

**Title: Rates of pelvic inflammatory disease and ectopic pregnancy in Australia, 2009 to 2014: ecological analysis of hospital data**

**Authors**

Jane L Goller, Centre for Epidemiology and Biostatistics, Melbourne School of Population & Global Health, University of Melbourne, Parkville, Victoria, 3010, Australia

Alysha M De Livera, Centre for Epidemiology and Biostatistics, Melbourne School of Population & Global Health, University of Melbourne, Parkville, Victoria, 3010, Australia

Rebecca J Guy, Kirby Institute, UNSW Sydney, Sydney, New South Wales, 2052, Australia

Nicola Low, Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland

Basil Donovan, Kirby Institute, UNSW Sydney, Sydney, New South Wales, 2052, Australia

Matthew Law, Kirby Institute, UNSW Sydney, Sydney, New South Wales, 2052, Australia

John M Kaldor, Kirby Institute, UNSW Sydney, Sydney, New South Wales, 2052, Australia

Christopher K Fairley, Central Clinical School, Monash University and Melbourne Sexual Health Centre, Carlton, Victoria, 3053, Australia

Jane S Hocking, Centre for Epidemiology and Biostatistics, Melbourne School of Population & Global Health, University of Melbourne, Parkville, Victoria, 3010, Australia

**Corresponding author:** Jane Louise Goller,

Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Level 3, 207 Bouverie St, Parkville, 3053. Australia

Email: [jane.goller@unimelb.edu.au](mailto:jane.goller@unimelb.edu.au), Telephone: + 61 3 9035 6612, Fax: +61 3 9349 5815

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## ABSTRACT

**Objectives:** To analyse yearly rates of pelvic inflammatory disease (PID) and ectopic pregnancy (EP) diagnosed in hospital settings in Australia from 2009 to 2014.

**Methods:** We calculated yearly PID and EP diagnosis rates in three states (Victoria, New South Wales, Queensland) for women aged 15 to 44 years using hospital admissions and emergency department (ED) attendance data, with population and live-birth denominators. We stratified PID diagnoses as chlamydial or gonorrheal-related (CT-or-NG-related), acute, unspecified and chronic and analysed variations by year, age and residential area using Poisson regression models.

**Results:** For PID, the rate of all admissions in 2014 was 63.3 per 100,000 women (95% confidence interval CI 60.8 to 65.9) and of all presentations in EDs was 97.0 per 100,000 women (95%CI 93.9 to 100.2). Comparing 2014 with 2009: the rate of all PID admissions did not change, but the rate of all presentations in ED increased (adjusted incidence rate ratio, aIRR 1.34, 95%CI 1.24 to 1.45), and for admissions by PID category was higher for CT-or-NG-related PID (aIRR 1.73, 95%CI 1.31 to 2.28) and unspecified-PID (aIRR 1.09, 95%CI 1.00 to 1.19) and lower for chronic-PID (aIRR 0.84, 95%CI 0.74 to 0.95). For EP, in 2014 the rate of all admissions was 17.4 (95% CI 16.9 to 17.9) per 1000 live births and of all ED presentations was 15.6 (95% CI 15.1 to 16.1). Comparing 2014 with 2009, rates of all EP-admissions (aIRR 1.06, 95%CI 1.04-1.08) and rates in ED (aIRR 1.24, 95%CI 1.18-1.31) were higher.

**Conclusions:** PID and EP remain important causes of hospital admissions for female sexually transmitted infection associated complications. Hospital EDs care for more PID cases than inpatient departments, particularly for young women. Updated primary care data are needed to better understand PID epidemiology and healthcare usage.

## INTRODUCTION

*Chlamydia trachomatis* and *Neisseria gonorrhoeae* can ascend to the upper genital tract and have serious health consequences for women, including pelvic inflammatory disease (PID), which can lead to ectopic pregnancy (EP), chronic pelvic pain or infertility<sup>1 2</sup> that maybe unrecognised until affected women try to conceive. These sequelae account for substantial health care costs<sup>3</sup> and their prevention is an important reason for sexually transmissible infection (STI) control policies.<sup>4</sup>

In many countries including Australia, PID and EP are not statutorily notifiable but datasets about diagnoses in hospitals provide information about rates over time. The gonorrhoea epidemics in many industrialised countries during the 1960s and 1970s were associated with increasing PID incidence followed by increasing EP incidence.<sup>5</sup> From the 1980s to 2010, declining PID rates in hospital admissions and general practice were reported in several countries including Australia<sup>5-14</sup> with some reports suggesting declines were influenced by STI control.<sup>12</sup> However, in the 1980s and 1990s falls in PID and STIs were also attributed to sexual behaviour changes in response to the HIV epidemic.<sup>6</sup> Stable or declining EP rates have been reported during the 1990s and 2000s in some countries,<sup>7-9</sup> but increasing rates have also been reported.<sup>10</sup>

In 2007 in Australia, the hospital admission rate for PID was 89 per 100,000 population and EP was 16 per 1000 live births, amongst women aged 15-39 years.<sup>8</sup> Since then, chlamydia and gonorrhea diagnoses patterns have changed. Amongst women, age-standardised chlamydia diagnosis rates increased from 2007-2011, were stable to 2015 then increased in 2016.<sup>15</sup> Although gonorrhoea occurs predominantly among men who have sex with men, notification rates in women more than doubled from 2007-2016, raising concerns about potential reproductive tract complications.<sup>15</sup> The primary objective of this study was to analyse yearly rates of PID and EP diagnosed in Australian hospital settings. A secondary objective was to examine associations between PID or EP diagnosis and characteristics of residential area.

## METHODS

We undertook an ecological study using data of numbers of hospital admissions and emergency department (ED) attendances for PID and EP in the three most populous Australian states, New South Wales, Victoria and Queensland. The study was approved by the Royal Australian College of General Practitioners National Research and Evaluation Ethics Committee (NREEC09.019).

We obtained data from state Departments of Health from separate hospital admissions and ED attendances registers (supplementary table 1). We received non-identifiable, line-listed records for 15-44-year-old female patients during 2009-2014. Hospital admission datasets included data from all public (government-funded) and private hospitals. ED datasets included data for presentations to public hospitals with a designated ED. Data reporting from EDs was voluntary and clinicians assigned diagnosis codes, making ED data more variable than admissions data. ED attendances can result in

discharge or hospital admission, the latter also counted in admissions datasets, but, we could not merge these datasets owing to de-identified records and different data systems.

Each patient record included a principal diagnosis for the main reason for care and ‘other’ diagnoses made, each coded using ICD10-AM or for some EDs, ICD9 or Systematized Nomenclature of Medicine. Data items included year, agegroup, residential postcode, and, principal diagnosis code on which a PID or EP diagnosis was assigned (table 1, supplementary table 2). Like other Australian studies,<sup>7 8</sup> we excluded records with an ‘other’ PID or EP diagnosis because they might represent pre-existing conditions. We categorised PID admissions further as chlamydial-or-gonorrhoeal-related (CT-or-NG-related PID), acute-PID, PID-unspecified, or, chronic-PID. As this analysis focussed on trends we only included ED records from hospitals contributing data in all years and if annual presentation numbers varied by <50%.

Denominator data were obtained from the Australian Bureau of Statistics (supplementary table 1). At postcode level these included estimated female residential population by year, age, remoteness, and index of relative socio-economic disadvantage (IRSD).<sup>16</sup> Like another Australian study<sup>8</sup> we obtained the number of live births by maternal age and year for our EP denominator. The three states comprised 1738 postcodes. Postcodes were excluded (n=18) if the population was zero (e.g. company postcodes) or off-shore island/s; or, recoded to a neighbouring postcode (n=42) if IRSD was unavailable or the population for some agegroups was zero (e.g. remote postcodes). The remaining 1678 postcodes were categorised for remoteness (metropolitan, inner-regional, outer-regional and/or remote using standard definitions) and deciles of increasing socio-economic disadvantage based on the IRSD.

We prepared three datasets. The all-admissions and all-ED datasets included all hospital admissions or ED presentations with a principal PID or EP diagnosis, and population by postcode, year and agegroup. The non-admitted-ED dataset was a subset comprising PID or EP episodes discharged from EDs without admission.

### **Statistical analysis**

We analysed datasets separately, using Stata 14 (StataCorp, College Station, Texas, USA). We calculated yearly PID and EP rates per 100,000 women using population denominators and EP rates per 1,000 live births. We examined variation in rates by year, agegroup, remoteness and socio-economic disadvantage of postcode using univariable and multivariable Poisson regression models with clustered sandwich estimator to account for intragroup correlation.<sup>17</sup> We included year as a categorical variable to see whether rates differed from the reference category of 2009. We report incidence rate ratios (IRR) with 95% confidence intervals (95% CI). Where necessary, we used zero-inflated Poisson (ZIP) regression to account for large numbers of postcodes with no cases, and compared the fit to ordinary Poisson models using the Vuong test.<sup>18</sup> Using likelihood ratio tests, we investigated interactions

between residential area and agegroup and reported them if statistically and clinically meaningful. We conducted a subgroup analysis of admission rates by PID category. Two sensitivity analyses were undertaken to examine robustness of our results. The first used linear splines to explore the rate of change in overall rates per two-year period. The second repeated our analysis of population rates, omitting postcodes recoded to neighbouring postcodes.

## **RESULTS**

From 2009-2014 we recorded totals of 14,271 admissions and 20,522 ED presentations with a principal PID diagnosis, and 23,579 admissions and 19,382 ED presentations with a principal EP diagnosis, across 1,678 postcodes (table 1, supplementary table 2). The median population of 15-44-year-old women in study postcodes in 2009 was 946 (interquartile range 212-3254). Two-fifths (42%) of postcodes were metropolitan (representing 76% of the population), 29% in outer-regional/remote areas (7% of the population) and 41% of the population lived in more disadvantaged (five most disadvantaged IRSD deciles) areas.

Table 1 Number of hospital admissions and emergency department presentations for PID and EP, and, age breakdown of the population and live birth denominators, by year, 2009-2014

	2009	2010	2011	2012	2013	2014	Overall
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	N (%)
<b>Pelvic inflammatory disease*</b>							
Total admissions	2,141	2,314	2,510	2,429	2,502	2,375	<b>14,271 (100)</b>
CT-or-NG-related-PID†	81 (3.8)	126 (5.4)	123 (4.9)	141 (5.8)	157 (6.3)	142 (6.0)	770 (5.4)
Acute PID‡	124 (5.8)	140 (6.1)	176 (7.0)	151 (6.2)	152 (6.1)	152 (6.4)	895 (6.3)
Unspecified PID§	1,379 (64.4)	1,513 (65.4)	1,674 (66.7)	1,614 (66.4)	1,613 (64.5)	1,592 (67.0)	9385 (65.8)
Chronic PID ¶	557 (26.0)	535 (23.1)	537 (21.4)	523 (21.5)	580 (23.2)	489 (20.6)	3221 (22.6)
Total ED presentations	2566	2971	3438	3838	4067	3642	<b>20522 (100)</b>
Admitted from ED	746 (29.1)	837 (28.2)	1,054 (30.7)	1,172 (30.5)	1,375 (33.8)	1,298 (35.6)	6482 (31.6)
Not admitted from ED	1,820 (70.9)	2,134 (71.8)	2,384 (69.3)	2,666 (69.5)	2,692 (66.2)	2,344 (64.4)	14040 (68.4)
<b>Ectopic pregnancy¶¶</b>							
Total admissions	3,870	3,768	3,981	3,841	4,072	4,047	<b>23,579 (100)</b>
Total ED presentations	2,974	2,840	2,996	3,394	3,549	3,629	<b>19382 (100)</b>
Admitted from ED	2,325 (78.2)	2,233 (78.6)	2,365 (78.9)	2,657 (78.3)	2,800 (78.9)	2,785 (76.7)	15165 (78.2)
Not admitted from ED	649 (21.8)	607 (21.4)	631 (21.1)	737 (21.7)	749 (21.1)	844 (23.3)	4217 (21.8)
<b>Denominator/s</b>							
Estimated residential population#	3,534,785	3,578,562	3,611,095	3,659,865	3,708,538	3,754,048	
(N)							
15-24 years (%)	32.2	32.1	33.8	31.6	31.4	31.2	
25-34 years (%)	33.4	33.7	34.0	34.2	34.8	35.2	
35-44 years (%)	34.4	34.2	34.2	34.0	33.8	33.5	
Live births** (N)	234,821	235,805	233,193	239,145	237,205	232,553	
15-24 years (%)	18.0	17.6	17.0	16.9	16.3	15.2	
25-34 years (%)	58.9	59.0	59.9	60.4	60.9	60.6	
35-44 years (%)	23.1	23.4	23.1	22.7	22.8	22.1	

\*PID, International Classification of Diseases (ICD10) codes N70.0, N70.1, N70.9, N71.0, N71.1, N71.9, N73.0, N73.1, N73.2, N73.3, N73.4, N73.5, N73.8, N73.9, (N74.4+A56.1), (N74.3+ A54.2)

†CT-or-NG-related PID, ICD-10 codes (chlamydial PID N74.4+A56.1) and (gonococcal PID N74.3+A54.2),

‡Acute-PID, ICD-10 codes N70.0, N71.0, N73.0

§ Unspecified-PID, ICD-10 codes N70.9, N71.9, N73.2, N73.5, N73.8, N73.9

¶ Chronic-PID, ICD-10 codes N70.1, N71.1, N73.1, N73.4

¶¶ Ectopic pregnancy, ICD-10 codes O00.0, O00.1, O00.2, O00.8, O00.9

# Estimated residential population for females aged 15-44 years in 1678 study postcodes

\*\* Live births, maternal age 15-44 years

## **Pelvic inflammatory disease**

Two-thirds (65.8%) of PID hospital admissions were unspecified-PID, the remainder were chronic-PID (22.6%), acute-PID (6.3%), CT-related-PID (5.3%) and NG-related-PID (0.1%). Most (93.7%) PID in ED was unspecified-PID, the remainder were acute-PID (6.0%), chronic-PID (0.1%) and CT-related-PID (0.2%). One third (32%) of PID in ED resulted in hospital admission (table 1).

Figure 1A and supplementary table 3 show annual PID rates per 100,000 women. The overall PID admission rate increased from 60.6 in 2009 to 69.5 in 2011 then decreased to 63.3 in 2014. Between 2009-2014, the overall PID rate in ED increased from 72.6 to 97.0.

In multivariable analysis (table 2) comparing 2014 with 2009; the rate of all PID admissions did not change (adjusted IRR 1.05, 95% CI 0.98-1.12), but within PID categories (table 3) were higher for CT-or-NG-related-PID (aIRR 1.73, 95% CI 1.31-2.28) and unspecified-PID (aIRR 1.09, 95% CI 1.00-1.19), similar for acute-PID and lower for chronic-PID (aIRR 0.84, 95% CI 0.74-0.95). PID admission rates were higher for women aged 15-24 than 35-44 years (aIRR 1.09, 95% CI 1.04-1.14) including CT-or-NG-related-PID (aIRR 11.68, 95% CI 8.60-15.85) and unspecified-PID. Chronic-PID admission rates were highest for women 35-44 years. In EDs, overall PID rates were higher in 2014 than 2009 (aIRR 1.34, 95% CI 1.24-1.45) including PID managed without admission, and, were more than twice as high for women aged 15-34 than 35-44 years. Higher PID rates were observed in more disadvantaged and non-metropolitan (regional or remote) than metropolitan areas.

Table 2: Factors associated with population rates of (A) PID and (B) ectopic pregnancy, and, (C) ectopic pregnancy rates per 1000 live births, 2009-2014

	All admissions		All emergency department		Non-admitted emergency department	
	Univariable	Multivariable	Univariable	Multivariable	Univariable	Multivariable
	IRR (95% CI)	aIRR (95% CI)	IRR (95% CI)	aIRR (95% CI)	IRR (95% CI)	aIRR (95% CI)
<b>A: PID</b>						
<b>Age group in years</b>						
15-24	1.11 (1.05-1.16)	1.09 (1.04-1.14)	2.78 (2.62-2.94)	2.72 (2.57-2.87)	3.12 (2.92-3.34)	3.02 (2.84-3.22)
25-34	1.02 (0.97-1.07)	1.01 (0.96-1.06)	2.09 (1.98-2.21)	2.11 (2.00-2.23)	2.25 (2.11-2.40)	2.26 (2.12-2.41)
35-44	1.0	1.0	1.0	1.0	1.0	1.0
<b>Area of residence</b>						
Metropolitan	1.0	1.0	1.0	1.0	1.0	1.0
Inner regional	1.23 (1.17-1.29)	1.12 (1.07-1.18)	1.63 (1.51-1.75)	1.46 (1.36-1.56)	1.72 (1.58-1.87)	1.53 (1.41-1.65)
Outer regional/remote	1.75 (1.63-1.87)	1.57 (1.47-1.69)	2.28 (2.02-2.57)	2.08 (1.87-2.32)	2.26 (1.96-2.60)	2.06 (1.81-2.34)
<b>Socioeconomic status of area</b>						
Deciles of increasing disadvantage	1.06 (1.05-1.07)	1.05 (1.04-1.06)	1.09 (1.08-1.10)	1.07 (1.06-1.08)	1.09 (1.08-1.10)	1.08 (1.07-1.09)
<b>Year</b>						
2009	1.0	1.0	1.0	1.0	1.0	1.0
2010	1.07 (1.00-1.15)	1.07 (1.00-1.15)	1.13 (1.04-1.23)	1.13 (1.05-1.22)	1.13 (1.02-1.24)	1.14 (1.04-1.24)
2011	1.14 (1.07-1.23)	1.14 (1.07-1.22)	1.32 (1.21-1.45)	1.32 (1.22-1.42)	1.30 (1.18-1.44)	1.29 (1.18-1.41)
2012	1.09 (1.01-1.16)	1.09 (1.02-1.16)	1.42 (1.30-1.55)	1.41 (1.31-1.53)	1.39 (1.26-1.54)	1.40 (1.28-1.53)
2013	1.12 (1.04-1.20)	1.12 (1.05-1.20)	1.48 (1.36-1.62)	1.50 (1.39-1.62)	1.37 (1.24-1.52)	1.40 (1.28-1.53)
2014	1.04 (0.97-1.12)	1.05 (0.98-1.12)	1.33 (1.22-1.45)	1.34 (1.24-1.45)	1.22 (1.11-1.35)	1.22 (1.12-1.33)
<b>B: ECTOPIC PREGNANCY (population rates)</b>						
<b>Age group in years</b>						
15-24	0.72 (0.69-0.76)	0.70 (0.67-0.74)	1.03 (0.97-1.10)	1.00 (0.95-1.06)	0.95 (0.82-1.09)	0.95 (0.83-1.09)
25-34	2.05 (1.98-2.13)	2.04 (1.96-2.12)	2.33 (2.21-2.45)	2.32 (2.20-2.44)	2.10 (1.84-2.40)	2.08 (1.82-2.38)
35-44	1.0	1.0	1.0	1.0	1.0	1.0
<b>Area of residence</b>						
Metropolitan	1.0	1.0	1.0	1.0	1.0	1.0
Inner regional	1.12 (1.06-1.19)	1.16 (1.10-1.22)	1.16 (1.08-1.24)	1.16 (1.09-1.23)	0.84 (0.69-1.03)	0.91 (0.75-1.11)
Outer regional/remote	1.46 (1.35-1.59)	1.43 (1.32-1.55)	1.19 (1.09-1.31)	1.13 (1.04-1.24)	0.64 (0.45-0.92)	0.69 (0.49-0.96)



**Socioeconomic status of area**

Deciles of increasing disadvantage	1.03 (1.02-1.04)	1.03 (1.03-1.04)	1.05 (1.04-1.06)	1.05 (1.04-1.06)	1.01 (1.00-1.03)	1.02 (1.00-1.04)
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**Year**

2009	1.0	1.0	1.0	1.0	1.0	1.0
2010	0.97 (0.91-1.03)	0.97 (0.92-1.02)	0.96 (0.89-1.03)	0.95 (0.89-1.02)	0.93 (0.79-1.10)	0.94 (0.80-1.10)
2011	1.01 (0.95-1.07)	1.01 (0.95-1.06)	0.98 (0.91-1.05)	0.97 (0.91-1.04)	0.92 (0.79-1.06)	0.92 (0.80-1.06)
2012	0.96 (0.91-1.03)	0.96 (0.90-1.01)	1.12 (1.04-1.20)	1.09 (1.02-1.17)	1.08 (0.93-1.27)	1.07 (0.92-1.25)
2013	1.01 (0.95-1.08)	1.00 (0.94-1.06)	1.14 (1.05-1.22)	1.12 (1.04-1.20)	1.08 (0.92-1.27)	1.08 (0.92-1.25)
2014	1.00 (0.94-1.06)	0.97 (0.92-1.03)	1.14 (1.06-1.24)	1.12 (1.05-1.20)	1.23 (1.04-1.44)	1.17 (1.00-1.37)

**C: ECTOPIC PREGNANCY (rates among live births)\*****Age group in years**

15-24	0.89 (0.85-0.93)	0.89 (0.87-0.91)	1.27 (1.15-1.40)	1.27 (1.24-1.31)	1.23 (0.83-1.83)	1.24 (0.83-1.83)
25-34	0.81 (0.77-0.85)	0.81 (0.80-0.83)	0.94 (0.84-1.05)	0.94 (0.92-0.95)	0.94 (0.62-1.42)	0.93 (0.62-1.40)
35-44	1.0	1.0	1.0	1.0	1.0	1.0

**Year**

2009	1.0	1.0	1.0	1.0	1.0	1.0
2010	0.97 (0.83-1.14)	0.97 (0.95-0.99)	0.95 (0.77-1.17)	0.95 (0.92-0.98)	0.93 (0.49-1.78)	0.93 (0.49-1.76)
2011	1.04 (0.89-1.20)	1.04 (1.00-1.07)	1.01 (0.83-1.24)	1.02 (0.98-1.05)	0.98 (0.53-1.80)	0.98 (0.54-1.79)
2012	0.97 (0.84-1.14)	0.98 (0.95-1.00)	1.12 (0.91-1.38)	1.13 (1.09-1.16)	1.12 (0.63-2.00)	1.12 (0.63-1.97)
2013	1.04 (0.88-1.24)	1.04 (1.02-1.07)	1.18 (0.97-1.44)	1.19 (1.15-1.22)	1.14 (0.63-2.06)	1.15 (0.64-2.05)
2014	1.06 (0.89-1.25)	1.06 (1.04-1.08)	1.23 (1.03-1.47)	1.24 (1.18-1.31)	1.31 (0.71-2.44)	1.32 (0.71-2.45)

IRR, incidence rate ratio; 95%CI, 95% confidence interval; aIRR, adjusted incidence rate ratio

\*Level of socio-economic disadvantage and remoteness of area were not included as variables in the analysis of EP rates among live births because these denominator data were not available at postcode level.

Table 3 Factors associated with PID admissions, by PID category, 2009-2014

	<b>CT-or-NG-related PID</b>		<b>Acute-PID</b>		<b>Unspecified-PID</b>		<b>Chronic-PID</b>	
	aIRR	(95% CI)	aIRR	(95% CI)	aIRR	(95% CI)	aIRR	(95% CI)
<b>Age group in years</b>								
15-24	11.68	(8.60-15.85)	0.74	(0.62-0.89)	1.46	(1.38-1.55)	0.20	(0.18-0.23)
25-34	2.95	(2.11-4.13)	0.93	(0.78-1.10)	1.18	(1.12-1.25)	0.69	(0.64-0.75)
35-44	1.0		1.0		1.0		1.0	
<b>Area of residence</b>								
Metropolitan	1.0		1.0		1.0		1.0	
Inner regional	0.88	(0.71-1.08)	1.31	(1.09-1.58)	1.13	(1.06-1.20)	1.10	(1.00-1.22)
Outer regional/remote	1.56	(1.24-1.96)	1.78	(1.43-2.22)	1.68	(1.54-1.83)	1.11	(0.97-1.27)
<b>Socioeconomic status of area</b>								
Deciles of increasing disadvantage	1.08	(1.05-1.11)	1.06	(1.03-1.09)	1.06	(1.05-1.07)	1.01	(1.00-1.03)
<b>Year</b>								
2009	1.0		1.0		1.0		1.0	
2010	1.56	(1.18-2.07)	1.08	(0.84-1.40)	1.09	(1.00-1.18)	0.96	(0.85-1.09)
2011	1.52	(1.15-2.01)	1.36	(1.06-1.75)	1.19	(1.09-1.29)	0.94	(0.83-1.06)
2012	1.72	(1.31-2.25)	1.18	(0.92-1.52)	1.12	(1.03-1.22)	0.92	(0.81-1.04)
2013	1.89	(1.44-2.47)	1.17	(0.91-1.52)	1.12	(1.03-1.22)	1.00	(0.88-1.13)
2014	1.73	(1.31-2.28)	1.15	(0.89-1.50)	1.09	(1.01-1.19)	0.83	(0.73-0.95)

CT-or-NG-related-PID, Chlamydial or gonococcal PID ; aIRR, adjusted incidence rate ratio; 95%CI, 95% confidence interval

### Ectopic pregnancy

The most frequent EP diagnoses codes were O00.1 tubal pregnancy (70% of admissions), and, O00.9 EP-unspecified (83% of ED) and 78% of EP in ED resulted in hospital admission. Yearly population rates of EP are shown in Figure 1B and supplementary table 3 and EP rates among live births in figure 1C.

**Population rates:** The overall EP hospital admission rate per 100,000 women in 2014 was 107.8 and did not differ from 2009 (Table 2). Between 2009-2014, EP rates in ED increased overall (84.1 to 96.7) and, for women discharged without admission (18.4 to 22.5).

In multivariable analysis (table 2), comparing 2014 with 2009, EP rates in hospital admissions did not change but were higher in EDs (aIRR 1.12, 95%CI 1.05-1.20). Admission and ED rates were highest for women aged 25-34 compared with 35-44 years and in more disadvantaged and non-metropolitan areas. Rates of EP discharged from ED without admission were higher in 2014 than 2009 (aIRR 1.17, 95%CI 1.00-1.37) and lowest in outer-regional/remote areas (aIRR 0.69, 95%CI 0.49-0.96).

**Live birth rates:** Overall EP rates per 1000 live births in 2014 were 17.4 in admissions, 15.6 in ED, and 3.6 for ED but not admitted. In multivariable analysis, EP admission rates (table 2) were higher in 2014 than 2009 (aIRR 1.06, 95%CI 1.04-1.08) and highest for women 35-44 years. In ED, EP rates were highest for women aged 15-24 years and in 2014 compared with 2009 (aIRR 1.24, 95%CI 1.18-1.3).

## **Sensitivity analyses**

Linear splines showed the rate of change for population rates did not alter during the study, and, the rate of change for ED-EP live birth rates during 2011-2012 was higher than for 2009-2010 (supplementary table 4). Omission of postcodes recoded to neighbouring postcodes showed negligible change to results (data available on request).

## **DISCUSSION**

This ecological study found that for reproductive age women, overall PID admission rates were similar between 2009 and 2014. Within PID categories, admission rates increased for CT-or-NG-related-PID and unspecified-PID, but declined for chronic-PID. PID rates in EDs increased and were 2.7 times higher among women aged 15-24 than 35-44 years. Age variability in overall PID admission rates was less pronounced. EP rates among live births were higher in 2014 compared with 2009 in admissions and EDs.

### **Strengths and weaknesses**

Our study had two main strengths. First, inclusion of ED data provided new information about PID and EP diagnoses in Australia, and, like other studies<sup>7 8</sup> included public and private hospital admissions for a complete picture of PID and EP admissions. PID rates for women admitted from ED showed a similar pattern between the admissions and ED datasets. Second, undertaking our analysis at postcode level allowed exploration of the relationship between area characteristics and population rates. Large numbers of postcodes with no diagnoses were accommodated by the multivariable ZIP analysis for which our findings were consistent with ordinary Poisson models.

An important study limitation is our PID rates included only women managed in hospital. Australian guidelines recommend inpatient management for severe PID and outpatient management for mild-moderate PID.<sup>19</sup> While admissions data can tell us about severe PID, most mild-moderate PID is managed in primary care,<sup>20</sup> general practice being Australia's mainstream primary care setting. Primary care data are needed for a more complete picture of PID, but aren't routinely available. Second, because ED data provision is voluntary, we consider our admission data more reliable than ED data. We minimised variability in ED rates by limiting our analysis to EDs contributing data for all study years and with high completeness. Third, clinical PID diagnosis has low sensitivity and specificity compared with laparoscopic visualisation.<sup>2</sup> Absolute diagnosis rates might be inaccurate but, if diagnostic practices were unchanged these trends should be reliable. Uterine, cervical motion or adnexal tenderness in sexually active women with pelvic pain are the mainstay of PID diagnosis<sup>2</sup> and until non-invasive biomarkers for upper genital tract inflammation are widely available,<sup>2</sup> large scale diagnostic changes that affect estimated rates are unanticipated. However, current policies promote opportunistic chlamydia testing<sup>4</sup> and could

contribute to identifying more STI-associated PID. Fourth, our birth denominator did not include all conceptions and EP rates could be influenced by other pregnancy outcomes (e.g. stillbirths, abortion) over time. We could not address this issue because data about all conceptions aren't routinely available, but live birth denominators have been accepted previously.<sup>8 21</sup> Finally, being an ecological study, we cannot make causal inferences about factors that might influence rates over time. We show yearly age-adjusted rates, and our area measures allowed comparisons between more or less affluent or urban and non-urban areas.

### **Comparison with other studies**

We found admission rates in 2009 per 100,000 of 61 for PID and 110 for EP among reproductive-aged women. An earlier Australian study (2001-2008) reported annual infertility admission rates for same-aged women of around 400 per 100,000.<sup>22</sup> Our overall PID admission rates were similar between 2009-2014 which is broadly consistent with a commissioned review presenting hospital discharge rates for inflammatory diseases of female pelvic organs (including any cause PID) during 1990-2014 across Europe, America and Australia, showing declining country specific rates to around 2007, that then appeared to plateau in several countries including Australia.<sup>23</sup> This is the first Australian study to assess PID rates using routinely collected ED data. Our findings of increasing PID rates contrasts with a study in the United States of America that found falling PID rates (2002-2009) among adolescents attending EDs.<sup>14</sup> For EP, stable or declining admission rates using live birth denominators have been reported in Australia and internationally until the 2000s, with increases in some groups.<sup>7 8 21</sup> We found EP admission rates among live births in 2014 were 8% higher than for 2009. We are unaware of other studies measuring EP trends in EDs.

### **Interpretation of the findings**

This study provides some evidence that declines in PID observed in Australia<sup>7 8</sup> and elsewhere<sup>8</sup> might have ceased or even reversed. Several factors might contribute to this. First, STI epidemiology and sexual behaviour might be changing, and, PID is most common among young sexually active women.<sup>2</sup> Population-based data show increasing numbers of lifetime sex partners for young Australians, potentially increasing STI risk<sup>24</sup> and surveillance data show increasing chlamydia and gonorrhoea rates among women that appear to reflect increased testing and transmission.<sup>15</sup> Other Australian data show higher risks for PID hospitalisation following gonorrhea or chlamydia compared with no infection.<sup>25</sup> Although we found increasing CT-related-PID rates and to a lesser extent NG, this might reflect increased testing or that clinicians are more likely to diagnose PID for women with lower abdominal symptoms and a positive test. Second, increased screening and treatment of diagnosed infections renders more women susceptible to reinfection. Chlamydia reinfection substantially increases PID risk<sup>1 2 23</sup> and is common, repeat

chlamydia diagnosis rates of 22%, in the year after treatment have been reported in Australia.<sup>26</sup> Third, most PID was unspecified so other causes should be considered. *Mycoplasma genitalium* has been detected in 2.4% of Australian women attending primary care<sup>27</sup> and is receiving attention worldwide as a PID pathogen with worrying levels of antimicrobial resistance.<sup>2 23</sup> Bacterial vaginosis has been diagnosed in up to 12% of Australian women, and BV-associated microbes are often found in the upper genital tract of women with PID.<sup>2 23</sup> PID can also develop after uterine instrumentation, although this risk is greatest if an STI is present.<sup>28</sup> The extent these factors contribute to our findings is unknown and further research about PID causes is needed.

Australian data for 1998-2003 have shown around 59,000 PID general practice encounters annually.<sup>20</sup> Factors restricting primary care access could also contribute to increased ED rates. Timely access to Australian general practice is a concern particularly in non-metropolitan areas where there are ongoing workforce shortages<sup>29</sup> that could contribute to higher STI rates<sup>15</sup> thereby increasing PID risk. Further, out-of-pocket expenses<sup>30</sup> in primary care might prompt women to attend ED instead for mild-moderate PID not requiring hospital admission. During the study period, average out-of-pocket costs increased by 41%.<sup>31</sup>

Increasing EP rates could reflect increased risk of extrauterine conception or increased detection of extrauterine pregnancy. Risk factors for extrauterine conception include smoking, post-infection tubal damage (particularly chlamydia), assisted-reproductive-technologies and older maternal age.<sup>32</sup> The extent these risks impact on EP rates is unknown, although, smoking rates in pregnancy have declined and maternal age has increased in Australia, where EP-related mortality is rare.<sup>33 34</sup> Factors that increase EP diagnosis include more sensitive  $\beta$ -HCG tests to detect EP that might previously have resulted in undiagnosed tubal abortion, high-resolution-transvaginal ultrasound, early pregnancy units, and close monitoring of assisted reproduction outcomes. Our finding that a fifth of EP in ED were managed without admission is consistent with increased use of non-surgical (methotrexate) or conservative (wait and see) management<sup>34</sup> in some areas.

### **Implications for research, practice and policy**

Prevention of PID and its associated complications is a key goal of STI control, yet trends in these conditions are generally not routinely monitored. The challenges in measuring PID and EP rates in this and other studies highlight the need for improved data sources and surveillance systems (reflecting hospital and primary care) that facilitate comparable measures over time. Australian policy identifies the need for interventions in primary care to enhance STI management, particularly partner notification and retesting.<sup>4 23</sup> Further analyses of hospital and primary care data can support evaluation of enhanced STI

management impacts. Research is also needed to better understand the role of other infections in PID, and, develop non-invasive and objective methods that can improve PID diagnosis in any setting.

In conclusion, we found increasing rates of PID and EP diagnosis in ED, and, EP hospital admissions. These results could represent changing sexual practices, increasing STI transmission and re-infections, changing healthcare usage or increased EP detection from improved diagnosis. Without primary care data knowledge of PID epidemiology and healthcare use in Australia is incomplete. PID and EP remain important causes of hospital admission for STI-associated complications. EDs provide care for many additional PID cases, particularly for young women warranting a strengthened focus on understanding drivers of these rates and on reducing risks of these sequelae.

#### **KEY MESSAGES**

- PID and EP remain important causes of hospital admissions for STI-associated complications among reproductive age women. EDs care for many more PID cases, particularly for young women.
- PID rates in EDs were substantially higher for younger than older women. PID hospital admission rates varied little by age.
- Updated primary care data are needed to better understand PID epidemiology and healthcare usage, particularly given different patterns between hospital admissions and ED attendances.

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