

# Trend and Outcomes of Inadvertent Isotretinoin Exposure in Pregnancy

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## Background

Isotretinoin is a known human teratogen (1).

Cases of isotretinoin use during pregnancy have been reported internationally, with one study in Berlin documenting 108 cases of exposure from 1993 to 2008 (2).

Unfortunately, there are a lack of studies describing trends of isotretinoin exposure in pregnancy in Australia, and their outcomes.

## Aim

To describe the trend of isotretinoin exposure in Australia amongst pregnant women or women planning pregnancy, and pregnancy outcomes following inadvertent exposure.

## Method

This retrospective, observational study examined antenatal isotretinoin exposures referred to the Women's Clinical Genetics Service (CGS) between January 2012 and June 2023. A retrospective review of the Medicines Information Services' (MIS) enquiries relating to isotretinoin and pregnancy during this period was also conducted.

- CGS data was collected through retrospective review of medical records and recorded on case report forms. CGS data included: age, gestational age at cessation of isotretinoin, outcome of pregnancy, gestational age at pregnancy outcome and contraceptive use.
- MIS data was collected through the MIS electronic database. Information collected included: type of enquirers and type of enquiries regarding isotretinoin in pregnancy.
- Data was then collated and reviewed using Microsoft Excel® and descriptive analysis.

## Results

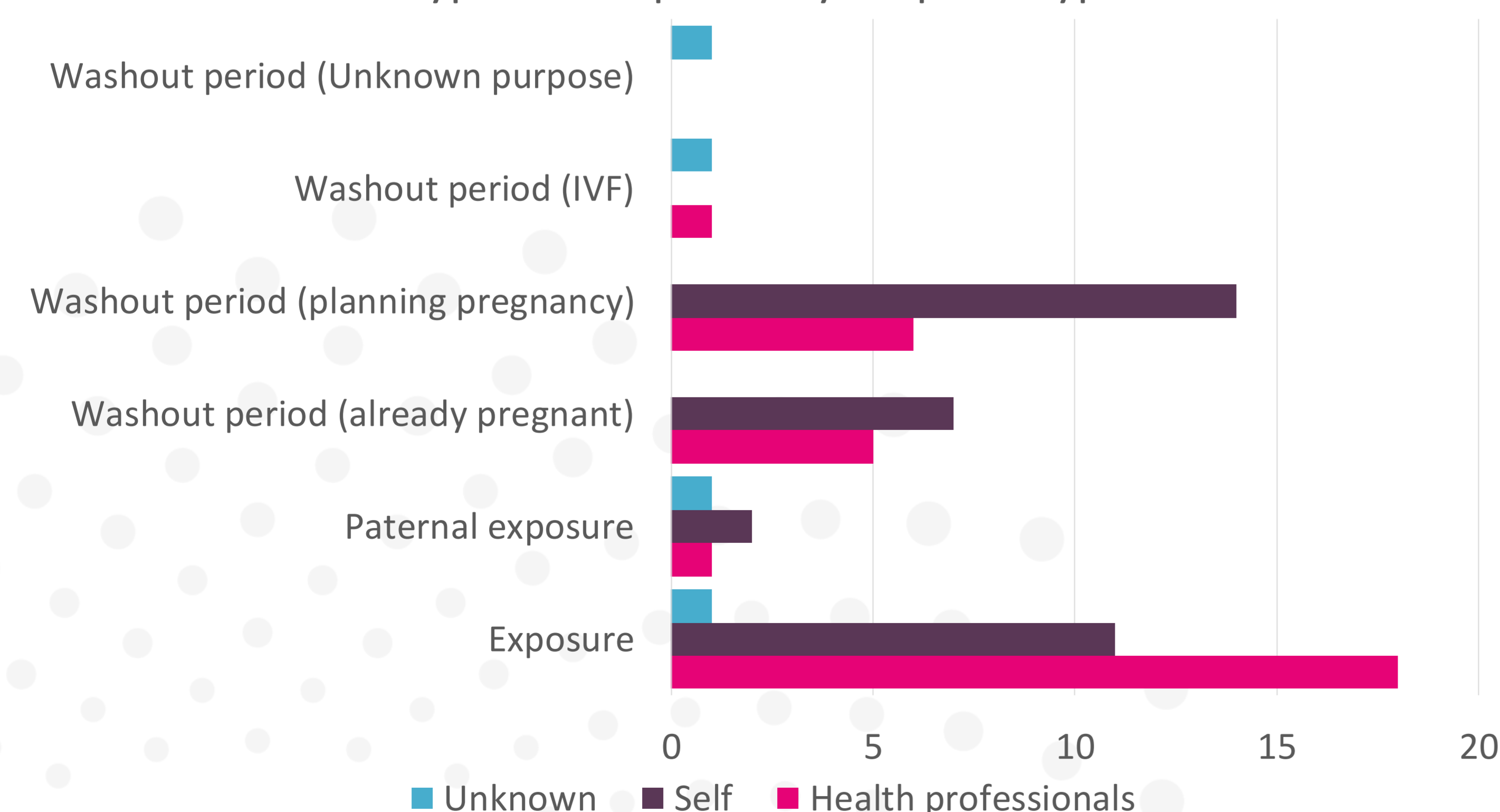
The MIS received 113 enquiries regarding isotretinoin exposure in the study period. Of this, 44 records were excluded due to: insufficient details (n=12), not related to oral isotretinoin (n=5), not pregnancy related (n=3), record not related to enquiry (n=12) and duplicate enquiry for the same patient (n=12).

69 enquiries met the inclusion criteria. Pregnancy planning following isotretinoin therapy (35/69, 51%), exposure to isotretinoin in pregnancy (30/69, 43%), and paternal exposure (4/69, 6%) were included in the study.

Patients (34, 50%), health professionals (31, 45%) or unknown/unrecorded (4, 5%) were identified as enquirers.

For enquiries about pregnancy planning after ceasing isotretinoin therapy (washout period), 2 (7%) were relating to *in-vitro* fertilization (IVF), 20 (57%) relating to patients currently planning pregnancy, 12 (34%) regarded patients who were already pregnant, and 1 (3%) unknown purpose (figure 1).

Types of enquiries by enquirer type



Graph 1. Enquiries received by MIS grouped by type of enquiry and type of enquirer.

A total of 10 pregnant women attended the CGS post-isotretinoin exposure in pregnancy (Table 1). Only two women reported the use of contraception whilst on isotretinoin.

No congenital malformations were reported in the three live births.

Case Number	Age (years)	Contraceptives	GA at last isotretinoin dose (weeks+ days)	Pregnancy outcome	GA at outcome (weeks+ days)
1	40	Unknown	8+0	Live birth	40+0
2	39	Unknown	2+5	Live birth	36+2
3	25	Unknown	* 2 weeks prior to conception	Live birth	41+0
4	18	No	3+4	Still birth	39+0
5	34	Unknown	6+1	Termination	9+5
6	28	Yes	6+0	Termination	8+0
7	27	No	4+2	Termination	19+2
8	30	Yes	4+1	Termination	9+2
9	40	No	5+1	Spontaneous abortion	9+4
10	22	Unknown	3+3	Unknown	NA

Table 1. Clinical Genetics Services (CGS) cases of patients exposure to isotretinoin during pregnancy or 4 weeks prior to conception. GA: Gestational age.

## Discussion

As prescribing of isotretinoin has several restrictions in Australia to protect against exposure in pregnancy, these findings are surprising.

Live births following isotretinoin exposure have been reported in previous literature, aligning with these findings (1). No malformations were described in this case series, but the small case number makes statistical analysis of the findings difficult.

The limited documentation of contraceptive use may indicate insufficient focus on preventing pregnancy in patients using isotretinoin.

The MIS enquiries received indicate vigilance about isotretinoin's teratogenicity is still needed. The enquiries also suggest there is poor knowledge of safe pregnancy planning after isotretinoin therapy.

Women taking isotretinoin should be encouraged to discuss pregnancy planning with their healthcare providers.

These findings are limited by the small sample size and by the information available when gathered retrospectively.

Further studies should examine the optimal management strategies of pregnancy following inadvertent isotretinoin exposure.



Image 1. Isotretinoin exposed fetus with defects: hydrocephalus, low set ears, micrognathia(4).



Image 2. Depiction of Cleft lip defect in baby(5).



Image 3. Depiction of Anencephaly defect in baby

## Conclusion

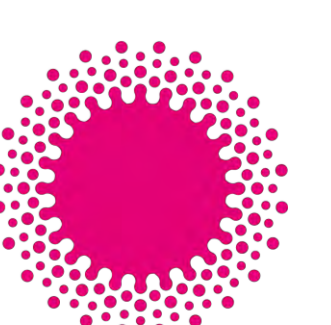
Through this case series, different pregnancy outcomes were able to be explored.

Use of contraceptives and gestation of pregnancy when isotretinoin was ceased were also explored.

Live births after isotretinoin exposure in early pregnancy has been observed, but more research is needed to explore management strategies for exposed pregnancies.

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