The suprachiasmatic nucleus in the hypothalamus relays circadian information to other circadian oscillators via regulation of clock-gene expression and neuroendocrine signalling. Clock-gene expression occurs in several reproductive tissues including the ovary, which may explain why alterations in endogenous levels of hormones have been observed among shift workers. Furthermore, there is some evidence that shift work adversely affects female fertility, which may lead to greater use of fertility treatment by these women.

During the pregnancy, melatonin is important as an antioxidant and in regulating the fetal circadian rhythm. Beyond disrupting this rhythm, night shift work has the potential to interfere with aspects of

Key messages

What is already known about this subject?

Night shift work is known to affect circadian rhythms, perturbing the endocrine system.

It is plausible that night shift work undertaken by women could contribute to urogenital anomalies in offspring.

Investigation is complicated because of evidence that night shift work impairs female fertility, and assisted conception is associated with elevated prevalence of urogenital anomalies.

What are the new findings?

Women whose occupations were imputed to involve night shift work had an elevated risk of urogenital defects among first born children, but only if they conceived with fertility treatment. This was not explained by differences in the types of fertility treatment administered to women who worked night shift compared with other women receiving treatment.

Results were similar for nurses and women in other occupations involving night shift work, when considered separately, as well as combined.

How might this impact on policy or clinical practice in the foreseeable future?

Women undertaking night shift work who experience fertility problems may benefit from choice of shift schedule and promotion of strategies to mitigate circadian disruption, pretreatment and through pregnancy.
fetal development that occur in a hormone-dependent manner, notably the urogenital system that undergoes a relatively long period of transformation, including sexual differentiation, which occurs until 18 weeks of gestation.9

Urogenital anomalies are among the most common congenital anomalies, affecting up to 16 per 1000 births,7 with a higher prevalence reported among males in some studies.4–10 Anomalies may affect the structure and function of kidneys, bladder and urinary tract. Genitals may be malformed, for example, by displacement of the urethral opening or in more extreme cases being ambiguous.11

Despite plausible mechanisms for teratogenicity of maternal circadian rhythm disturbance, there has been little investigation of maternal night shift work and fetal urogenital anomalies. One recent study found no association between maternal self-reported night shift work and cryptorchidism (undescended testis) among 53 316 newborn males.12

Mode of conception has yet to be considered in studies of maternal night shift work and congenital anomalies,13 important given the impact of night shift work on female fertility,3 4 and since certain fertility treatments have been identified as a risk factor for urogenital anomalies.6–14 Endocrine disruption is complex, defying older ideas about dose–response relationships, and little is known about multiple exposures or interactions.15

Further intricacy arises because night shift work has been linked to unhealthy lifestyles, including poor diet and smoking, and can induce or exacerbate obesity and poor insulin-glucose metabolism.16 Working at night may also affect intimate relationships and sexual behaviours.17 A number of these factors are alternative pathways to (perceived) infertility and/or urogenital anomalies (see figure 1).3 6 18

Our aim was to investigate the role of maternal night shift work in urogenital anomalies in offspring, using a population-based data linkage study, taking into account the potential interaction with mode of conception. We considered nurses separately from other occupational groups undertaking night shift work, then combined these groups.

**MATERIALS AND METHODS**

**Data sources and study population**

As described previously,19 the study cohort was assembled by linking data on all patients undergoing fertility assessment and treatment in South Australia (SA) with two registries, the SA Perinatal Registry and SA Birth Defects Registry. Linked data were available for the period 1986–2002. The cohort (n=327 369) thus comprised all live births, fetal deaths and terminations (after 20 weeks) occurring among women residing in SA between 1986 and 2002. For this study, the focus was first births to women in paid employment (n=98 103).

**Night shift work**

The title of the mother’s usual occupation prior to and/or during pregnancy was recorded in the Perinatal Registry, coded using the Australian Standard Classification of Occupation (V1). A job-exposure matrix (JEM) was applied in order to infer night shift work exposure.20

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**Figure 1** Schematic diagram of a model for the occurrence of urogenital defects, developed based on existing literature.

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The JEM was based on data from 1789 control participants in a population-based case-control study examining the association between different night shift work factors and breast cancer. Detailed information on shift work was collected in a structured telephone interview with algorithms used to calculate the probability of exposure to shift work variables. In a validation study, the JEM performed almost as well as job-specific questionnaires in reproducing an established association. Using the JEM, a probability of exposure to light at night can correspond to an occupation (probably through educational requirements) and specific health risks of shift work. Occupations in which at least 30% of workers reported exposure to light at night, an optimal threshold as determined in previous studies, were labelled ‘night shift workers’. Others were assumed to be day workers.

Urogenital anomalies
Structural, biochemical, chromosomal and other congenital anomalies are reported to the SA Birth Defects Registry and classified according to the British Paediatric Association Modification of the International Classification of Diseases Ninth Revision (ICD-9 BPA). Anomalies are reportable until a child’s fifth birthday. Minor anomalies are excluded unless they are disfiguring or require treatment (thus, for example, hydrocele testis is not included). All codes relating to urogenital anomalies in both males and females, ICD-9 BPA 75200 to ICD-9 BPA 75399 were considered as outcomes in the present study.

Mode of conception
Mode of conception was classified as natural or occurring with clinical assistance. The latter were further classified as minimal intervention (timed intercourse, semen tests or low-dose hormonal stimulation), ovulation induction only, in vitro fertilisation (IVF), intracytoplasmic sperm injection, intratubal insemination, gamete intrafallopian transfer or use of donor oocytes. We excluded 400 births for which mode of conception was unclear (with infertility noted on the birth record but no corresponding fertility clinic record).

Other variables
A model for the occurrence of urogenital defects was developed based on existing literature, as depicted in figure 1. In view of the substantial uncertainty about aetiology, we included several factors thought to be associated with increased risk of congenital anomalies, so these effects (if present) could be removed through inclusion as covariates. For example, both obesity and impaired glucose-insulin metabolism may be induced or exacerbated as a consequence of night shift work and these increase the likelihood of infertility as well as being directly associated with congenital anomalies. Maternal age at family formation is linked to occupation (probably through educational requirements) and older age is associated with both infertility and congenital anomalies. For the exposure of infertility treatment, it is necessary to take into account fetal sex and multiplicity (twins, triplets, etc) as some procedures affect the ratio of male to female fetuses and some affect the frequency of multiple pregnancy, and our
interest was in associations that were not driven by either of these considerations.

Covariates obtained from the Perinatal Registry included maternal age (5 years age bands) and maternal ethnicity (Caucasian or non-Caucasian). Socioeconomic status was assigned based on postcode of residence and the Socio-Economic Indexes for Areas, and classified as quartiles, with 236 (0.26%) women for whom this information was missing. Exclusion of night shift work exposure and used a method to estimate the frequency of specific treatment types according to night shift work status, mode of conception and multiplicity, although there was little difference between the two groups. Around 3% of births were multiple gestations (91% twins, 9% higher order multiples), and this prevalence did not appear to vary with night shift work status. Births conceived with fertility treatment comprised 3462 (3.5%). The prevalence of night shift work was higher among births conceived with fertility treatment (13.1%) compared with naturally conceived births (11.4%).

The population for these analyses was restricted to primiparous women in paid employment (online supplemental figure 1). This increases the likelihood of participants being employed in their designated usual occupation around the time of conception and reduces the potential for bias associated with the ‘infertile woman’ effect. Also, the great majority of Australian women return to work part-time after they have a child, so work-related exposures are quite different from those of childless or primiparous women.

Use of fertility treatment was tabulated for individual occupations with probable night shift work exposure as per the JEM and for the most common day working occupations. Among probable night shift workers, nurses and other occupations were considered separately, then together. We tabulated maternal health and sociodemographic characteristics, as well as pregnancy and birth characteristics stratified by night shift work exposure, mode of conception and multiplicity (singleton vs twins and triplets combined).

Offspring of indeterminate or unknown sex (n=24, 0.03%) were coded as male in the primary analysis. These births should not be excluded as this does not occur at random and can be a manifestation of serious urogenital anomalies. The other extreme was examined in sensitivity analyses by recoding these births as female; as no differences in results were observed, results are not presented.

In multivariable logistic regression, in addition to the inclusion of night shift work and mode of conception as main effects, an interaction term was included to account for the multiplicative joint effects of these exposures. Generalised estimating equations with exchangeable correlation matrix structure were applied to account for clustering, specifically births resulting from multiple gestations that cannot be treated as independent observations.

Within the group that received fertility treatment, we examined the frequency of specific treatment types according to night shift work exposure and used a \( \chi^2 \) test to determine whether any treatment types were more commonly administered to night shift workers than day workers. We also compared BMI, where data were available, for night shift and day workers who conceived with fertility treatment.

Finally, pregnancy outcomes including fetal death, overall congenital anomalies and urogenital anomalies were tabulated by night shift exposure, treatment type and multiplicity. This is presented descriptively for clinical interest, as data were too sparse for statistical analysis.

All data analyses were performed using Stata V.14. (StataCorp).

**RESULTS**

There were 98 103 primiparous women in paid employment who gave birth during the study period. Occupations for 11 227 (11.4%) women were likely to have involved night shift work. Over half of the night shift workers were nurses, with other occupations including other personal service workers and police officers (online supplemental table 1). The prevalence of shift work as determined by the JEM corresponded with contemporaneous Australian workforce data, which indicated that 11% of full-time and 16% of part-time female workers were engaged in shift work.

Births conceived with fertility treatment comprised 3462 (3.5%). The prevalence of night shift work was higher among births conceived with fertility treatment (13.1%) compared with naturally conceived births (11.4%).

**Statistical analysis**

Among births conceived naturally (table 2), perinatal profiles for singletons were similar across the three occupational exposure groups. Around 2% of natural conceptions were multiple gestations (98% of these comprising twins, 2% higher order multiples), and this prevalence did not appear to vary with night shift work exposure.

Among births arising from fertility treatment (table 2), there was considerable variation in the prevalence of urogenital anomalies in singletons. Around a quarter of births arising from fertility treatment were multiple gestations (91% twins, 9% higher order multiples), with multiples most frequent where the mother undertook day work.

Multivariable logistic regression analysis was undertaken with models including relevant maternal factors as well as fetal sex and multiplicity, although there was little difference between unadjusted and adjusted results (table 3). A multiplicative interaction term between night shift work and mode of conception in relation to the outcome of urogenital anomalies in offspring was included. The interaction term was statistically significant in the model for nurses (adjusted \( \beta=0.73, SE=0.31, \ p=0.02 \)). The coefficients in the model for other night shift workers were similar, but the interaction was not statistically significant (adjusted \( \beta=0.66, SE=0.55, \ p=0.2 \)). Results for the model in which night shift occupations were combined were compatible (adjusted \( \beta=0.74, SE=0.29, \ p=0.01 \)). Overall, among naturally conceived first births, maternal night shift work was not associated with urogenital anomalies in offspring when other factors were considered (OR=0.99, 95% CI 0.84 to 1.15). Where
conception arose from fertility treatment, the odds of urogenital defects was elevated among births to night shift workers compared with day workers (OR=2.07, 95% CI 1.20 to 3.55).

The type of fertility treatment received by night shift and day workers was compared with see whether this was a potential explanation for differences in the prevalence of urogenital anomalies in offspring (table 4). Around one-third of women conceived with IVF and a quarter with ICSI. There was no statistically significant difference in the types of treatment received by night shift exposure status. Among women who conceived with fertility treatment and for whom BMI data was available (n=3053), on average, maternal BMI was 25.1 kg/m² for night shift workers and 24.6 kg/m² for day workers (p=0.07).

We attempted to investigate whether specific treatment modalities and multiplicity were associated with an excess of urogenital defects for night shift workers but data were sparse (see online supplemental table 2).

### DISCUSSION

This study demonstrated an interaction between maternal night shift work and the use of fertility treatment to conceive in relation to the prevalence of urogenital anomalies in first births. This was not explained by differences in the types of fertility treatment administered to women who worked night shift.

Interest in the occurrence of urogenital anomalies among births to nurses, in particular, has been motivated by concerns about the range of potential chemical, biological and physical exposures in the healthcare setting. A case–control study in the USA comprising 4915 cases and 3027 controls reported significantly higher prevalence of any congenital anomalies, genital anomalies and urinary anomalies among children of female nurses.29 The study did not consider mode of conception.

A recent systematic review by Warembourg et al identified four relevant studies (three cohort, one case–control) published

### Table 2

| Naturally conceived births | Other shift workers | Day workers | Births from fertility treatment | Other shift workers | Day workers |
|---------------------------|---------------------|-------------|--------------------------------|---------------------|-------------|
| Nurses                    | (n=7820)            | (n=2954)    | (n=83 867)                     | (n=343)             | (n=110)     |
| Male births n (%)        | 7660 (98.0)         | 2902 (98.2) | 82 037 (97.8)                  | 269 (78.4)          | 79 (71.8)   |
| Female births n (%)      | 3989 (52.0)         | 1477 (50.9) | 42 245 (51.5)                  | 118 (43.9)          | 40 (50.6)   |
| Fetal deaths n (per 1000 births) | 43 (5.6)     | 18 (6.2)    | 423 (5.2)                      | 1 (0.3)             | 2 (25.3)    |
| Birth weight in grams (mean±SD)†‡ | 3433±455 | 3417±462    | 3409±457                       | 3325±481            | 3466±479    |
| Gestational age† n (%)  | ≥37 weeks           | 7191 (94.6) | 2701 (94.0)                    | 76 427 (94.0)       | 238 (89.5)  |
| ≤36 weeks                | 409 (5.4)           | 174 (6.0)   | 4925 (6.0)                     | 28 (10.5)           | 5 (6.5)     |
| Any congenital anomalies n (per 1000 births) | 461 (60.2) | 178 (61.3) | 4817 (58.7)                   | 30 (111.5)          | 6 (75.9)    |
| Urogenital anomalies n (per 1000 births) | 132 (17.2) | 51 (17.6)   | 1401 (17.1)                    | 9 (33.5)            | 3 (38.0)    |
| Multiples* n (%)         | 160 (2.0)           | 52 (1.8)    | 1830 (2.2)                     | 74 (26.6)           | 31 (28.2)   |
| Male births n (%)        | 70 (43.8)           | 24 (46.2)   | 861 (47.1)                     | 41 (55.4)           | 19 (61.3)   |
| Fetal deaths n (per 1000 births) | 5 (31.3)    | 2 (38.5)    | 39 (21.3)                      | 4 (54.1)            | 5 (161.3)   |
| Birth weight, grams (mean±SD)†‡ | 2649±310 | 2680±392    | 2713±363                       | 2755±424            | 2759±418    |
| Gestational age† n (%)  | ≥37 weeks           | 80 (51.6)   | 26 (52.0)                      | 773 (43.2)          | 24 (34.3)   |
| ≤36 weeks                | 75 (48.4)           | 24 (48.0)   | 1016 (56.8)                    | 46 (65.7)           | 8 (33.3)    |
| Any congenital anomalies n (per 1000 births) | 5 (31.3)    | 4 (76.9)    | 140 (76.5)                     | 10 (135.1)          | 2 (64.5)    |
| Urogenital anomalies n (per 1000 births) | 1 (6.3)     | 1 (19.2)    | 42 (23.0)                      | 6 (81.1)            | 2 (64.5)    |

* Ninety-eight per cent of naturally conceived multiple births and 91% of multiple births from fertility treatment were twins.
† Excluding terminations for defect (n=308) and fetal deaths (n=589).
‡ Term births only. Birthweight information was missing for 213 births.

### Table 3

| Mode of conception | Interaction with | n    | Urogenital anomaly | Unadjusted OR (95% CI) | Adjusted* OR (95% CI) |
|--------------------|------------------|------|--------------------|------------------------|-----------------------|
| Natural            | Day work         | 83 867| Reference          | 0.99 (0.83 to 1.19)    | 0.97 (0.81 to 1.16)   |
|                    | Nurses            | 7820 | 1.03 (0.78 to 1.36) | 1.04 (0.78 to 1.37)   |
|                    | Other night shift workers | 2954 | 1.00 (0.86 to 1.17) | 0.99 (0.84 to 1.15)   |
|                    | All night shift workers | 10 774 | Reference          | 1.84 (1.02 to 3.31)   | 2.01 (1.11 to 3.62)   |
| Fertility treatment| Day work         | 3009 | Reference          | 2.07 (0.72 to 5.92)   | 2.00 (0.70 to 5.73)   |
|                    | Nurses            | 343  | 1.95 (1.14 to 3.33) | 2.07 (1.20 to 3.55)   |
|                    | Other night shift workers | 110 | Reference          | 2.07 (0.72 to 5.92)   | 2.00 (0.70 to 5.73)   |
|                    | All night shift workers | 453 | Reference          | 2.07 (1.20 to 3.55)   |

* Adjusted for maternal age, ethnicity, socioeconomic status, smoking, prepregnancy diabetes, gestational diabetes, prepregnancy hypertension, pregnancy induced hypertension, fetal sex and multiplicity.
between 2000 and 2013. Three of the included studies found no association between maternal healthcare work and offspring urogenital anomalies. The fourth study, a cohort study of 23,222 nurses, found that the prevalence of urogenital anomalies among children of nurses was significantly lower than the rate in the general population, although potential confounding factors could not be taken into account. Only one of the four included studies considered mode of conception, finding no impact on the results. That study included first births to 5976 healthcare workers and 60,890 other workers form the Danish National Birth Cohort, with a prevalence of fertility treatment of 8.1% and 7.1% respectively. Within the systematic review no study had specific information on work schedules.

While we also do not have information on actual work schedules, an advantage of our study is that we included potential night shift workers from other industries who are unlikely to be exposed to the infections, solvents and other hazards experienced by some nurses. The relationships were similar, pointing to a factor these industries have in common, but this needs investigation in a sample with more detailed exposure information.

One previous study has considered the impact of maternal night shift work across a broader range of industries. This Japanese study of 51,316 newborn males examined the contribution of maternal occupational environment during gestation to the frequency of cryptorchidism. No association between self-reported maternal night shift work in either early or mid-late gestation and cryptorchidism was found.

Our results concur with existing research indicating that urogenital anomalies are more common among males than female births. Detection bias may contribute to this finding since the male sex organs are located externally, so anomalies may be more readily identified during routine examinations. However, congenital anomalies of the kidney and urinary tract have also been shown to occur more frequently in males. Our findings also confirm that urogenital anomalies are more common among babies conceived with fertility treatment. While detection bias might contribute to this through greater treatment seeking of mothers on behalf of these children, or greater healthcare needs, that anomalies were reported up to the child’s fifth birthday mitigates this. The variability in the ratio of males to females born after fertility treatment is consistent with published work showing this is affected by specific components of treatment.

Mechanistically it is possible that altered endocrinology produced by circadian misalignment in female night shift workers may contribute to the increased prevalence of urogenital anomalies in offspring. However, if either altered androgen-oestrogen balance or melatonin secretion were driving the association between night shift work and urogenital anomalies, we might expect to see an effect regardless of mode of conception. Instead, urogenital anomalies were increased only when conception involved fertility treatment.

This might be explained by differences between night shift workers who required fertility treatment to conceive and their coworkers. An important possibility is differences in shift schedules entailing greater duration and/or intensity of night shift work, hence greater interference with reproductive function. A study by Schernhammer et al found higher rates of endometriosis among rotating shift workers, but only among those with concurrent infertility. This led the authors to raise the idea of an interaction between the pathophysiology of infertility and the physiological disturbances produced by night and rotating shift work. Although we found an interaction, we cannot address this specific proposition as we do not have individual-level information on shift schedules. Another possibility relates to tolerance of night shift work, which has been shown to vary between individuals. Those with poor tolerance have greater sleep disturbance, fatigue, low mood, irritability and other symptoms, and could also experience greater endocrine disturbance. Again, we lack specific information relevant to this.

Elsewhere we showed that women undertaking night shift work who receive fertility treatment are more likely than other women receiving treatment to have menstrual irregularity. It is possible that some of these women have menstrual disturbances produced by circadian disruption, in the absence of underlying clinical infertility.

Strengths of this study include the use of large, population-based datasets. The SA Birth Defects Registry provides high-quality information on congenital anomalies diagnosed up to age 5 years, allowing ascertainment beyond those detectable at birth. Linkage of fertility clinic data provided information on specific treatment modalities.

This study also has several limitations. JEMs provide a rather crude classification of exposure. Lack of individual-level information on shift schedules for women means we were unable to investigate possible roles of intensity and duration of night shift work. As well, use of a JEM limits the ability to control for other potentially hazardous exposures occurring within an occupation which may also be relevant. Use of occupational title to impute night shift work involves a degree of misclassification of exposure but as this occurs independently of outcome status, our effect estimates are likely to be conservative. Smoking data were of fairly poor quality but previous studies suggest no association between maternal smoking and urogenital anomalies. High maternal BMI has been identified as a risk factor for urogenital anomalies and is associated with shift work, but we did not have information on BMI where women conceived naturally. Lastly, linked data were available for the period 1986–2002 only, as data linkage for more recent years had not been completed. Examination of a longer time series would be valuable for future studies.

Maternal shift work involving exposure to light at night was significantly associated with urogenital anomalies in offspring, but only when women conceived with fertility treatment. The interaction between maternal night shift work and use of fertility treatment suggests that individual susceptibility to circadian disruption and the impact of this on severity of infertility may be important factors in determining adverse outcomes, such as urogenital anomalies.
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REFERENCES

1 Gamble KL, Resuehr D, Johnson CH. Shift work and circadian disruption of reproduction. Front Endocrinol 2013;4:92.

2 Schenhammer ES, Rosner B, Willett WC, et al. Epidemiology of urinary melanin in women and its relation to other hormones and night work. Cancer Epidemiol Biomarkers Prev 2004;13:936–43.

3 Fernandez RC, Marino JL, Varcoe T, et al. Fixed or rotating night shift work undertaken by women: implications for fertility and miscarriage. Semin Reprod Med 2016;34:74–82.

4 Fernandez RC, Moore VM, Marino JL, et al. Night shift among women: is it associated with difficulty Conceiving a first birth? Front Public Health 2020;8:676.

5 Reiter RJ, Tan DX, Korkmaz A, et al. Melatonin and stable circadian rhythms optimize maternal, placental and fetal physiology. Hum Reprod Update 2014;20:293–307.

6 van der Zanden LFM, van Rooij IALM, Feitz WFJ, et al. Aetiology of hypospadias: a systematic review of genes and environment. Front Public Health 2016;3:179–83.

7 Lary JM, Paulozzi LJ. Sex differences in the prevalence of human birth defects: a population-based study. Teratology 2001;64:237–51.

8 Sokal R, Tata LJ, Fleming KM. Sex prevalence of major congenital anomalies in the United Kingdom: a national population-based study and international comparison meta-analysis. Birth Defects Res A Clin Mol Teratol 2014;100:79–91.

9 Tennant PWC, Samarasekera SD, Fries-Axlsdotter T, et al. Sex differences in the prevalence of congenital anomalies: a population-based study. Birth Defects Res A Clin Mol Teratol 2011;91:894–901.

10 Moore KL, Persaud TNV, Torchia MG. Urogenital system. the developing human: clinically orientated embryology. Philadelphia: Elsevier, 2011: 245–88.