

Temporal trends in tranexamic acid prescribing by Australian general practice registrars for heavy menstrual bleeding

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Background and objective

Evidence-based prescribing for heavy menstrual bleeding (HMB) can improve quality of life, iron deficiency and anaemia. Tranexamic acid (TXA) is more effective than oral hormonal medications (OHMs). This study aimed to establish temporal trends (2010–23) in TXA prescribing for HMB by Australian general practice registrars.

Methods

Cross-sectional analyses were conducted within an ongoing inception cohort study (Registrar Clinical Encounters in Training [ReCEnT]), using multivariable mixed logistic regression models.

Results

In 4717 registrars (response rate 93.4%), adjusted odds of prescribing TXA for HMB increased by 12% annually (odds ratio [OR] 1.12, 95% confidence interval [CI]: 1.04–1.20, $P=0.004$), and 18% annually when compared to OHMs (OR 1.18, 95% CI: 1.03–1.36, $P=0.019$). General practice registrars who consulted their supervisor were less likely to prescribe TXA compared to OHMs (OR 0.36, 95% CI: 0.14–0.92, $P=0.034$).

Discussion

Registrars' increasing TXA prescribing suggests an appropriate response to evidence. Supervisors may be slower to implement this evidence, warranting further investigation to inform evidence-based prescribing strategies.

HEAVY MENSTRUAL BLEEDING (HMB), previously known as menorrhagia, is an important health concern, affecting one in four women of reproductive age.¹ HMB is defined as excessive menstrual blood loss that interferes with quality of life.² In addition to reducing quality of life,² HMB leads to iron deficiency, anaemia,³ hysterectomy⁴ and preventable hospitalisations. HMB has several causes, including structural pathologies, such as fibroids and endometrial cancer, and non-structural causes, such as ovulatory dysfunction and coagulopathies.³ A Cochrane meta-analysis clarified the comparative effectiveness of medical treatment options for HMB.⁵ The levonorgestrel intrauterine system (LNG-IUS) was most effective, followed by tranexamic acid (TXA), long-cycle oral progestogens, then non-steroidal anti-inflammatory drugs (NSAIDs).⁵

Despite the hierarchy of most effective medications, oral hormonal medications (OHMs) are more frequently prescribed for HMB in Australia and the UK than the more effective TXA and LNG-IUS.^{6,7} In an Australian general practice study, the LNG-IUS was prescribed for HMB in 4.3% of cases and TXA in 7.6%.⁶ Combined oral contraceptives (COCs) were the most prescribed medicines (15%), despite a Cochrane review finding uncertain evidence of effectiveness for these medicines.⁵ Oral progestogens, such as norethisterone, are similarly more often prescribed than more effective options.⁶

The low use of TXA could be because of clotting-risk concerns.⁸ Meta-analysis has shown, however, that thrombosis events are not significantly increased with TXA use, compared to placebo.⁵ LNG-IUS prescribing in general practice is likely to be reduced by the low rates of general practitioners (GPs) trained to insert them⁹, leading to either prescription of another medication option or gynaecology referral. TXA, however, is readily accessible by prescription.

To our knowledge, no studies have investigated whether HMB prescribing in general practice has changed over time with emerging evidence. This would help in determining whether further measures, such as education or resource development, need to be taken to improve evidence-based prescribing for HMB in general practice. Increased prescribing of the most effective medications in general practice has the potential to lower rates of iron

deficiency and anaemia and provide women with an improved quality of life.

General practice registrars are an important component of the general practice workforce, comprising 16% by headcount of Australian GPs.¹⁰ General practice registrars have prescribing rights identical to their more senior GP colleagues, but are still forming their patterns of practice. Whether general practice registrars' HMB prescribing has adapted to evolving evidence has implications for general practice registrars' education regarding HMB, and also more broadly for evidence-based prescribing education.

We aimed to investigate temporal trends, from 2010 to 2023, in TXA prescribing for HMB by Australian general practice registrars. We hypothesised TXA prescribing would increase during this period, both overall and relative to OHMs. This is because, according to 'diffusion of innovation theory', we would expect the more evidence-based prescribing practice to gradually increase over time as knowledge 'diffuses' into practice.¹¹

Methods

Design

We report cross-sectional analyses conducted within the Registrar Clinical Encounters in Training (ReCEnT) project; an ongoing inception cohort study (2010 to present).¹²

Study setting

ReCEnT participants are registrars from the Australian General Practice Training (AGPT) program. From 2010 to 2015, the study was conducted in regions in New South Wales, Queensland, Victoria, Tasmania and South Australia. Because of a major restructuring of GP training from 2016 to 2023, the study was conducted in New South Wales, Australian Capital Territory, eastern Victoria and Tasmania (accounting for 44% of Australian general practice registrars¹³). Data were collected during office-based consultations. Participation is a routine component of the registrars' educational program.^{14,15} Registrars can consent for their data to be used for research purposes.

Eligibility criterion

Registrars needed to be in one of their first three community-based general practice training terms at participating general

practice training organisations from 2010 to 2023 to be eligible to participate in the study.

Data collection methods

General practice registrars recorded the details of 60 consecutive patient consultations on case report forms at the time of consultation (via hardcopy 2010–19, online portal 2020–23), in addition to questionnaire-elicited participant and practice demographics. Problems/diagnoses managed in the consultations were coded via International Classification for Primary Care version 2 (ICPC-2 PLUS).¹⁶ Medications prescribed were coded via Anatomical Therapeutic Chemical (ATC) classification.¹⁷

Outcomes

The outcome measure was prescription of tranexamic acid (ATC code B02AA02).

Independent variables

Independent variables in analyses were at patient, registrar, practice and consultation levels (Appendix 1, available online only).

Statistical methods

HMB problems were defined by ICPC-2 PLUS codes¹⁶ (refer to Appendix 2, available online only) as determined by a panel of consulting gynaecologists and the clinician authors. The panel also defined OHMs prescribed (Appendix 3, available online only).

Cross-sectional analysis was undertaken at the level of problems/diagnosis. Descriptive statistics included frequencies for categorical variables and mean with standard deviation (SD) for continuous variables.

The following proportions were calculated with 95% confidence intervals (CI):

- Proportion of all problems/diagnoses that were HMB problem/diagnoses.
- Proportion of all HMB problems/diagnoses that were treated with TXA.
- Proportion of HMB problems/diagnoses treated with TXA, of the population of HMB that were treated with TXA or OHMs.

Further analyses were restricted to: (1) problems/diagnoses categorised as HMB; and (2) problems/diagnoses categorised as HMB for which TXA or OHMs was prescribed.

The effects of explanatory variables on prescribing TXA were estimated using

univariable and multivariable mixed effects logistic regression. This was used because of our binary outcome factor and aim of modelling longitudinal change with repeated measures on participating registrars.¹⁸ Repeated measures of registrars were accounted for by specifying a random intercept for a registrar. Year was treated as continuous, and its corresponding parameter estimate represents the estimated average change per year in the odds of: (1) prescribing TXA for HMB; and (2) prescribing TXA rather than OHMs for HMB. All other variables were modelled as fixed effects.

An augmented backwards selection process was used for model specification. Variables in the model with $P > 0.2$ were tested for removal and removed if it did not substantively change the effect size (beta coefficient). Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test (HL test) applied to a standard logistic model. The logistic model assumption of linearity in the log-odds for continuous variables was also checked. Effects were expressed as odds ratios (ORs) with 95% CI. Significance was declared at the conventional 0.05 level.

Regression models estimated proportions of problems for which TXA was prescribed, by year, adjusted for other variables in the model. Analyses were programmed using STATA 18.0 (StataCorp LLC, College Station, TX, USA; 2023) and SAS V9.4 (SAS Institute, Cary, NC, USA; 2010). Excel V16.8 (Microsoft Corporation, Redmond, WA, USA; 2016) was used for descriptive statistics.

Ethics

Ethics approval was by the human research ethics committees at the University of Newcastle (H-2009-0323), University of Notre Dame Australia (2023-034S), and The Royal Australian College of General Practitioners (NREEC-23-161).

Results

Descriptive statistics

The total sample of 4717 registrars (response rate 93.4%) provided 12,009 registrar-rounds of data, for a total of 713,480 consultations and 1,068,912 diagnoses/problems. Participating registrars were 60% female, and 81% had an Australian medical degree (refer to detailed

Table 1. General practice registrar and practice demographics of participants in the ReCEnT cohort study (2010–23)

Variables	Class	All registrars n (%)
<i>Registrar characteristics</i>		
<i>n=4717</i>		
Registrar gender	Female	2816 (60)
Country of primary medical degree	Australia	3744 (81)
Pathway registrar enrolled in	Rural	1481 (32)
Has postgraduate qualifications	Yes	1403 (30)
Training college seeking Fellowship	RACGP	4437 (94)
	ACCRM	114 (2.4)
	Both	36 (0.8)
Year of graduation	Mean±SD	2011.7 (5.9)
<i>Registrar round/practice characteristics</i>		
<i>n=12,009</i>		
Registrar training term	Term 1	4528 (38)
	Term 2	4021 (34)
	Term 3	3460 (29)
Registrar does other medical work	Yes	1922 (17)
Practice routinely bulk bills	Yes	3623 (31)
Rurality of practice	Major city	7194 (60)
	Inner regional	3861 (32)
	Outer regional/remote/ very remote	949 (7.9)
SEIFA-IRSD decile of practice ²⁰	Mean±SD	5.4 (2.8)

ACCRM, Australian College of Rural and Remote Medicine; RACGP, The Royal Australian College of General Practitioners; ReCEnT, Registrar Clinical Encounters in Training; SD, standard deviation; SEIFA-IRSD, Socio-Economic Indexes for Areas - Index of Relative Socio-economic Disadvantage.

characteristics in Table 1). There were 2438 HMB problems/diagnoses (0.2% of all problems/diagnoses).

Medications were prescribed for 47% (n=1156) of HMB problems/diagnoses. The most prescribed medications were TXA (n=415, 17%), NSAIDs (n=315, 13%), COCs (n=254, 10%) and oral progestogens (n=144, 5.9%). Less prescribed medications included the LNG-IUS (n=54, 2.2%), etonogestrel implant (n=17, 0.7%) and hormonal injections (n=19, 0.8%). When point-of-care resources other than a supervisor were used, Therapeutic Guidelines was used most often (32%), followed by Health Pathways

(15%) and the Australian Medicines Handbook (8.6%).

Temporal trends in TXA prescribing

The odds of prescribing TXA for HMB increased approximately linearly over the study period (2010–23). Increasingly, TXA was chosen over OHMs, with the proportion of TXA compared to OHMs prescribed doubling in the treatment period from 2010 (0.3, 95% CI: 0.16–0.43) to 2023 (0.6, 95% CI: 0.51–0.68), as shown in Appendix 4 (available online only). The adjusted odds of prescribing TXA for all HMB problems increased by 12% per

year in the multivariable model (OR 1.12, 95% CI: 1.04–1.20, $P=0.004$), as shown in Figure 1 and Table 2. The adjusted odds of prescribing TXA compared to OHMs increased by 18% per year in the multivariable model (OR 1.18, 95% CI: 1.03–1.36, $P=0.019$), as shown in Figure 2 and Table 3. Among the variables, the proportion of missing data was low (Appendix 5, available online only).

Associations of prescribing tranexamic acid compared to oral hormonal medications

General practice registrars who consulted their GP supervisor had approximately one-third the odds of prescribing TXA compared to OHMs (OR 0.36, 95% CI: 0.14–0.92, $P=0.034$). Consulting sources other than a supervisor was strongly associated with prescribing TXA overall (OR 2.69, 95% CI: 1.84–3.93, $P<0.001$). General practice registrars in term 3, compared to term 1, had approximately twice the odds of prescribing TXA overall (OR 2.31, 95% CI: 1.54–3.46, $P<0.001$), and compared to OHMs (OR 2.30, 95% CI: 1.06–4.98, $P=0.035$). Characteristics associated with prescription of TXA are presented in Appendix 6 (available online only). The univariable and multivariable regression models are presented in Table 2 (all HMB problems) and Table 3 (among HMB problems where TXA or OHMs were prescribed).

Discussion

This study aimed to investigate the temporal trends in TXA prescribing for HMB by Australian general practice registrars. Over the study period (2010–23), TXA prescribing for HMB steadily increased. The proportion of TXA prescribed compared to OHMs doubled in the study period. General practice registrars in a later stage of training had increased odds of choosing TXA. Consulting a GP supervisor was associated with reduced odds of prescribing TXA by almost three-fold compared to OHMs.

The increase in TXA prescribing for HMB over time suggests an appropriate response by general practice registrars to current evidence of TXA's superior efficacy to OHMs. The approximately linear increase in odds of TXA

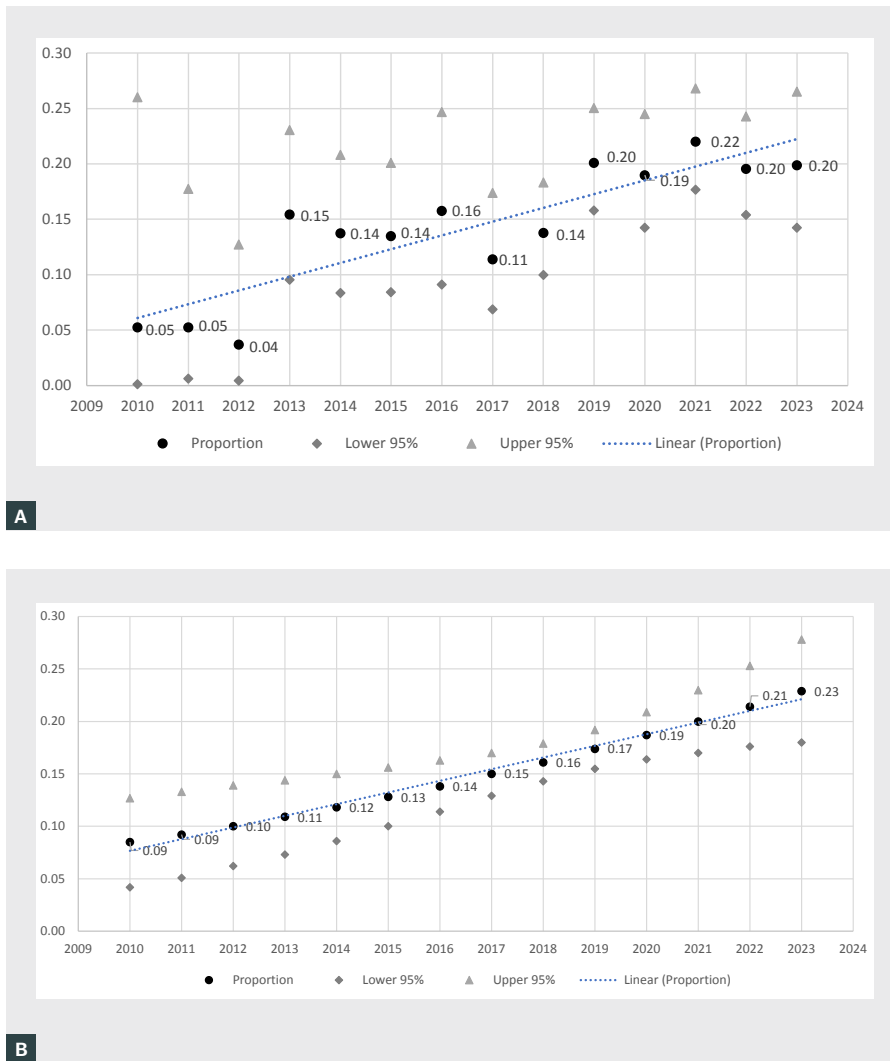


Figure 1. Proportion of tranexamic acid prescribed for heavy menstrual bleeding overall, by year, raw and adjusted. **(A)** Raw proportion of tranexamic acid prescribed by year of consultation. **(B)** Adjusted proportion of tranexamic acid prescribed by year of consultation.

prescribing suggests that the implementation of evidence into clinical practice has occurred in a steady manner, in keeping with ‘diffusion of innovation’ theory.¹¹

Although TXA exceeded OHM prescribing by the end of the study period, this proportion may still be less than optimal given TXA’s superior efficacy. Generalisability to Australian registrars is strong (the study includes 44% of Australian general practice registrars¹³ with similar demographics), as is generalisability to trainees in countries with

similar apprenticeship-like training systems.

The association of OHM prescribing with GP supervisor consultation could reflect GP supervisors being slower than registrars to adjust their practice to current evidence. Point-of-care resource use was associated with TXA prescribing. However, it is unclear whether resource use changed prescribing choice or was used to check details such as dosing for an already chosen medication.

Therapeutic Guidelines was the most utilised source, and still lists COCs, TXA

and NSAIDs as equivalent second-line agents for HMB.¹⁹ This is a possible reason for the slow uptake of TXA. The delay in guidelines’ representation of research evidence is a broader issue that needs to be addressed, as it likely contributes to delays in implementing the best evidence into practice.

Comparison with other research

To our knowledge, this is the first study to report the temporal trends of TXA prescribing for HMB. Compared to established GPs in a previous Australian study (2008–16),⁶ the general practice registrars in our study prescribed more TXA (17% vs 8%) and less COCs (10% vs 15%). Medications were prescribed in approximately half the consultations for both (47% registrars, 53% established GPs).

Limitations

A limitation of this study is that the reported consultations lack contextual clinical details. This includes severity of the HMB, duration, requirement for contraception, comorbidities and patient preferences. Dispensing and use is also unknown; however, the focus of this study was clinician prescribing. Both new and repeat prescriptions of TXA and OHMs were included in the analysis, so repeat prescriptions may reflect previous decision making by other clinicians.

Implications for future research

The potentially delayed uptake of evidence-based prescribing by GP supervisors, and its impact on general practice registrars, is an issue in general practice training that warrants further exploration. Broader prescribing patterns in GP supervisors, and its impact on registrars, could be studied to assess whether this is a widespread issue in evidence-based prescribing, or isolated to conditions like HMB. Qualitative research into the reasons for OHM choice over TXA in the GP supervisor group could help to direct improvement, such as education and access to appropriate resources. Further research into how general practice registrars and established GPs use point-of-care resources to make HMB prescribing decisions could assist resource development that supports evidence-based decisions.

Conclusion

General practice registrars steadily increased their TXA prescribing for HMB in the study period. Registrars' increasing preference for TXA over the less effective

OHMs suggests an appropriate response to evidence. However, the strong association of GP supervisor consultation with prescribing OHMs over TXA is concerning. Next steps would include investigating the reasons for

the GP supervisors' preferences and whether this pattern occurs in other conditions, and to identify strategies to increase evidence-based prescribing.

Table 2. Associations with general practice registrar prescribing of TXA for HMB (2010–23): time, patient, registrar, practice and consultation variables^A

Variable group	Variable	Class	Univariable		Adjusted	
			OR (95% CI)	P	OR (95% CI)	P
Time	Year of consultation		1.10 (1.05–1.15)	<0.001	1.12 (1.04–1.20)	0.004
Patient	Patient age		1.00 (0.99–1.01)	0.47	1.01 (0.99–1.02)	0.45
	Patient/practice status	New to registrar	1.04 (0.80–1.36)	0.77	1.07 (0.77–1.49)	0.68
	Referent: Existing patient	New to practice	1.47 (0.93–2.34)	0.10	1.60 (0.90–2.86)	0.11
	NESB	Yes	0.94 (0.57–1.55)	0.81	1.01 (0.57–1.79)	0.97
	Aboriginal and/or Torres Strait Islander background	Yes	1.93 (0.96–3.90)	0.065	1.41 (0.58–3.43)	0.45
Registrar	Registrar gender	Female	0.90 (0.65–1.25)	0.54	0.82 (0.55–1.22)	0.32
	Training term/post	Term 2	1.27 (0.92–1.75)	0.14	1.26 (0.86–1.86)	0.24
	Referent: Term 1	Term 3	2.09 (1.51–2.90)	<0.001	2.31 (1.54–3.46)	<0.001
	Additional training in women's health	Yes	1.11 (0.70–1.77)	0.65	1.36 (0.80–2.31)	0.26
	Qualified as doctor in Australia	Yes	0.75 (0.53–1.05)	0.095	0.90 (0.53–1.53)	0.68
	Year of graduation		1.01 (0.99–1.04)	0.30	0.99 (0.95–1.03)	0.60
Practice	Practice routinely bulk bills	Yes	0.98 (0.72–1.32)	0.87	0.99 (0.67–1.47)	0.96
	Rurality	Inner regional	0.99 (0.74–1.33)	0.96	0.78 (0.49–1.24)	0.30
	Referent: Major cities	Outer regional remote	1.27 (0.78–2.07)	0.33	0.96 (0.46–1.98)	0.90
	SEIFA-IRSD index ²⁰		1.00 (0.95–1.05)	0.97	0.99 (0.93–1.05)	0.73
	Training region	Region 2	1.00 (0.43–2.32)	1.00	1.59 (0.56–4.48)	0.38
	Referent: Region 1	Region 3	1.10 (0.62–1.97)	0.74	1.03 (0.49–2.17)	0.94
		Region 4	1.24 (0.81–1.89)	0.33	1.34 (0.79–2.27)	0.28
		Region 5	0.84 (0.19–3.83)	0.83	1.18 (0.16–8.77)	0.87
	Region 6	1.23 (0.78–1.92)	0.37	0.89 (0.47–1.67)	0.71	
	Region 7	1.73 (1.11–2.68)	0.015	1.46 (0.84–2.54)	0.18	

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Table 2. Associations with general practice registrar prescribing of TXA for HMB (2010–23): time, patient, registrar, practice and consultation variables^A (cont'd)

Variable group	Variable	Class	Univariable		Adjusted	
			OR (95% CI)	P	OR (95% CI)	P
Consultation	Consultation duration		1.00 (0.99–1.01)	0.99	1.00 (0.98–1.01)	0.90
	New problem	Yes	1.03 (0.80–1.34)	0.81	0.97 (0.70–1.36)	0.87
	Sought assistance	Other sources	2.63 (1.92–3.61)	<0.001	2.69 (1.84–3.93)	<0.001
	Referent: No source	Supervisor	1.15 (0.70–1.91)	0.58	1.68 (0.92–3.05)	0.09
	Pathology ordered	Yes	1.16 (0.90–1.50)	0.26	1.00 (0.71–1.39)	0.99
	Imaging ordered	Yes	1.37 (1.05–1.79)	0.021	1.21 (0.85–1.71)	0.29
	Referral ordered	Yes	0.77 (0.55–1.08)	0.12	0.87 (0.57–1.32)	0.51

^AThe multivariable model had a good fit (*HL goodness of fit* $P=0.075$) and good predictive accuracy (*C-statistic*=0.76).

CI, confidence interval; HMB, heavy menstrual bleeding; NESB, Non-English-speaking background; OR, odds ratio; SEIFA-IRSD, Socio-Economic Indexes for Areas – Index of Relative Socio-economic Disadvantage; TXA, tranexamic acid.

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Table 3. Associations with general practice registrar prescribing of TXA compared to OHMs for HMB (2010–23): Time, patient, registrar, practice and consultation variables^A

Variable group	Variable	Class	Univariable		Adjusted	
			OR (95% CI)	P	OR (95% CI)	P
Time	Year of consultation		1.17 (1.08–1.26)	<0.001	1.18 (1.03–1.36)	0.019
Patient	Patient age		1.06 (1.04–1.09)	<0.001	1.06 (1.03–1.09)	<0.001
	Patient/practice status	New to registrar	0.83 (0.54–1.25)	0.36	0.67 (0.38–1.19)	0.17
	Referent: Existing patient	New to practice	1.61 (0.74–3.51)	0.23	1.05 (0.37–2.97)	0.92
	NESB	Yes	2.61 (0.95–7.18)	0.063	2.10 (0.64–6.90)	0.22
	Aboriginal and/or Torres Strait Islander background	Yes	1.14 (0.38–3.43)	0.82	1.55 (0.36–6.59)	0.55
Registrar	Registrar gender	Female	1.00 (0.58–1.72)	1.00	0.99 (0.49–1.99)	0.98
	Training term/post	Term 2	1.25 (0.73–2.13)	0.42	0.93 (0.48–1.80)	0.83
	Referent: Term 1	Term 3	2.34 (1.30–4.23)	0.005	2.30 (1.06–4.98)	0.035
	Additional training in women's health	Yes	1.00 (0.47–2.13)	0.99	0.86 (0.35–2.08)	0.73
	Qualified as a doctor in Australia	Yes	0.61 (0.34–1.11)	0.10	0.64 (0.25–1.66)	0.35
	Year of graduation		1.02 (0.98–1.07)	0.29	0.98 (0.91–1.06)	0.67
Practice	Practice routinely bulk bills	Yes	1.37 (0.81–2.32)	0.24	1.07 (0.53–2.17)	0.84
	Rurality	Inner regional	0.63 (0.39–1.03)	0.063	0.35 (0.15–0.83)	0.019
	Referent: Major city	Outer regional remote	0.78 (0.36–1.68)	0.52	0.51 (0.14–1.88)	0.31
	SEIFA-IRSD index ²⁰		1.01 (0.94–1.09)	0.79	0.96 (0.85–1.07)	0.42
	Training region	Region 2	0.76 (0.20–2.85)	0.68	2.70 (0.41–17.9)	0.30
	Referent: Region 1	Region 3	0.84 (0.35–2.01)	0.69	1.36 (0.41–4.48)	0.61
		Region 4	1.76 (0.88–3.53)	0.11	2.06 (0.82–5.18)	0.12
		Region 5	0.43 (0.05–3.51)	0.43	0.53 (0.02–11.3)	0.68
	Region 6	1.95 (0.93–4.08)	0.078	1.23 (0.40–3.82)	0.71	
	Region 7	2.29 (1.10–4.73)	0.026	2.45 (0.91–6.59)	0.076	
Consultation	Consultation duration		1.01 (0.99–1.03)	0.22	1.01 (0.98–1.03)	0.66
	New problem	Yes	1.26 (0.82–1.95)	0.29	1.11 (0.62–2.01)	0.72
	Sought assistance	Other sources	1.64 (1.00–2.69)	0.052	1.45 (0.76–2.78)	0.25
	Referent: No sources	Supervisor	0.37 (0.18–0.77)	0.008	0.36 (0.14–0.92)	0.034
	Pathology ordered	Yes	2.15 (1.32–3.48)	0.002	1.48 (0.78–2.83)	0.23
	Imaging ordered	Yes	5.86 (3.06–11.22)	<0.001	3.37 (1.58–7.19)	0.002
	Referral ordered	Yes	1.19 (0.67–2.13)	0.55	1.10 (0.53–2.32)	0.79

^AThe multivariable model had a good fit (*H-L goodness of fit* $P=0.075$) and good predictive accuracy (*C-statistic*=0.76).

HMB, heavy menstrual bleeding; NESB, non-English-speaking background; OHM, oral hormone medication; TXA, tranexamic acid.

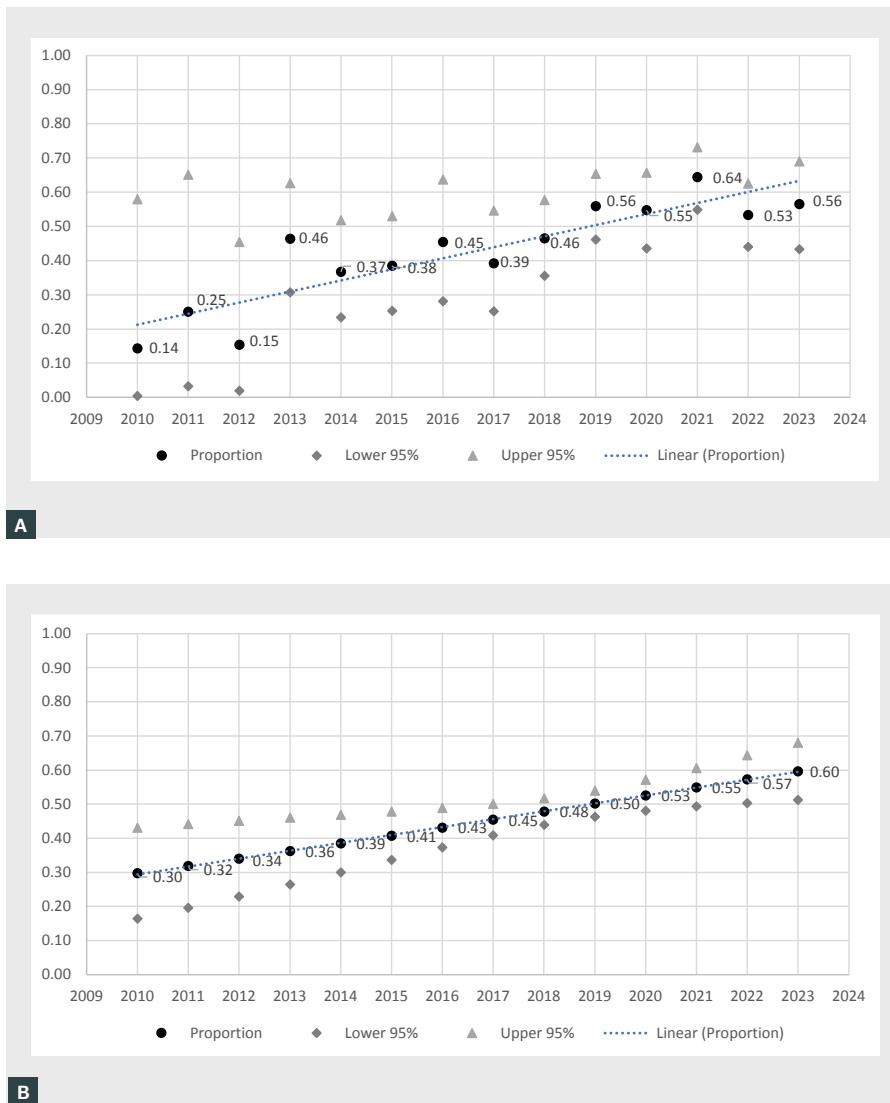


Figure 2. Proportion of tranexamic acid compared to oral hormonal medication prescribed by general practice registrars for heavy menstrual bleeding, raw and adjusted. **(A)** Raw proportion of tranexamic acid prescribing compared to oral hormonal medications by year. **(B)** Adjusted proportion of tranexamic acid prescribing compared to oral hormonal medications by year.

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