



BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Trends in clinical management of lactational mastitis among women attending Australian general practice: a national longitudinal study using MedicineInsight, 2011-2022

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-080128
Article Type:	Original research
Date Submitted by the Author:	22-Sep-2023
Complete List of Authors:	Grzeskowiak, Luke; Flinders University, College of Medicine and Public Health; South Australian Health and Medical Research Institute Limited, SAHMRI Women and Kids Kunne, Aline; South Australian Health and Medical Research Institute Limited, SAHMRI Women and Kids Crawford, Sharinne; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery Cullinane, Meabh; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery Amir, Lisa; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery; The Royal Women's Hospital, Breastfeeding service
Keywords:	Epidemiology < TROPICAL MEDICINE, Primary Care < Primary Health Care, Public health < INFECTIOUS DISEASES, MICROBIOLOGY, Pharmacology < TROPICAL MEDICINE

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES).

Title: Trends in clinical management of lactational mastitis among women attending Australian general practice: a national longitudinal study using MedicineInsight, 2011-2022

Luke E Grzeskowiak^{1,2,3}, Aline Kunnel², Sharinne B Crawford⁴, Meabh Cullinane⁴, Lisa H Amir^{4,5}

¹ Flinders Health and Medical Research Institute, College of Medicine and Public Health, Flinders University, Adelaide, South Australia, Australia

² South Australian Health and Medical Research Institute, Adelaide, South Australia, Australia

³ Adelaide Medical School, University of Adelaide

⁴ Judith Lumley Centre, School of Nursing and Midwifery, La Trobe University, Victoria, Australia

⁵ Breastfeeding service, Royal Women's Hospital, VIC, Australia

Corresponding Author:

Name: Associate Professor Luke Grzeskowiak, Flinders University

Email: luke.grzeskowiak@flinders.edu.au

Address: SAHMRI Women and Kids, Level 7, Clarence Rieger Building, Women's and Children's Hospital - 72 King William Road, North Adelaide, SA, 5006, Australia

Word Count

Abstract: 299

Main Text: 3369

Keywords: lactational mastitis; breastfeeding; epidemiology; primary care; public health; antibiotics; medications

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

ABSTRACT

Objective: To examine longitudinal trends in clinical management of lactational mastitis in women attending general practice.

Design: Open cohort study.

Setting: Australian general practice using data from MedicineInsight

Participants: Women aged 18 to 44 years with one or more clinical encounters for lactational mastitis between January 2011 and July 2022.

Primary and Secondary Outcome Measures: The primary outcome measure was the proportion prescribed oral antibiotics, according to antibiotic type. Secondary outcome measures were the proportion of women prescribed other medications (e.g. antifungals, lactation suppressants) or ordered selected clinical investigations including breast ultrasound, blood test, breast milk culture, nipple swab culture, or breast aspirate. Outcomes were examined according to calendar year and individual or clinic practice level characteristics.

Results: Among 25,002 women who had one or more clinical encounters related to mastitis, 90.9% were prescribed oral antibiotics. While the proportion of women prescribed an oral antibiotic remained consistent from 2011 to 2022 (91.1% vs. 92.5%), there were changes in the proportion receiving prescriptions for di/flucloxacillin (46.1% vs. 60.4%) and cefalexin (38.6% vs. 26.5%). Fewer than 12% of women received a clinical investigation related to their mastitis encounter, most commonly a breast ultrasound (7.1%), followed by a selected blood test (3.8%). Requests for breast milk cultures, nipple swab cultures, or breast aspirates occurred in less than 1.1% of individuals. Significant increases were evident with respect to ordering of all clinical investigations, with rates at least doubling between 2011 and 2022 (6.6% vs 14.7%). Large variability in clinical management was evident according to both individual characteristics (e.g. concessional status) and also at the clinical practice-level (e.g. remoteness).

Conclusions: Australian general practitioners commonly prescribe oral antibiotics for women with mastitis and largely in line with clinical guidelines. Their use of clinical investigations as part of mastitis management has increased over the last decade.

Strengths and limitation of this study

The study includes information about >25,000 lactational mastitis encounters extracted from electronic medical records in Australian general practice which are nationally representative.

We explored longitudinal changes in the frequency of oral antibiotic prescribing and selected requested tests related to mastitis encounter and examined how these differed according to patient- and practice-level characteristics.

The quality and accuracy of 'real-world' data captured through electronic medical records might be affected by clinician behaviour, the type of health information system used in each general practice, and algorithms used for data extraction.

Funding: This project was funded by a Therapeutic Guidelines Ltd (TGL) / RACGP Foundation Research Grant (TGL2020-02) awarded to LEG, SBC, MC, and LHA. LEG receives salary support from the Channel 7 Children's Research Foundation (CRF-210323).

Competing interest statement: The authors report no conflicts of interest.

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

INTRODUCTION

Lactational mastitis is a common breastfeeding complication in women, which is characterised by localized breast pain, tenderness, erythema and engorgement, and systemic symptoms such as fever, accompanied by malaise and rigors.^{1,2} Mastitis can significantly disrupt activities of daily living, and is associated with significant maternal morbidity^{1,2} and premature breastfeeding cessation.³ Mastitis prevalence ranges from 3% to 20%⁴ and most commonly occurs within the first four weeks postpartum.⁵ Diagnosis is based on symptoms, which range from mild inflammation to more severe disease which can include bacterial infection and abscess development.^{6,7} Early and appropriate treatment of mastitis is important to prevent adverse sequelae.

Early or mild cases of mastitis are treated symptomatically, with the use of self-management strategies aimed at ensuring effective drainage of breast milk, such as continued regular breastfeeding and/or expressing, gently massaging the affected breast, applying warmth to assist with let-down reflex and cold to reduce swelling.⁶ Analgesics and anti-inflammatories may be useful in the management of pain and/or fevers.⁸ In cases where symptoms do not resolve within 24-48 hours, or are moderate or severe, treatment with antibiotics may be required.⁸ In Australia, the *Therapeutic Guidelines* advise initial empirical treatment with narrow-spectrum di/flucloxacillin,⁹ targeting the most likely pathogens associated with mastitis, including *Staphylococcus aureus*.^{5,10} In the case of penicillin allergy, cefalexin or clindamycin may be used, depending on the severity of the penicillin allergy.⁹ In contrast to antibiotics, there is less guidance regarding the use of clinical investigations as part of mastitis management. Use of breast milk or nipple swab cultures are only recommended for patients with sepsis or who are not responding to first-line treatment.^{6,11} Similarly, diagnostic ultrasound of the breast is recommended when a fluctuant breast mass is present, or where mastitis is not resolving or an abscess is suspected.^{6,11} Less clear is the role of blood tests such as C-reactive protein (CRP) to guide antibiotic treatment.^{12,13}

There are few studies examining clinical management of mastitis, particularly in a primary care or community setting. Most studies have focused on prescribing of oral antibiotics, with prevalence ranging from 38% to 86%.¹⁴⁻¹⁹ In contrast, there has been limited exploration of

clinical investigations such as ultrasound or breast milk or swab cultures. Foxman et al appears to be the only study assessing the prevalence of culture analysis, with no participants reporting having this performed.¹⁴

Given the lack of research internationally on the clinical management of lactational mastitis in general practice settings, this study aimed to investigate longitudinal trends in the clinical management of lactational mastitis among women attending Australian general practice between 2011 and 2022.

METHODS

Ethics

The independent MedicineInsight Data Governance Committee approved the study (protocol 2019-003) and the Human Research Ethics Committee of the University of Adelaide exempted it from ethical review due to the use of non-identifiable data.

Study design, setting and data source

This was an open cohort study using data from the NPS MedicineWise MedicineInsight dataset. The study period spanned 1 January 2011 to 31 July 2022. MedicineInsight is a large-scale, national general practice dataset established by NPS MedicineWise with core funding from the Australian Government Department of Health. The MedicineInsight dataset has been described in detail elsewhere.²⁰ In summary, MedicineInsight uses third-party extraction tools (GRHANITE™ and Precedence Health Care's cdmNet™) which extract, de-identify and securely transmit patient data from participating practices' clinical information systems (CISs), such as Best Practice and Medical Director, to a secure data repository. The extraction tool collects incremental data regularly, allowing the development of a longitudinal database in which individuals within each practice can be tracked over time. The MedicineInsight dataset collects data on individual demographic characteristics, practice encounters (not including progress notes), diagnoses, prescribed medication, pathology tests and referrals. Insights are enriched through selected free text data. MedicineInsight contains electronic health records (EHRs) from

approximately 2,700 General Practitioners (GP) and 662 general practices across Australia (8.2% of all Australian practices).²⁰ The characteristics of MedicineInsight patients have been previously demonstrated to be nationally representative of the Australian population.²⁰

Study population

We restricted our analysis to females of reproductive age (18-44 years inclusive) with one or more documented clinical encounters related to mastitis and documentation relating to a pregnancy within the previous 12-months of the encounter. Mastitis encounters were identified by searching the 'Encounter reason' free text field for the term 'mastitis'. We also searched the 'Diagnosis reason', 'Test reason' and 'Prescription reason' free text field for the term 'mastitis' to identify encounters related to mastitis. We excluded the free text term 'granulomatous mastitis' as this was considered unlikely to be related to lactational mastitis. Clinical encounters for mastitis occurring within 14 days of a previous mastitis encounter were defined as belonging to the same treatment episode. Only the first episode per individual was included in the analysis. Documented pregnancies were identified using the separate 'pregnancy' dataset which included data on date of last menstrual period and estimated date of confinement. We also searched the 'Encounter reason' free text field using terms related to pregnancy (i.e. 'Antenatal', 'Pregnancy', 'Hyperemesis gravidarum', 'Morning sickness'), postpartum ('postnatal', 'postpartum', 'baby check', '6-week check'), or breast feeding (i.e. 'breast feeding', 'breastfeeding', 'lactation') to identify women with a recent pregnancy. This was undertaken to increase the likelihood of the clinical encounter being related to lactational mastitis.

Outcome

The primary outcome assessed was the proportion of women prescribed oral antibiotics on the same data as a mastitis encounter. Prescribed antibiotics were identified from the corresponding 'Prescriptions' dataset. Secondary outcomes included the proportion of women ordered clinical investigations for mastitis including breast ultrasound, breast milk culture, nipple swab culture, blood test (i.e. CRP, Erythrocyte sedimentation rate [ESR], full blood examination [FBE]), and breast aspirate. These were identified by searching the 'Requested tests' free text field for the previously listed terms. Additional secondary outcomes included the proportion of women

prescribed other medications, including topical or intravenous antibiotics, antifungals, lactation suppressants (i.e. cabergoline, bromocriptine), or lactation stimulants (i.e. domperidone).

Patient and public involvement

There was no direct patient or public involvement in this research. The research used an established de-identified general practice dataset.

Covariates

Patient characteristics included age (based on year of birth), remoteness, socio-economic indexes for areas (SEIFA), state/territory, Indigenous status, Commonwealth concession card status and smoking status. Females for whom Indigenous status was recorded as unknown or missing were re-categorised as non-Indigenous, as done in other studies.²¹ Remoteness, socio-economic indexes for areas (SEIFA) and state/territory were based on patients' residential postcodes. Remoteness was determined in accordance with the Australian Bureau of Statistics' (ABS) Australian Statistical Geography Standard (ASGS) Remoteness Areas, with 1 being a 'Major City' and 5 a 'Very Remote' area. Due to small population sizes, data for 'Remote' and 'Very Remote' were combined. SEIFA was determined according to the ABS Index of Relative Socio-Economic Advantage and Disadvantage (IRSAD) codes. We also extracted data from the clinical observations dataset to determine which individuals had a temperature recorded on the same day as the clinical encounter and whether the patient was considered febrile or not (temperature >38.5 degrees Celsius).

Statistical analysis

Descriptive statistics (counts and percentages) were used to describe the study population.

The proportion of women who were prescribed medications or ordered selected clinical investigations was calculated based on the year of first clinical encounter for mastitis and expressed as a percentage, with corresponding 95% confidence intervals. Proportions were

calculated separately based on management occurring on the same day as the first documented clinical encounter for mastitis, or on the same day as any clinical encounter for mastitis within the same episode. The proportion of women prescribed antibiotics or who received selected clinical investigations were stratified by calendar year to examine longitudinal trends.

We examined practice-level variation in the proportion of women receiving selected management for mastitis by stratifying proportions based on individual general practices, restricting the comparison to general practices that included data on ≥ 10 patients with mastitis.

We used univariable logistic regression analyses to compare the likelihood of women being prescribed oral antibiotics or receiving various clinical investigations related to mastitis based on individual characteristics. These analyses were undertaken separately according to clinical management at the first encounter, or any clinical encounter within the same mastitis episode.

All analyses were based on two-sided P-values, which statistical define by $p<0.05$. The statistical analysis was performed using STATA MP 17 (Stata, College Station, Texas), with graphs prepared using R, version 4.3.0 (R Core Team).

RESULTS

A total of 25,002 females aged 18 to 44 years had one or more clinical encounters related to mastitis recorded in this general practice dataset between January 2011 and July 2022, as well as documented evidence of a recent pregnancy.

A greater proportion of women were aged 30-34 (39.3%), were never smokers (54.6%), lived in a major city (65.6%), and had a very high socioeconomic status (27.5%). A small proportion of women held a Commonwealth Concession card (15.6%) or were Aboriginal and/or Torres Strait Islander (2.2%) (**Table 1**). Approximately one quarter (27.8%) of women had a documented temperature at their first encounter, with 1.6% of the entire cohort being febrile.

Most (90.1%; $n = 22,523$) women received a prescription for oral antibiotics at their first encounter. With respect to clinical investigations, 5.6% were ordered a breast ultrasound, 3.3% a blood test, 0.9% a nipple swab culture, and 0.8% breast milk culture (**Table 2**). Only very small numbers were prescribed oral (1.1%) or topical (1.2%) antifungals, topical antibiotics (0.5%),

lactation suppressants (1.1%) or lactation stimulants (1.0%). Di/flucloxacillin and cefalexin accounted for >90% of oral antibiotic prescriptions. Only 3,006 (12.0%) women had two or more clinical encounters related to the same mastitis episode. When including clinical management across all clinical encounters, the proportion prescribed oral antibiotics increased only marginally to 90.9%. When considering investigations ordered at any clinical encounter, the largest increase was observed for breast ultrasound, which increased from 5.6% to 7.1% (**Table 2**). Approximately 1 in 10 (12.1%) women prescribed cefalexin had a documented penicillin allergy, whereas 64.4% of women prescribed clindamycin had a documented penicillin allergy.

When stratified by calendar year, the proportion of women prescribed oral antibiotics remained consistent across 2011 to 2022 ($p=0.559$). In contrast, significant increases from 2011 to 2022 were evident with respect to increases in proportions receiving breast ultrasound (3.4% to 8.5%), blood test (2.6% to 5.2%), breast milk culture (0.8% to 1.4%), swab culture (0.5% to 1.7%), and breast aspirate (<0.1% to 0.4%) (**Figure 1, Supplemental Table 1**). The proportion of women prescribed di/flucloxacillin increased from 46.1% in 2011 to 60.4% in 2022, whereas the proportion prescribed cefalexin decreased from 38.6% to 26.5% (**Supplemental Table 2**). From 2011 to 2022, the median treatment duration based on the initial prescription was 6 days, however there was a significant reduction in the proportion issued repeats from 31.5% to 3.0%.

Significant variability was evident with respect to overall clinical management of mastitis according to individual general practices, with the proportion of patients prescribed oral antibiotics ranging from 56.9% to 100% (**Figure 2**). Likewise, variation was seen with breast ultrasound (range: 0% to 40.6%), breast milk culture (0% to 14.7%), swab culture (0% to 9.2%), breast aspirate (0% to 3.8%) and blood test (0% to 31.2%).

Women prescribed oral antibiotics at the first encounter were less likely to receive a breast ultrasound, blood test, and breast aspirate. Similarly, they were less likely to be co-prescribed topical antibiotics, and oral/topical antifungals (**Supplemental Table 3**).

The only consistent factor associated with an increased likelihood of being prescribed oral antibiotics at the first or any encounter was the general practice being located in a regional or

remote area, but the absolute differences were small (~1.0%) (**Table 3**). In comparison, factors associated with increased likelihood of breast ultrasound included older age (>30 years), being a current smoker, living in a major city, and higher socioeconomic status (**Supplemental Table 4**). The likelihood of receiving a blood test was increased for those in the youngest (18-24 years) and oldest (40-44 years) age groups, with a concession card (**Supplemental Table 5**). Factors associated with an increased likelihood of a breast milk culture included having a concession card, being a previous or current smoker, and the general practice being located in a regional or remote area (**Supplemental Table 6**). In contrast, the only factor associated with an increased likelihood of receiving a nipple swab culture was the general practice being located in a regional or remote area (**Supplemental Table 7**). In addition, however, the likelihood of receiving a breast milk culture was lower for those with a concession card or who were previous or current smokers. Only lower socioeconomic status was associated with a lower likelihood of breast aspirate (**Supplemental Table 8**), although none were ordered for individuals who identified as Aboriginal and/or Torres Strait Islanders or who were identified as being febrile at the time of the first encounter.

DISCUSSION

Principal findings

Evidence from this large national database indicate that most women presenting to Australian general practice for lactational mastitis are prescribed oral antibiotics, with prescribing practices appearing to largely be in adherence to Australian clinical guidelines. While there has been no change in overall oral antibiotic prescribing rates over the past decade, we observed an increase in narrow spectrum antibiotics (i.e. di/flucloxacillin) indicating closer adherence to local guidelines and improved antibiotic stewardship. In addition, there were significant increases in the use of selected clinical investigations as part of mastitis management, including breast ultrasound and milk and nipple swab cultures. This suggests increased awareness of the use of clinical investigations in supporting optimal clinical management of lactational mastitis. The observed variation in clinical management of lactational mastitis according to patient- and practice-level characteristics warrants further investigation to determine whether there may be further opportunities to improve standardization of clinical care.

Strengths and weaknesses

Study strengths include use of a large high-quality general practice database containing longitudinal individual-level data from 2011 to 2022 that is considered nationally representative. Multiple strategies were used to improve data quality, including restricting the cohort to those with a likely recent pregnancy and the use of different fields for data extraction. Nonetheless, our study has some important limitations. The quality and accuracy of 'real-world' data captured through electronic medical records might be affected by clinician behaviour and the type of health information system used in each general practice. For example, differences in recording may exist based on non-mandatory fields, free-text entries and use of system coding vocabularies. It is possible that this may result in possible misclassification and under-reporting of lactational mastitis encounters or associated clinical management. We made the assumption that prescriptions or clinical investigations ordered on the same day as a clinical encounter for mastitis were related to that encounter reason, where they may have been provided for alternative indications. In addition, GPs commonly provide a prescription for antibiotics (or other medications) with directions only to get it dispensed if symptoms don't improve in the subsequent days ('delayed prescribing').²² The database doesn't contain information on referrals made to other health care providers or hospitals. In the case of severe mastitis, some clinicians may have opted to direct the patient to a hospital emergency department, rather than provide treatment. While data are recorded at the individual patient level, patient data are not linked across different general practices. Therefore, it is possible that individuals presenting to different general practices with the same symptoms were counted twice. Lastly, MedicineInsight uses a non-random sampling process to recruit the practices, however, the distribution of the sample has previously been shown to closely resemble figures from the last Australian census.²⁰

Comparison to other studies

To our knowledge, this is the first evaluation of clinical management of lactational mastitis in a primary care setting. Most previous studies are limited to small numbers of women with mastitis (often less than 100) and lack contemporary data. In a prospective cohort study, Foxman et al followed 946 women recruited between 1994-1998, of which 77 women developed mastitis.¹⁴ Of these women, 86% were prescribed antibiotics, with the most common being cefalexin (46%),

followed by amoxicillin (7%), ampicillin (7%), and amoxicillin and clavulanic acid (7%). No cultures were performed for any women and no data were reported for ultrasound or blood tests. A more recent study from Scott et al followed 420 breastfeeding women recruited between 2004 and 2005 in Scotland, with 74 developing mastitis.¹⁹ Among those women with mastitis, 78% were prescribed antibiotics, with the most common being flucloxacillin (30%), followed by amoxicillin (17%), erythromycin (7%), and amoxicillin and clavulanic acid (7%). Notably, 33% couldn't remember what antibiotic they were prescribed. The largest study evaluated data from almost 80,000 women recruited to the Norwegian Mother, Father and Child Cohort Study between 1999 to 2008.³ Among the 15,014 who reported experiencing mastitis, 5,524 (36.8%) reported using antibiotics. Of those who could remember which antibiotic they received, the most common antibiotics included penicillins (83.8%), followed by macrolides (15.2%) and cephalosporins (2.6%).

Implications

While the observed rates of antibiotic prescribing are very high, it is not possible to determine the appropriateness of prescribing practices based on available data. It is possible that women presenting to general practice with mastitis symptoms may represent those with more severe disease, corresponding to high rates of treatment. Further, it is likely that not all prescriptions for antibiotics were dispensed, and even when dispensed, not all antibiotics were commenced.²³ Also, it is possible that GPs are issuing prescriptions (or repeats) to women to be dispensed only if symptoms do not improve, representing delayed prescribing. However, the role of delayed prescribing in the context of antimicrobial stewardship for mastitis has not been evaluated and requires further investigation. Further, there was much larger observed variation in antibiotic prescribing practices at the practice-level compared with patient-level characteristics and this warrants further exploration as to underlying causes.

Increasing rates of ordering of clinical investigations over the decade suggests increased awareness of the potential value of such investigations in the diagnosis and/or management of mastitis. The observed higher frequency of ultrasound in older women and current smokers suggest ultrasounds may be being used to rule out differential diagnoses.^{24,25} However, lower rates of ultrasound in those of lower socioeconomic status raises questions about potential equity issues and whether access or affordability negatively impacts uptake. A similar picture emerged

for other investigations such as breast aspirate, breast milk culture, and nipple swab culture which were lower in those with lower socioeconomic status or a concession card. The lower rate of ultrasounds in those visiting a general practice located in remote or regional areas may be reflective of access difficulties, however, this is contrasted with higher rates of milk and swab cultures in these areas. Higher culture rates in rural settings may reflect observed higher rates of antimicrobial resistance, including Methicillin resistant *S. aureus* (MRSA) in these settings.²⁶ Similar to antibiotic prescribing practices, the large variation in frequency of clinical investigations warrants further examination, particularly appropriateness of these investigations and their impact on mastitis management.

Lactational mastitis has frequently been considered to be a topic that has not received the attention it deserves.²⁷ Research is needed to determine when antibiotics are needed for mastitis; which are the most appropriate antibiotic and what is the most appropriate duration. Clinical guidelines for management of mastitis have changed little over the last couple of decades, and GPs are assumed to be familiar with managing this common problem. It is timely to recommend an education program to alert clinicians that prescribing antibiotics for mastitis is not always straightforward: it should not be assumed that all lactating women with inflammatory breast symptoms require antibiotic treatment, and the potential need for breast milk culture should be considered. Breast milk culture may be appropriate at first presentation in locations with high rates of MRSA or in mothers with known antibiotic allergies, and should be ordered if the condition is not responding to first line antibiotics within 48 hours.

CONCLUSION

Australian GPs commonly prescribe oral antibiotics for women with mastitis and largely in line with clinical guidelines. Over the last decade, GPs have increased prescriptions for narrow spectrum antibiotics indicating closer adherence to local guidelines and improved antibiotic stewardship. Their use of clinical investigations as part of mastitis management has increased over the last decade but there may be the opportunity for increased use of breast milk culture to understand and manage local bacterial sensitivities.

Author contributions

All authors made significant contributions to the manuscript and are responsible for its content. LEG, SBC, MC and LHA conceived the idea, obtained grant funding and planned this study. LEG and AK were responsible for data extraction and analysis. LEG, SBC, MC and LHA were responsible for interpretation of study findings, while LEG and AK were responsible for presenting the results. LEG wrote the first draft and all authors contributed to the manuscript refinement. All authors have read and approved the final manuscript.

Data Sharing Statement

Data may be obtained from MedicineInsight and are not publicly available. Third parties may express an interest in the information collected through MedicineInsight. The provision of information in these instances undergoes a formal approval process and is guided by the MedicineInsight independent external Data Governance Committee. This Committee includes general practitioners, consumer advocates, privacy experts and researchers.

Ethics statements

Patient consent for publication

Not required.

Ethics approval

The independent MedicineInsight Data Governance Committee approved the study (protocol 2019-003) and the Human Research Ethics Committee of the University of Adelaide exempted it from ethical review due to the use of non-identifiable data.

Acknowledgments

The authors would like to thank NPS MedicineWise for their support in the development of this research.

Figure legends:

Figure 1. Longitudinal trends in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations, Australia 2011 to 2022

Figure 2. Variation in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations according to each individual general practice, Australia 2011 to 2022

References

1. Cooney F, Petty-Saphon N. The burden of severe lactational mastitis in Ireland from 2006 to 2015. *Ir Med J* 2019; **112**(1): 855.
2. De Groot N, Birnie E, Vermolen JH, Dorscheidt JJ, Bonsel GJ. The prevalence of adverse postnatal outcomes for mother and infant in the Netherlands. *PloS One* 2018; **13**(9): e0202960.
3. Grzeskowiak LE, Saha MR, Ingman WV, Nordeng H, Ystrom E, Amir LH. Incidence, antibiotic treatment and outcomes of lactational mastitis: findings from the Norwegian mother, father and child cohort study (MoBa). *Paediatr Perinat Epidemiol* 2022; **36**(2): 254-63.
4. Wilson E, Woodd SL, Benova L. Incidence of and risk factors for lactational mastitis: a systematic review. *J Hum Lact* 2020; **36**(4): 673-86.
5. Cullinane M, Amir LH, Donath SM, et al. Determinants of mastitis in women in the CASTLE study: a cohort study. *BMC Fam Pract* 2015; **16**: 181.
6. Scott DM. Inflammatory diseases of the breast. *Best Pract Res Clin Obstet Gynaecol* 2022; **83**: 72-87.
7. Bhatt AA, Woodard GA, Lee CU, Hesley GK. Urgent and emergent breast lesions—a primer for the general radiologist, on-call resident and sonographer. *Australas J Ultrasound Med* 2022; **25**(2): 54-65.
8. Mitchell KB, Johnson HM, Rodriguez JM, et al. Academy of Breastfeeding Medicine Clinical Protocol# 36: the mastitis spectrum, revised 2022. *Breastfeed Med* 2022; **17**(5): 360-76.
9. Therapeutic Guidelines: Antibiotic: eTG complete. In: Lactational mastitis. 2020.
10. Rimoldi SG, Pileri P, Mazzocco MI, et al. The role of Staphylococcus aureus in mastitis: A multidisciplinary working group experience. *J Hum Lact* 2020; **36**(3): 503-9.
11. Wheaton N, Al-Abdullah A, Haertlein T. Postdelivery emergencies. *Emerg Med Clin North Am* 2019; **37**(2): 287-300.
12. Fetherston CM, Wells JI, Hartmann PE. Severity of mastitis symptoms as a predictor of C-reactive protein in milk and blood during lactation. *Breastfeed Med* 2006; **1**(3): 127-35.
13. Petel D, Winters N, Gore GC, et al. Use of C-reactive protein to tailor antibiotic use: a systematic review and meta-analysis. *BMJ Open* 2018; **8**(12): e022133.
14. Foxman B, D'Arcy H, Gillespie B, Bobo JK, Schwartz K. Lactation mastitis: occurrence and medical management among 946 breastfeeding women in the United States. *Am J Epidemiol* 2002; **155**(2): 103-14.
15. Fetherston C. Characteristics of lactation mastitis in a Western Australian cohort. *Breastfeed Rev* 1997; **5**(2): 5-11.
16. Kinlay JR, O'Connell DL, Kinlay S. Incidence of mastitis in breastfeeding women during the six months after delivery: a prospective cohort study. *Med J Aust* 1998; **169**(6): 310-2.
17. Jonsson S, Pulkkinen M. Mastitis today: incidence, prevention and treatment. *Ann Chir Gynaecol Suppl* 1994; (83): 84-7.
18. Lin C-H, Yang P-R, Lee C-P, Huang W-Y, Shih W-T, Yang Y-H. Descriptive study of mastitis in postpartum women in Taiwan: incidence and related factors. *J Womens Health (Larchmt)* 2023; **32**(5): 616-22.
19. Scott JA, Robertson M, Fitzpatrick J, Knight C, Mulholland S. Occurrence of lactational mastitis and medical management: a prospective cohort study in Glasgow. *Int Breastfeed J* 2008; **3**: 21.

20. Busingye D, Gianacas C, Pollack A, et al. Data Resource Profile: MedicineInsight, an Australian national primary health care database. *Int J Epidemiol* 2019; **48**(6): 1741-h.
21. Gilbert E, Rumbold A, Campbell S, Boyle J, Grzeskowiak L. Management of encounters related to subfertility and infertility among Aboriginal and Torres Strait Islander females in Australian general practice. *BMC Women's Health* 2023; **23**: 410.
22. Thursky KA, Hardefeldt LY, Rajkhowa A, et al. Antimicrobial stewardship in Australia: The role of qualitative research in programme development. *JAC Antimicrob Resist* 2021; **3**(4): dlab166.
23. Ito S, Koren G, Einarson TR. Maternal noncompliance with antibiotics during breastfeeding. *Ann Pharmacother* 1993; **27**(1): 40-2.
24. Moore DA, Bracewell SL, Smith EB, Jordan SG. A new search pattern for emergency breast exams: the clinical picture. *Emerg Radiol* 2021; **29**: 207-13.
25. Porembka JH, Compton L, Omar L, et al. Breast ultrasound utilization in a safety net emergency department. *Emerg Radiol* 2019; **26**: 123-31.
26. Cameron JK, Hall L, Tong SY, Paterson DL, Halton K. Incidence of community onset MRSA in Australia: least reported where it is Most prevalent. *Antimicrob Resist Infect Control* 2019; **8**: 33.
27. Amir LH, Ingram J. Health professionals' advice for breastfeeding problems: Not good enough! *Int Breastfeed J* 2008; **3**: 22.

Table 1. Characteristics of 25,002 women presenting to Australian General Practice between 2011 and 2022 for Lactational Mastitis

	N (%)
Year	
2011-2012	3448 (13.8%)
2013-2014	4135 (16.5%)
2015-2016	4633 (18.5%)
2017-2018	4657 (18.6%)
2019-2020	4723 (18.9%)
2021-2022	3406 (13.6%)
Age group	
18-24	1991 (8.0%)
25-29	5830 (23.3%)
30-34	9821 (39.3%)
35-39	5900 (23.6%)
40-44	1460 (5.8%)
Concession status	
No Concession	21111 (84.4%)
Concession Card	3891 (15.6%)
Smoking status	
Never Smoker	13653 (54.6%)
Ex Smoker	8675 (34.7%)
Current Smoker	808 (3.2%)
Missing	1866 (7.5%)
Patient SES	
Very Low	3139 (12.6%)
Low	4215 (16.9%)
Middle	5143 (20.6%)
High	5533 (22.1%)
Very High	6872 (27.5%)
Missing	100 (0.4%)
Indigenous status	
Aboriginal and/or TSI	547 (2.2%)
Neither Aboriginal or TSI	24455 (97.8%)
Fever	
No	6551 (26.2%)
Yes	401 (1.6%)
Not recorded	18050 (72.2%)
Remoteness of general practice	
Major city	16397 (65.6%)
Inner regional	8162 (32.6%)
Remote & very remote	339 (1.4%)
Missing	104 (0.4%)

SES, socioeconomic status; TSI, Torres Strait Islander

Table 2. Selected clinical investigations and medications prescribed during the first or any encounter within the same episode of treatment for lactational mastitis in women attending general practice, Australia 2011 to 2022

	First encounter	Any encounter*
Clinical investigations		
Breast ultrasound	1 393 (5.6%)	1 771 (7.1%)
Milk culture	195 (0.8%)	235 (0.9%)
Nipple swab culture	237 (0.9%)	283 (1.1%)
Breast aspirate	37 (0.1%)	64 (0.3%)
Blood test	835 (3.3%)	962 (3.8%)
FBE	823 (3.3%)	947 (3.8%)
CRP	278 (1.1%)	350 (1.4%)
ESR	179 (0.7%)	212 (0.8%)
Medication prescriptions		
Antibiotics		
Oral	22 523 (90.1%)	22 739 (90.9%)
Di/flucloxacillin	12 477 (49.9%)	12 794 (51.2%)
Cefalexin	8 223 (32.9%)	8 501 (34.0%)
Amoxicillin	754 (3.0%)	772 (3.1%)
Amoxicillin clavulanate	594 (2.4%)	664 (2.7%)
Clindamycin	315 (1.3%)	354 (1.4%)
Erythromycin	289 (1.2%)	308 (1.2%)
Other	174 (0.7%)	215 (0.9%)
Intravenous	20 (0.1%)	32 (0.1%)
Topical	125 (0.5%)	149 (0.6%)
Antifungals		
Oral	275 (1.1%)	326 (1.3%)
Topical	303 (1.2%)	349 (1.4%)
Other medications		
Lactation suppressants	270 (1.1%)	310 (1.2%)
Lactation stimulants	256 (1.0%)	295 (1.2%)

*at any encounter for mastitis, including additional encounter occurring within two-week period of a previous mastitis encounter

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FBE: Full blood examination;

Table 3. Proportion of women attending general practice who were prescribed oral antibiotics during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	88.6 (87.2, 90.0)	0.89 (0.75, 1.04)	89.4 (88.0, 90.7)	0.88 (0.74, 1.03)
25-29	89.8 (89.0, 90.6)	Reference	90.6 (89.8, 91.3)	Reference
30-34	90.3 (89.7, 90.8)	1.05 (0.94, 1.17)	91.2 (90.7, 91.8)	1.08 (0.96, 1.21)
35-39	90.4 (89.6, 91.1)	1.07 (0.95, 1.21)	91.3 (90.5, 92.0)	1.08 (0.95, 1.23)
40-44	90.6 (89.0, 92.1)	1.10 (0.90, 1.33)	91.3 (89.7, 92.7)	1.09 (0.89, 1.33)
Concession status				
No concession	90.3 (89.8, 90.7)	Reference	91.2 (90.8, 91.5)	Reference
Concession holder	89.2 (88.1, 90.1)	0.89 (0.79, 0.99)	89.8 (88.8, 90.7)	0.85 (0.76, 0.95)
Smoking status				
Current smoker	90.7 (88.5, 92.6)	1.12 (0.88, 1.43)	91.1 (88.9, 93.0)	1.05 (0.82, 1.35)
Ex-smoker	91.4 (90.8, 92.0)	1.22 (1.11, 1.34)	92.1 (91.5, 92.7)	1.20 (1.09, 1.32)
Never smoker	89.7 (89.2, 90.2)	Reference	90.7 (90.2, 91.1)	Reference
Patient SES				
Very low	90.5 (89.4, 91.5)	1.04 (0.90, 1.20)	91.0 (89.9, 91.9)	0.99 (0.85, 1.15)
Low	89.4 (88.5, 90.3)	0.93 (0.82, 1.05)	90.5 (89.6, 91.4)	0.93 (0.82, 1.07)
Middle	90.3 (89.4, 91.1)	1.02 (0.90, 1.15)	91.2 (90.3, 91.9)	1.01 (0.89, 1.15)
High	90.3 (89.5, 91.0)	1.02 (0.90, 1.14)	91.2 (90.4, 91.9)	1.01 (0.90, 1.15)
Very high	90.1 (89.4, 90.8)	Reference	91.1 (90.4, 91.7)	Reference
Indigenous status				
Aboriginal and/or TSI	89.0 (86.1, 91.5)	0.89 (0.68, 1.17)	89.6 (86.7, 92.0)	0.85 (0.65, 1.13)
Neither Aboriginal or TSI	90.1 (89.7, 90.5)	Reference	91.0 (90.6, 91.3)	Reference
Fever				
No	94.1 (93.5, 94.6)	Reference	94.6 (94.1, 95.2)	Reference
Yes	92.8 (89.8, 95.1)	0.81 (0.55, 1.19)	94.3 (91.5, 96.3)	0.93 (0.60, 1.44)
Not Documented	88.6 (88.1, 89.0)	0.49 (0.44, 0.55)	89.5 (89.1, 90.0)	0.49 (0.43, 0.55)
Remoteness of general practice				
Major city	89.7 (89.2, 90.2)	Reference	90.6 (90.2, 91.1)	Reference
Inner/Outer regional	90.8 (90.0, 91.5)	1.13 (1.02, 1.26)	91.6 (90.8, 92.3)	1.12 (1.00, 1.25)
Remote/Very remote	91.2 (90.1, 92.1)	1.19 (1.04, 1.36)	91.7 (90.7, 92.7)	1.15 (1.00, 1.32)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

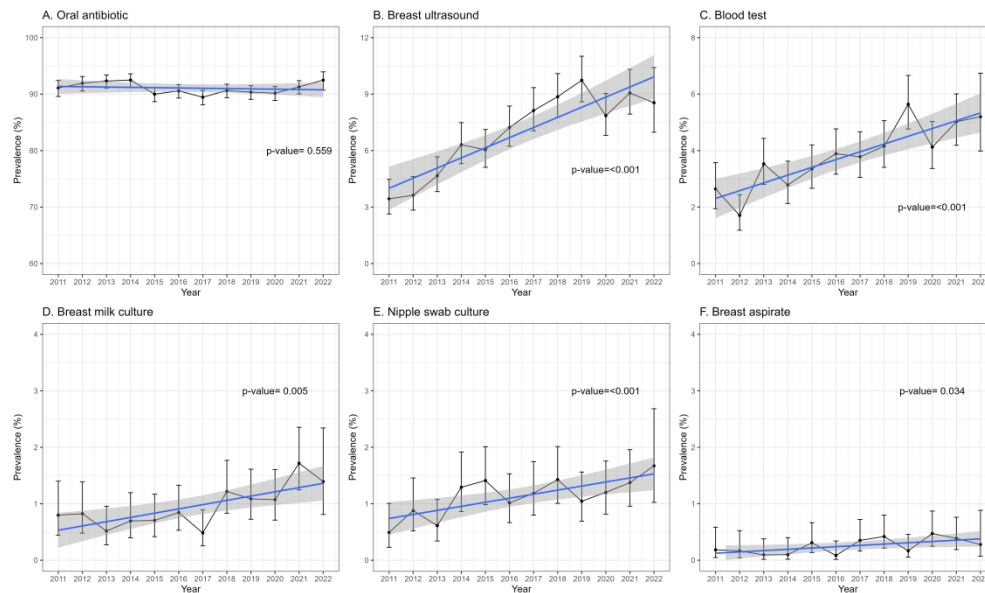


Figure 1. Longitudinal trends in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations, Australia 2011 to 2022

1291x774mm (118 x 118 DPI)

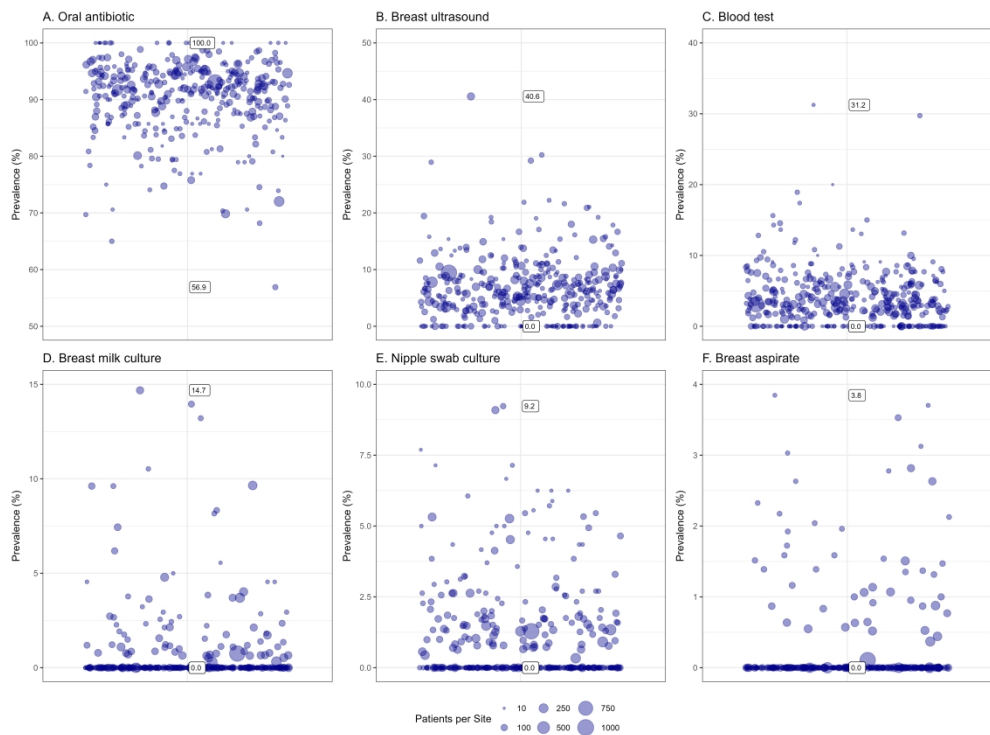


Figure 2. Variation in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations according to each individual general practice, Australia 2011 to 2022

1035x776mm (157 x 157 DPI)

Supplemental Table 1. Clinical management of in women attending general practice during the first or any encounter within the same treatment episode for lactational mastitis according to calendar year, Australia 2011 to 2022

		2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022†	Total
N		1 628	1 820	2 123	2 012	2 268	2 365	2 276	2 381	2 393	2 330	1 329	1 077	25 002
Oral antibiotic	First	1 465 (90.0%)	1 652 (90.8%)	1 942 (91.5%)	1 850 (92.0%)	2 028 (89.4%)	2 130 (90.1%)	2 011 (88.4%)	2 133 (89.6%)	2 143 (89.6%)	2 079 (89.2%)	1 103 (80.3%)	987 (91.6%)	22 523 (90.1%)
	Any	1 483 (91.1%)	1 673 (91.9%)	1 960 (92.3%)	1 861 (92.5%)	2 041 (90.0%)	2 142 (90.6%)	2 036 (89.5%)	2 158 (90.6%)	2 162 (90.3%)	2 101 (90.2%)	1 126 (81.3%)	996 (92.5%)	22 739 (90.9%)
Breast ultrasound	First	45 (2.8%)	45 (2.5%)	76 (3.6%)	107 (5.3%)	103 (4.5%)	139 (5.9%)	147 (6.5%)	159 (6.7%)	196 (8.2%)	132 (5.7%)	169 (12.3%)	75 (7.0%)	1393 (5.6%)
	Any	56 (3.4%)	66 (3.6%)	99 (4.7%)	127 (6.3%)	137 (6.0%)	171 (7.2%)	185 (8.1%)	211 (8.9%)	233 (9.7%)	183 (7.9%)	111 (8.1%)	92 (8.5%)	1771 (7.1%)
Breast milk culture	First	11 (0.7%)	11 (0.6%)	10 (0.5%)	8 (0.4%)	13 (0.6%)	18 (0.8%)	10 (0.4%)	26 (1.1%)	25 (1.0%)	21 (0.9%)	31 (2.3%)	11 (1.0%)	195 (0.8%)
	Any	13 (0.8%)	15 (0.8%)	11 (0.5%)	14 (0.7%)	16 (0.7%)	20 (0.8%)	11 (0.5%)	29 (1.2%)	26 (1.1%)	25 (1.1%)	40 (2.7%)	15 (1.4%)	235 (0.9%)
Nipple swab culture	First	8 (0.5%)	13 (0.7%)	13 (0.6%)	24 (1.2%)	26 (1.1%)	17 (0.7%)	23 (1.0%)	30 (1.3%)	18 (0.8%)	22 (0.9%)	26 (1.9%)	17 (1.6%)	237 (0.9%)
	Any	8 (0.5%)	16 (0.9%)	13 (0.6%)	26 (1.3%)	32 (1.4%)	24 (1.0%)	27 (1.2%)	34 (1.4%)	25 (1.0%)	28 (1.2%)	32 (2.4%)	18 (1.7%)	283 (1.1%)
Blood test‡	First	41 (2.5%)	27 (1.5%)	64 (3.0%)	49 (2.4%)	62 (2.7%)	84 (3.6%)	69 (3.0%)	88 (3.7%)	117 (4.9%)	82 (3.5%)	104 (7.5%)	48 (4.5%)	835 (3.3%)
	Any	43 (2.6%)	31 (1.7%)	75 (3.5%)	56 (2.8%)	76 (3.4%)	92 (3.9%)	86 (3.8%)	99 (4.2%)	135 (5.6%)	96 (4.1%)	117 (8.0%)	56 (5.2%)	962 (3.8%)
Breast aspirate	First	NR	NR	NR	NR	NR	NR	5 (0.2%)	9 (0.4%)	NR	6 (0.3%)	5 (0.2%)	NR	37 (0.1%)
	Any	NR	NR	NR	NR	7 (0.3%)	NR	8 (0.4%)	10 (0.4%)	NR	11 (0.5%)	9 (0.4%)	NR	64 (0.3%)

NR, not reportable due to small cell size

† 2022 calendar year includes January to July data only

‡ Includes ordering of full blood count, c-reactive protein, or erythrocyte sedimentation rate

Supplemental Table 2. The proportion of women attending general practice who were prescribed oral antibiotics during the first or any encounter within the same treatment episode for lactational mastitis according to antibiotic type and calendar year, Australia 2011 to 2022

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022†
N	1 628	1 820	2 123	2 012	2 268	2 365	2 276	2 381	2 393	2 330	2 329	1 077
Di/flucloxacillin												
First	719 (44.2%)	816 (44.8%)	981 (46.2%)	922 (45.8%)	1038 (45.8%)	1142 (48.3%)	1098 (48.2%)	1273 (53.5%)	1244 (52.0%)	1263 (54.2%)	1340 (57.5%)	641 (59.5%)
Any*	751 (46.1%)	830 (45.6%)	1010 (47.6%)	945 (47.0%)	1068 (47.1%)	1172 (49.6%)	1130 (49.6%)	1310 (55.0%)	1264 (52.8%)	1292 (55.5%)	1371 (58.9%)	651 (60.4%)
Cefalexin												
First	607 (37.3%)	678 (37.3%)	775 (36.5%)	765 (38.0%)	780 (34.4%)	825 (34.9%)	737 (32.4%)	690 (29.0%)	782 (32.7%)	884 (38.4%)	626 (26.9%)	274 (25.4%)
Any*	629 (38.6%)	704 (38.7%)	800 (37.7%)	780 (38.8%)	804 (35.4%)	850 (35.9%)	765 (33.6%)	714 (30.0%)	805 (33.6%)	913 (39.6%)	652 (28.0%)	285 (26.5%)
Amoxicillin												
First	65 (4.0%)	93 (5.1%)	84 (4.0%)	57 (2.8%)	95 (4.2%)	75 (3.2%)	72 (3.2%)	59 (2.5%)	40 (1.7%)	38 (1.6%)	53 (2.3%)	23 (2.1%)
Any*	68 (4.2%)	94 (5.2%)	86 (4.1%)	59 (2.9%)	96 (4.2%)	77 (3.3%)	74 (3.3%)	62 (2.6%)	40 (1.7%)	38 (1.6%)	55 (2.4%)	23 (2.1%)
Amoxicillin and clavulanate												
First	28 (1.7%)	27 (1.5%)	63 (3.0%)	48 (2.4%)	48 (2.1%)	54 (2.3%)	64 (2.8%)	72 (3.0%)	71 (3.0%)	43 (1.8%)	48 (2.1%)	28 (2.6%)
Any*	29 (1.8%)	32 (1.8%)	69 (3.3%)	54 (2.7%)	59 (2.6%)	63 (2.7%)	71 (3.1%)	81 (3.4%)	74 (3.1%)	48 (2.1%)	53 (2.3%)	31 (2.9%)
Erythromycin												
First	22 (1.4%)	27 (1.5%)	34 (1.6%)	43 (2.1%)	34 (1.5%)	34 (1.4%)	23 (1.0%)	22 (0.9%)	21 (0.9%)	17 (0.7%)	5 (0.2%)	7 (0.6%)
Any*	23 (1.4%)	30 (1.6%)	39 (1.8%)	44 (2.2%)	35 (1.5%)	35 (1.5%)	26 (1.1%)	24 (1.0%)	23 (1.0%)	17 (0.7%)	5 (0.2%)	7 (0.6%)
Clindamycin												
First	21 (1.3%)	20 (1.1%)	20 (0.9%)	22 (1.1%)	34 (1.5%)	23 (1.0%)	28 (1.2%)	28 (1.2%)	26 (1.1%)	13 (0.8%)	32 (1.4%)	18 (1.7%)
Any*	22 (1.4%)	22 (1.2%)	23 (1.1%)	23 (1.1%)	39 (1.7%)	28 (1.2%)	32 (1.4%)	30 (1.3%)	28 (1.2%)	49 (2.1%)	38 (1.6%)	20 (1.9%)
Other												
First	20 (1.2%)	17 (0.9%)	19 (0.9%)	20 (1.0%)	19 (0.8%)	11 (0.5%)	15 (0.7%)	8 (0.3%)	14 (0.6%)	11 (0.5%)	13 (0.6%)	7 (0.6%)
Any*	22 (1.4%)	25 (1.4%)	25 (1.2%)	23 (1.1%)	22 (1.0%)	14 (0.6%)	16 (0.7%)	12 (0.5%)	19 (0.8%)	15 (0.6%)	15 (0.6%)	7 (0.6%)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

† 2022 calendar year includes January to July data only

For peer review only

Supplemental Table 3. The proportion of women attending general practice for lactational mastitis who received selected clinical investigations or prescribed medications according to whether or not they were prescribed oral antibiotics during the same encounter, Australia 2011 to 2022

	Antibiotics prescribed at first encounter		p-value
	No (N = 2 479)	Yes (N = 22 523)	
Clinical Investigations			
Breast ultrasound	174 (7.0%)	1 219 (5.4%)	<0.001
Breast milk culture	26 (1.0%)	169 (0.8%)	0.109
Nipple swab culture	28 (1.1%)	209 (0.9%)	0.326
Blood Test	109 (4.4%)	726 (3.2%)	0.002
Breast Aspirate	8 (0.3%)	29 (0.1%)	0.017
Medication Prescriptions			
Antibiotics			
Topical	25 (1.0%)	100 (0.4%)	<0.001
Intravenous	8 (0.3%)	12 (0.1%)	<0.001
Antifungals			
Oral	97 (3.9%)	178 (0.8%)	<0.001
Topical	53 (2.1%)	250 (1.1%)	<0.001
Other Medications			
Lactation Suppressant	26 (1.0%)	244 (1.1%)	0.875
Lactation Stimulant	30 (1.2%)	226 (1.0%)	0.332

Supplemental Table 4. Proportion of women attending general practice who received a breast ultrasound during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	4.4 (3.6, 5.4)	0.97 (0.76, 1.25)	5.2 (4.3, 6.3)	0.88 (0.71, 1.11)
25-29	4.5 (4.0, 5.1)	Reference	5.9 (5.3, 6.5)	Reference
30-34	5.6 (5.2, 6.1)	1.25 (1.08, 1.46)	7.2 (6.7, 7.7)	1.24 (1.08, 1.41)
35-39	6.5 (5.9, 7.1)	1.46 (1.24, 1.71)	8.2 (7.5, 8.9)	1.43 (1.24, 1.65)
40-44	7.4 (6.1, 8.9)	1.68 (1.34, 2.12)	9.5 (8.1, 11.1)	1.69 (1.37, 2.07)
Concession status				
No concession	5.5 (5.2, 5.8)	Reference	7.1 (6.8, 7.5)	Reference
Concession holder	5.8 (5.1, 6.6)	1.05 (0.91, 1.22)	6.8 (6.1, 7.7)	0.96 (0.84, 1.09)
Smoking status				
Current smoker	7.9 (6.2, 10.0)	1.44 (1.11, 1.88)	9.4 (7.5, 11.6)	1.30 (1.02, 1.66)
Ex-smoker	5.2 (4.7, 5.7)	0.91 (0.81, 1.03)	6.3 (5.8, 6.8)	0.84 (0.76, 0.94)
Never smoker	5.6 (5.3, 6.0)	Reference	7.4 (7.0, 7.8)	Reference
Patient SES				
Very low	5.2 (4.5, 6.1)	0.91 (0.75, 1.09)	6.3 (5.5, 7.2)	0.82 (0.69, 0.97)
Low	5.3 (4.6, 6.0)	0.92 (0.78, 1.09)	6.6 (5.9, 7.4)	0.87 (0.74, 1.01)
Middle	5.3 (4.7, 6.0)	0.93 (0.79, 1.08)	6.7 (6.0, 7.4)	0.87 (0.76, 1.01)
High	6.0 (5.4, 6.6)	1.05 (0.90, 1.22)	7.6 (6.9, 8.3)	1.00 (0.88, 1.15)
Very high	5.7 (5.2, 6.3)	Reference	7.6 (7.0, 8.2)	Reference
Indigenous status				
Aboriginal and/or TSI	5.7 (3.9, 7.9)	1.02 (0.71, 1.47)	6.6 (4.7, 9.0)	0.92 (0.66, 1.30)
Neither Aboriginal or TSI	5.6 (5.3, 5.9)	Reference	7.1 (6.8, 7.4)	Reference
Fever				
No	6.5 (5.9, 7.1)	Reference	8.3 (7.6, 9.0)	Reference
Yes	3.0 (1.6, 5.2)	0.45 (0.25, 0.80)	5.5 (3.5, 8.2)	0.64 (0.41, 1.00)
Not Documented	5.3 (5.0, 5.6)	0.81 (0.72, 0.91)	6.7 (6.3, 7.1)	0.79 (0.71, 0.88)
Remoteness of general practice				
Major City	5.7 (5.4, 6.1)	Reference	7.4 (7.0, 7.8)	Reference
Inner/Outer Regional	5.0 (4.5, 5.7)	0.87 (0.75, 1.00)	6.4 (5.8, 7.1)	0.86 (0.76, 0.97)
Remote/Very Remote	5.5 (4.7, 6.3)	0.95 (0.80, 1.12)	6.5 (5.6, 7.4)	0.87 (0.75, 1.01)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 5. Proportion of women attending general practice who received a blood test (FBE, CRP, or ESR) during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	4.0 (3.2, 4.9)	1.30 (1.00, 1.71)	4.6 (3.7, 5.6)	1.30 (1.01, 1.67)
25-29	3.1 (2.6, 3.5)	Reference	3.6 (3.1, 4.1)	Reference
30-34	3.4 (3.0, 3.7)	1.10 (0.92, 1.32)	3.8 (3.4, 4.2)	1.06 (0.89, 1.26)
35-39	3.2 (2.8, 3.7)	1.04 (0.84, 1.28)	3.7 (3.2, 4.2)	1.02 (0.84, 1.23)
40-44	4.0 (3.0, 5.1)	1.31 (0.97, 1.77)	4.7 (3.7, 5.9)	1.33 (1.01, 1.75)
Concession status				
No concession	3.2 (2.9, 3.4)	Reference	3.7 (3.4, 3.9)	Reference
Concession holder	4.3 (3.7, 5.0)	1.37 (1.15, 1.63)	4.8 (4.1, 5.5)	1.31 (1.11, 1.54)
Smoking status				
Current Smoker	4.0 (2.7, 5.5)	1.21 (0.84, 1.74)	4.5 (3.1, 6.1)	1.14 (0.81, 1.61)
Ex Smoker	3.4 (3.0, 3.8)	1.02 (0.88, 1.18)	3.7 (3.3, 4.1)	0.93 (0.81, 1.07)
Never Smoker	3.3 (3.0, 3.6)	Reference	3.9 (3.6, 4.3)	Reference
Patient SES				
Very Low	3.5 (2.9, 4.2)	1.07 (0.85, 1.35)	3.8 (3.1, 4.5)	0.99 (0.79, 1.23)
Low	3.5 (3.0, 4.1)	1.08 (0.88, 1.34)	4.2 (3.6, 4.9)	1.11 (0.92, 1.35)
Middle	3.4 (2.9, 4.0)	1.05 (0.86, 1.28)	3.8 (3.3, 4.4)	1.00 (0.83, 1.21)
High	3.1 (2.7, 3.6)	0.95 (0.78, 1.17)	3.7 (3.2, 4.2)	0.97 (0.81, 1.17)
Very High	3.3 (2.9, 3.7)	Reference	3.8 (3.4, 4.3)	Reference
Indigenous status				
Aboriginal and/or TSI	4.6 (3.0, 6.7)	1.40 (0.93, 2.10)	5.1 (3.4, 7.3)	1.36 (0.92, 2.00)
Neither	3.3 (3.1, 3.5)	Reference	3.8 (3.6, 4.1)	Reference
Fever				
No	3.9 (3.5, 4.4)	Reference	4.5 (4.0, 5.0)	Reference
Yes	2.5 (1.2, 4.5)	0.63 (0.33, 1.19)	3.0 (1.6, 5.2)	0.66 (0.37, 1.18)
Not Documented	3.2 (2.9, 3.4)	0.80 (0.69, 0.93)	3.6 (3.4, 3.9)	0.81 (0.70, 0.93)
Remoteness of general practice				
Major City	3.4 (3.1, 3.7)	Reference	3.9 (3.7, 4.3)	Reference
Inner/Outer	3.1 (2.6, 3.6)	0.90 (0.75, 1.08)	3.6 (3.1, 4.2)	0.91 (0.77, 1.07)
Regional				
Remote/Very	3.2 (2.6, 3.9)	0.95 (0.76, 1.17)	3.6 (3.0, 4.3)	0.92 (0.75, 1.12)
Remote				

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 6. Proportion of women attending general practice who received a breast milk culture during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.8 (0.5, 1.3)	0.78 (0.45, 1.36)	1.0 (0.6, 1.5)	0.83 (0.51, 1.38)
25-29	1.0 (0.8, 1.3)	Reference	1.2 (0.9, 1.5)	Reference
30-34	0.9 (0.8, 1.1)	0.91 (0.66, 1.26)	1.1 (0.9, 1.3)	0.91 (0.67, 1.23)
35-39	0.8 (0.6, 1.1)	0.77 (0.53, 1.13)	1.0 (0.8, 1.3)	0.85 (0.60, 1.20)
40-44	1.5 (0.9, 2.3)	1.47 (0.90, 2.41)	1.8 (1.2, 2.6)	1.49 (0.95, 2.35)
Concession status				
No concession	1.0 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Concession holder	0.9 (0.6, 1.2)	0.91 (0.63, 1.31)	1.1 (0.8, 1.4)	0.92 (0.66, 1.28)
Smoking Status				
Current Smoker	1.4 (0.7, 2.4)	1.41 (0.76, 2.63)	1.4 (0.7, 2.4)	1.15 (0.62, 2.13)
Ex Smoker	0.9 (0.7, 1.1)	0.89 (0.67, 1.19)	1.0 (0.8, 1.2)	0.83 (0.64, 1.08)
Never Smoker	1.0 (0.8, 1.1)	Reference	1.2 (1.0, 1.4)	Reference
Patient SES				
Very Low	1.0 (0.7, 1.4)	0.90 (0.59, 1.36)	1.3 (0.9, 1.8)	1.03 (0.71, 1.50)
Low	0.7 (0.5, 1.0)	0.62 (0.41, 0.95)	0.8 (0.6, 1.2)	0.65 (0.44, 0.97)
Middle	0.8 (0.6, 1.1)	0.72 (0.49, 1.05)	1.1 (0.8, 1.4)	0.86 (0.61, 1.20)
High	0.9 (0.7, 1.2)	0.83 (0.58, 1.18)	1.1 (0.8, 1.4)	0.87 (0.63, 1.21)
Very High	1.1 (0.9, 1.4)	Reference	1.3 (1.0, 1.6)	Reference
Indigenous Status				
Aboriginal and/or TSI	0.9 (0.3, 2.1)	0.96 (0.40, 2.35)	0.9 (0.3, 2.1)	0.80 (0.33, 1.95)
Neither Aboriginal or TSI	0.9 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Fever				
No	1.1 (0.9, 1.4)	Reference	1.3 (1.1, 1.6)	Reference
Yes	0.2 (0.0, 1.4)	0.22 (0.03, 1.60)	0.5 (0.1, 1.8)	0.37 (0.09, 1.52)
Not Documented	0.9 (0.8, 1.1)	0.81 (0.61, 1.07)	1.1 (0.9, 1.2)	0.81 (0.63, 1.04)
Remoteness of general practice				
Major City	0.9 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Inner/Outer Regional	0.7 (0.5, 0.9)	0.71 (0.49, 1.03)	0.9 (0.6, 1.2)	0.77 (0.56, 1.07)
Remote/Very Remote	1.4 (1.0, 1.9)	1.48 (1.05, 2.07)	1.6 (1.2, 2.1)	1.44 (1.05, 1.98)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 7. Proportion of women attending general practice who received a nipple swab culture during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.7 (0.4, 1.2)	0.84 (0.46, 1.52)	0.9 (0.5, 1.4)	0.87 (0.51, 1.50)
25-29	0.8 (0.6, 1.1)	Reference	1.0 (0.7, 1.3)	Reference
30-34	0.9 (0.7, 1.1)	1.04 (0.73, 1.48)	1.0 (0.8, 1.2)	1.04 (0.75, 1.44)
35-39	0.6 (0.4, 0.9)	0.74 (0.49, 1.14)	0.8 (0.6, 1.1)	0.81 (0.55, 1.20)
40-44	0.6 (0.3, 1.2)	0.73 (0.36, 1.49)	1.0 (0.5, 1.6)	0.98 (0.54, 1.76)
Concession status				
No concession	0.8 (0.7, 1.0)	Reference	1.0 (0.9, 1.1)	Reference
Concession holder	0.5 (0.3, 0.8)	0.58 (0.36, 0.94)	0.6 (0.4, 0.9)	0.61 (0.40, 0.94)
Smoking Status				
Current Smoker	0.1 (0.0, 0.7)	0.14 (0.02, 0.98)	0.1 (0.0, 0.7)	0.11 (0.02, 0.81)
Ex Smoker	0.6 (0.5, 0.8)	0.68 (0.49, 0.94)	0.7 (0.6, 0.9)	0.67 (0.50, 0.90)
Never Smoker	0.9 (0.7, 1.1)	Reference	1.1 (0.9, 1.3)	Reference
Patient SES				
Very Low	0.4 (0.2, 0.7)	0.59 (0.33, 1.06)	0.6 (0.4, 0.9)	0.59 (0.36, 0.98)
Low	1.0 (0.7, 1.3)	1.32 (0.88, 1.99)	1.1 (0.8, 1.5)	1.07 (0.74, 1.56)
Middle	0.8 (0.6, 1.1)	1.08 (0.72, 1.62)	1.0 (0.7, 1.3)	0.95 (0.66, 1.37)
High	0.7 (0.5, 1.0)	0.96 (0.63, 1.44)	0.8 (0.6, 1.1)	0.80 (0.55, 1.16)
Very High	0.8 (0.6, 1.0)	Reference	1.0 (0.8, 1.3)	Reference
Indigenous Status				
Aboriginal and/or TSI	0.5 (0.1, 1.6)	0.70 (0.22, 2.19)	0.5 (0.1, 1.6)	0.58 (0.18, 1.80)
Neither Aboriginal or TSI	0.8 (0.7, 0.9)	Reference	0.9 (0.8, 1.1)	Reference
Fever				
No	0.8 (0.6, 1.1)	Reference	1.0 (0.8, 1.3)	Reference
Yes	0.7 (0.2, 2.2)	0.89 (0.28, 2.86)	1.0 (0.3, 2.5)	0.98 (0.35, 2.69)
Not Documented	0.8 (0.6, 0.9)	0.90 (0.66, 1.24)	0.9 (0.8, 1.1)	0.89 (0.67, 1.18)
Remoteness of general practice				
Major City	0.8 (0.6, 0.9)	Reference	0.9 (0.8, 1.1)	Reference
Inner/Outer Regional	0.3 (0.2, 0.5)	0.46 (0.28, 0.75)	0.5 (0.3, 0.7)	0.53 (0.35, 0.81)
Remote/Very Remote	1.3 (0.9, 1.8)	1.76 (1.24, 2.52)	1.4 (1.0, 1.9)	1.49 (1.06, 2.09)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 8. Proportion of women attending general practice who received a breast aspirate during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.1 (0.0, 0.3)	0.37 (0.05, 2.93)	0.1 (0.0, 0.4)	0.53 (0.12, 2.40)
25-29	0.1 (0.1, 0.3)	Reference	0.2 (0.1, 0.3)	Reference
30-34	0.1 (0.1, 0.2)	0.96 (0.40, 2.33)	0.3 (0.2, 0.4)	1.57 (0.78, 3.14)
35-39	0.2 (0.1, 0.4)	1.48 (0.61, 3.63)	0.3 (0.2, 0.5)	1.53 (0.72, 3.27)
40-44	0.2 (0.0, 0.6)	1.50 (0.40, 5.66)	0.3 (0.1, 0.8)	1.82 (0.63, 5.24)
Concession status				
No concession	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.3)	Reference
Concession holder	0.1 (0.0, 0.3)	0.85 (0.33, 2.18)	0.2 (0.1, 0.4)	0.67 (0.30, 1.46)
Smoking status				
Current Smoker	0.4 (0.1, 1.1)	2.42 (0.72, 8.13)	0.4 (0.1, 1.1)	1.34 (0.41, 4.33)
Ex Smoker	0.1 (0.1, 0.2)	0.75 (0.35, 1.59)	0.2 (0.1, 0.3)	0.70 (0.40, 1.25)
Never Smoker	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.4)	Reference
Patient SES				
Very Low	0.1 (0.0, 0.2)	0.27 (0.06, 1.19)	0.1 (0.0, 0.2)	0.14 (0.03, 0.57)
Low	0.1 (0.0, 0.3)	0.51 (0.19, 1.39)	0.2 (0.1, 0.4)	0.41 (0.19, 0.88)
Middle	0.1 (0.0, 0.2)	0.33 (0.11, 1.00)	0.2 (0.1, 0.3)	0.33 (0.15, 0.72)
High	0.2 (0.1, 0.3)	0.78 (0.35, 1.71)	0.3 (0.1, 0.4)	0.54 (0.29, 1.02)
Very High	0.2 (0.1, 0.4)	Reference	0.5 (0.3, 0.7)	Reference
Indigenous status				
Aboriginal and/or TSI	0	NR	0	NR
Neither	0.2 (0.1-0.2)	Reference	0.3 (0.2-0.3)	Reference
Aboriginal or TSI				
Fever				
No	0.2 (0.1, 0.3)	Reference	0.3 (0.2, 0.4)	Reference
Yes	0.0 (0.0, 0.9)	NR	0.0 (0.0, 0.9)	NR
Not Documented	0.1 (0.1, 0.2)	0.98 (0.47, 2.03)	0.3 (0.2, 0.3)	1.00 (0.58, 1.75)
Remoteness of general practice				
Major City	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.4)	Reference
Inner/Outer	0.1 (0.0, 0.2)	0.56 (0.22, 1.45)	0.2 (0.1, 0.3)	0.59 (0.29, 1.20)
Regional				
Remote/Very Remote	0.1 (0.0, 0.3)	0.75 (0.26, 2.14)	0.2 (0.1, 0.5)	0.77 (0.35, 1.70)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	6-7
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8-9
		(c) Explain how missing data were addressed	8-9
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed	N/A

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures in each exposure	N/A
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	N/A
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Figure 1, Table 3-4
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Trends in clinical management of lactational mastitis among women attending Australian general practice: a national longitudinal study using MedicineInsight, 2011-2022

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-080128.R1
Article Type:	Original research
Date Submitted by the Author:	24-Jan-2024
Complete List of Authors:	Grzeskowiak, Luke; Flinders University, College of Medicine and Public Health; South Australian Health and Medical Research Institute Limited, SAHMRI Women and Kids Kunne, Aline; South Australian Health and Medical Research Institute Limited, SAHMRI Women and Kids Crawford, Sharinne; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery Cullinane, Meabh; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery Amir, Lisa; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery; The Royal Women's Hospital, Breastfeeding service
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	General practice / Family practice, Obstetrics and gynaecology
Keywords:	Epidemiology < TROPICAL MEDICINE, Primary Care < Primary Health Care, Public health < INFECTIOUS DISEASES, MICROBIOLOGY, Pharmacology < TROPICAL MEDICINE

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES).

Title: Trends in clinical management of lactational mastitis among women attending Australian general practice: a national longitudinal study using MedicineInsight, 2011-2022

Luke E Grzeskowiak^{1,2,3}, Aline Kunnel², Sharinne B Crawford⁴, Meabh Cullinane⁴, Lisa H Amir^{4,5}

¹ Flinders Health and Medical Research Institute, College of Medicine and Public Health, Flinders University, Adelaide, South Australia, Australia

² South Australian Health and Medical Research Institute, Adelaide, South Australia, Australia

³ Adelaide Medical School, University of Adelaide

⁴ Judith Lumley Centre, School of Nursing and Midwifery, La Trobe University, Victoria, Australia

⁵ Breastfeeding service, Royal Women's Hospital, VIC, Australia

Corresponding Author:

Name: Associate Professor Luke Grzeskowiak, Flinders University

Email: luke.grzeskowiak@flinders.edu.au

Address: SAHMRI Women and Kids, Level 7, Clarence Rieger Building, Women's and Children's Hospital - 72 King William Road, North Adelaide, SA, 5006, Australia

Word Count

Abstract: 299

Main Text: 3369

Keywords: lactational mastitis; breastfeeding; epidemiology; primary care; public health; antibiotics; medications

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

ABSTRACT

Objective: To examine longitudinal trends in clinical management of lactational mastitis in women attending general practice.

Design: Open cohort study.

Setting: Australian general practice using data from MedicineInsight

Participants: Women aged 18 to 44 years with one or more clinical encounters for lactational mastitis between January 2011 and July 2022.

Primary and Secondary Outcome Measures: The primary outcome measure was the proportion prescribed oral antibiotics, according to antibiotic type. Secondary outcome measures were the proportion of women prescribed other medications (e.g. antifungals, lactation suppressants) or ordered selected clinical investigations including breast ultrasound, blood test, breast milk culture, nipple swab culture, or breast aspirate. Outcomes were examined according to calendar year and individual or clinic practice level characteristics.

Results: Among 25,002 women who had one or more clinical encounters related to mastitis, 90.9% were prescribed oral antibiotics. While the proportion of women prescribed an oral antibiotic remained consistent from 2011 to 2022 (91.1% vs. 92.5%), there were changes in the proportion receiving prescriptions for di/flucloxacillin (46.1% vs. 60.4%) and cefalexin (38.6% vs. 26.5%). Fewer than 12% of women received a clinical investigation related to their mastitis encounter, most commonly a breast ultrasound (7.1%), followed by a selected blood test (3.8%). Requests for breast milk cultures, nipple swab cultures, or breast aspirates occurred in less than 1.1% of individuals. Significant increases were evident with respect to ordering of all clinical investigations, with rates at least doubling between 2011 and 2022 (6.6% vs 14.7%). Large variability in clinical management was evident according to both individual characteristics (e.g. concessional status) and also at the clinical practice-level (e.g. remoteness).

Conclusions: Australian general practitioners commonly prescribe oral antibiotics for women with mastitis and largely in line with clinical guidelines. Their use of clinical investigations as part of mastitis management has increased over the last decade.

Strengths and limitation of this study

The study includes information about >25,000 lactational mastitis encounters extracted from electronic medical records in Australian general practice which are nationally representative.

We explored longitudinal changes in the frequency of oral antibiotic prescribing and selected requested tests related to mastitis encounter and examined how these differed according to patient- and practice-level characteristics.

The quality and accuracy of 'real-world' data captured through electronic medical records might be affected by clinician behaviour, the type of health information system used in each general practice, and algorithms used for data extraction.

Funding: This project was funded by a Therapeutic Guidelines Ltd (TGL) / RACGP Foundation Research Grant (TGL2020-02) awarded to LEG, SBC, MC, and LHA. LEG receives salary support from the Channel 7 Children's Research Foundation (CRF-210323).

Competing interest statement: The authors report no conflicts of interest.

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

INTRODUCTION

Lactational mastitis is a common breastfeeding complication, which is characterised by localized breast pain, tenderness, erythema and engorgement, and systemic symptoms such as fever, accompanied by malaise and rigors.[1,2] Mastitis can significantly disrupt activities of daily living, and is associated with significant maternal morbidity[1,2] and premature breastfeeding cessation.[3] Mastitis prevalence ranges from 3% to 20%[4] and most commonly occurs within the first four weeks postpartum.[5] Diagnosis is based on symptoms, which range from mild inflammation to more severe disease which can include bacterial infection and abscess development.[6,7] Early and appropriate treatment of mastitis is important to prevent adverse sequelae.

Early or mild cases of mastitis are treated symptomatically, with the use of self-management strategies aimed at ensuring effective drainage of breast milk, such as continued regular breastfeeding and/or expressing, gently massaging the affected breast, applying warmth to assist with let-down reflex and cold to reduce swelling.[6] Analgesics and anti-inflammatories may be useful in the management of pain and/or fevers.[8] In cases where symptoms do not resolve within 24-48 hours, or are moderate or severe, treatment with antibiotics may be required.[8] In Australia, the *Therapeutic Guidelines* advise initial empirical treatment with narrow-spectrum di/flucloxacillin,[9] targeting the most likely pathogens associated with mastitis, including *Staphylococcus aureus*. [5,10] In the case of penicillin allergy, cefalexin or clindamycin may be used, depending on the severity of the penicillin allergy.[9] In contrast to antibiotics, there is less guidance regarding the use of clinical investigations as part of mastitis management. Use of breast milk or nipple swab cultures are only recommended for patients with sepsis or who are not responding to first-line treatment.[6,11] Similarly, diagnostic ultrasound of the breast is recommended when a fluctuant breast mass is present, or where mastitis is not resolving or an abscess is suspected.[6,11] Less clear is the role of blood tests such as C-reactive protein (CRP) to guide antibiotic treatment.[12,13]

There are few studies examining clinical management of mastitis, particularly in a primary care or community setting. Most studies have focused on prescribing of oral antibiotics, with prevalence ranging from 38% to 86%.[14-19] In contrast, there has been limited exploration of

clinical investigations such as ultrasound or breast milk or swab cultures. Foxman et al appears to be the only study assessing the prevalence of culture analysis, with no participants reporting having this performed.[14]

Given the lack of research internationally on the clinical management of lactational mastitis in general practice settings, this study aimed to investigate longitudinal trends in the clinical management of lactational mastitis among women attending Australian general practice between 2011 and 2022.

METHODS

Ethics

The independent MedicineInsight Data Governance Committee approved the study (protocol 2019-003) and the Human Research Ethics Committee of the University of Adelaide exempted it from ethical review due to the use of non-identifiable data.

Study design, setting and data source

This was an open cohort study using data from the NPS MedicineWise MedicineInsight dataset. The study period spanned 1 January 2011 to 31 July 2022. MedicineInsight is a large-scale, national general practice dataset established by NPS MedicineWise with core funding from the Australian Government Department of Health. The MedicineInsight dataset has been described in detail elsewhere.[20] In summary, MedicineInsight uses third-party extraction tools (GRHANITE™ and Precedence Health Care's cdmNet™) which extract, de-identify and securely transmit patient data from participating practices' clinical information systems (CISs), such as Best Practice and Medical Director, to a secure data repository. The extraction tool collects incremental data regularly, allowing the development of a longitudinal database in which individuals within each practice can be tracked over time. The MedicineInsight dataset collects data on individual demographic characteristics, practice encounters (not including progress notes), diagnoses, prescribed medication, pathology tests and referrals. Insights are enriched through selected free text data. MedicineInsight contains electronic health records (EHRs) from

approximately 2,700 General Practitioners (GP) and 662 general practices across Australia (8.2% of all Australian practices).[20] The characteristics of MedicineInsight patients have been previously demonstrated to be nationally representative of the Australian population.[20]

Study population

We restricted our analysis to females of reproductive age (18-44 years inclusive) with one or more documented clinical encounters related to mastitis and documentation relating to a pregnancy within the previous 12-months of the encounter. Mastitis encounters were identified by searching the ‘Encounter reason’ free text field for the term ‘mastitis’. We also searched the ‘Diagnosis reason’, ‘Test reason’ and ‘Prescription reason’ free text field for the term ‘mastitis’ to identify encounters related to mastitis. We excluded the free text term ‘granulomatous mastitis’ as this was considered unlikely to be related to lactational mastitis. Clinical encounters for mastitis occurring within 14 days of a previous mastitis encounter were defined as belonging to the same treatment episode. Only the first episode per individual was included in the analysis. Documented pregnancies were identified using the separate ‘pregnancy’ dataset which included data on date of last menstrual period and estimated date of confinement. We also searched the ‘Encounter reason’ free text field using terms related to pregnancy (i.e. ‘Antenatal’, ‘Pregnancy’, ‘Hyperemesis gravidarum’, ‘Morning sickness’), postpartum (‘postnatal’, ‘postpartum’, ‘baby check’, ‘6-week check’), or breast feeding (i.e. ‘breast feeding’, ‘breastfeeding’, ‘lactation’) to identify women with a recent pregnancy. This was undertaken to increase the likelihood of the clinical encounter being related to lactational mastitis.

Outcome

The primary outcome assessed was the proportion of women prescribed oral antibiotics on the same date as a mastitis encounter. Prescribed antibiotics were identified from the corresponding ‘Prescriptions’ dataset. We extracted data on antibiotic type, quantity supplied, and whether any repeat prescriptions (for subsequent medication supplies) were issued. Secondary outcomes included the proportion of women ordered clinical investigations for mastitis including breast ultrasound, breast milk culture, nipple swab culture, blood test (i.e. CRP, Erythrocyte sedimentation rate [ESR], full blood examination [FBE]), and breast aspirate. These were identified by searching the ‘Requested tests’ free text field for the previously listed terms.

Additional secondary outcomes included the proportion of women prescribed other medications, including topical or intravenous antibiotics, antifungals, lactation suppressants (i.e. cabergoline, bromocriptine), or lactation stimulants (i.e. domperidone).

Patient and public involvement

There was no direct patient or public involvement in this research. The research used an established de-identified general practice dataset.

Covariates

Patient characteristics included age (based on year of birth), remoteness, socio-economic indexes for areas (SEIFA), state/territory, Indigenous status, Commonwealth concession card status and smoking status. Females for whom Indigenous status was recorded as unknown or missing were re-categorised as non-Indigenous, as done in other studies.[21] Remoteness, socio-economic indexes for areas (SEIFA) and state/territory were based on patients' residential postcodes. Remoteness was determined in accordance with the Australian Bureau of Statistics' (ABS) Australian Statistical Geography Standard (ASGS) Remoteness Areas, with 1 being a 'Major City' and 5 a 'Very Remote' area. Due to small population sizes, data for 'Remote' and 'Very Remote' were combined. SEIFA was determined according to the ABS Index of Relative Socio-Economic Advantage and Disadvantage (IRSAD) codes. We also extracted data from the clinical observations dataset to determine which individuals had a temperature recorded on the same day as the clinical encounter and whether the patient was considered febrile or not (temperature >38.5 degrees Celsius).

Statistical analysis

Descriptive statistics (counts and percentages) were used to describe the study population.

The proportion of women who were prescribed medications or ordered selected clinical investigations was calculated based on the year of first clinical encounter for mastitis and

expressed as a percentage, with corresponding 95% confidence intervals. Proportions were calculated separately based on management occurring on the same day as the first documented clinical encounter for mastitis, or on the same day as any clinical encounter for mastitis within the same episode. The proportion of women prescribed antibiotics or who received selected clinical investigations were stratified by calendar year to examine longitudinal trends.

We examined practice-level variation in the proportion of women receiving selected management for mastitis by stratifying proportions based on individual general practices, restricting the comparison to general practices that included data on ≥ 10 patients with mastitis.

We used univariable logistic regression analyses to compare the likelihood of women being prescribed oral antibiotics or receiving various clinical investigations related to mastitis based on individual characteristics. These analyses were undertaken separately according to clinical management at the first encounter, or any clinical encounter within the same mastitis episode.

All analyses were based on two-sided P-values, which statistical define by $p < 0.05$. The statistical analysis was performed using STATA MP 17 (Stata, College Station, Texas), with graphs prepared using R, version 4.3.0 (R Core Team).

RESULTS

A total of 25,002 females aged 18 to 44 years had one or more clinical encounters related to mastitis recorded in this general practice dataset between January 2011 and July 2022, as well as documented evidence of a recent pregnancy.

A greater proportion of women were aged 30-34 (39.3%), were never smokers (54.6%), lived in a major city (65.6%), and had a very high socioeconomic status (27.5%). A small proportion of women held a Commonwealth Concession card (15.6%) or were Aboriginal and/or Torres Strait Islander (2.2%) (**Table 1**). Approximately one quarter (27.8%) of women had a documented temperature at their first encounter, with 5.8% of those with a documented temperature being febrile.

Most (90.1%; $n = 22,523$) women received a prescription for oral antibiotics at their first encounter. With respect to clinical investigations, 5.6% were ordered a breast ultrasound, 3.3% a

blood test, 0.9% a nipple swab culture, and 0.8% breast milk culture (**Table 2**). Only very small numbers were prescribed oral (1.1%) or topical (1.2%) antifungals, topical antibiotics (0.5%), lactation suppressants (1.1%) or lactation stimulants (1.0%). Di/flucloxacillin and cefalexin accounted for >90% of oral antibiotic prescriptions. Only 3,006 (12.0%) women had two or more clinical encounters related to the same mastitis episode. When including clinical management across all clinical encounters, the proportion prescribed oral antibiotics increased only marginally to 90.9%. When considering investigations ordered at any clinical encounter, the largest increase was observed for breast ultrasound, which increased from 5.6% to 7.1% (**Table 2**). Approximately 1 in 10 (12.1%) women prescribed cefalexin had a documented penicillin allergy, whereas 64.4% of women prescribed clindamycin had a documented penicillin allergy.

When stratified by calendar year, the proportion of women prescribed oral antibiotics remained consistent across 2011 to 2022 ($p=0.559$). In contrast, significant increases from 2011 to 2022 were evident with respect to increases in proportions receiving breast ultrasound (3.4% to 8.5%), blood test (2.6% to 5.2%), breast milk culture (0.8% to 1.4%), swab culture (0.5% to 1.7%), and breast aspirate (<0.1% to 0.4%) (**Figure 1, Supplemental Table 1**). The proportion of women prescribed di/flucloxacillin increased from 46.1% in 2011 to 60.4% in 2022, whereas the proportion prescribed cefalexin decreased from 38.6% to 26.5% (**Supplemental Table 2**). From 2011 to 2022, the median treatment duration based on the initial prescription was 6 days, however there was a significant reduction in the proportion issued repeats from 31.5% to 3.0%.

Significant variability was evident with respect to overall clinical management of mastitis according to individual general practices, with the proportion of patients prescribed oral antibiotics ranging from 56.9% to 100% (**Figure 2**). Likewise, variation was seen with breast ultrasound (range: 0% to 40.6%), breast milk culture (0% to 14.7%), swab culture (0% to 9.2%), breast aspirate (0% to 3.8%) and blood test (0% to 31.2%).

Women prescribed oral antibiotics at the first encounter were less likely to receive a breast ultrasound, blood test, and breast aspirate. Similarly, they were less likely to be co-prescribed topical antibiotics, and oral/topical antifungals (**Supplemental Table 3**).

The only consistent factor associated with an increased likelihood of being prescribed oral antibiotics at the first or any encounter was the general practice being located in a regional or remote area, but the absolute differences were small (~1.0%) (**Table 3**). In comparison, factors associated with increased likelihood of breast ultrasound included older age (>30 years), being a current smoker, living in a major city, and higher socioeconomic status (**Supplemental Table 4**). The likelihood of receiving a blood test was increased for those in the youngest (18-24 years) and oldest (40-44 years) age groups, with a concession card (**Supplemental Table 5**). Factors associated with an increased likelihood of a breast milk culture included having a concession card, being a previous or current smoker, and the general practice being located in a regional or remote area (**Supplemental Table 6**). In contrast, the only factor associated with an increased likelihood of receiving a nipple swab culture was the general practice being located in a regional or remote area (**Supplemental Table 7**). In addition, however, the likelihood of receiving a breast milk culture was lower for those with a concession card or who were previous or current smokers. Only lower socioeconomic status was associated with a lower likelihood of breast aspirate (**Supplemental Table 8**), although none were ordered for individuals who identified as Aboriginal and/or Torres Strait Islanders or who were identified as being febrile at the time of the first encounter.

DISCUSSION

Principal findings

Evidence from this large national database indicate that most women presenting to Australian general practice for lactational mastitis are prescribed oral antibiotics, with prescribing practices appearing to largely be in adherence to Australian clinical guidelines. While there has been no change in overall oral antibiotic prescribing rates over the past decade, we observed an increase in prescribing of narrow spectrum antibiotics (i.e. di/flucloxacillin). This, combined with a lower rate of repeat prescriptions orders over time, indicate closer adherence to local guidelines and improved antibiotic stewardship. In addition, there were significant increases in the use of selected clinical investigations as part of mastitis management, including breast ultrasound and milk and nipple swab cultures. This suggests increased awareness of the use of clinical investigations in supporting optimal clinical management of lactational mastitis. The observed

variation in clinical management of lactational mastitis according to patient- and practice-level characteristics warrants further investigation to determine whether there may be further opportunities to improve standardization of clinical care.

Strengths and weaknesses

Study strengths include use of a large high-quality general practice database containing longitudinal individual-level data from 2011 to 2022 that is considered nationally representative. Multiple strategies were used to improve data quality, including restricting the cohort to those with a likely recent pregnancy and the use of different fields for data extraction. Nonetheless, our study has some important limitations. The quality and accuracy of ‘real-world’ data captured through electronic medical records might be affected by clinician behaviour and the type of health information system used in each general practice. For example, differences in recording may exist based on non-mandatory fields, free-text entries and use of system coding vocabularies. It is possible that this may result in possible misclassification and under-reporting of lactational mastitis encounters or associated clinical management. We made the assumption that prescriptions or clinical investigations ordered on the same day as a clinical encounter for mastitis were related to that encounter reason, where they may have been provided for alternative indications. In addition, GPs commonly provide a prescription for antibiotics (or other medications) with directions only to get it dispensed if symptoms don’t improve in the subsequent days (‘delayed prescribing’).[22] The database doesn’t contain information on referrals made to other health care providers or hospitals. In the case of severe mastitis, some clinicians may have opted to direct the patient to a hospital emergency department, rather than provide treatment. While data are recorded at the individual patient level, patient data are not linked across different general practices. Therefore, it is possible that individuals presenting to different general practices with the same symptoms were counted twice. Lastly, MedicineInsight uses a non-random sampling process to recruit the practices, however, the distribution of the sample has previously been shown to closely resemble figures from the last Australian census.[20]

Comparison to other studies

To our knowledge, this is the first evaluation of clinical management of lactational mastitis in a primary care setting. Most previous studies are limited to small numbers of women with mastitis (often less than 100) and lack contemporary data. In a prospective cohort study, Foxman et al followed 946 women recruited between 1994-1998, of which 77 women developed mastitis.[14] Of these women, 86% were prescribed antibiotics, with the most common being cefalexin (46%), followed by amoxicillin (7%), ampicillin (7%), and amoxicillin and clavulanic acid (7%). No cultures were performed for any women and no data were reported for ultrasound or blood tests. A more recent study from Scott et al followed 420 breastfeeding women recruited between 2004 and 2005 in Scotland, with 74 developing mastitis.[19] Among those women with mastitis, 78% were prescribed antibiotics, with the most common being flucloxacillin (30%), followed by amoxicillin (17%), erythromycin (7%), and amoxicillin and clavulanic acid (7%). Notably, 33% couldn't remember what antibiotic they were prescribed. The largest study evaluated data from almost 80,000 women recruited to the Norwegian Mother, Father and Child Cohort Study between 1999 to 2008.[3] Among the 15,014 who reported experiencing mastitis, 5,524 (36.8%) reported using antibiotics. Of those who could remember which antibiotic they received, the most common antibiotics included penicillins (83.8%), followed by macrolides (15.2%) and cephalosporins (2.6%).

Implications

While the observed proportion of antibiotic prescribing are very high, it is not possible to determine the appropriateness of prescribing practices based on available data. It is possible that women presenting to general practice with mastitis symptoms may represent those with more severe disease, corresponding to high rates of treatment. Further, it is likely that not all prescriptions for antibiotics were dispensed, and even when dispensed, not all antibiotics were commenced.[23] Also, it is possible that GPs are issuing prescriptions (or repeats) to women to be dispensed only if symptoms do not improve, representing delayed prescribing. However, the role of delayed prescribing in the context of antimicrobial stewardship for mastitis has not been evaluated and requires further investigation. Further, there was much larger observed variation in antibiotic prescribing practices at the practice-level compared with patient-level characteristics and this warrants further exploration as to underlying causes.

Increasing rates of ordering of clinical investigations over the decade suggests increased awareness of the potential value of such investigations in the diagnosis and/or management of mastitis. The observed higher frequency of ultrasound in older women and current smokers suggest ultrasounds may be being used to rule out differential diagnoses.[24,25] However, lower rates of ultrasound in those of lower socioeconomic status raises questions about potential equity issues and whether access or affordability negatively impacts uptake. A similar picture emerged for other investigations such as breast aspirate, breast milk culture, and nipple swab culture which were lower in those with lower socioeconomic status or a concession card. The lower rate of ultrasounds in those visiting a general practice located in remote or regional areas may be reflective of access difficulties, however, this is contrasted with higher rates of milk and swab cultures in these areas. Higher culture rates in rural settings may reflect observed higher rates of antimicrobial resistance, including Methicillin resistant *S. aureus* (MRSA) in these settings.[26] Similar to antibiotic prescribing practices, the large variation in frequency of clinical investigations warrants further examination, particularly appropriateness of these investigations and their impact on mastitis management.

Lactational mastitis has frequently been considered to be a topic that has not received the attention it deserves.[27] Research is needed to determine when antibiotics are needed for mastitis; which are the most appropriate antibiotic and what is the most appropriate duration. Clinical guidelines for management of mastitis have changed little over the last couple of decades, and GPs are assumed to be familiar with managing this common problem. It is timely to recommend an education program to alert clinicians that prescribing antibiotics for mastitis is not always straightforward: it should not be assumed that all lactating women with inflammatory breast symptoms require antibiotic treatment, and the potential need for breast milk culture should be considered. Breast milk culture may be appropriate at first presentation in locations with high rates of MRSA or in mothers with known antibiotic allergies, and should be ordered if the condition is not responding to first line antibiotics within 48 hours.[8]

CONCLUSION

Australian GPs commonly prescribe oral antibiotics for women with mastitis and largely in line with clinical guidelines. Over the last decade, GPs have increased prescriptions for narrow

spectrum antibiotics indicating closer adherence to local guidelines and improved antibiotic stewardship. Their use of clinical investigations as part of mastitis management has increased over the last decade but there may be the opportunity for increased use of breast milk culture to understand and manage local bacterial sensitivities.

Author contributions

All authors made significant contributions to the manuscript and are responsible for its content. LEG, SBC, MC and LHA conceived the idea, obtained grant funding and planned this study. LEG and AK were responsible for data extraction and analysis. LEG, SBC, MC and LHA were responsible for interpretation of study findings, while LEG and AK were responsible for presenting the results. LEG wrote the first draft and all authors contributed to the manuscript refinement. All authors have read and approved the final manuscript.

Data Sharing Statement

Data may be obtained from MedicineInsight and are not publicly available. Third parties may express an interest in the information collected through MedicineInsight. The provision of information in these instances undergoes a formal approval process and is guided by the MedicineInsight independent external Data Governance Committee. This Committee includes general practitioners, consumer advocates, privacy experts and researchers.

Ethics statements

Patient consent for publication

Not required.

Ethics approval

The independent MedicineInsight Data Governance Committee approved the study (protocol 2019-003) and the Human Research Ethics Committee of the University of Adelaide exempted it from ethical review due to the use of non-identifiable data.

Acknowledgments

The authors would like to thank NPS MedicineWise for their support in the development of this research.

Figure legends:

Figure 1. Longitudinal trends in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations, Australia 2011 to 2022

Figure 2. Variation in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations according to each individual general practice, Australia 2011 to 2022. Each circle corresponds to an individual site.

References

1. Cooney F, Petty-Saphon N. The burden of severe lactational mastitis in Ireland from 2006 to 2015. *Ir Med J* 2019; 112(1): 855.
2. De Groot N, Birnie E, Vermolen JH, et al. The prevalence of adverse postnatal outcomes for mother and infant in the Netherlands. *PloS One* 2018; 13(9): e0202960.
3. Grzeskowiak LE, Saha MR, Ingman WV, et al. Incidence, antibiotic treatment and outcomes of lactational mastitis: findings from the Norwegian mother, father and child cohort study (MoBa). *Paediatr Perinat Epidemiol* 2022; 36(2): 254-63.
4. Wilson E, Woodd SL, Benova L. Incidence of and risk factors for lactational mastitis: a systematic review. *J Hum Lact* 2020; 36(4): 673-86.
5. Cullinane M, Amir LH, Donath SM, et al. Determinants of mastitis in women in the CASTLE study: a cohort study. *BMC Fam Pract* 2015; 16: 181.
6. Scott DM. Inflammatory diseases of the breast. *Best Pract Res Clin Obstet Gynaecol* 2022; 83: 72-87.
7. Bhatt AA, Woodard GA, Lee CU, Hesley GK. Urgent and emergent breast lesions—a primer for the general radiologist, on-call resident and sonographer. *Australas J Ultrasound Med* 2022; 25(2): 54-65.
8. Mitchell KB, Johnson HM, Rodríguez JM, et al. Academy of Breastfeeding Medicine Clinical Protocol# 36: the mastitis spectrum, revised 2022. *Breastfeed Med* 2022; 17(5): 360-76.
9. Therapeutic Guidelines: Antibiotic: eTG complete. In: Lactational mastitis. 2020.
10. Rimoldi SG, Pileri P, Mazzocco MI, et al. The role of *Staphylococcus aureus* in mastitis: A multidisciplinary working group experience. *J Hum Lact* 2020; 36(3): 503-9.
11. Wheaton N, Al-Abdullah A, Haertlein T. Postdelivery emergencies. *Emerg Med Clin North Am* 2019; 37(2): 287-300.
12. Fetherston CM, Wells JI, Hartmann PE. Severity of mastitis symptoms as a predictor of C-reactive protein in milk and blood during lactation. *Breastfeed Med* 2006; 1(3): 127-35.
13. Petel D, Winters N, Gore GC, et al. Use of C-reactive protein to tailor antibiotic use: a systematic review and meta-analysis. *BMJ Open* 2018; 8(12): e022133.
14. Foxman B, D'Arcy H, Gillespie B, et al. Lactation mastitis: occurrence and medical management among 946 breastfeeding women in the United States. *Am J Epidemiol* 2002; 155(2): 103-14.
15. Fetherston C. Characteristics of lactation mastitis in a Western Australian cohort. *Breastfeed Rev* 1997; 5(2): 5-11.
16. Kinlay JR, O'Connell DL, Kinlay S. Incidence of mastitis in breastfeeding women during the six months after delivery: a prospective cohort study. *Med J Aust* 1998; 169(6): 310-2.
17. Jonsson S, Pulkkinen M. Mastitis today: incidence, prevention and treatment. *Ann Chir Gynaecol Suppl* 1994; (83): 84-7.
18. Lin C-H, Yang P-R, Lee C-P, et al. Descriptive study of mastitis in postpartum women in Taiwan: incidence and related factors. *J Womens Health (Larchmt)* 2023; 32(5): 616-22.
19. Scott JA, Robertson M, Fitzpatrick J, et al. Occurrence of lactational mastitis and medical management: a prospective cohort study in Glasgow. *Int Breastfeed J* 2008; 3: 21.
20. Busingye D, Gianacas C, Pollack A, et al. Data Resource Profile: MedicineInsight, an Australian national primary health care database. *Int J Epidemiol* 2019; 48(6): 1741-h.

21. Gilbert E, Rumbold A, Campbell S, et al. Management of encounters related to subfertility and infertility among Aboriginal and Torres Strait Islander females in Australian general practice. *BMC Women's Health* 2023; 23: 410.

22. Thursky KA, Hardefeldt LY, Rajkhowa A, et al. Antimicrobial stewardship in Australia: The role of qualitative research in programme development. *JAC Antimicrob Resist* 2021; 3(4): dlab166.

23. Ito S, Koren G, Einarson TR. Maternal noncompliance with antibiotics during breastfeeding. *Ann Pharmacother* 1993; 27(1): 40-2.

24. Moore DA, Bracewell SL, Smith EB, Jordan SG. A new search pattern for emergency breast exams: the clinical picture. *Emerg Radiol* 2021; 29: 207-13.

25. Porembka JH, Compton L, Omar L, et al. Breast ultrasound utilization in a safety net emergency department. *Emerg Radiol* 2019; 26: 123-31.

26. Cameron JK, Hall L, Tong SY, et al. Incidence of community onset MRSA in Australia: least reported where it is Most prevalent. *Antimicrob Resist Infect Control* 2019; 8: 33.

27. Amir LH, Ingram J. Health professionals' advice for breastfeeding problems: Not good enough! *Int Breastfeed J* 2008; 3: 22.

Table 1. Characteristics of 25,002 women presenting to Australian General Practice between 2011 and 2022 for Lactational Mastitis

	N (%)
Year	
2011-2012	3448 (13.8%)
2013-2014	4135 (16.5%)
2015-2016	4633 (18.5%)
2017-2018	4657 (18.6%)
2019-2020	4723 (18.9%)
2021-2022	3406 (13.6%)
Age group	
18-24	1991 (8.0%)
25-29	5830 (23.3%)
30-34	9821 (39.3%)
35-39	5900 (23.6%)
40-44	1460 (5.8%)
Concession status	
No Concession	21111 (84.4%)
Concession Card	3891 (15.6%)
Smoking status	
Never Smoker	13653 (54.6%)
Ex Smoker	8675 (34.7%)
Current Smoker	808 (3.2%)
Missing	1866 (7.5%)
Patient SES	
Very Low	3139 (12.6%)
Low	4215 (16.9%)
Middle	5143 (20.6%)
High	5533 (22.1%)
Very High	6872 (27.5%)
Missing	100 (0.4%)
Indigenous status	
Aboriginal and/or TSI	547 (2.2%)
Neither Aboriginal or TSI	24455 (97.8%)
Fever	
No	6551 (26.2%)
Yes	401 (1.6%)
Not recorded	18050 (72.2%)
Remoteness of general practice	
Major city	16397 (65.6%)
Inner regional	8162 (32.6%)
Remote & very remote	339 (1.4%)
Missing	104 (0.4%)

SES, socioeconomic status; TSI, Torres Strait Islander

Table 2. Selected clinical investigations and medications prescribed during the first or any encounter within the same episode of treatment for lactational mastitis in women attending general practice, Australia 2011 to 2022

	First encounter	Any encounter*
Clinical investigations		
Breast ultrasound	1 393 (5.6%)	1 771 (7.1%)
Milk culture	195 (0.8%)	235 (0.9%)
Nipple swab culture	237 (0.9%)	283 (1.1%)
Breast aspirate	37 (0.1%)	64 (0.3%)
Blood test	835 (3.3%)	962 (3.8%)
FBE	823 (3.3%)	947 (3.8%)
CRP	278 (1.1%)	350 (1.4%)
ESR	179 (0.7%)	212 (0.8%)
Medication prescriptions		
Antibiotics		
Oral	22 523 (90.1%)	22 739 (90.9%)
Di/flucloxacillin	12 477 (49.9%)	12 794 (51.2%)
Cefalexin	8 223 (32.9%)	8 501 (34.0%)
Amoxicillin	754 (3.0%)	772 (3.1%)
Amoxicillin clavulanate	594 (2.4%)	664 (2.7%)
Clindamycin	315 (1.3%)	354 (1.4%)
Erythromycin	289 (1.2%)	308 (1.2%)
Other	174 (0.7%)	215 (0.9%)
Intravenous	20 (0.1%)	32 (0.1%)
Topical	125 (0.5%)	149 (0.6%)
Antifungals		
Oral	275 (1.1%)	326 (1.3%)
Topical	303 (1.2%)	349 (1.4%)
Other medications		
Lactation suppressants	270 (1.1%)	310 (1.2%)
Lactation stimulants	256 (1.0%)	295 (1.2%)

*at any encounter for mastitis, including additional encounter occurring within two-week period of a previous mastitis encounter

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FBE: Full blood examination;

Table 3. Proportion of women attending general practice who were prescribed oral antibiotics during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	88.6 (87.2, 90.0)	0.89 (0.75, 1.04)	89.4 (88.0, 90.7)	0.88 (0.74, 1.03)
25-29	89.8 (89.0, 90.6)	Reference	90.6 (89.8, 91.3)	Reference
30-34	90.3 (89.7, 90.8)	1.05 (0.94, 1.17)	91.2 (90.7, 91.8)	1.08 (0.96, 1.21)
35-39	90.4 (89.6, 91.1)	1.07 (0.95, 1.21)	91.3 (90.5, 92.0)	1.08 (0.95, 1.23)
40-44	90.6 (89.0, 92.1)	1.10 (0.90, 1.33)	91.3 (89.7, 92.7)	1.09 (0.89, 1.33)
Concession status				
No concession	90.3 (89.8, 90.7)	Reference	91.2 (90.8, 91.5)	Reference
Concession holder	89.2 (88.1, 90.1)	0.89 (0.79, 0.99)	89.8 (88.8, 90.7)	0.85 (0.76, 0.95)
Smoking status				
Current smoker	90.7 (88.5, 92.6)	1.12 (0.88, 1.43)	91.1 (88.9, 93.0)	1.05 (0.82, 1.35)
Ex-smoker	91.4 (90.8, 92.0)	1.22 (1.11, 1.34)	92.1 (91.5, 92.7)	1.20 (1.09, 1.32)
Never smoker	89.7 (89.2, 90.2)	Reference	90.7 (90.2, 91.1)	Reference
Patient SES				
Very low	90.5 (89.4, 91.5)	1.04 (0.90, 1.20)	91.0 (89.9, 91.9)	0.99 (0.85, 1.15)
Low	89.4 (88.5, 90.3)	0.93 (0.82, 1.05)	90.5 (89.6, 91.4)	0.93 (0.82, 1.07)
Middle	90.3 (89.4, 91.1)	1.02 (0.90, 1.15)	91.2 (90.3, 91.9)	1.01 (0.89, 1.15)
High	90.3 (89.5, 91.0)	1.02 (0.90, 1.14)	91.2 (90.4, 91.9)	1.01 (0.90, 1.15)
Very high	90.1 (89.4, 90.8)	Reference	91.1 (90.4, 91.7)	Reference
Indigenous status				
Aboriginal and/or TSI	89.0 (86.1, 91.5)	0.89 (0.68, 1.17)	89.6 (86.7, 92.0)	0.85 (0.65, 1.13)
Neither Aboriginal or TSI	90.1 (89.7, 90.5)	Reference	91.0 (90.6, 91.3)	Reference
Fever				
No	94.1 (93.5, 94.6)	Reference	94.6 (94.1, 95.2)	Reference
Yes	92.8 (89.8, 95.1)	0.81 (0.55, 1.19)	94.3 (91.5, 96.3)	0.93 (0.60, 1.44)
Not Documented	88.6 (88.1, 89.0)	0.49 (0.44, 0.55)	89.5 (89.1, 90.0)	0.49 (0.43, 0.55)
Remoteness of general practice				
Major city	89.7 (89.2, 90.2)	Reference	90.6 (90.2, 91.1)	Reference
Inner/Outer regional	90.8 (90.0, 91.5)	1.13 (1.02, 1.26)	91.6 (90.8, 92.3)	1.12 (1.00, 1.25)
Remote/Very remote	91.2 (90.1, 92.1)	1.19 (1.04, 1.36)	91.7 (90.7, 92.7)	1.15 (1.00, 1.32)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

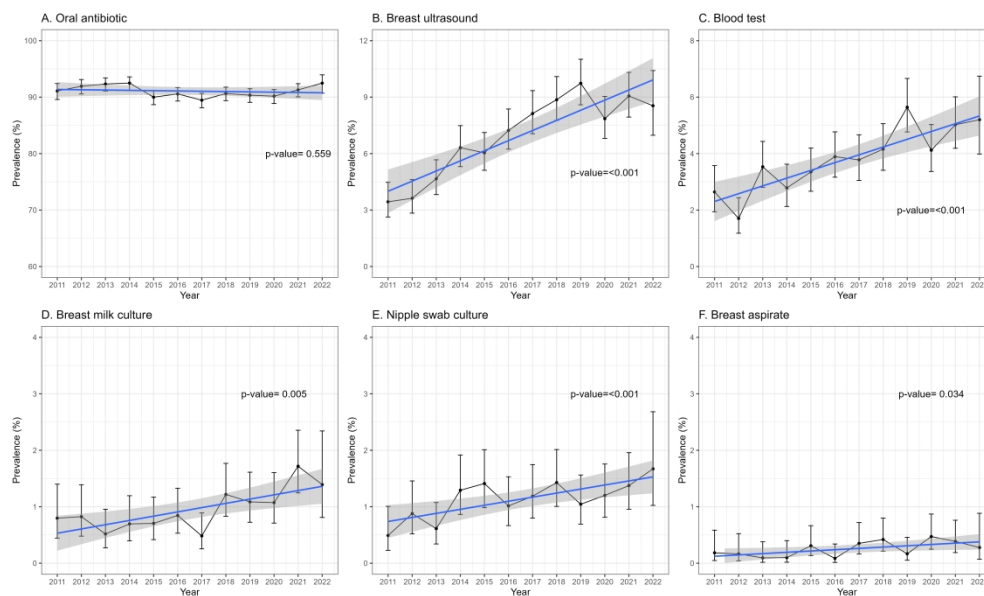


Figure 1. Longitudinal trends in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations, Australia 2011 to 2022

1291x774mm (118 x 118 DPI)

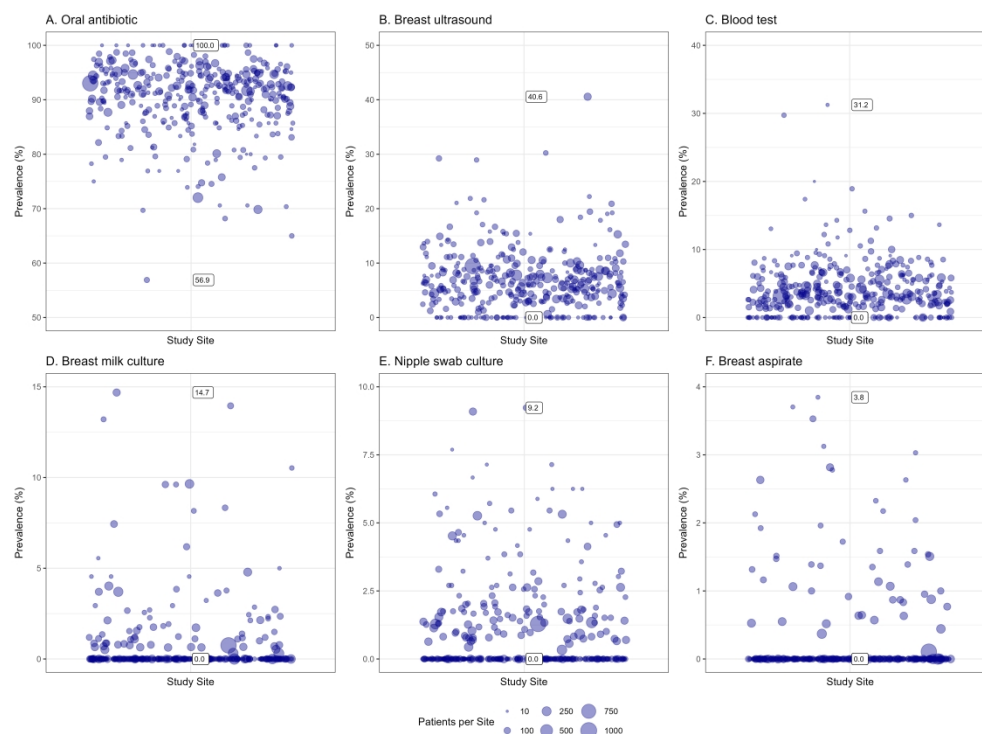


Figure 2. Variation in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations according to each individual general practice, Australia 2011 to 2022

1035x776mm (157 x 157 DPI)

Supplemental Table 1. Clinical management of in women attending general practice during the first or any encounter within the same treatment episode for lactational mastitis according to calendar year, Australia 2011 to 2022

		2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022†	Total
N		1 628	1 820	2 123	2 012	2 268	2 365	2 276	2 381	2 393	2 330	2 329	1 077	25 002
Oral antibiotic														
	First	1 465 (90.0%)	1 652 (90.8%)	1 942 (91.5%)	1 850 (92.0%)	2 028 (89.4%)	2 130 (90.1%)	2 011 (88.4%)	2 133 (89.6%)	2 143 (89.6%)	2 079 (89.2%)	2 103 (90.3%)	987 (91.6%)	22 523 (90.1%)
	Any	1 483 (91.1%)	1 673 (91.9%)	1 960 (92.3%)	1 861 (92.5%)	2 041 (90.0%)	2 142 (90.6%)	2 036 (89.5%)	2 158 (90.6%)	2 162 (90.3%)	2 101 (90.2%)	2 126 (91.3%)	996 (92.5%)	22 739 (90.9%)
Breast ultrasound														
	First	45 (2.8%)	45 (2.5%)	76 (3.6%)	107 (5.3%)	103 (4.5%)	139 (5.9%)	147 (6.5%)	159 (6.7%)	196 (8.2%)	132 (5.7%)	169 (7.3%)	75 (7.0%)	1393 (5.6%)
	Any	56 (3.4%)	66 (3.6%)	99 (4.7%)	127 (6.3%)	137 (6.0%)	171 (7.2%)	185 (8.1%)	211 (8.9%)	233 (9.7%)	183 (7.9%)	211 (9.1%)	92 (8.5%)	1771 (7.1%)
Breast milk culture														
	First	11 (0.7%)	11 (0.6%)	10 (0.5%)	8 (0.4%)	13 (0.6%)	18 (0.8%)	10 (0.4%)	26 (1.1%)	25 (1.0%)	21 (0.9%)	31 (1.3%)	11 (1.0%)	195 (0.8%)
	Any	13 (0.8%)	15 (0.8%)	11 (0.5%)	14 (0.7%)	16 (0.7%)	20 (0.8%)	11 (0.5%)	29 (1.2%)	26 (1.1%)	25 (1.1%)	40 (1.7%)	15 (1.4%)	235 (0.9%)
Nipple swab culture														
	First	8 (0.5%)	13 (0.7%)	13 (0.6%)	24 (1.2%)	26 (1.1%)	17 (0.7%)	23 (1.0%)	30 (1.3%)	18 (0.8%)	22 (0.9%)	26 (1.1%)	17 (1.6%)	237 (0.9%)
	Any	8 (0.5%)	16 (0.9%)	13 (0.6%)	26 (1.3%)	32 (1.4%)	24 (1.0%)	27 (1.2%)	34 (1.4%)	25 (1.0%)	28 (1.2%)	32 (1.4%)	18 (1.7%)	283 (1.1%)
Blood test‡														
	First	41 (2.5%)	27 (1.5%)	64 (3.0%)	49 (2.4%)	62 (2.7%)	84 (3.6%)	69 (3.0%)	88 (3.7%)	117 (4.9%)	82 (3.5%)	104 (4.5%)	48 (4.5%)	835 (3.3%)
	Any	43 (2.6%)	31 (1.7%)	75 (3.5%)	56 (2.8%)	76 (3.4%)	92 (3.9%)	86 (3.8%)	99 (4.2%)	135 (5.6%)	96 (4.1%)	117 (5.0%)	56 (5.2%)	962 (3.8%)
Breast aspirate														
	First	NR	NR	NR	NR	NR	NR	5 (0.2%)	9 (0.4%)	NR	6 (0.3%)	5 (0.2%)	NR	37 (0.1%)
	Any	NR	NR	NR	NR	7 (0.3%)	NR	8 (0.4%)	10 (0.4%)	NR	11 (0.5%)	9 (0.4%)	NR	64 (0.3%)

NR, not reportable due to small cell size
† 2022 calendar year includes January to July data only
‡ Includes ordering of full blood count, c-reactive protein, or erythrocyte sedimentation rate

Supplemental Table 2. The proportion of women attending general practice who were prescribed oral antibiotics during the first or any encounter within the same treatment episode for lactational mastitis according to antibiotic type and calendar year, Australia 2011 to 2022

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022†
N	1 628	1 820	2 123	2 012	2 268	2 365	2 276	2 381	2 393	2 330	2 329	1 077
Di/flucloxacillin												
First	719 (44.2%)	816 (44.8%)	981 (46.2%)	922 (45.8%)	1038 (45.8%)	1142 (48.3%)	1098 (48.2%)	1273 (53.5%)	1244 (52.0%)	1263 (54.2%)	1340 (57.5%)	641 (59.5%)
Any*	751 (46.1%)	830 (45.6%)	1010 (47.6%)	945 (47.0%)	1068 (47.1%)	1172 (49.6%)	1130 (49.6%)	1310 (55.0%)	1264 (52.8%)	1292 (55.5%)	1371 (58.9%)	651 (60.4%)
Cefalexin												
First	607 (37.3%)	678 (37.3%)	775 (36.5%)	765 (38.0%)	780 (34.4%)	825 (34.9%)	737 (32.4%)	690 (29.0%)	782 (32.7%)	684 (29.4%)	626 (26.9%)	274 (25.4%)
Any*	629 (38.6%)	704 (38.7%)	800 (37.7%)	780 (38.8%)	804 (35.4%)	850 (35.9%)	765 (33.6%)	714 (30.0%)	805 (33.6%)	713 (30.6%)	652 (28.0%)	285 (26.5%)
Amoxicillin												
First	65 (4.0%)	93 (5.1%)	84 (4.0%)	57 (2.8%)	95 (4.2%)	75 (3.2%)	72 (3.2%)	59 (2.5%)	40 (1.7%)	38 (1.6%)	53 (2.3%)	23 (2.1%)
Any*	68 (4.2%)	94 (5.2%)	86 (4.1%)	59 (2.9%)	96 (4.2%)	77 (3.3%)	74 (3.3%)	62 (2.6%)	40 (1.7%)	38 (1.6%)	55 (2.4%)	23 (2.1%)
Amoxicillin and clavulanate												
First	28 (1.7%)	27 (1.5%)	63 (3.0%)	48 (2.4%)	48 (2.1%)	54 (2.3%)	64 (2.8%)	72 (3.0%)	71 (3.0%)	43 (1.8%)	48 (2.1%)	28 (2.6%)
Any*	29 (1.8%)	32 (1.8%)	69 (3.3%)	54 (2.7%)	59 (2.6%)	63 (2.7%)	71 (3.1%)	81 (3.4%)	74 (3.1%)	48 (2.1%)	53 (2.3%)	31 (2.9%)
Erythromycin												
First	22 (1.4%)	27 (1.5%)	34 (1.6%)	43 (2.1%)	34 (1.5%)	34 (1.4%)	23 (1.0%)	22 (0.9%)	21 (0.9%)	17 (0.7%)	5 (0.2%)	7 (0.6%)
Any*	23 (1.4%)	30 (1.6%)	39 (1.8%)	44 (2.2%)	35 (1.5%)	35 (1.5%)	26 (1.1%)	24 (1.0%)	23 (1.0%)	17 (0.7%)	5 (0.2%)	7 (0.6%)
Clindamycin												
First	21 (1.3%)	20 (1.1%)	20 (0.9%)	22 (1.1%)	34 (1.5%)	23 (1.0%)	28 (1.2%)	28 (1.2%)	26 (1.1%)	43 (1.8%)	32 (1.4%)	18 (1.7%)
Any*	22 (1.4%)	22 (1.2%)	23 (1.1%)	23 (1.1%)	39 (1.7%)	28 (1.2%)	32 (1.4%)	30 (1.3%)	28 (1.2%)	49 (2.1%)	38 (1.6%)	20 (1.9%)
Other												
First	20 (1.2%)	17 (0.9%)	19 (0.9%)	20 (1.0%)	19 (0.8%)	11 (0.5%)	15 (0.7%)	8 (0.3%)	14 (0.6%)	11 (0.5%)	13 (0.6%)	7 (0.6%)
Any*	22 (1.4%)	25 (1.4%)	25 (1.2%)	23 (1.1%)	22 (1.0%)	14 (0.6%)	16 (0.7%)	12 (0.5%)	19 (0.8%)	15 (0.6%)	15 (0.6%)	7 (0.6%)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

† 2022 calendar year includes January to July data only

Supplemental Table 3. The proportion of women attending general practice for lactational mastitis who received selected clinical investigations or prescribed medications according to whether or not they were prescribed oral antibiotics during the same encounter, Australia 2011 to 2022

	Antibiotics prescribed at first encounter		p-value
	No (N = 2 479)	Yes (N = 22 523)	
Clinical Investigations			
Breast ultrasound	174 (7.0%)	1 219 (5.4%)	<0.001
Breast milk culture	26 (1.0%)	169 (0.8%)	0.109
Nipple swab culture	28 (1.1%)	209 (0.9%)	0.326
Blood Test	109 (4.4%)	726 (3.2%)	0.002
Breast Aspirate	8 (0.3%)	29 (0.1%)	0.017
Medication Prescriptions			
Antibiotics			
Topical	25 (1.0%)	100 (0.4%)	<0.001
Intravenous	8 (0.3%)	12 (0.1%)	<0.001
Antifungals			
Oral	97 (3.9%)	178 (0.8%)	<0.001
Topical	53 (2.1%)	250 (1.1%)	<0.001
Other Medications			
Lactation Suppressant	26 (1.0%)	244 (1.1%)	0.875
Lactation Stimulant	30 (1.2%)	226 (1.0%)	0.332

Supplemental Table 4. Proportion of women attending general practice who received a breast ultrasound during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	4.4 (3.6, 5.4)	0.97 (0.76, 1.25)	5.2 (4.3, 6.3)	0.88 (0.71, 1.11)
25-29	4.5 (4.0, 5.1)	Reference	5.9 (5.3, 6.5)	Reference
30-34	5.6 (5.2, 6.1)	1.25 (1.08, 1.46)	7.2 (6.7, 7.7)	1.24 (1.08, 1.41)
35-39	6.5 (5.9, 7.1)	1.46 (1.24, 1.71)	8.2 (7.5, 8.9)	1.43 (1.24, 1.65)
40-44	7.4 (6.1, 8.9)	1.68 (1.34, 2.12)	9.5 (8.1, 11.1)	1.69 (1.37, 2.07)
Concession status				
No concession	5.5 (5.2, 5.8)	Reference	7.1 (6.8, 7.5)	Reference
Concession holder	5.8 (5.1, 6.6)	1.05 (0.91, 1.22)	6.8 (6.1, 7.7)	0.96 (0.84, 1.09)
Smoking status				
Current smoker	7.9 (6.2, 10.0)	1.44 (1.11, 1.88)	9.4 (7.5, 11.6)	1.30 (1.02, 1.66)
Ex-smoker	5.2 (4.7, 5.7)	0.91 (0.81, 1.03)	6.3 (5.8, 6.8)	0.84 (0.76, 0.94)
Never smoker	5.6 (5.3, 6.0)	Reference	7.4 (7.0, 7.8)	Reference
Patient SES				
Very low	5.2 (4.5, 6.1)	0.91 (0.75, 1.09)	6.3 (5.5, 7.2)	0.82 (0.69, 0.97)
Low	5.3 (4.6, 6.0)	0.92 (0.78, 1.09)	6.6 (5.9, 7.4)	0.87 (0.74, 1.01)
Middle	5.3 (4.7, 6.0)	0.93 (0.79, 1.08)	6.7 (6.0, 7.4)	0.87 (0.76, 1.01)
High	6.0 (5.4, 6.6)	1.05 (0.90, 1.22)	7.6 (6.9, 8.3)	1.00 (0.88, 1.15)
Very high	5.7 (5.2, 6.3)	Reference	7.6 (7.0, 8.2)	Reference
Indigenous status				
Aboriginal and/or TSI	5.7 (3.9, 7.9)	1.02 (0.71, 1.47)	6.6 (4.7, 9.0)	0.92 (0.66, 1.30)
Neither Aboriginal or TSI	5.6 (5.3, 5.9)	Reference	7.1 (6.8, 7.4)	Reference
Fever				
No	6.5 (5.9, 7.1)	Reference	8.3 (7.6, 9.0)	Reference
Yes	3.0 (1.6, 5.2)	0.45 (0.25, 0.80)	5.5 (3.5, 8.2)	0.64 (0.41, 1.00)
Not Documented	5.3 (5.0, 5.6)	0.81 (0.72, 0.91)	6.7 (6.3, 7.1)	0.79 (0.71, 0.88)
Remoteness of general practice				
Major City	5.7 (5.4, 6.1)	Reference	7.4 (7.0, 7.8)	Reference
Inner/Outer Regional	5.0 (4.5, 5.7)	0.87 (0.75, 1.00)	6.4 (5.8, 7.1)	0.86 (0.76, 0.97)
Remote/Very Remote	5.5 (4.7, 6.3)	0.95 (0.80, 1.12)	6.5 (5.6, 7.4)	0.87 (0.75, 1.01)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 5. Proportion of women attending general practice who received a blood test (FBE, CRP, or ESR) during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	4.0 (3.2, 4.9)	1.30 (1.00, 1.71)	4.6 (3.7, 5.6)	1.30 (1.01, 1.67)
25-29	3.1 (2.6, 3.5)	Reference	3.6 (3.1, 4.1)	Reference
30-34	3.4 (3.0, 3.7)	1.10 (0.92, 1.32)	3.8 (3.4, 4.2)	1.06 (0.89, 1.26)
35-39	3.2 (2.8, 3.7)	1.04 (0.84, 1.28)	3.7 (3.2, 4.2)	1.02 (0.84, 1.23)
40-44	4.0 (3.0, 5.1)	1.31 (0.97, 1.77)	4.7 (3.7, 5.9)	1.33 (1.01, 1.75)
Concession status				
No concession	3.2 (2.9, 3.4)	Reference	3.7 (3.4, 3.9)	Reference
Concession holder	4.3 (3.7, 5.0)	1.37 (1.15, 1.63)	4.8 (4.1, 5.5)	1.31 (1.11, 1.54)
Smoking status				
Current Smoker	4.0 (2.7, 5.5)	1.21 (0.84, 1.74)	4.5 (3.1, 6.1)	1.14 (0.81, 1.61)
Ex Smoker	3.4 (3.0, 3.8)	1.02 (0.88, 1.18)	3.7 (3.3, 4.1)	0.93 (0.81, 1.07)
Never Smoker	3.3 (3.0, 3.6)	Reference	3.9 (3.6, 4.3)	Reference
Patient SES				
Very Low	3.5 (2.9, 4.2)	1.07 (0.85, 1.35)	3.8 (3.1, 4.5)	0.99 (0.79, 1.23)
Low	3.5 (3.0, 4.1)	1.08 (0.88, 1.34)	4.2 (3.6, 4.9)	1.11 (0.92, 1.35)
Middle	3.4 (2.9, 4.0)	1.05 (0.86, 1.28)	3.8 (3.3, 4.4)	1.00 (0.83, 1.21)
High	3.1 (2.7, 3.6)	0.95 (0.78, 1.17)	3.7 (3.2, 4.2)	0.97 (0.81, 1.17)
Very High	3.3 (2.9, 3.7)	Reference	3.8 (3.4, 4.3)	Reference
Indigenous status				
Aboriginal and/or TSI	4.6 (3.0, 6.7)	1.40 (0.93, 2.10)	5.1 (3.4, 7.3)	1.36 (0.92, 2.00)
Neither	3.3 (3.1, 3.5)	Reference	3.8 (3.6, 4.1)	Reference
Fever				
No	3.9 (3.5, 4.4)	Reference	4.5 (4.0, 5.0)	Reference
Yes	2.5 (1.2, 4.5)	0.63 (0.33, 1.19)	3.0 (1.6, 5.2)	0.66 (0.37, 1.18)
Not Documented	3.2 (2.9, 3.4)	0.80 (0.69, 0.93)	3.6 (3.4, 3.9)	0.81 (0.70, 0.93)
Remoteness of general practice				
Major City	3.4 (3.1, 3.7)	Reference	3.9 (3.7, 4.3)	Reference
Inner/Outer	3.1 (2.6, 3.6)	0.90 (0.75, 1.08)	3.6 (3.1, 4.2)	0.91 (0.77, 1.07)
Regional				
Remote/Very	3.2 (2.6, 3.9)	0.95 (0.76, 1.17)	3.6 (3.0, 4.3)	0.92 (0.75, 1.12)
Remote				

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 6. Proportion of women attending general practice who received a breast milk culture during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.8 (0.5, 1.3)	0.78 (0.45, 1.36)	1.0 (0.6, 1.5)	0.83 (0.51, 1.38)
25-29	1.0 (0.8, 1.3)	Reference	1.2 (0.9, 1.5)	Reference
30-34	0.9 (0.8, 1.1)	0.91 (0.66, 1.26)	1.1 (0.9, 1.3)	0.91 (0.67, 1.23)
35-39	0.8 (0.6, 1.1)	0.77 (0.53, 1.13)	1.0 (0.8, 1.3)	0.85 (0.60, 1.20)
40-44	1.5 (0.9, 2.3)	1.47 (0.90, 2.41)	1.8 (1.2, 2.6)	1.49 (0.95, 2.35)
Concession status				
No concession	1.0 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Concession holder	0.9 (0.6, 1.2)	0.91 (0.63, 1.31)	1.1 (0.8, 1.4)	0.92 (0.66, 1.28)
Smoking Status				
Current Smoker	1.4 (0.7, 2.4)	1.41 (0.76, 2.63)	1.4 (0.7, 2.4)	1.15 (0.62, 2.13)
Ex Smoker	0.9 (0.7, 1.1)	0.89 (0.67, 1.19)	1.0 (0.8, 1.2)	0.83 (0.64, 1.08)
Never Smoker	1.0 (0.8, 1.1)	Reference	1.2 (1.0, 1.4)	Reference
Patient SES				
Very Low	1.0 (0.7, 1.4)	0.90 (0.59, 1.36)	1.3 (0.9, 1.8)	1.03 (0.71, 1.50)
Low	0.7 (0.5, 1.0)	0.62 (0.41, 0.95)	0.8 (0.6, 1.2)	0.65 (0.44, 0.97)
Middle	0.8 (0.6, 1.1)	0.72 (0.49, 1.05)	1.1 (0.8, 1.4)	0.86 (0.61, 1.20)
High	0.9 (0.7, 1.2)	0.83 (0.58, 1.18)	1.1 (0.8, 1.4)	0.87 (0.63, 1.21)
Very High	1.1 (0.9, 1.4)	Reference	1.3 (1.0, 1.6)	Reference
Indigenous Status				
Aboriginal and/or TSI	0.9 (0.3, 2.1)	0.96 (0.40, 2.35)	0.9 (0.3, 2.1)	0.80 (0.33, 1.95)
Neither Aboriginal or TSI	0.9 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Fever				
No	1.1 (0.9, 1.4)	Reference	1.3 (1.1, 1.6)	Reference
Yes	0.2 (0.0, 1.4)	0.22 (0.03, 1.60)	0.5 (0.1, 1.8)	0.37 (0.09, 1.52)
Not Documented	0.9 (0.8, 1.1)	0.81 (0.61, 1.07)	1.1 (0.9, 1.2)	0.81 (0.63, 1.04)
Remoteness of general practice				
Major City	0.9 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Inner/Outer	0.7 (0.5, 0.9)	0.71 (0.49, 1.03)	0.9 (0.6, 1.2)	0.77 (0.56, 1.07)
Regional				
Remote/Very Remote	1.4 (1.0, 1.9)	1.48 (1.05, 2.07)	1.6 (1.2, 2.1)	1.44 (1.05, 1.98)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 7. Proportion of women attending general practice who received a nipple swab culture during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.7 (0.4, 1.2)	0.84 (0.46, 1.52)	0.9 (0.5, 1.4)	0.87 (0.51, 1.50)
25-29	0.8 (0.6, 1.1)	Reference	1.0 (0.7, 1.3)	Reference
30-34	0.9 (0.7, 1.1)	1.04 (0.73, 1.48)	1.0 (0.8, 1.2)	1.04 (0.75, 1.44)
35-39	0.6 (0.4, 0.9)	0.74 (0.49, 1.14)	0.8 (0.6, 1.1)	0.81 (0.55, 1.20)
40-44	0.6 (0.3, 1.2)	0.73 (0.36, 1.49)	1.0 (0.5, 1.6)	0.98 (0.54, 1.76)
Concession status				
No concession	0.8 (0.7, 1.0)	Reference	1.0 (0.9, 1.1)	Reference
Concession holder	0.5 (0.3, 0.8)	0.58 (0.36, 0.94)	0.6 (0.4, 0.9)	0.61 (0.40, 0.94)
Smoking Status				
Current Smoker	0.1 (0.0, 0.7)	0.14 (0.02, 0.98)	0.1 (0.0, 0.7)	0.11 (0.02, 0.81)
Ex Smoker	0.6 (0.5, 0.8)	0.68 (0.49, 0.94)	0.7 (0.6, 0.9)	0.67 (0.50, 0.90)
Never Smoker	0.9 (0.7, 1.1)	Reference	1.1 (0.9, 1.3)	Reference
Patient SES				
Very Low	0.4 (0.2, 0.7)	0.59 (0.33, 1.06)	0.6 (0.4, 0.9)	0.59 (0.36, 0.98)
Low	1.0 (0.7, 1.3)	1.32 (0.88, 1.99)	1.1 (0.8, 1.5)	1.07 (0.74, 1.56)
Middle	0.8 (0.6, 1.1)	1.08 (0.72, 1.62)	1.0 (0.7, 1.3)	0.95 (0.66, 1.37)
High	0.7 (0.5, 1.0)	0.96 (0.63, 1.44)	0.8 (0.6, 1.1)	0.80 (0.55, 1.16)
Very High	0.8 (0.6, 1.0)	Reference	1.0 (0.8, 1.3)	Reference
Indigenous Status				
Aboriginal and/or TSI	0.5 (0.1, 1.6)	0.70 (0.22, 2.19)	0.5 (0.1, 1.6)	0.58 (0.18, 1.80)
Neither Aboriginal or TSI	0.8 (0.7, 0.9)	Reference	0.9 (0.8, 1.1)	Reference
Fever				
No	0.8 (0.6, 1.1)	Reference	1.0 (0.8, 1.3)	Reference
Yes	0.7 (0.2, 2.2)	0.89 (0.28, 2.86)	1.0 (0.3, 2.5)	0.98 (0.35, 2.69)
Not Documented	0.8 (0.6, 0.9)	0.90 (0.66, 1.24)	0.9 (0.8, 1.1)	0.89 (0.67, 1.18)
Remoteness of general practice				
Major City	0.8 (0.6, 0.9)	Reference	0.9 (0.8, 1.1)	Reference
Inner/Outer	0.3 (0.2, 0.5)	0.46 (0.28, 0.75)	0.5 (0.3, 0.7)	0.53 (0.35, 0.81)
Regional				
Remote/Very Remote	1.3 (0.9, 1.8)	1.76 (1.24, 2.52)	1.4 (1.0, 1.9)	1.49 (1.06, 2.09)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 8. Proportion of women attending general practice who received a breast aspirate during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.1 (0.0, 0.3)	0.37 (0.05, 2.93)	0.1 (0.0, 0.4)	0.53 (0.12, 2.40)
25-29	0.1 (0.1, 0.3)	Reference	0.2 (0.1, 0.3)	Reference
30-34	0.1 (0.1, 0.2)	0.96 (0.40, 2.33)	0.3 (0.2, 0.4)	1.57 (0.78, 3.14)
35-39	0.2 (0.1, 0.4)	1.48 (0.61, 3.63)	0.3 (0.2, 0.5)	1.53 (0.72, 3.27)
40-44	0.2 (0.0, 0.6)	1.50 (0.40, 5.66)	0.3 (0.1, 0.8)	1.82 (0.63, 5.24)
Concession status				
No concession	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.3)	Reference
Concession holder	0.1 (0.0, 0.3)	0.85 (0.33, 2.18)	0.2 (0.1, 0.4)	0.67 (0.30, 1.46)
Smoking status				
Current Smoker	0.4 (0.1, 1.1)	2.42 (0.72, 8.13)	0.4 (0.1, 1.1)	1.34 (0.41, 4.33)
Ex Smoker	0.1 (0.1, 0.2)	0.75 (0.35, 1.59)	0.2 (0.1, 0.3)	0.70 (0.40, 1.25)
Never Smoker	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.4)	Reference
Patient SES				
Very Low	0.1 (0.0, 0.2)	0.27 (0.06, 1.19)	0.1 (0.0, 0.2)	0.14 (0.03, 0.57)
Low	0.1 (0.0, 0.3)	0.51 (0.19, 1.39)	0.2 (0.1, 0.4)	0.41 (0.19, 0.88)
Middle	0.1 (0.0, 0.2)	0.33 (0.11, 1.00)	0.2 (0.1, 0.3)	0.33 (0.15, 0.72)
High	0.2 (0.1, 0.3)	0.78 (0.35, 1.71)	0.3 (0.1, 0.4)	0.54 (0.29, 1.02)
Very High	0.2 (0.1, 0.4)	Reference	0.5 (0.3, 0.7)	Reference
Indigenous status				
Aboriginal and/or TSI	0	NR	0	NR
Neither	0.2 (0.1-0.2)	Reference	0.3 (0.2-0.3)	Reference
Aboriginal or TSI				
Fever				
No	0.2 (0.1, 0.3)	Reference	0.3 (0.2, 0.4)	Reference
Yes	0.0 (0.0, 0.9)	NR	0.0 (0.0, 0.9)	NR
Not Documented	0.1 (0.1, 0.2)	0.98 (0.47, 2.03)	0.3 (0.2, 0.3)	1.00 (0.58, 1.75)
Remoteness of general practice				
Major City	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.4)	Reference
Inner/Outer	0.1 (0.0, 0.2)	0.56 (0.22, 1.45)	0.2 (0.1, 0.3)	0.59 (0.29, 1.20)
Regional				
Remote/Very	0.1 (0.0, 0.3)	0.75 (0.26, 2.14)	0.2 (0.1, 0.5)	0.77 (0.35, 1.70)
Remote				

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	6-7
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8-9
		(c) Explain how missing data were addressed	8-9
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed	N/A

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures in each exposure	N/A
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	N/A
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Figure 1, Table 3-4
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Trends in clinical management of lactational mastitis among women attending Australian general practice: a national longitudinal study using MedicineInsight, 2011-2022

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-080128.R2
Article Type:	Original research
Date Submitted by the Author:	25-Mar-2024
Complete List of Authors:	Grzeskowiak, Luke; Flinders University, College of Medicine and Public Health; South Australian Health and Medical Research Institute Limited, SAHMRI Women and Kids Kunne, Aline; South Australian Health and Medical Research Institute Limited, SAHMRI Women and Kids Crawford, Sharinne; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery Cullinane, Meabh; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery Amir, Lisa; La Trobe University, Judith Lumley Centre, School of Nursing and Midwifery; The Royal Women's Hospital, Breastfeeding service
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	General practice / Family practice, Obstetrics and gynaecology
Keywords:	Epidemiology < TROPICAL MEDICINE, Primary Care < Primary Health Care, Public health < INFECTIOUS DISEASES, MICROBIOLOGY, Pharmacology < TROPICAL MEDICINE

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Supérieur (ABES).

Title: Trends in clinical management of lactational mastitis among women attending Australian general practice: a national longitudinal study using MedicineInsight, 2011-2022

Luke E Grzeskowiak^{1,2,3}, Aline Kunnel², Sharinne B Crawford⁴, Meabh Cullinane⁴, Lisa H Amir^{4,5}

¹ Flinders Health and Medical Research Institute, College of Medicine and Public Health, Flinders University, Adelaide, South Australia, Australia

² South Australian Health and Medical Research Institute, Adelaide, South Australia, Australia

³ Adelaide Medical School, University of Adelaide

⁴ Judith Lumley Centre, School of Nursing and Midwifery, La Trobe University, Victoria, Australia

⁵ Breastfeeding service, Royal Women's Hospital, VIC, Australia

Corresponding Author:

Name: Associate Professor Luke Grzeskowiak, Flinders University

Email: luke.grzeskowiak@flinders.edu.au

Address: SAHMRI Women and Kids, Level 7, Clarence Rieger Building, Women's and Children's Hospital - 72 King William Road, North Adelaide, SA, 5006, Australia

Word Count

Abstract: 299

Main Text: 3369

Keywords: lactational mastitis; breastfeeding; epidemiology; primary care; public health; antibiotics; medications

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

ABSTRACT

Objective: To examine longitudinal trends in clinical management of lactational mastitis in women attending general practice.

Design: Open cohort study.

Setting: Australian general practice using data from MedicineInsight

Participants: Women aged 18 to 44 years with one or more clinical encounters for lactational mastitis between January 2011 and July 2022.

Primary and Secondary Outcome Measures: The primary outcome measure was the proportion prescribed oral antibiotics, according to antibiotic type. Secondary outcome measures were the proportion of women prescribed other medications (e.g. antifungals, lactation suppressants) or ordered selected clinical investigations including breast ultrasound, blood test, breast milk culture, nipple swab culture, or breast aspirate. Outcomes were examined according to calendar year and individual or clinic practice level characteristics.

Results: Among 25,002 women who had one or more clinical encounters related to mastitis, 90.9% were prescribed oral antibiotics. While the proportion of women prescribed an oral antibiotic remained consistent from 2011 to 2022 (91.1% vs. 92.5%), there were changes in the proportion receiving prescriptions for di/flucloxacillin (46.1% vs. 60.4%) and cefalexin (38.6% vs. 26.5%). Fewer than 12% of women received a clinical investigation related to their mastitis encounter, most commonly a breast ultrasound (7.1%), followed by a selected blood test (3.8%). Requests for breast milk cultures, nipple swab cultures, or breast aspirates occurred in less than 1.1% of individuals. Significant increases were evident with respect to ordering of all clinical investigations, with rates at least doubling between 2011 and 2022 (6.6% vs 14.7%). Large variability in clinical management was evident according to both individual characteristics (e.g. concessional status) and also at the clinical practice-level (e.g. remoteness).

Conclusions: Australian general practitioners commonly prescribe oral antibiotics for women with mastitis and largely in line with clinical guidelines. Their use of clinical investigations as part of mastitis management has increased over the last decade.

Strengths and limitation of this study

The study includes information about >25,000 lactational mastitis encounters extracted from electronic medical records in Australian general practice which are nationally representative.

We explored longitudinal changes in the frequency of oral antibiotic prescribing and selected requested tests related to mastitis encounter and examined how these differed according to patient- and practice-level characteristics.

The quality and accuracy of 'real-world' data captured through electronic medical records might be affected by clinician behaviour, the type of health information system used in each general practice, and algorithms used for data extraction.

Funding: This project was funded by a Therapeutic Guidelines Ltd (TGL) / RACGP Foundation Research Grant (TGL2020-02) awarded to LEG, SBC, MC, and LHA. LEG receives salary support from the Channel 7 Children's Research Foundation (CRF-210323).

Competing interest statement: The authors report no conflicts of interest.

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

INTRODUCTION

Lactational mastitis is a common breastfeeding complication, which is characterised by localized breast pain, tenderness, erythema and engorgement, and systemic symptoms such as fever, accompanied by malaise and rigors.[1,2] Mastitis can significantly disrupt activities of daily living, and is associated with significant maternal morbidity[1,2] and premature breastfeeding cessation.[3] Mastitis prevalence ranges from 3% to 20%[4] and most commonly occurs within the first four weeks postpartum.[5] Diagnosis is based on symptoms, which range from mild inflammation to more severe disease which can include bacterial infection and abscess development.[6,7] Early and appropriate treatment of mastitis is important to prevent adverse sequelae.

Early or mild cases of mastitis are treated symptomatically, with the use of self-management strategies aimed at ensuring effective drainage of breast milk, such as continued regular breastfeeding and/or expressing, gently massaging the affected breast, applying warmth to assist with let-down reflex and cold to reduce swelling.[6] Analgesics and anti-inflammatories may be useful in the management of pain and/or fevers.[8] In cases where symptoms do not resolve within 24-48 hours, or are moderate or severe, treatment with antibiotics may be required.[8] In Australia, the *Therapeutic Guidelines* advise initial empirical treatment with narrow-spectrum di/flucloxacillin,[9] targeting the most likely pathogens associated with mastitis, including *Staphylococcus aureus*. [5,10] In the case of penicillin allergy, cefalexin or clindamycin may be used, depending on the severity of the penicillin allergy.[9] In contrast to antibiotics, there is less guidance regarding the use of clinical investigations as part of mastitis management. Use of breast milk or nipple swab cultures are only recommended for patients with sepsis or who are not responding to first-line treatment.[6,11] Similarly, diagnostic ultrasound of the breast is recommended when a fluctuant breast mass is present, or where mastitis is not resolving or an abscess is suspected.[6,11] Less clear is the role of blood tests such as C-reactive protein (CRP) to guide antibiotic treatment.[12,13]

There are few studies examining clinical management of mastitis, particularly in a primary care or community setting. Most studies have focused on prescribing of oral antibiotics, with prevalence ranging from 38% to 86%.[14-19] In contrast, there has been limited exploration of

clinical investigations such as ultrasound or breast milk or swab cultures. Foxman et al appears to be the only study assessing the prevalence of culture analysis, with no participants reporting having this performed.[14]

Given the lack of research internationally on the clinical management of lactational mastitis in general practice settings, this study aimed to investigate longitudinal trends in the clinical management of lactational mastitis among women attending Australian general practice between 2011 and 2022.

METHODS

Ethics

The independent MedicineInsight Data Governance Committee approved the study (protocol 2019-003) and the Human Research Ethics Committee of the University of Adelaide exempted it from ethical review due to the use of non-identifiable data.

Study design, setting and data source

This was an open cohort study using data from the NPS MedicineWise MedicineInsight dataset. The study period spanned 1 January 2011 to 31 July 2022. MedicineInsight is a large-scale, national general practice dataset established by NPS MedicineWise with core funding from the Australian Government Department of Health. The MedicineInsight dataset has been described in detail elsewhere.[20] In summary, MedicineInsight uses third-party extraction tools (GRHANITE™ and Precedence Health Care's cdmNet™) which extract, de-identify and securely transmit patient data from participating practices' clinical information systems (CISs), such as Best Practice and Medical Director, to a secure data repository. The extraction tool collects incremental data regularly, allowing the development of a longitudinal database in which individuals within each practice can be tracked over time. The MedicineInsight dataset collects data on individual demographic characteristics, practice encounters (not including progress notes), diagnoses, prescribed medication, pathology tests and referrals. Insights are enriched through selected free text data. MedicineInsight contains electronic health records (EHRs) from

approximately 2,700 General Practitioners (GP) and 662 general practices across Australia (8.2% of all Australian practices).[20] The characteristics of MedicineInsight patients have been previously demonstrated to be nationally representative of the Australian population.[20]

Study population

We restricted our analysis to females of reproductive age (18-44 years inclusive) with one or more documented clinical encounters related to mastitis and documentation relating to a pregnancy within the previous 12-months of the encounter. Mastitis encounters were identified by searching the ‘Encounter reason’ free text field for the term ‘mastitis’. We also searched the ‘Diagnosis reason’, ‘Test reason’ and ‘Prescription reason’ free text field for the term ‘mastitis’ to identify encounters related to mastitis. We excluded the free text term ‘granulomatous mastitis’ as this was considered unlikely to be related to lactational mastitis. Clinical encounters for mastitis occurring within 14 days of a previous mastitis encounter were defined as belonging to the same treatment episode. Only the first episode per individual was included in the analysis. Documented pregnancies were identified using the separate ‘pregnancy’ dataset which included data on date of last menstrual period and estimated date of confinement. We also searched the ‘Encounter reason’ free text field using terms related to pregnancy (i.e. ‘Antenatal’, ‘Pregnancy’, ‘Hyperemesis gravidarum’, ‘Morning sickness’), postpartum (‘postnatal’, ‘postpartum’, ‘baby check’, ‘6-week check’), or breast feeding (i.e. ‘breast feeding’, ‘breastfeeding’, ‘lactation’) to identify women with a recent pregnancy. This was undertaken to increase the likelihood of the clinical encounter being related to lactational mastitis.

Outcome

The primary outcome assessed was the proportion of women prescribed oral antibiotics on the same date as a mastitis encounter. Prescribed antibiotics were identified from the corresponding ‘Prescriptions’ dataset. We extracted data on antibiotic type, quantity supplied, and whether any repeat prescriptions (for subsequent medication supplies) were issued. Secondary outcomes included the proportion of women ordered clinical investigations for mastitis including breast ultrasound, breast milk culture, nipple swab culture, blood test (i.e. CRP, Erythrocyte sedimentation rate [ESR], full blood examination [FBE]), and breast aspirate. These were identified by searching the ‘Requested tests’ free text field for the previously listed terms.

Additional secondary outcomes included the proportion of women prescribed other medications, including topical or intravenous antibiotics, antifungals, lactation suppressants (i.e. cabergoline, bromocriptine), or lactation stimulants (i.e. domperidone).

Patient and public involvement

There was no direct patient or public involvement in this research. The research used an established de-identified general practice dataset.

Covariates

Patient characteristics included age (based on year of birth), remoteness, socio-economic indexes for areas (SEIFA), state/territory, Indigenous status, Commonwealth concession card status and smoking status. Females for whom Indigenous status was recorded as unknown or missing were re-categorised as non-Indigenous, as done in other studies.[21] Remoteness, socio-economic indexes for areas (SEIFA) and state/territory were based on patients' residential postcodes. Remoteness was determined in accordance with the Australian Bureau of Statistics' (ABS) Australian Statistical Geography Standard (ASGS) Remoteness Areas, with 1 being a 'Major City' and 5 a 'Very Remote' area. Due to small population sizes, data for 'Remote' and 'Very Remote' were combined. SEIFA was determined according to the ABS Index of Relative Socio-Economic Advantage and Disadvantage (IRSAD) codes. We also extracted data from the clinical observations dataset to determine which individuals had a temperature recorded on the same day as the clinical encounter and whether the patient was considered febrile or not (temperature >38.5 degrees Celsius).

Statistical analysis

Descriptive statistics (counts and percentages) were used to describe the study population.

The proportion of women who were prescribed medications or ordered selected clinical investigations was calculated based on the year of first clinical encounter for mastitis and

expressed as a percentage, with corresponding 95% confidence intervals. Proportions were calculated separately based on management occurring on the same day as the first documented clinical encounter for mastitis, or on the same day as any clinical encounter for mastitis within the same episode. The proportion of women prescribed antibiotics or who received selected clinical investigations were stratified by calendar year to examine longitudinal trends.

We examined practice-level variation in the proportion of women receiving selected management for mastitis by stratifying proportions based on individual general practices, restricting the comparison to general practices that included data on ≥ 10 patients with mastitis.

We used univariable logistic regression analyses to compare the likelihood of women being prescribed oral antibiotics or receiving various clinical investigations related to mastitis based on individual characteristics. These analyses were undertaken separately according to clinical management at the first encounter, or any clinical encounter within the same mastitis episode.

All analyses were based on two-sided P-values, which statistical define by $p < 0.05$. The statistical analysis was performed using STATA MP 17 (Stata, College Station, Texas), with graphs prepared using R, version 4.3.0 (R Core Team).

RESULTS

A total of 25,002 females aged 18 to 44 years had one or more clinical encounters related to mastitis recorded in this general practice dataset between January 2011 and July 2022, as well as documented evidence of a recent pregnancy.

A greater proportion of women were aged 30-34 (39.3%), were never smokers (54.6%), lived in a major city (65.6%), and had a very high socioeconomic status (27.5%). A small proportion of women held a Commonwealth Concession card (15.6%) or were Aboriginal and/or Torres Strait Islander (2.2%) (**Table 1**). Approximately one quarter (27.8%) of women had a documented temperature at their first encounter, with 5.8% of those with a documented temperature being febrile.

Most (90.1%; $n = 22,523$) women received a prescription for oral antibiotics at their first encounter. With respect to clinical investigations, 5.6% were ordered a breast ultrasound, 3.3% a

blood test, 0.9% a nipple swab culture, and 0.8% breast milk culture (**Table 2**). Only very small numbers were prescribed oral (1.1%) or topical (1.2%) antifungals, topical antibiotics (0.5%), lactation suppressants (1.1%) or lactation stimulants (1.0%). Di/flucloxacillin and cefalexin accounted for >90% of oral antibiotic prescriptions. Only 3,006 (12.0%) women had two or more clinical encounters related to the same mastitis episode. When including clinical management across all clinical encounters, the proportion prescribed oral antibiotics increased only marginally to 90.9%. When considering investigations ordered at any clinical encounter, the largest increase was observed for breast ultrasound, which increased from 5.6% to 7.1% (**Table 2**). Approximately 1 in 10 (12.1%) women prescribed cefalexin had a documented penicillin allergy, whereas 64.4% of women prescribed clindamycin had a documented penicillin allergy.

When stratified by calendar year, the proportion of women prescribed oral antibiotics remained consistent across 2011 to 2022 ($p=0.559$). In contrast, significant increases from 2011 to 2022 were evident with respect to increases in proportions receiving breast ultrasound (3.4% to 8.5%), blood test (2.6% to 5.2%), breast milk culture (0.8% to 1.4%), swab culture (0.5% to 1.7%), and breast aspirate (<0.1% to 0.4%) (**Figure 1, Supplemental Table 1**). The proportion of women prescribed di/flucloxacillin increased from 46.1% in 2011 to 60.4% in 2022, whereas the proportion prescribed cefalexin decreased from 38.6% to 26.5% (**Supplemental Table 2**). From 2011 to 2022, the median treatment duration based on the initial prescription was 6 days, however there was a significant reduction in the proportion issued repeats from 31.5% to 3.0%.

Significant variability was evident with respect to overall clinical management of mastitis according to individual general practices, with the proportion of patients prescribed oral antibiotics ranging from 56.9% to 100% (**Figure 2**). Likewise, variation was seen with breast ultrasound (range: 0% to 40.6%), breast milk culture (0% to 14.7%), swab culture (0% to 9.2%), breast aspirate (0% to 3.8%) and blood test (0% to 31.2%).

Women prescribed oral antibiotics at the first encounter were less likely to receive a breast ultrasound, blood test, and breast aspirate. Similarly, they were less likely to be co-prescribed topical antibiotics, and oral/topical antifungals (**Supplemental Table 3**).

The only consistent factor associated with an increased likelihood of being prescribed oral antibiotics at the first or any encounter was the general practice being located in a regional or remote area, but the absolute differences were small (~1.0%) (**Table 3**). In comparison, factors associated with increased likelihood of breast ultrasound included older age (>30 years), being a current smoker, living in a major city, and higher socioeconomic status (**Supplemental Table 4**). The likelihood of receiving a blood test was increased for those in the youngest (18-24 years) and oldest (40-44 years) age groups, with a concession card (**Supplemental Table 5**). Factors associated with an increased likelihood of a breast milk culture included having a concession card, being a previous or current smoker, and the general practice being located in a regional or remote area (**Supplemental Table 6**). In contrast, the only factor associated with an increased likelihood of receiving a nipple swab culture was the general practice being located in a regional or remote area (**Supplemental Table 7**). In addition, however, the likelihood of receiving a breast milk culture was lower for those with a concession card or who were previous or current smokers. Only lower socioeconomic status was associated with a lower likelihood of breast aspirate (**Supplemental Table 8**), although none were ordered for individuals who identified as Aboriginal and/or Torres Strait Islanders or who were identified as being febrile at the time of the first encounter.

DISCUSSION

Principal findings

Evidence from this large national database indicate that most women presenting to Australian general practice for lactational mastitis are prescribed oral antibiotics, with prescribing practices appearing to largely be in adherence to Australian clinical guidelines. While there has been no change in overall oral antibiotic prescribing rates over the past decade, we observed an increase in prescribing of narrow spectrum antibiotics (i.e. di/flucloxacillin). This, combined with a lower rate of repeat prescriptions orders over time, indicate closer adherence to local guidelines and improved antibiotic stewardship. In addition, there were significant increases in the use of selected clinical investigations as part of mastitis management, including breast ultrasound and milk and nipple swab cultures. This suggests increased awareness of the use of clinical investigations in supporting optimal clinical management of lactational mastitis. The observed

variation in clinical management of lactational mastitis according to patient- and practice-level characteristics warrants further investigation to determine whether there may be further opportunities to improve standardization of clinical care.

Strengths and weaknesses

Study strengths include use of a large high-quality general practice database containing longitudinal individual-level data from 2011 to 2022 that is considered nationally representative. Multiple strategies were used to improve data quality, including restricting the cohort to those with a likely recent pregnancy and the use of different fields for data extraction. Nonetheless, our study has some important limitations. The quality and accuracy of ‘real-world’ data captured through electronic medical records might be affected by clinician behaviour and the type of health information system used in each general practice. For example, differences in recording may exist based on non-mandatory fields, free-text entries and use of system coding vocabularies. It is possible that this may result in possible misclassification and over-reporting or under-reporting of lactational mastitis encounters or associated clinical management. As the study team were only provided access to de-identified data, we were unable to undertake chart reviews to validate our approach for identifying women diagnosed with lactational mastitis. Further, we made the assumption that prescriptions or clinical investigations ordered on the same day as a clinical encounter for mastitis were related to that encounter reason, where they may have been provided for alternative indications. Also, given clinical investigations may have been undertaken to rule out diagnoses of lactational mastitis, it is possible that individuals identified as having clinical investigations may be more likely to have been misclassified as having lactational mastitis. In addition, GPs commonly provide a prescription for antibiotics (or other medications) with directions only to get it dispensed if symptoms don’t improve in the subsequent days (‘delayed prescribing’).[22] The database doesn’t contain information on referrals made to other health care providers or hospitals. In the case of severe mastitis, some clinicians may have opted to direct the patient to a hospital emergency department, rather than provide treatment. While data are recorded at the individual patient level, patient data are not linked across different general practices. Therefore, it is possible that individuals presenting to different general practices with the same symptoms were counted twice. Lastly, MedicineInsight uses a non-

random sampling process to recruit the practices, however, the distribution of the sample has previously been shown to closely resemble figures from the last Australian census.[20]

Comparison to other studies

To our knowledge, this is the first evaluation of clinical management of lactational mastitis in a primary care setting. Most previous studies are limited to small numbers of women with mastitis (often less than 100) and lack contemporary data. In a prospective cohort study, Foxman et al followed 946 women recruited between 1994-1998, of which 77 women developed mastitis.[14] Of these women, 86% were prescribed antibiotics, with the most common being cefalexin (46%), followed by amoxicillin (7%), ampicillin (7%), and amoxicillin and clavulanic acid (7%). No cultures were performed for any women and no data were reported for ultrasound or blood tests. A more recent study from Scott et al followed 420 breastfeeding women recruited between 2004 and 2005 in Scotland, with 74 developing mastitis.[19] Among those women with mastitis, 78% were prescribed antibiotics, with the most common being flucloxacillin (30%), followed by amoxicillin (17%), erythromycin (7%), and amoxicillin and clavulanic acid (7%). Notably, 33% couldn't remember what antibiotic they were prescribed. The largest study evaluated data from almost 80,000 women recruited to the Norwegian Mother, Father and Child Cohort Study between 1999 to 2008.[3] Among the 15,014 who reported experiencing mastitis, 5,524 (36.8%) reported using antibiotics. Of those who could remember which antibiotic they received, the most common antibiotics included penicillins (83.8%), followed by macrolides (15.2%) and cephalosporins (2.6%).

Implications

While the observed proportion of antibiotic prescribing are very high, it is not possible to determine the appropriateness of prescribing practices based on available data. It is possible that women presenting to general practice with mastitis symptoms may represent those with more severe disease, corresponding to high rates of treatment. Further, it is likely that not all prescriptions for antibiotics were dispensed, and even when dispensed, not all antibiotics were commenced.[23] Also, it is possible that GPs are issuing prescriptions (or repeats) to women to be dispensed only if symptoms do not improve, representing delayed prescribing. However, the role of delayed prescribing in the context of antimicrobial stewardship for mastitis has not been evaluated and requires further investigation. Further, there was much larger observed variation in

antibiotic prescribing practices at the practice-level compared with patient-level characteristics and this warrants further exploration as to underlying causes.

Increasing rates of ordering of clinical investigations over the decade suggests increased awareness of the potential value of such investigations in the diagnosis and/or management of mastitis. The observed higher frequency of ultrasound in older women and current smokers suggest ultrasounds may be being used to rule out differential diagnoses.[24,25] However, lower rates of ultrasound in those of lower socioeconomic status raises questions about potential equity issues and whether access or affordability negatively impacts uptake. A similar picture emerged for other investigations such as breast aspirate, breast milk culture, and nipple swab culture which were lower in those with lower socioeconomic status or a concession card. The lower rate of ultrasounds in those visiting a general practice located in remote or regional areas may be reflective of access difficulties, however, this is contrasted with higher rates of milk and swab cultures in these areas. Higher culture rates in rural settings may reflect observed higher rates of antimicrobial resistance, including Methicillin resistant *S. aureus* (MRSA) in these settings.[26] Similar to antibiotic prescribing practices, the large variation in frequency of clinical investigations warrants further examination, particularly appropriateness of these investigations and their impact on mastitis management.

Lactational mastitis has frequently been considered to be a topic that has not received the attention it deserves.[27] Research is needed to determine when antibiotics are needed for mastitis; which are the most appropriate antibiotic and what is the most appropriate duration. Clinical guidelines for management of mastitis have changed little over the last couple of decades, and GPs are assumed to be familiar with managing this common problem. It is timely to recommend an education program to alert clinicians that prescribing antibiotics for mastitis is not always straightforward: it should not be assumed that all lactating women with inflammatory breast symptoms require antibiotic treatment, and the potential need for breast milk culture should be considered. Breast milk culture may be appropriate at first presentation in locations with high rates of MRSA or in mothers with known antibiotic allergies, and should be ordered if the condition is not responding to first line antibiotics within 48 hours.[8]

CONCLUSION

Australian GPs commonly prescribe oral antibiotics for women with mastitis and largely in line with clinical guidelines. Over the last decade, GPs have increased prescriptions for narrow spectrum antibiotics indicating closer adherence to local guidelines and improved antibiotic stewardship. Their use of clinical investigations as part of mastitis management has increased over the last decade but there may be the opportunity for increased use of breast milk culture to understand and manage local bacterial sensitivities.

Author contributions

All authors made significant contributions to the manuscript and are responsible for its content. LEG, SBC, MC and LHA conceived the idea, obtained grant funding and planned this study. LEG and AK were responsible for data extraction and analysis. LEG, SBC, MC and LHA were responsible for interpretation of study findings, while LEG and AK were responsible for presenting the results. LEG wrote the first draft and all authors contributed to the manuscript refinement. All authors have read and approved the final manuscript.

Data Sharing Statement

Data may be obtained from MedicineInsight and are not publicly available. Third parties may express an interest in the information collected through MedicineInsight. The provision of information in these instances undergoes a formal approval process and is guided by the MedicineInsight independent external Data Governance Committee. This Committee includes general practitioners, consumer advocates, privacy experts and researchers.

Ethics statements

Patient consent for publication

Not required.

Ethics approval

The independent MedicineInsight Data Governance Committee approved the study (protocol 2019-003) and the Human Research Ethics Committee of the University of Adelaide exempted it from ethical review due to the use of non-identifiable data.

Acknowledgments

The authors would like to thank NPS MedicineWise for their support in the development of this research.

Figure legends:

Figure 1. Longitudinal trends in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations, Australia 2011 to 2022

Figure 2. Variation in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations according to each individual general practice, Australia 2011 to 2022. Each circle corresponds to an individual site.

References

1. Cooney F, Petty-Saphon N. The burden of severe lactational mastitis in Ireland from 2006 to 2015. *Ir Med J* 2019; 112(1): 855.
2. De Groot N, Birnie E, Vermolen JH, et al. The prevalence of adverse postnatal outcomes for mother and infant in the Netherlands. *PloS One* 2018; 13(9): e0202960.
3. Grzeskowiak LE, Saha MR, Ingman WV, et al. Incidence, antibiotic treatment and outcomes of lactational mastitis: findings from the Norwegian mother, father and child cohort study (MoBa). *Paediatr Perinat Epidemiol* 2022; 36(2): 254-63.
4. Wilson E, Woodd SL, Benova L. Incidence of and risk factors for lactational mastitis: a systematic review. *J Hum Lact* 2020; 36(4): 673-86.
5. Cullinane M, Amir LH, Donath SM, et al. Determinants of mastitis in women in the CASTLE study: a cohort study. *BMC Fam Pract* 2015; 16: 181.
6. Scott DM. Inflammatory diseases of the breast. *Best Pract Res Clin Obstet Gynaecol* 2022; 83: 72-87.
7. Bhatt AA, Woodard GA, Lee CU, Hesley GK. Urgent and emergent breast lesions—a primer for the general radiologist, on-call resident and sonographer. *Australas J Ultrasound Med* 2022; 25(2): 54-65.
8. Mitchell KB, Johnson HM, Rodríguez JM, et al. Academy of Breastfeeding Medicine Clinical Protocol# 36: the mastitis spectrum, revised 2022. *Breastfeed Med* 2022; 17(5): 360-76.
9. Therapeutic Guidelines: Antibiotic: eTG complete. In: Lactational mastitis. 2020.
10. Rimoldi SG, Pileri P, Mazzocco MI, et al. The role of *Staphylococcus aureus* in mastitis: A multidisciplinary working group experience. *J Hum Lact* 2020; 36(3): 503-9.
11. Wheaton N, Al-Abdullah A, Haertlein T. Postdelivery emergencies. *Emerg Med Clin North Am* 2019; 37(2): 287-300.
12. Fetherston CM, Wells JI, Hartmann PE. Severity of mastitis symptoms as a predictor of C-reactive protein in milk and blood during lactation. *Breastfeed Med* 2006; 1(3): 127-35.
13. Petel D, Winters N, Gore GC, et al. Use of C-reactive protein to tailor antibiotic use: a systematic review and meta-analysis. *BMJ Open* 2018; 8(12): e022133.
14. Foxman B, D'Arcy H, Gillespie B, et al. Lactation mastitis: occurrence and medical management among 946 breastfeeding women in the United States. *Am J Epidemiol* 2002; 155(2): 103-14.
15. Fetherston C. Characteristics of lactation mastitis in a Western Australian cohort. *Breastfeed Rev* 1997; 5(2): 5-11.
16. Kinlay JR, O'Connell DL, Kinlay S. Incidence of mastitis in breastfeeding women during the six months after delivery: a prospective cohort study. *Med J Aust* 1998; 169(6): 310-2.
17. Jonsson S, Pulkkinen M. Mastitis today: incidence, prevention and treatment. *Ann Chir Gynaecol Suppl* 1994; (83): 84-7.
18. Lin C-H, Yang P-R, Lee C-P, et al. Descriptive study of mastitis in postpartum women in Taiwan: incidence and related factors. *J Womens Health (Larchmt)* 2023; 32(5): 616-22.
19. Scott JA, Robertson M, Fitzpatrick J, et al. Occurrence of lactational mastitis and medical management: a prospective cohort study in Glasgow. *Int Breastfeed J* 2008; 3: 21.
20. Busingye D, Gianacas C, Pollack A, et al. Data Resource Profile: MedicineInsight, an Australian national primary health care database. *Int J Epidemiol* 2019; 48(6): 1741-h.

21. Gilbert E, Rumbold A, Campbell S, et al. Management of encounters related to subfertility and infertility among Aboriginal and Torres Strait Islander females in Australian general practice. BMC Women's Health 2023; 23: 410.

22. Thursky KA, Hardefeldt LY, Rajkhowa A, et al. Antimicrobial stewardship in Australia: The role of qualitative research in programme development. JAC Antimicrob Resist 2021; 3(4): dlab166.

23. Ito S, Koren G, Einarson TR. Maternal noncompliance with antibiotics during breastfeeding. Ann Pharmacother 1993; 27(1): 40-2.

24. Moore DA, Bracewell SL, Smith EB, Jordan SG. A new search pattern for emergency breast exams: the clinical picture. Emerg Radiol 2021; 29: 207-13.

25. Porembka JH, Compton L, Omar L, et al. Breast ultrasound utilization in a safety net emergency department. Emerg Radiol 2019; 26: 123-31.

26. Cameron JK, Hall L, Tong SY, et al. Incidence of community onset MRSA in Australia: least reported where it is Most prevalent. Antimicrob Resist Infect Control 2019; 8: 33.

27. Amir LH, Ingram J. Health professionals' advice for breastfeeding problems: Not good enough! Int Breastfeed J 2008; 3: 22.

Table 1. Characteristics of 25,002 women presenting to Australian General Practice between 2011 and 2022 for Lactational Mastitis

	N (%)
Year	
2011-2012	3448 (13.8%)
2013-2014	4135 (16.5%)
2015-2016	4633 (18.5%)
2017-2018	4657 (18.6%)
2019-2020	4723 (18.9%)
2021-2022	3406 (13.6%)
Age group	
18-24	1991 (8.0%)
25-29	5830 (23.3%)
30-34	9821 (39.3%)
35-39	5900 (23.6%)
40-44	1460 (5.8%)
Concession status	
No Concession	21111 (84.4%)
Concession Card	3891 (15.6%)
Smoking status	
Never Smoker	13653 (54.6%)
Ex Smoker	8675 (34.7%)
Current Smoker	808 (3.2%)
Missing	1866 (7.5%)
Patient SES	
Very Low	3139 (12.6%)
Low	4215 (16.9%)
Middle	5143 (20.6%)
High	5533 (22.1%)
Very High	6872 (27.5%)
Missing	100 (0.4%)
Indigenous status	
Aboriginal and/or TSI	547 (2.2%)
Neither Aboriginal or TSI	24455 (97.8%)
Fever	
No	6551 (26.2%)
Yes	401 (1.6%)
Not recorded	18050 (72.2%)
Remoteness of general practice	
Major city	16397 (65.6%)
Inner regional	8162 (32.6%)
Remote & very remote	339 (1.4%)
Missing	104 (0.4%)

SES, socioeconomic status; TSI, Torres Strait Islander

Table 2. Selected clinical investigations and medications prescribed during the first or any encounter within the same episode of treatment for lactational mastitis in women attending general practice, Australia 2011 to 2022

	First encounter	Any encounter*
Clinical investigations		
Breast ultrasound	1 393 (5.6%)	1 771 (7.1%)
Milk culture	195 (0.8%)	235 (0.9%)
Nipple swab culture	237 (0.9%)	283 (1.1%)
Breast aspirate	37 (0.1%)	64 (0.3%)
Blood test	835 (3.3%)	962 (3.8%)
FBE	823 (3.3%)	947 (3.8%)
CRP	278 (1.1%)	350 (1.4%)
ESR	179 (0.7%)	212 (0.8%)
Medication prescriptions		
Antibiotics		
Oral	22 523 (90.1%)	22 739 (90.9%)
Di/flucloxacillin	12 477 (49.9%)	12 794 (51.2%)
Cefalexin	8 223 (32.9%)	8 501 (34.0%)
Amoxicillin	754 (3.0%)	772 (3.1%)
Amoxicillin clavulanate	594 (2.4%)	664 (2.7%)
Clindamycin	315 (1.3%)	354 (1.4%)
Erythromycin	289 (1.2%)	308 (1.2%)
Other	174 (0.7%)	215 (0.9%)
Intravenous	20 (0.1%)	32 (0.1%)
Topical	125 (0.5%)	149 (0.6%)
Antifungals		
Oral	275 (1.1%)	326 (1.3%)
Topical	303 (1.2%)	349 (1.4%)
Other medications		
Lactation suppressants	270 (1.1%)	310 (1.2%)
Lactation stimulants	256 (1.0%)	295 (1.2%)

*at any encounter for mastitis, including additional encounter occurring within two-week period of a previous mastitis encounter

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FBE: Full blood examination;

Table 3. Proportion of women attending general practice who were prescribed oral antibiotics during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	88.6 (87.2, 90.0)	0.89 (0.75, 1.04)	89.4 (88.0, 90.7)	0.88 (0.74, 1.03)
25-29	89.8 (89.0, 90.6)	Reference	90.6 (89.8, 91.3)	Reference
30-34	90.3 (89.7, 90.8)	1.05 (0.94, 1.17)	91.2 (90.7, 91.8)	1.08 (0.96, 1.21)
35-39	90.4 (89.6, 91.1)	1.07 (0.95, 1.21)	91.3 (90.5, 92.0)	1.08 (0.95, 1.23)
40-44	90.6 (89.0, 92.1)	1.10 (0.90, 1.33)	91.3 (89.7, 92.7)	1.09 (0.89, 1.33)
Concession status				
No concession	90.3 (89.8, 90.7)	Reference	91.2 (90.8, 91.5)	Reference
Concession holder	89.2 (88.1, 90.1)	0.89 (0.79, 0.99)	89.8 (88.8, 90.7)	0.85 (0.76, 0.95)
Smoking status				
Current smoker	90.7 (88.5, 92.6)	1.12 (0.88, 1.43)	91.1 (88.9, 93.0)	1.05 (0.82, 1.35)
Ex-smoker	91.4 (90.8, 92.0)	1.22 (1.11, 1.34)	92.1 (91.5, 92.7)	1.20 (1.09, 1.32)
Never smoker	89.7 (89.2, 90.2)	Reference	90.7 (90.2, 91.1)	Reference
Patient SES				
Very low	90.5 (89.4, 91.5)	1.04 (0.90, 1.20)	91.0 (89.9, 91.9)	0.99 (0.85, 1.15)
Low	89.4 (88.5, 90.3)	0.93 (0.82, 1.05)	90.5 (89.6, 91.4)	0.93 (0.82, 1.07)
Middle	90.3 (89.4, 91.1)	1.02 (0.90, 1.15)	91.2 (90.3, 91.9)	1.01 (0.89, 1.15)
High	90.3 (89.5, 91.0)	1.02 (0.90, 1.14)	91.2 (90.4, 91.9)	1.01 (0.90, 1.15)
Very high	90.1 (89.4, 90.8)	Reference	91.1 (90.4, 91.7)	Reference
Indigenous status				
Aboriginal and/or TSI	89.0 (86.1, 91.5)	0.89 (0.68, 1.17)	89.6 (86.7, 92.0)	0.85 (0.65, 1.13)
Neither Aboriginal or TSI	90.1 (89.7, 90.5)	Reference	91.0 (90.6, 91.3)	Reference
Fever				
No	94.1 (93.5, 94.6)	Reference	94.6 (94.1, 95.2)	Reference
Yes	92.8 (89.8, 95.1)	0.81 (0.55, 1.19)	94.3 (91.5, 96.3)	0.93 (0.60, 1.44)
Not Documented	88.6 (88.1, 89.0)	0.49 (0.44, 0.55)	89.5 (89.1, 90.0)	0.49 (0.43, 0.55)
Remoteness of general practice				
Major city	89.7 (89.2, 90.2)	Reference	90.6 (90.2, 91.1)	Reference
Inner/Outer regional	90.8 (90.0, 91.5)	1.13 (1.02, 1.26)	91.6 (90.8, 92.3)	1.12 (1.00, 1.25)
Remote/Very remote	91.2 (90.1, 92.1)	1.19 (1.04, 1.36)	91.7 (90.7, 92.7)	1.15 (1.00, 1.32)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

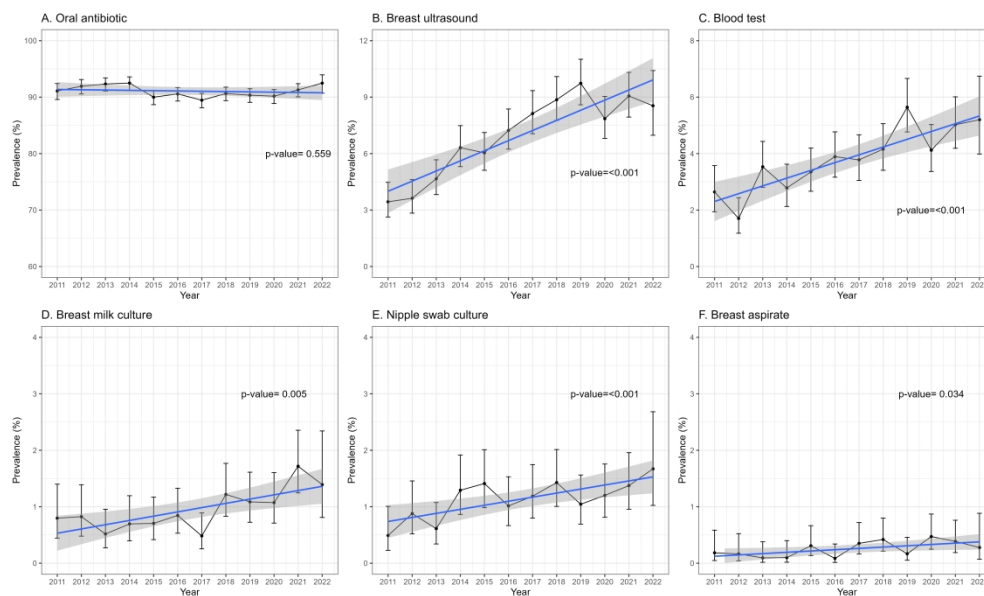


Figure 1. Longitudinal trends in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations, Australia 2011 to 2022

1291x774mm (118 x 118 DPI)

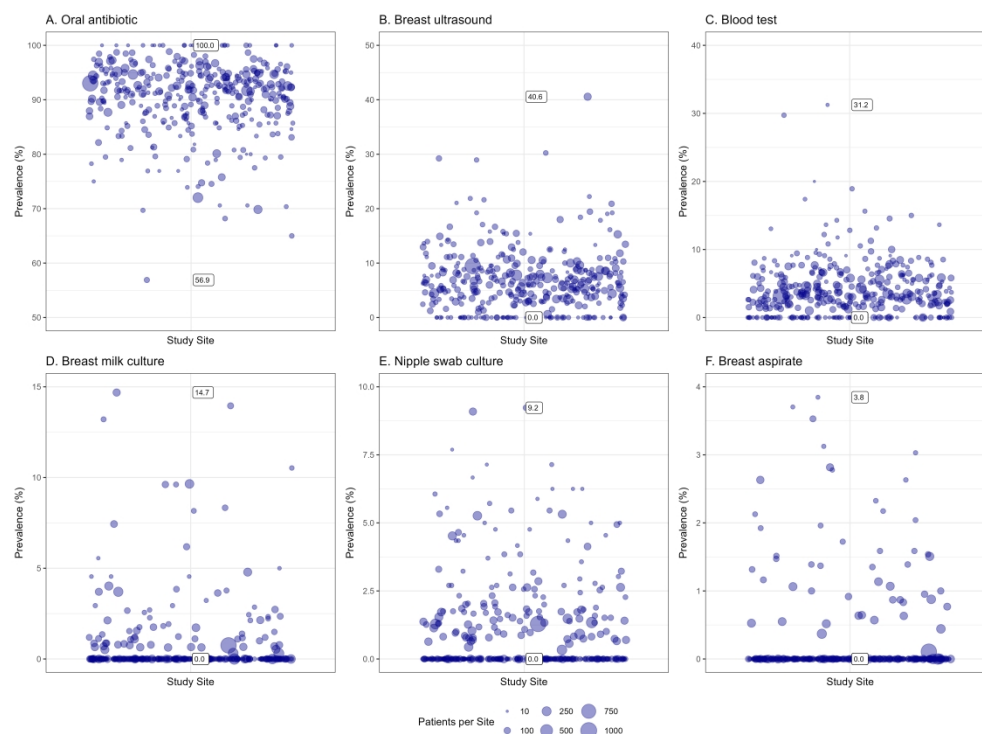


Figure 2. Variation in proportion of women attending general practice for lactational mastitis who are prescribed oral antibiotics or receive selected clinical investigations according to each individual general practice, Australia 2011 to 2022

1035x776mm (157 x 157 DPI)

Supplemental Table 1. Clinical management of in women attending general practice during the first or any encounter within the same treatment episode for lactational mastitis according to calendar year, Australia 2011 to 2022

		2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022†	Total
N		1 628	1 820	2 123	2 012	2 268	2 365	2 276	2 381	2 393	2 330	2 329	1 077	25 002
Oral antibiotic														
	First	1 465 (90.0%)	1 652 (90.8%)	1 942 (91.5%)	1 850 (92.0%)	2 028 (89.4%)	2 130 (90.1%)	2 011 (88.4%)	2 133 (89.6%)	2 143 (89.6%)	2 079 (89.2%)	2 103 (90.3%)	987 (91.6%)	22 523 (90.1%)
	Any	1 483 (91.1%)	1 673 (91.9%)	1 960 (92.3%)	1 861 (92.5%)	2 041 (90.0%)	2 142 (90.6%)	2 036 (89.5%)	2 158 (90.6%)	2 162 (90.3%)	2 101 (90.2%)	2 126 (91.3%)	996 (92.5%)	22 739 (90.9%)
Breast ultrasound														
	First	45 (2.8%)	45 (2.5%)	76 (3.6%)	107 (5.3%)	103 (4.5%)	139 (5.9%)	147 (6.5%)	159 (6.7%)	196 (8.2%)	132 (5.7%)	169 (7.3%)	75 (7.0%)	1393 (5.6%)
	Any	56 (3.4%)	66 (3.6%)	99 (4.7%)	127 (6.3%)	137 (6.0%)	171 (7.2%)	185 (8.1%)	211 (8.9%)	233 (9.7%)	183 (7.9%)	211 (9.1%)	92 (8.5%)	1771 (7.1%)
Breast milk culture														
	First	11 (0.7%)	11 (0.6%)	10 (0.5%)	8 (0.4%)	13 (0.6%)	18 (0.8%)	10 (0.4%)	26 (1.1%)	25 (1.0%)	21 (0.9%)	31 (1.3%)	11 (1.0%)	195 (0.8%)
	Any	13 (0.8%)	15 (0.8%)	11 (0.5%)	14 (0.7%)	16 (0.7%)	20 (0.8%)	11 (0.5%)	29 (1.2%)	26 (1.1%)	25 (1.1%)	40 (1.7%)	15 (1.4%)	235 (0.9%)
Nipple swab culture														
	First	8 (0.5%)	13 (0.7%)	13 (0.6%)	24 (1.2%)	26 (1.1%)	17 (0.7%)	23 (1.0%)	30 (1.3%)	18 (0.8%)	22 (0.9%)	26 (1.1%)	17 (1.6%)	237 (0.9%)
	Any	8 (0.5%)	16 (0.9%)	13 (0.6%)	26 (1.3%)	32 (1.4%)	24 (1.0%)	27 (1.2%)	34 (1.4%)	25 (1.0%)	28 (1.2%)	32 (1.4%)	18 (1.7%)	283 (1.1%)
Blood test‡														
	First	41 (2.5%)	27 (1.5%)	64 (3.0%)	49 (2.4%)	62 (2.7%)	84 (3.6%)	69 (3.0%)	88 (3.7%)	117 (4.9%)	82 (3.5%)	104 (4.5%)	48 (4.5%)	835 (3.3%)
	Any	43 (2.6%)	31 (1.7%)	75 (3.5%)	56 (2.8%)	76 (3.4%)	92 (3.9%)	86 (3.8%)	99 (4.2%)	135 (5.6%)	96 (4.1%)	117 (5.0%)	56 (5.2%)	962 (3.8%)
Breast aspirate														
	First	NR	NR	NR	NR	NR	NR	5 (0.2%)	9 (0.4%)	NR	6 (0.3%)	5 (0.2%)	NR	37 (0.1%)
	Any	NR	NR	NR	NR	7 (0.3%)	NR	8 (0.4%)	10 (0.4%)	NR	11 (0.5%)	9 (0.4%)	NR	64 (0.3%)

NR, not reportable due to small cell size
† 2022 calendar year includes January to July data only
‡ Includes ordering of full blood count, c-reactive protein, or erythrocyte sedimentation rate

Supplemental Table 2. The proportion of women attending general practice who were prescribed oral antibiotics during the first or any encounter within the same treatment episode for lactational mastitis according to antibiotic type and calendar year, Australia 2011 to 2022

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022†
N	1 628	1 820	2 123	2 012	2 268	2 365	2 276	2 381	2 393	2 330	2 329	1 077
Di/flucloxacillin												
First	719 (44.2%)	816 (44.8%)	981 (46.2%)	922 (45.8%)	1038 (45.8%)	1142 (48.3%)	1098 (48.2%)	1273 (53.5%)	1244 (52.0%)	1263 (54.2%)	1340 (57.5%)	641 (59.5%)
Any*	751 (46.1%)	830 (45.6%)	1010 (47.6%)	945 (47.0%)	1068 (47.1%)	1172 (49.6%)	1130 (49.6%)	1310 (55.0%)	1264 (52.8%)	1292 (55.5%)	1371 (58.9%)	651 (60.4%)
Cefalexin												
First	607 (37.3%)	678 (37.3%)	775 (36.5%)	765 (38.0%)	780 (34.4%)	825 (34.9%)	737 (32.4%)	690 (29.0%)	782 (32.7%)	684 (29.4%)	626 (26.9%)	274 (25.4%)
Any*	629 (38.6%)	704 (38.7%)	800 (37.7%)	780 (38.8%)	804 (35.4%)	850 (35.9%)	765 (33.6%)	714 (30.0%)	805 (33.6%)	713 (30.6%)	652 (28.0%)	285 (26.5%)
Amoxicillin												
First	65 (4.0%)	93 (5.1%)	84 (4.0%)	57 (2.8%)	95 (4.2%)	75 (3.2%)	72 (3.2%)	59 (2.5%)	40 (1.7%)	38 (1.6%)	53 (2.3%)	23 (2.1%)
Any*	68 (4.2%)	94 (5.2%)	86 (4.1%)	59 (2.9%)	96 (4.2%)	77 (3.3%)	74 (3.3%)	62 (2.6%)	40 (1.7%)	38 (1.6%)	55 (2.4%)	23 (2.1%)
Amoxicillin and clavulanate												
First	28 (1.7%)	27 (1.5%)	63 (3.0%)	48 (2.4%)	48 (2.1%)	54 (2.3%)	64 (2.8%)	72 (3.0%)	71 (3.0%)	43 (1.8%)	48 (2.1%)	28 (2.6%)
Any*	29 (1.8%)	32 (1.8%)	69 (3.3%)	54 (2.7%)	59 (2.6%)	63 (2.7%)	71 (3.1%)	81 (3.4%)	74 (3.1%)	48 (2.1%)	53 (2.3%)	31 (2.9%)
Erythromycin												
First	22 (1.4%)	27 (1.5%)	34 (1.6%)	43 (2.1%)	34 (1.5%)	34 (1.4%)	23 (1.0%)	22 (0.9%)	21 (0.9%)	17 (0.7%)	5 (0.2%)	7 (0.6%)
Any*	23 (1.4%)	30 (1.6%)	39 (1.8%)	44 (2.2%)	35 (1.5%)	35 (1.5%)	26 (1.1%)	24 (1.0%)	23 (1.0%)	17 (0.7%)	5 (0.2%)	7 (0.6%)
Clindamycin												
First	21 (1.3%)	20 (1.1%)	20 (0.9%)	22 (1.1%)	34 (1.5%)	23 (1.0%)	28 (1.2%)	28 (1.2%)	26 (1.1%)	43 (1.8%)	32 (1.4%)	18 (1.7%)
Any*	22 (1.4%)	22 (1.2%)	23 (1.1%)	23 (1.1%)	39 (1.7%)	28 (1.2%)	32 (1.4%)	30 (1.3%)	28 (1.2%)	49 (2.1%)	38 (1.6%)	20 (1.9%)
Other												
First	20 (1.2%)	17 (0.9%)	19 (0.9%)	20 (1.0%)	19 (0.8%)	11 (0.5%)	15 (0.7%)	8 (0.3%)	14 (0.6%)	11 (0.5%)	13 (0.6%)	7 (0.6%)
Any*	22 (1.4%)	25 (1.4%)	25 (1.2%)	23 (1.1%)	22 (1.0%)	14 (0.6%)	16 (0.7%)	12 (0.5%)	19 (0.8%)	15 (0.6%)	15 (0.6%)	7 (0.6%)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

† 2022 calendar year includes January to July data only

Supplemental Table 3. The proportion of women attending general practice for lactational mastitis who received selected clinical investigations or prescribed medications according to whether or not they were prescribed oral antibiotics during the same encounter, Australia 2011 to 2022

	Antibiotics prescribed at first encounter		p-value
	No (N = 2 479)	Yes (N = 22 523)	
Clinical Investigations			
Breast ultrasound	174 (7.0%)	1 219 (5.4%)	<0.001
Breast milk culture	26 (1.0%)	169 (0.8%)	0.109
Nipple swab culture	28 (1.1%)	209 (0.9%)	0.326
Blood Test	109 (4.4%)	726 (3.2%)	0.002
Breast Aspirate	8 (0.3%)	29 (0.1%)	0.017
Medication Prescriptions			
Antibiotics			
Topical	25 (1.0%)	100 (0.4%)	<0.001
Intravenous	8 (0.3%)	12 (0.1%)	<0.001
Antifungals			
Oral	97 (3.9%)	178 (0.8%)	<0.001
Topical	53 (2.1%)	250 (1.1%)	<0.001
Other Medications			
Lactation Suppressant	26 (1.0%)	244 (1.1%)	0.875
Lactation Stimulant	30 (1.2%)	226 (1.0%)	0.332

Supplemental Table 4. Proportion of women attending general practice who received a breast ultrasound during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	4.4 (3.6, 5.4)	0.97 (0.76, 1.25)	5.2 (4.3, 6.3)	0.88 (0.71, 1.11)
25-29	4.5 (4.0, 5.1)	Reference	5.9 (5.3, 6.5)	Reference
30-34	5.6 (5.2, 6.1)	1.25 (1.08, 1.46)	7.2 (6.7, 7.7)	1.24 (1.08, 1.41)
35-39	6.5 (5.9, 7.1)	1.46 (1.24, 1.71)	8.2 (7.5, 8.9)	1.43 (1.24, 1.65)
40-44	7.4 (6.1, 8.9)	1.68 (1.34, 2.12)	9.5 (8.1, 11.1)	1.69 (1.37, 2.07)
Concession status				
No concession	5.5 (5.2, 5.8)	Reference	7.1 (6.8, 7.5)	Reference
Concession holder	5.8 (5.1, 6.6)	1.05 (0.91, 1.22)	6.8 (6.1, 7.7)	0.96 (0.84, 1.09)
Smoking status				
Current smoker	7.9 (6.2, 10.0)	1.44 (1.11, 1.88)	9.4 (7.5, 11.6)	1.30 (1.02, 1.66)
Ex-smoker	5.2 (4.7, 5.7)	0.91 (0.81, 1.03)	6.3 (5.8, 6.8)	0.84 (0.76, 0.94)
Never smoker	5.6 (5.3, 6.0)	Reference	7.4 (7.0, 7.8)	Reference
Patient SES				
Very low	5.2 (4.5, 6.1)	0.91 (0.75, 1.09)	6.3 (5.5, 7.2)	0.82 (0.69, 0.97)
Low	5.3 (4.6, 6.0)	0.92 (0.78, 1.09)	6.6 (5.9, 7.4)	0.87 (0.74, 1.01)
Middle	5.3 (4.7, 6.0)	0.93 (0.79, 1.08)	6.7 (6.0, 7.4)	0.87 (0.76, 1.01)
High	6.0 (5.4, 6.6)	1.05 (0.90, 1.22)	7.6 (6.9, 8.3)	1.00 (0.88, 1.15)
Very high	5.7 (5.2, 6.3)	Reference	7.6 (7.0, 8.2)	Reference
Indigenous status				
Aboriginal and/or TSI	5.7 (3.9, 7.9)	1.02 (0.71, 1.47)	6.6 (4.7, 9.0)	0.92 (0.66, 1.30)
Neither Aboriginal or TSI	5.6 (5.3, 5.9)	Reference	7.1 (6.8, 7.4)	Reference
Fever				
No	6.5 (5.9, 7.1)	Reference	8.3 (7.6, 9.0)	Reference
Yes	3.0 (1.6, 5.2)	0.45 (0.25, 0.80)	5.5 (3.5, 8.2)	0.64 (0.41, 1.00)
Not Documented	5.3 (5.0, 5.6)	0.81 (0.72, 0.91)	6.7 (6.3, 7.1)	0.79 (0.71, 0.88)
Remoteness of general practice				
Major City	5.7 (5.4, 6.1)	Reference	7.4 (7.0, 7.8)	Reference
Inner/Outer Regional	5.0 (4.5, 5.7)	0.87 (0.75, 1.00)	6.4 (5.8, 7.1)	0.86 (0.76, 0.97)
Remote/Very Remote	5.5 (4.7, 6.3)	0.95 (0.80, 1.12)	6.5 (5.6, 7.4)	0.87 (0.75, 1.01)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 5. Proportion of women attending general practice who received a blood test (FBE, CRP, or ESR) during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	4.0 (3.2, 4.9)	1.30 (1.00, 1.71)	4.6 (3.7, 5.6)	1.30 (1.01, 1.67)
25-29	3.1 (2.6, 3.5)	Reference	3.6 (3.1, 4.1)	Reference
30-34	3.4 (3.0, 3.7)	1.10 (0.92, 1.32)	3.8 (3.4, 4.2)	1.06 (0.89, 1.26)
35-39	3.2 (2.8, 3.7)	1.04 (0.84, 1.28)	3.7 (3.2, 4.2)	1.02 (0.84, 1.23)
40-44	4.0 (3.0, 5.1)	1.31 (0.97, 1.77)	4.7 (3.7, 5.9)	1.33 (1.01, 1.75)
Concession status				
No concession	3.2 (2.9, 3.4)	Reference	3.7 (3.4, 3.9)	Reference
Concession holder	4.3 (3.7, 5.0)	1.37 (1.15, 1.63)	4.8 (4.1, 5.5)	1.31 (1.11, 1.54)
Smoking status				
Current Smoker	4.0 (2.7, 5.5)	1.21 (0.84, 1.74)	4.5 (3.1, 6.1)	1.14 (0.81, 1.61)
Ex Smoker	3.4 (3.0, 3.8)	1.02 (0.88, 1.18)	3.7 (3.3, 4.1)	0.93 (0.81, 1.07)
Never Smoker	3.3 (3.0, 3.6)	Reference	3.9 (3.6, 4.3)	Reference
Patient SES				
Very Low	3.5 (2.9, 4.2)	1.07 (0.85, 1.35)	3.8 (3.1, 4.5)	0.99 (0.79, 1.23)
Low	3.5 (3.0, 4.1)	1.08 (0.88, 1.34)	4.2 (3.6, 4.9)	1.11 (0.92, 1.35)
Middle	3.4 (2.9, 4.0)	1.05 (0.86, 1.28)	3.8 (3.3, 4.4)	1.00 (0.83, 1.21)
High	3.1 (2.7, 3.6)	0.95 (0.78, 1.17)	3.7 (3.2, 4.2)	0.97 (0.81, 1.17)
Very High	3.3 (2.9, 3.7)	Reference	3.8 (3.4, 4.3)	Reference
Indigenous status				
Aboriginal and/or TSI	4.6 (3.0, 6.7)	1.40 (0.93, 2.10)	5.1 (3.4, 7.3)	1.36 (0.92, 2.00)
Neither	3.3 (3.1, 3.5)	Reference	3.8 (3.6, 4.1)	Reference
Fever				
No	3.9 (3.5, 4.4)	Reference	4.5 (4.0, 5.0)	Reference
Yes	2.5 (1.2, 4.5)	0.63 (0.33, 1.19)	3.0 (1.6, 5.2)	0.66 (0.37, 1.18)
Not Documented	3.2 (2.9, 3.4)	0.80 (0.69, 0.93)	3.6 (3.4, 3.9)	0.81 (0.70, 0.93)
Remoteness of general practice				
Major City	3.4 (3.1, 3.7)	Reference	3.9 (3.7, 4.3)	Reference
Inner/Outer	3.1 (2.6, 3.6)	0.90 (0.75, 1.08)	3.6 (3.1, 4.2)	0.91 (0.77, 1.07)
Regional				
Remote/Very	3.2 (2.6, 3.9)	0.95 (0.76, 1.17)	3.6 (3.0, 4.3)	0.92 (0.75, 1.12)
Remote				

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter
Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 6. Proportion of women attending general practice who received a breast milk culture during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.8 (0.5, 1.3)	0.78 (0.45, 1.36)	1.0 (0.6, 1.5)	0.83 (0.51, 1.38)
25-29	1.0 (0.8, 1.3)	Reference	1.2 (0.9, 1.5)	Reference
30-34	0.9 (0.8, 1.1)	0.91 (0.66, 1.26)	1.1 (0.9, 1.3)	0.91 (0.67, 1.23)
35-39	0.8 (0.6, 1.1)	0.77 (0.53, 1.13)	1.0 (0.8, 1.3)	0.85 (0.60, 1.20)
40-44	1.5 (0.9, 2.3)	1.47 (0.90, 2.41)	1.8 (1.2, 2.6)	1.49 (0.95, 2.35)
Concession status				
No concession	1.0 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Concession holder	0.9 (0.6, 1.2)	0.91 (0.63, 1.31)	1.1 (0.8, 1.4)	0.92 (0.66, 1.28)
Smoking Status				
Current Smoker	1.4 (0.7, 2.4)	1.41 (0.76, 2.63)	1.4 (0.7, 2.4)	1.15 (0.62, 2.13)
Ex Smoker	0.9 (0.7, 1.1)	0.89 (0.67, 1.19)	1.0 (0.8, 1.2)	0.83 (0.64, 1.08)
Never Smoker	1.0 (0.8, 1.1)	Reference	1.2 (1.0, 1.4)	Reference
Patient SES				
Very Low	1.0 (0.7, 1.4)	0.90 (0.59, 1.36)	1.3 (0.9, 1.8)	1.03 (0.71, 1.50)
Low	0.7 (0.5, 1.0)	0.62 (0.41, 0.95)	0.8 (0.6, 1.2)	0.65 (0.44, 0.97)
Middle	0.8 (0.6, 1.1)	0.72 (0.49, 1.05)	1.1 (0.8, 1.4)	0.86 (0.61, 1.20)
High	0.9 (0.7, 1.2)	0.83 (0.58, 1.18)	1.1 (0.8, 1.4)	0.87 (0.63, 1.21)
Very High	1.1 (0.9, 1.4)	Reference	1.3 (1.0, 1.6)	Reference
Indigenous Status				
Aboriginal and/or TSI	0.9 (0.3, 2.1)	0.96 (0.40, 2.35)	0.9 (0.3, 2.1)	0.80 (0.33, 1.95)
Neither Aboriginal or TSI	0.9 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Fever				
No	1.1 (0.9, 1.4)	Reference	1.3 (1.1, 1.6)	Reference
Yes	0.2 (0.0, 1.4)	0.22 (0.03, 1.60)	0.5 (0.1, 1.8)	0.37 (0.09, 1.52)
Not Documented	0.9 (0.8, 1.1)	0.81 (0.61, 1.07)	1.1 (0.9, 1.2)	0.81 (0.63, 1.04)
Remoteness of general practice				
Major City	0.9 (0.8, 1.1)	Reference	1.1 (1.0, 1.3)	Reference
Inner/Outer	0.7 (0.5, 0.9)	0.71 (0.49, 1.03)	0.9 (0.6, 1.2)	0.77 (0.56, 1.07)
Regional				
Remote/Very Remote	1.4 (1.0, 1.9)	1.48 (1.05, 2.07)	1.6 (1.2, 2.1)	1.44 (1.05, 1.98)

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 7. Proportion of women attending general practice who received a nipple swab culture during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.7 (0.4, 1.2)	0.84 (0.46, 1.52)	0.9 (0.5, 1.4)	0.87 (0.51, 1.50)
25-29	0.8 (0.6, 1.1)	Reference	1.0 (0.7, 1.3)	Reference
30-34	0.9 (0.7, 1.1)	1.04 (0.73, 1.48)	1.0 (0.8, 1.2)	1.04 (0.75, 1.44)
35-39	0.6 (0.4, 0.9)	0.74 (0.49, 1.14)	0.8 (0.6, 1.1)	0.81 (0.55, 1.20)
40-44	0.6 (0.3, 1.2)	0.73 (0.36, 1.49)	1.0 (0.5, 1.6)	0.98 (0.54, 1.76)
Concession status				
No concession	0.8 (0.7, 1.0)	Reference	1.0 (0.9, 1.1)	Reference
Concession holder	0.5 (0.3, 0.8)	0.58 (0.36, 0.94)	0.6 (0.4, 0.9)	0.61 (0.40, 0.94)
Smoking Status				
Current Smoker	0.1 (0.0, 0.7)	0.14 (0.02, 0.98)	0.1 (0.0, 0.7)	0.11 (0.02, 0.81)
Ex Smoker	0.6 (0.5, 0.8)	0.68 (0.49, 0.94)	0.7 (0.6, 0.9)	0.67 (0.50, 0.90)
Never Smoker	0.9 (0.7, 1.1)	Reference	1.1 (0.9, 1.3)	Reference
Patient SES				
Very Low	0.4 (0.2, 0.7)	0.59 (0.33, 1.06)	0.6 (0.4, 0.9)	0.59 (0.36, 0.98)
Low	1.0 (0.7, 1.3)	1.32 (0.88, 1.99)	1.1 (0.8, 1.5)	1.07 (0.74, 1.56)
Middle	0.8 (0.6, 1.1)	1.08 (0.72, 1.62)	1.0 (0.7, 1.3)	0.95 (0.66, 1.37)
High	0.7 (0.5, 1.0)	0.96 (0.63, 1.44)	0.8 (0.6, 1.1)	0.80 (0.55, 1.16)
Very High	0.8 (0.6, 1.0)	Reference	1.0 (0.8, 1.3)	Reference
Indigenous Status				
Aboriginal and/or TSI	0.5 (0.1, 1.6)	0.70 (0.22, 2.19)	0.5 (0.1, 1.6)	0.58 (0.18, 1.80)
Neither Aboriginal or TSI	0.8 (0.7, 0.9)	Reference	0.9 (0.8, 1.1)	Reference
Fever				
No	0.8 (0.6, 1.1)	Reference	1.0 (0.8, 1.3)	Reference
Yes	0.7 (0.2, 2.2)	0.89 (0.28, 2.86)	1.0 (0.3, 2.5)	0.98 (0.35, 2.69)
Not Documented	0.8 (0.6, 0.9)	0.90 (0.66, 1.24)	0.9 (0.8, 1.1)	0.89 (0.67, 1.18)
Remoteness of general practice				
Major City	0.8 (0.6, 0.9)	Reference	0.9 (0.8, 1.1)	Reference
Inner/Outer	0.3 (0.2, 0.5)	0.46 (0.28, 0.75)	0.5 (0.3, 0.7)	0.53 (0.35, 0.81)
Regional				
Remote/Very	1.3 (0.9, 1.8)	1.76 (1.24, 2.52)	1.4 (1.0, 1.9)	1.49 (1.06, 2.09)
Remote				

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

Supplemental Table 8. Proportion of women attending general practice who received a breast aspirate during the first, or any, encounter for lactational mastitis according to individual and practice-level characteristics, Australia 2011 to 2022

Category	First		Any*	
	Proportion (95% CI)	OR (95% CI)	Proportion (95% CI)	OR (95% CI)
Age group				
18-24	0.1 (0.0, 0.3)	0.37 (0.05, 2.93)	0.1 (0.0, 0.4)	0.53 (0.12, 2.40)
25-29	0.1 (0.1, 0.3)	Reference	0.2 (0.1, 0.3)	Reference
30-34	0.1 (0.1, 0.2)	0.96 (0.40, 2.33)	0.3 (0.2, 0.4)	1.57 (0.78, 3.14)
35-39	0.2 (0.1, 0.4)	1.48 (0.61, 3.63)	0.3 (0.2, 0.5)	1.53 (0.72, 3.27)
40-44	0.2 (0.0, 0.6)	1.50 (0.40, 5.66)	0.3 (0.1, 0.8)	1.82 (0.63, 5.24)
Concession status				
No concession	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.3)	Reference
Concession holder	0.1 (0.0, 0.3)	0.85 (0.33, 2.18)	0.2 (0.1, 0.4)	0.67 (0.30, 1.46)
Smoking status				
Current Smoker	0.4 (0.1, 1.1)	2.42 (0.72, 8.13)	0.4 (0.1, 1.1)	1.34 (0.41, 4.33)
Ex Smoker	0.1 (0.1, 0.2)	0.75 (0.35, 1.59)	0.2 (0.1, 0.3)	0.70 (0.40, 1.25)
Never Smoker	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.4)	Reference
Patient SES				
Very Low	0.1 (0.0, 0.2)	0.27 (0.06, 1.19)	0.1 (0.0, 0.2)	0.14 (0.03, 0.57)
Low	0.1 (0.0, 0.3)	0.51 (0.19, 1.39)	0.2 (0.1, 0.4)	0.41 (0.19, 0.88)
Middle	0.1 (0.0, 0.2)	0.33 (0.11, 1.00)	0.2 (0.1, 0.3)	0.33 (0.15, 0.72)
High	0.2 (0.1, 0.3)	0.78 (0.35, 1.71)	0.3 (0.1, 0.4)	0.54 (0.29, 1.02)
Very High	0.2 (0.1, 0.4)	Reference	0.5 (0.3, 0.7)	Reference
Indigenous status				
Aboriginal and/or TSI	0	NR	0	NR
Neither	0.2 (0.1-0.2)	Reference	0.3 (0.2-0.3)	Reference
Aboriginal or TSI				
Fever				
No	0.2 (0.1, 0.3)	Reference	0.3 (0.2, 0.4)	Reference
Yes	0.0 (0.0, 0.9)	NR	0.0 (0.0, 0.9)	NR
Not Documented	0.1 (0.1, 0.2)	0.98 (0.47, 2.03)	0.3 (0.2, 0.3)	1.00 (0.58, 1.75)
Remoteness of general practice				
Major City	0.2 (0.1, 0.2)	Reference	0.3 (0.2, 0.4)	Reference
Inner/Outer	0.1 (0.0, 0.2)	0.56 (0.22, 1.45)	0.2 (0.1, 0.3)	0.59 (0.29, 1.20)
Regional				
Remote/Very	0.1 (0.0, 0.3)	0.75 (0.26, 2.14)	0.2 (0.1, 0.5)	0.77 (0.35, 1.70)
Remote				

*at any encounter for mastitis, including additional encounter occurring within two week period of a previous mastitis encounter

Abbreviations: OR, odds ratio; SES, socioeconomic status; TSI, Torres Strait Islander

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	6-7
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8-9
		(c) Explain how missing data were addressed	8-9
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed	N/A

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures in each exposure	N/A
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	N/A
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Figure 1, Table 3-4
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiple comparisons, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.