

# BMJ Open Variations in outcomes by residential location for women with breast cancer: a systematic review

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## ABSTRACT

**Objectives** To systematically assess the evidence for variations in outcomes at each step along the breast cancer continuum of care for Australian women by residential location.

**Design** Systematic review.

**Methods** Systematic searches of peer-reviewed articles in English published from 1 January 1990 to 24 November 2017 using PubMed, EMBASE, CINAHL and Informat databases. Inclusion criteria were: population was adult female patients with breast cancer; Australian setting; outcome measure was survival, patient or tumour characteristics, screening rates or frequencies, clinical management, patterns of initial care or post-treatment follow-up with analysis by residential location or studies involving non-metropolitan women only. Included studies were critically appraised using a modified Newcastle–Ottawa Scale.

**Results** Seventy-four quantitative studies met the inclusion criteria. Around 59% were considered high quality, 34% moderate and 7% low. No eligible studies examining treatment choices or post-treatment follow-up were identified. Non-metropolitan women consistently had poorer survival, with most of this differential being attributed to more advanced disease at diagnosis, treatment-related factors and socioeconomic disadvantage. Compared with metropolitan women, non-metropolitan women were more likely to live in disadvantaged areas and had differing clinical management and patterns of care. However, findings regarding geographical variations in tumour characteristics or diagnostic outcomes were inconsistent.

**Conclusions** A general pattern of poorer survival and variations in clinical management for Australian female patients with breast cancer from non-metropolitan areas was evident. However, the wide variability in data sources, measures, study quality, time periods and geographical classification made direct comparisons across studies challenging. The review highlighted the need to promote standardisation of geographical classifications and increased comparability of data systems. It also identified key gaps in the existing literature including a lack of studies on advanced breast cancer, geographical variations in treatment choices from the perspective of patients and post-treatment follow-up.

## INTRODUCTION

Worldwide, breast cancer is the most frequently diagnosed cancer among women,

## Strengths and limitations of this study

- First systematic review examining evidence for geographical variations in breast cancer outcomes across the continuum of care for Australian women.
- Review was conducted according to published guidelines.
- All included articles were subject to quality assessment.
- Wide heterogeneity across studies in study quality, levels of evidence, methodology, data sources, time period and terminology.
- No meta-analysis was possible.

accounting for 25% of all new diagnoses in 2012, and is the leading cause of female cancer mortality (15% of total cancer deaths).<sup>1</sup> Among Australian women, breast cancer is also the most common cancer and the second leading cause of cancer mortality.<sup>2</sup> Like other developed countries, Australia has high breast cancer incidence rates but relatively low-mortality rates<sup>1</sup> with significant and ongoing improvements in survival, most likely due to earlier detection, screening mammography and improved treatments.<sup>3</sup> However, not all women have benefited equally from these improvements with international studies consistently reporting geographical variations in survival<sup>4–6</sup> and across the breast cancer continuum of care (such as screening, diagnosis, treatment, post-treatment and psychosocial care).<sup>7–9</sup> While Australia has relatively high-survival rates compared with international benchmarks,<sup>10</sup> significant variations exist with poorer survival for rural and disadvantaged women.<sup>11 12</sup>

Australia has a universal healthcare system; however, it is also a country of vast distances with cancer-related services typically being concentrated in major cities<sup>13</sup> so that those living elsewhere often face long travel times and limited access to specialised care.<sup>11 14</sup>

Although about 20% of the total Australian population live outside a major city, for some states and territories, this percentage increases to over one-third.<sup>15</sup> There is also considerable overlap between remoteness and socioeconomic status; around one-third of the population living in major cities in Australia also live in areas classified as least disadvantaged, compared with only 2% of those from very remote areas.<sup>16</sup> Current strategies to better address the needs of rural patients with cancer and to make cancer care more accessible include the Australian Government's establishment of cancer centres and radiation facilities in regional Australia, exploring innovative models of care and other local-level initiatives.<sup>14 17</sup>

A comprehensive understanding of the drivers of variations in outcomes across population groups is a prerequisite for ensuring equitable cancer care and improving outcomes for all Australians. This systematic review aimed to identify, assess and synthesise the current evidence relating to geographical variations in survival, patient and tumour characteristics and diagnostic and clinical outcomes for female Australian patients with breast cancer. It was conducted as part of a larger systematic review that also investigated psychosocial outcomes<sup>18</sup> and variations by indigenous status.<sup>19</sup> Such a review may help identify gaps in knowledge, formulate strategic research priorities and develop evidence-based interventions to reduce the observed inequities.

## METHODS

### Terminology

Due to the range of definitions used to define geographical areas, geographical remoteness was categorised into 'metropolitan' areas (typically 'major cities' or 'urban') and 'non-metropolitan' areas (comprising the remaining localities). However, where relevant, important patterns observed within the remoteness categories were described in greater detail such as studies relating specifically to remote or very remote areas.

## CLINICAL QUESTIONS

The published Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting systematic reviews<sup>20</sup> were followed for this review. As a first step, a series of clinical questions to guide the review were clearly defined and agreed on before commencing the review process in consultation with a Project Steering Group that included clinicians, researchers, allied health practitioners, consumer advocates with experience in breast cancer and health policy representatives. All questions conformed to PICO guidelines<sup>20</sup> in which the target population (P), intervention/exposure (I), comparator (C) and outcomes (O) are clearly defined and used to guide the review process, with the comparator being the only optional component.<sup>21</sup>

Eleven clinical questions examining variations between non-metropolitan and metropolitan women with breast

## Box 1 Clinical questions guiding the systematic review

### Survival outcomes

- ▶ In women diagnosed with breast cancer, do non-metropolitan women have poorer breast cancer survival compared with metropolitan women in Australia?

### Patient and tumour characteristics

- ▶ In women diagnosed with breast cancer, do non-metropolitan women have different sociodemographic characteristics compared with metropolitan women in Australia?
- ▶ In women diagnosed with breast cancer, do non-metropolitan women have more advanced tumour characteristics compared with metropolitan women in Australia?

### Diagnostic and treatment outcomes

- ▶ In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to access breast screening services compared with metropolitan women in Australia?
- ▶ In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to adhere to recommended breast screening intervals (2 yearly) compared with metropolitan women in Australia?
- ▶ In women diagnosed with breast cancer, are there differences in the clinical management between non-metropolitan and metropolitan women in Australia?
- ▶ In women diagnosed with breast cancer, are non-metropolitan women less likely to receive the recommended clinical management compared with metropolitan women in Australia?
- ▶ In women diagnosed with breast cancer, are non-metropolitan women more likely to experience delays in referral to breast cancer specialist clinicians compared with metropolitan women in Australia?
- ▶ In women diagnosed with breast cancer, do non-metropolitan women experience fewer treatment options compared with metropolitan women in Australia?
- ▶ In women diagnosed with breast cancer, are non-metropolitan women less likely to complete prescribed treatment compared with metropolitan women in Australia?
- ▶ In women diagnosed with breast cancer, are non-metropolitan women less likely to participate in recommended follow-up compared with metropolitan women in Australia?

cancer (collectively referred to as 'residential location') were grouped according to (1) survival (one question), (2) patient/tumour characteristics (two questions) and (3) diagnostic and treatment outcomes (eight questions) (box 1).

## LITERATURE SEARCHES

The electronic databases: PubMed, EMBASE, CINAHL and Informit were systematically searched for all indexed articles from 1 January 1990 to 24 November 2017. The Web of Science database was used for cited reference searches.

Search strategies were based on keywords and subject headings to reflect the review aim with separate queries designed for each clinical question (see online supplementary appendix 1). Key terms of 'breast neoplasms', 'female' and 'Australia' were combined with terms

relating to geographical aspects including 'rural health', 'geographic inequalities', 'spatial', 'health services accessibility' and 'remoteness' and outcome measures of interest notably 'survival', 'stage', 'diagnosis age', 'socioeconomic', 'mammography', 'screening rate', 're-screening', 'clinical management', 'patterns of care', 'mastectomy', 'breast reconstruction', 'chemotherapy', 'radiotherapy', 'lymph node' and 'guideline adherence'. Additional synonyms reflecting each of the key terms were also included.

### INCLUSION CRITERIA

Studies were eligible if they met the following inclusion criteria:

1. the population included adult female patients with breast cancer or focused on a breast cancer-specific subgroup
2. had an Australian setting
3. the outcome measure was survival, patient or tumour characteristics, screening participation or frequency, clinical management, patterns of initial care or post-treatment follow-up
4. was
  - a. a quantitative study on non-metropolitan versus metropolitan comparisons
  - b. a qualitative study on geographical inequalities
  - c. quantitative or qualitative studies reporting on relevant outcomes for non-metropolitan women only.

The scope of the review was limited to English language peer-reviewed original research articles. Reviews, editorials, books, conference abstracts and commentaries were excluded, although when identified through the systematic searches their reference lists were examined for relevant articles.

### REVIEW PROCESS

After removing duplicates, the titles and abstracts of all articles identified during the searches were independently reviewed by two authors (first PD, second PHY, DRY or PDB) for possible inclusion based on their relevance to each clinical question. Discrepancies were clarified through discussion between the two reviewers, and if necessary, the other reviewers were consulted. Full-text versions of all articles of potential relevance were then retrieved for more detailed independent assessment by two reviewers as before. During this process, articles were classified as 'include' or 'exclude' with reasons for exclusion being documented. Reviewer decisions were compared, and any disagreements resolved by consensus.

### CRITICAL APPRAISAL

The quality of all included articles was critically assessed by two independent reviewers using the Newcastle-Ottawa Scale (NOS),<sup>22</sup> a risk of bias assessment tool for

non-randomised studies recommended by the Cochrane Collaboration<sup>23</sup> that can be readily tailored for the critical appraisal of quantitative cohort studies.<sup>9</sup> The NOS assesses studies on six items over five broad perspectives: (1) selection bias, (2) measurement of confounders, (3) outcome assessment, (4) follow-up and (5) adjustments for residual confounders (two items). We extended this tool by incorporating features from other published checklists<sup>24 25</sup> to include three additional items to assess (1) study attrition (missing data), (2) statistical methods and (3) data presentation. Studies were scored according to the extent that they met each of the nine assessed criterion (see online supplementary appendix 2) using an ordinal scale to rate the risk of bias as 0 (high), 1 (intermediate) and 2 (low), and the individual item scores then summed to give a total quality score. Instances of major differences in total scores between the two reviewers for individual articles were resolved by consensus, and each article was then assigned a summary score (averaged across the two scores). The total average score (range of 0–18) achieved across the nine criterion was categorised as 'high' (14–18), 'moderate' (9–13.5) or 'low' (<9) quality. Studies were not excluded based specifically on their quality rating.

Studies were also classified according to the published levels of evidence for quantitative observational studies from the Australian National Health and Medical Research Council<sup>24</sup> in decreasing order of strength as Level I, Level II, Level III-1, Level III-2, Level III-3 or Level IV.

### DATA EXTRACTION

For all included articles, study characteristics including author(s), publication year, title, population, design and outcomes were recorded in a customised database by one reviewer and subsequently checked by another. Any errors or inconsistencies were resolved after consulting the original source.

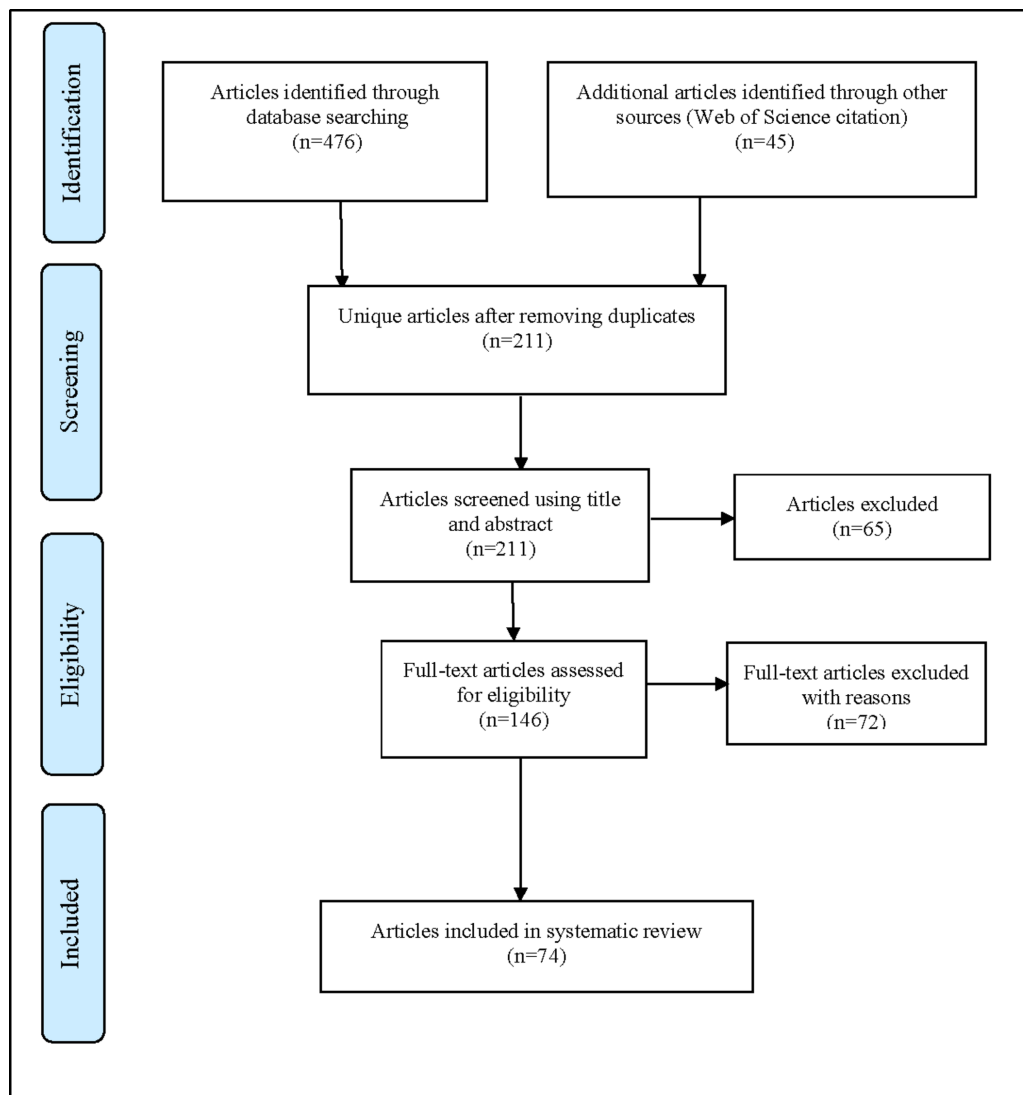
### RESULTS

#### Study selection

The steps in the review process are illustrated in a PRISMA diagram (figure 1). A total of 476 articles were identified across combined databases with an additional 45 citations from other sources. After removing duplicates, an initial pool of 211 articles remained of which 65 were excluded after initial scanning of title/abstracts. Of the 146 retrieved full-text articles, 74 met the inclusion criteria and were considered relevant to at least one of the clinical questions. Excluded studies are listed in online supplementary appendix 3, including reasons for exclusion.

### STUDY CHARACTERISTICS

All included articles were quantitative, and around 80% used administrative data sources such as population-based



**Figure 1** Process of inclusion and exclusion of studies for the systematic review.

cancer registries, screening databases or the non-representative (not population based) National Breast Cancer Audit database which has collected data on about 60% of invasive early breast cancers treated by participating Australian (and New Zealand) breast surgeons since 1998.<sup>26</sup> Remaining studies were based on medical record reviews and cross-sectional surveys.

There was considerable heterogeneity in the definition of non-metropolitan and metropolitan populations. While more than half (57%) of the included studies used standardised definitions such as the Rural, Remote and Metropolitan Areas system, the Accessibility/Remoteness Index of Australia (ARIA) or ARIA+ or remoteness areas defined by the Australian Standard Geographical Classification,<sup>27</sup> others defined non-metropolitan and metropolitan areas based on distances to services, population density or postcodes. Two studies did not provide detailed information regarding the basis of their geographical classification (table 1).

Around 59% of included studies were graded as high quality, 34% moderate and 7% low quality, with a mean

score of 13.0 and range of 6.5–17.0. Key limiting factors for these scores were that around one-third (30%) of studies did not use a population-based representative sample, whereas 20% did not adjust for confounders (including age and sociodemographics). Studies based on reliable and objective data sources (cancer registries) were limited in their ability to control for clinical and treatment factors. The use of highly selective or convenience samples and lack of follow-up also reduced study quality. No studies provided Level I evidence, whereas more than half (57%) gave Level II evidence, 34% Level III-3 and 9% Level IV evidence (table 1).

## KEY FINDINGS

Studies are summarised below (tables 2–5, also online supplementary appendix 4) according to clinical questions within each of the key themes: (1) survival outcomes, (2) patient/tumour characteristics and (3) diagnostic and treatment outcomes. Several studies reported on multiple outcomes. The emphasis is on whether there was evidence of variations

**Table 1** Summary scores, overall grades and levels of evidence for included studies

Study	Metropolitan/non-metropolitan definition	Score*	Quality†	Level‡
Adelson <i>et al</i> , 1997 <sup>73</sup>	Based on health services	15	High	III-3
Ahern <i>et al</i> , 2015 <sup>84</sup>	ARIA+	7	Low	IV
Ahern <i>et al</i> , 2016 <sup>94</sup>	ARIA+	7	Low	IV
Australian Institute of Health and Welfare, 2013 <sup>12</sup>	ARIA+	14.5	High	II
Azzopardi <i>et al</i> , 2014 <sup>72</sup>	ASGC	9	Moderate	II
Baade <i>et al</i> , 2011 <sup>51</sup>	ARIA+	16.5	High	II
Baade <i>et al</i> , 2016 <sup>77</sup>	Distance to radiation treatment facilities	16	High	II
Barratt <i>et al</i> , 1997 <sup>62</sup>	RRMA Classification	9.5	Moderate	II
Bell <i>et al</i> , 2012 <sup>88</sup>	Postcodes§	15	High	II
Bonett <i>et al</i> , 1990 <sup>29</sup>	Postcodes§	14.5	High	II
Budden <i>et al</i> , 2014 <sup>97</sup>	NA: regional women only	10	Moderate	IV
Campbell <i>et al</i> , 2006 <sup>95</sup>	Based on residential area	9.5	Moderate	III-3
Chen <i>et al</i> , 2015 <sup>30</sup>	ARIA+	15.5	High	II
Clayforth <i>et al</i> , 2007 <sup>31</sup>	Postcodes§	15	High	II
Cockburn <i>et al</i> , 1997 <sup>67</sup>	NA: rural and remote women only	10	Moderate	III-3
Chong <i>et al</i> , 2015 <sup>85</sup>	ASGC	13	Moderate	III-3
Collins <i>et al</i> , 2017 <sup>101</sup>	NA: regional women only	14	High	II
Craft <i>et al</i> , 1997 <sup>78</sup>	RRMA Classification	12	Moderate	III-3
Cramb <i>et al</i> , 2012 <sup>32</sup>	Distance to radiation treatment facilities	15.5	High	II
Cramb <i>et al</i> , 2016a <sup>34</sup>	ASGC	14	High	II
Cramb <i>et al</i> , 2016b <sup>33</sup>	ASGC	15	High	II
Cramb <i>et al</i> , 2017 <sup>35</sup>	ASGS	15	High	II
Dasgupta <i>et al</i> , 2012 <sup>36</sup>	ARIA	16.5	High	II
Dasgupta <i>et al</i> , 2017a <sup>52</sup>	Distance to radiation treatment facilities	16	High	II
Dasgupta <i>et al</i> , 2017b <sup>86</sup>	Distance to radiation treatment facilities	16	High	II
Dasgupta <i>et al</i> , 2017c <sup>89</sup>	Distance to radiation treatment facilities	16	High	II
Depczynski <i>et al</i> , 2018 <sup>54</sup>	ARIA+	13	Moderate	III-3
Eley <i>et al</i> , 2008 <sup>96</sup>	NA: rural and remote women only	7.5	Low	IV
Flitcroft <i>et al</i> , 2016 <sup>90</sup>	ARIA+	10	Moderate	III-3
Fox <i>et al</i> , 2013 <sup>55</sup>	RRMA Classification	10.5	Moderate	III-3
Hall and Holman, 2003 <sup>92</sup>	ARIA	14.5	High	II
Hall <i>et al</i> , 2004a <sup>37</sup>	ARIA	15	High	II
Hall <i>et al</i> , 2004b <sup>80</sup>	ARIA	14.5	High	II
Hill <i>et al</i> , 1994 <sup>79</sup>	Postcodes§	12.5	Moderate	II
Hsieh <i>et al</i> , 2013 <sup>48</sup>	ARIA+	14	High	II
Hsieh <i>et al</i> , 2015 <sup>83</sup>	Distance to radiation treatment facilities	14	High	II
Hsieh <i>et al</i> , 2016a <sup>38</sup>	ASGC	14	High	II
Hsieh <i>et al</i> , 2016b <sup>47</sup>	ARIA+	15	High	II
Hughes <i>et al</i> , 2014 <sup>68</sup>	Postcodes§	10.5	Moderate	III-3
Kok <i>et al</i> , 2006 <sup>53</sup>	RRMA Classification	14.5	High	III-3
Koshy <i>et al</i> , 2005 <sup>81</sup>	Postcodes§	9.5	Moderate	III-3
Kricker <i>et al</i> , 2001 <sup>82</sup>	Unclear	16	High	II
Lai <i>et al</i> , 2007 <sup>93</sup>	RRMA Classification	15	High	II
Lam <i>et al</i> , 2015 <sup>100</sup>	NA: regional women only	10	Moderate	IV

Continued

Table 1 Continued

Study	Metropolitan/non-metropolitan definition	Score*	Quality†	Level‡
Leung <i>et al</i> , 2014 <sup>60</sup>	ARIA+	12.5	Moderate	III-3
Leung <i>et al</i> , 2015 <sup>61</sup>	ARIA+	12	Moderate	III-3
Leung <i>et al</i> , 2016 <sup>57</sup>	ARIA+	13	Moderate	III-3
Lord <i>et al</i> , 2012 <sup>56</sup>	ARIA	14	High	II
Luke <i>et al</i> , 2004 <sup>58</sup>	Postcodes§	14	High	II
Martin <i>et al</i> , 2006 <sup>74</sup>	Based on residential area	14.5	High	II
Mastaglia and Kristjanson, 2001 <sup>75</sup>	Unclear	6.5	Low	IV
Mitchell <i>et al</i> , 2006 <sup>39</sup>	Postcodes§	16	High	II
Morris <i>et al</i> , 2012 <sup>87</sup>	ASGC	10.5	Moderate	III-3
O'Byrne <i>et al</i> , 2000 <sup>69</sup>	RRMA Classification	15.5	High	III-3
Ristevski <i>et al</i> , 2012 <sup>98</sup>	NA: regional women only	9	Moderate	IV
Roder <i>et al</i> , 2012a <sup>28</sup>	ASGC	14.5	High	III-3
Roder <i>et al</i> , 2012b <sup>108</sup>	ASGC	14	High	III-3
Roder <i>et al</i> , 2013a <sup>49</sup>	ASGC	14	High	III-3
Roder <i>et al</i> , 2013b <sup>26</sup>	ASGC	14.5	High	III-3
Roder <i>et al</i> , 2013c <sup>91</sup>	ASGC	14.5	High	III-3
Roder <i>et al</i> , 2014 <sup>50</sup>	ASGC	15	High	III-3
Schofield <i>et al</i> , 1994 <sup>65</sup>	Distance to screening services	10.5	Moderate	II
Siahpush and Singh, 2002 <sup>66</sup>	Based on residential area	12.5	Moderate	II
Spilsbury <i>et al</i> , 2005 <sup>40</sup>	Postcodes§	16	High	II
Sullivan <i>et al</i> , 2003 <sup>63</sup>	Postcodes§	11	Moderate	III-3
Supramaniam <i>et al</i> , 2014 <sup>41</sup>	ARIA+	17	High	II
Taylor, 1997 <sup>46</sup>	Capital city, other metropolitan, rural	14.5	High	II
Tervonen <i>et al</i> , 2017 <sup>42</sup>	ARIA+	14	High	II
Thompson <i>et al</i> , 2008 <sup>76</sup>	ARIA+	14.5	High	II
Tracey <i>et al</i> , 2008 <sup>43</sup>	ARIA	15	High	II
Tulloh and Goldsworthy, 1997 <sup>99</sup>	NA: rural and remote women only	7	Low	III-3
Weber <i>et al</i> , 2014 <sup>64</sup>	ARIA+	10.5	Moderate	III-3
Wilkinson and Cameron, 2004 <sup>45</sup>	Postcodes§	9.5	Moderate	II
Yu <i>et al</i> , 2015 <sup>44</sup>	ARIA+	12	Moderate	II

\*Average score over scores from two independent reviewers. Please refer to text for further details.

†Quality categories: high (score 14–18), moderate (score 9–13.5) or low (score <9). Please refer to text for further details.

‡Australian National Health and Medical Research Council<sup>24</sup> levels of evidence in decreasing order of strength are Level I, Level II, Level III-1, Level III-2, Level III-3 and Level IV.

§Postcodes within state capital were considered metropolitan, remaining were non-metropolitan.

ARIA, Accessibility/Remoteness Index of Australia; ASGC, Australian Standard Geographical Classification; NA, not applicable; RRMA, Rural, Remote and Metropolitan Area.

in relevant outcomes by residential location and, if so, the direction and a quantitative estimate of the magnitude of the effect. Given the considerable heterogeneity among studies in terms of their quality, levels of evidence, time period and geographical definitions, we have deliberately interpreted any summary patterns with caution.

## SURVIVAL OUTCOMES

There was a consistent pattern of significantly poorer survival (in unadjusted analyses) for women in non-metropolitan areas compared with metropolitan

women across 21 (19 high and 2 moderate quality) of 22 included studies both nationally<sup>12 28</sup> and at the state level (table 3).<sup>29–45</sup> The 5-year unadjusted relative survival for female breast cancers was about 2%–5% (absolute) lower for non-metropolitan than metropolitan women. The one exception was an early high-quality study involving women in New South Wales (diagnosed from 1980 to 1991) who did not report any survival differential.<sup>46</sup>

However, no geographical differential in survival was evident across 11<sup>28 32 36 37 39–43 46 47</sup> of 20 studies that also

**Table 2** Summary of included studies on differentials in breast cancer survival outcomes by residential location

Author, year	Location*	Period (follow-up)	Sample size	Poorer survival	
				Unadjusted	Adjusted†
Australian Institute of Health and Welfare, 2013 <sup>12</sup>	National	1982–2007 (end 2010)	NS	Non-metropolitan	NR
Wilkinson and Cameron, 2004 <sup>45</sup>	SA	1977–1993 (to 2000)	NS	Non-metropolitan	NR
Cramb <i>et al</i> , 2012 <sup>32</sup>	Qld	1996–2007	25 202	Non-metropolitan	No difference (s, d)
Dasgupta <i>et al</i> , 2012 <sup>36</sup>	Qld	1997–2006 (end 2007)	18 568	Non-metropolitan	No difference (s, d)
Hsieh <i>et al</i> , 2016b <sup>47</sup>	Qld	1997–2007 (end 2008)	9741	Non-metropolitan	No difference (s, d)
Tervonen <i>et al</i> , 2017 <sup>42</sup>	NSW	1980–2008 (end 2009)	88 768	Non-metropolitan	No difference (s, d)
Tracey <i>et al</i> , 2008 <sup>43</sup>	NSW	1980–2003 (end 2004)	59 731	Non-metropolitan	No difference (s, d)
Mitchell <i>et al</i> , 2006 <sup>39</sup>	WA	1999 (end 2004)	899	Non-metropolitan	No difference (s, t)
Supramaniam <i>et al</i> , 2014 <sup>41</sup>	NSW	2001–2007 (end 2008)	27 850	Non-metropolitan	No difference (s, d, t, c)
Roder <i>et al</i> , 2012a <sup>28</sup>	National	1991–2006	62 082	Non-metropolitan	No difference (d)
Hall <i>et al</i> , 2004a <sup>37</sup>	WA	1991–2001	7117	Non-metropolitan	No difference (d, t, c)
Spilsbury <i>et al</i> , 2005 <sup>40</sup>	WA	1982–2000	11 445	Non-metropolitan	No difference (d, t, c)
Taylor, 1997 <sup>46</sup>	NSW	1980–1991 (end 1992)	25 793	No difference	No difference (s)
Bonett <i>et al</i> , 1990 <sup>29</sup>	SA	1980–1986 (end 1988)	2565	Non-metropolitan	Non-metropolitan (s)
Chen <i>et al</i> , 2015 <sup>30</sup>	NSW	2000–2008	36 867	Non-metropolitan	Non-metropolitan (s)
Cramb <i>et al</i> , 2016a <sup>34</sup>	Qld	1997–2011	NS	Non-metropolitan	Non-metropolitan *(s)
Cramb <i>et al</i> , 2016b <sup>33</sup>	Qld	1997–2011	34 231	Non-metropolitan	Non-metropolitan (s)
Hsieh <i>et al</i> , 2013 <sup>48</sup>	Qld	1997–2007 (end 2008)	23 766	Non-metropolitan	Non-metropolitan (s, d)
Hsieh <i>et al</i> , 2016a <sup>38</sup>	Qld	1997–2007 (end 2008)	23 766	Non-metropolitan	Non-metropolitan (s)
Yu <i>et al</i> , 2015 <sup>44</sup>	NSW	1987–2007 (end 2007)	63 757	Non-metropolitan	Non-metropolitan (s, d)
Clayforth <i>et al</i> , 2007 <sup>31</sup>	WA	1989, 1994, 1999 (end 2005)	1729	Non-metropolitan	Non-metropolitan (s, t)
Cramb <i>et al</i> , 2017 <sup>35</sup>	Qld	1997–2004 (end 2005); 2005–2012 (end 2013)	38 204	Non-metropolitan	Non-metropolitan

\*National: all states/territories. NSW, New South Wales; Qld, Queensland; SA, South Australia; WA, Western Australia.

†All adjusted for age except Bonett *et al*, 1990.<sup>29</sup>

(s) Also adjusted for some measure of spread of diagnosis, such as stage at diagnosis or tumour diameter.

(t) Also adjusted for treatment-related factors.

(d) Also adjusted for area disadvantage.

(c) Also adjusted for comorbidities.

NR, not relevant; NS, not stated.

reported survival estimates after adjustment for various combinations of known survival determinants including demographics, area-level disadvantage, spread of disease, comorbidities and treatment-related factors. The remaining nine studies<sup>29–31 33–35 44 48</sup> all reported poorer survival for non-metropolitan women even after adjustment.

The adjusted results varied according to the combination of variables included in the statistical models. Six of the seven papers that reported significant differentials after adjusting for a measure of stage at diagnosis did not consider comorbidities or treatment-related factors.<sup>29 30 33 34 38 44</sup> Of the five studies that adjusted for treatment-related factors, four reported no evidence of a survival differential,<sup>37 39–41</sup> whereas the finding of a

significant difference was likely to be limited to women diagnosed prior to the mid-1990s in the remaining study.<sup>31</sup>

Most of the 22 included studies focused on medium-term survival, with only one<sup>43</sup> following women for longer than 5 years after their breast cancer diagnosis.

## PATIENT AND TUMOUR CHARACTERISTICS

### Patient characteristics

Both of the included high-quality studies that reported a positive association between area-disadvantage and non-metropolitan residence were based on analysis of 30 299 early invasive female breast cancer cases from the National Breast Cancer Audit (table 4).<sup>49 50</sup> For example,

**Table 3** Summary of included studies on differentials in patient and tumour characteristics by residential location

Author, year	Location*	Period	Sample size	Finding†
Patient characteristics (higher area-level socioeconomic disadvantage)				
Roder <i>et al</i> , 2013a <sup>49</sup>	National	1998–2010	30 299	Non-metropolitan
Roder <i>et al</i> , 2014 <sup>50</sup>	National	1998–2010	30 299	Non-metropolitan
Tumour characteristics (higher spread of disease) <sup>3</sup>				
Bonett <i>et al</i> , 1990 <sup>29</sup>	SA	1980–1986	1 171	No difference
Depczynski <i>et al</i> , 2018 <sup>54</sup>	NSW	2006–2009	726	No difference
Fox <i>et al</i> , 2013 <sup>55</sup>	NSW	2008–2011	400	No difference
Leung <i>et al</i> , 2016 <sup>57</sup>	NSW, Qld, Vic	1997–2011	195	No difference
Lord <i>et al</i> , 2012 <sup>56</sup>	NSW	2001–2002	6 664	No difference
Luke <i>et al</i> , 2004 <sup>58</sup>	SA	1997–2002	4 912	No difference
Mitchell <i>et al</i> , 2006 <sup>39</sup>	WA	1999	899	No difference
Wilkinson and Cameron, 2004 <sup>45</sup>	SA	1980–1998	NS	No difference
Baade <i>et al</i> , 2011 <sup>51</sup>	Qld	1997–2006	18 568	Non-metropolitan
Dasgupta <i>et al</i> , 2017a <sup>52</sup>	Qld	1997–2014	38 706	Non-metropolitan
Kok <i>et al</i> , 2006 <sup>53</sup>	Vic	1993–2000	5 294	Non-metropolitan
Roder <i>et al</i> , 2013b <sup>26</sup>	National	1998–2010	30 299	Non-metropolitan
Tracey <i>et al</i> , 2008 <sup>43</sup>	NSW	1980–2003	59 731	Metropolitan

\*National: all states/territories. NSW, New South Wales; Qld, Queensland; SA, South Australia; Vic, Victoria; WA, Western Australia.

†Some measure of spread of disease such as stage at diagnosis or tumour size.

**Table 4** Summary of included studies on differentials in diagnostic outcomes by residential location

Author, year	Location*	Period	Sample size†	Finding
Higher screening rate‡				
Barratt <i>et al</i> , 1997 <sup>62</sup>	National	1996	1 035	No difference
Leung <i>et al</i> , 2014 <sup>60</sup>	National	2001–2010	11 200	No difference
Leung <i>et al</i> , 2015 <sup>61</sup>	National	2010	10 011	No difference
Sullivan <i>et al</i> , 2003 <sup>63</sup>	WA	1982–2000	380	Non-metropolitan
Weber <i>et al</i> , 2014 <sup>64</sup>	NSW	2006–2010	101 063	Non-metropolitan
Schofield <i>et al</i> , 1994 <sup>65</sup>	Vic	1988–1990	668	Metropolitan
Siahpush and Singh, 2002 <sup>66</sup>	National	1995	10 179	Metropolitan
Cockburn <i>et al</i> , 1997 <sup>67</sup>	Vic	1995	180 non-metropolitan	No screening history and knowing service locations screening predictors
Higher rescreening rate§				
Hughes <i>et al</i> , 2014 <sup>68</sup>	WA	1999–2008	NS	No difference
Leung <i>et al</i> , 2014 <sup>60</sup>	National	2001–2010	11 200	Non-metropolitan
Leung <i>et al</i> , 2015 <sup>61</sup>	National	2010	10 011	Non-metropolitan
O'Byrne <i>et al</i> , 2000 <sup>69</sup>	Vic	1995–1996	121 889	Non-metropolitan
Siahpush and Singh, 2002 <sup>66</sup>	National	1995	10 179	Metropolitan

\*National: all states/territories. NSW, New South Wales; Vic, Victoria; WA, Western Australia.

†Only aged 50–69 years who were eligible at time of this review and all included studies for publicly funded BreastScreen programme in Australia.

‡Having had at least one screening mammogram.

§Having another screening mammogram within 2 years of the initial screen.



**Table 5** Summary of included studies on differentials in treatment outcomes by residential location

Author, year	Location*	Period	Sample size	Finding
<b>Higher mastectomy</b>				
Koshy <i>et al</i> , 2005 <sup>81</sup>	NSW, ACT	1997–2002	1069	No difference
Kricker <i>et al</i> , 2001 <sup>82</sup>	NSW	1992, 1995	2020 or 2883	No difference
Adelson <i>et al</i> , 1997 <sup>73</sup>	NSW	1991–1992	4038	Non-metropolitan
Azzopardi <i>et al</i> , 2014 <sup>72</sup>	National	1998–2012	21 643	Non-metropolitan
Martin <i>et al</i> , 2006 <sup>74</sup>	WA	1990–1999	2713	Non-metropolitan
Mastaglia and Kristjanson, 2001 <sup>75</sup>	WA	1996–1997	160	Non-metropolitan
Roder <i>et al</i> , 2013b <sup>26</sup>	National	1998–2010	30 299	Non-metropolitan
Thompson <i>et al</i> , 2008 <sup>76</sup>	Qld	2004–2005	1274	Non-metropolitan
<b>Higher breast-conserving surgery</b>				
Hall <i>et al</i> , 2004b <sup>80</sup>	WA	1991–2000	7304	No difference
Adelson <i>et al</i> , 1997 <sup>73</sup>	NSW	1991–1992	4038	Metropolitan
Azzopardi <i>et al</i> , 2014 <sup>72</sup>	National	1998–2012	21 643	Metropolitan
Baade <i>et al</i> , 2016 <sup>77</sup>	Qld	1997–2011	11 631	Metropolitan
Craft <i>et al</i> , 1997 <sup>78</sup>	National	1993	4683	Metropolitan
Hill <i>et al</i> , 1994 <sup>79</sup>	Vic	1990	856	Metropolitan
Kok <i>et al</i> , 2006 <sup>53</sup>	Vic	1993–2000	5294	Metropolitan
Mitchell <i>et al</i> , 2006 <sup>39</sup>	WA	1999	899	Metropolitan
Roder <i>et al</i> , 2013a <sup>49</sup>	National	1998–2010	30 299	Metropolitan
<b>Lower radiotherapy</b>				
Azzopardi <i>et al</i> , 2014 <sup>72</sup>	National	1998–2012	21 643	Non-metropolitan
Hsieh <i>et al</i> , 2015 <sup>83</sup>	Qld	1997–2008	6357	Non-metropolitan
Kok <i>et al</i> , 2006 <sup>53</sup>	Vic	1993–2000	5294	Non-metropolitan
Mitchell <i>et al</i> , 2006 <sup>39</sup>	WA	1999	899	Non-metropolitan
Hsieh <i>et al</i> , 2013a <sup>48</sup>	National	1998–2010	30 299	Non-metropolitan
<b>Lower hormonal therapy</b>				
Ahern <i>et al</i> , 2015 <sup>84</sup>	National	2013	325	No difference
Hsieh <i>et al</i> , 2015 <sup>83</sup>	Qld	1997–2008	6357	No difference
Mitchell <i>et al</i> , 2006 <sup>39</sup>	WA	1999	899	Non-metropolitan
<b>Lower chemotherapy</b>				
Hsieh <i>et al</i> , 2015 <sup>83</sup>	Qld	1997–2008	6357	No difference
Hill <i>et al</i> , 1994 <sup>79</sup>	Vic	1990	856	No difference
Mitchell <i>et al</i> , 2006 <sup>39</sup>	WA	1999	899	No difference
Roder <i>et al</i> , 2013a <sup>49</sup>	National	1998–2010	30 299	Metropolitan
<b>Lower sentinel node biopsy</b>				
Chong <i>et al</i> , 2015 <sup>85</sup>	National	2008–2010	18 737	Non-metropolitan
Dasgupta <i>et al</i> , 2017b <sup>86</sup>	Qld	July 2008–December 2012	5577	Non-metropolitan
Morris <i>et al</i> , 2012 <sup>87</sup>	National	2008 (last 6 months)	1267 to	Non-metropolitan
<b>Lower axillary surgery</b>				
Craft <i>et al</i> , 1997 <sup>78</sup>	National	1993	4683	No difference
Kricker <i>et al</i> , 2001 <sup>82</sup>	NSW	1992, 1995	2020 or 2883	No difference
Thompson <i>et al</i> , 2008 <sup>76</sup>	Qld	2004–2005	1274	No difference
<b>Lower breast reconstruction</b>				

Continued

Table 5 Continued

Author, year	Location*	Period	Sample size	Finding
Hall and Holman, 2003 <sup>92</sup>	WA	1991–2000	7303	No difference
Bell <i>et al</i> , 2012 <sup>88</sup>	Vic	2004–2006	366	Non-metropolitan
Dasgupta <i>et al</i> , 2017c <sup>89</sup>	Qld	1997–2012	4104	Non-metropolitan
Flitcroft <i>et al</i> , 2016 <sup>90</sup>	National	2013	3786	Non-metropolitan
Roder <i>et al</i> , 2013c <sup>91</sup>	National	1998–2010	12 207	Non-metropolitan
Higher unplanned admissions				
Lai <i>et al</i> , 2007 <sup>93</sup>	WA	1995–1999	2703	Non-metropolitan
Access breast care nurses				
Ahern <i>et al</i> , 2016 <sup>94</sup>	National	2013	902	No difference
Campbell <i>et al</i> , 2006 <sup>95</sup>	National	1997	544	No difference
Longer treatment delays				
Fox <i>et al</i> , 2013 <sup>55</sup>	NSW	2008–2011	400	Non-metropolitan
Poorer quality of care				
Hill <i>et al</i> , 1994 <sup>79</sup>	Vic	1990	856	Non-metropolitan
Fox <i>et al</i> , 2013 <sup>55</sup>	NSW	2008–2011	400	Non-metropolitan
Baade <i>et al</i> , 2016 <sup>77</sup>	Qld	1997–2011	11 631	Non-metropolitan
Mitchell <i>et al</i> , 2006 <sup>39</sup>	WA	1999	899	Non-metropolitan
Roder <i>et al</i> , 2013a <sup>49</sup>	National	1998–2010	30 299	Non-metropolitan
Roder <i>et al</i> , 2013b <sup>26</sup>	National	1998–2010	30 299	Non-metropolitan
Treatment completion				
Fox <i>et al</i> , 2013 <sup>55</sup>	NSW	2008–2011	400	Non-metropolitan more likely to complete chemotherapy
Roder <i>et al</i> , 2012b <sup>108</sup>	National	1998–2005	36 775	Non-metropolitan less likely to follow clinician-recommended treatments
Non-metropolitan				
Budden <i>et al</i> , 2014 <sup>97</sup>	Qld	NS	104	High-level satisfaction with treatment decisions
Eley <i>et al</i> , 2008 <sup>96</sup>	Qld	2005–2006	51	Breast cancer nurses important source of care
Ristevski <i>et al</i> , 2012 <sup>98</sup>	Vic	NS	70	High-level satisfaction with treatment decisions
Tulloh and Goldsworthy, 1997 <sup>99</sup>	Vic	1992–1995	28	Rural setting did not influence quality of care
Lam <i>et al</i> , 2015 <sup>100</sup>	NSW	2010–2014	574	A locally available publicly funded radiotherapy service increased breast-conserving surgery uptake
Collins <i>et al</i> , 2017 <sup>101</sup>	Vic	2009–2014	1213	Access to radiotherapy impacts surgical management

\*National: all states/territories. NSW, New South Wales; ACT, Australian Capital Territory; Qld, Queensland; Vic, Victoria; WA, Western Australia.

NS, not stated.

compared with affluent women, socioeconomically disadvantaged women diagnosed with breast cancer were 17 times more likely to live in remote areas (than metropolitan areas),<sup>49</sup> whereas compared with metropolitan women, those from remote areas were 13 times more likely to live in a disadvantaged rather than more advantaged region.<sup>50</sup>

### Tumour characteristics

No consistent pattern of variations in tumour characteristics by residential location was evident across the 13 included studies (table 4). Nationally, one high-quality study found that non-metropolitan women were 15% more likely to present with tumours >40 mm (vs <30 mm),<sup>26</sup> whereas three state-based high-quality studies also reported

similar patterns,<sup>51–53</sup> despite using different definitions of advanced disease. However, eight others (four high and four moderate quality) showed no differences,<sup>29 39 45 54–58</sup> and one (high quality) that metropolitan women were 11% more likely to present with regional disease than non-metropolitan patients, but equally likely to present with distant tumours.<sup>43</sup>

### Diagnostic and treatment outcomes

Studies described here assessed geographical variations in relation to two broad topics: breast cancer screening (table 4) and treatment (table 5). The target group for the two screening questions refers to women aged 50 to 69 years who were eligible (at the time of this review) for the free population-based national mammographic programme in Australia (BreastScreen Australia).<sup>59</sup>

#### Screening rate

All eight of the included moderate quality studies relate to the publicly funded BreastScreen programme, as there were no data available to assess variations in private mammography, and provided mixed results. Analyses of self-reported data for more than 10 000 women nationally found that despite poorer access to mammography services,<sup>60</sup> non-metropolitan women had similar screening rates to metropolitan women,<sup>60 61</sup> consistent with an earlier cross-sectional survey.<sup>62</sup> Two state-based studies, however, reported higher participation rates in the BreastScreen programme for non-metropolitan women.<sup>63 64</sup> In contrast, women who lived within 10–20 km of a relocatable BreastScreen service were 43% less likely to have been screened than those residing within 2 km of the service.<sup>65</sup> Another study found that non-metropolitan women in the target age group were 39% more likely to report never having been screened through BreastScreen Australia than metropolitan women.<sup>66</sup> Screening history, perceived breast cancer risk and knowledge about service location were among key predictors of accessing a relocatable screening service in a study involving only 180 non-metropolitan women.<sup>67</sup>

#### Rescreening

Results were inconsistent across the five included studies, with a dependence on the time period of data collection. One early (moderate quality) study showed that metropolitan women had higher rescreening rates through the national BreastScreen programme than non-metropolitan women,<sup>66</sup> whereas among four other studies from 1995 onwards, one (moderate quality) study showed no difference in rescreening rates<sup>68</sup> and three studies (two moderate and one high quality) showed that non-metropolitan women had higher rescreening rates.<sup>60 69</sup>

#### Clinical management

Given there are separate Australian guidelines for clinical management of early<sup>70</sup> and advanced stage breast cancer,<sup>71</sup> the descriptions of variations in clinical management are categorised accordingly.

A consistent pattern of variations in the clinical management of early breast cancer by residential location was evident across 21 (14 high, 6 moderate and 1 low quality) of 28 included studies with 7 (3 high, 2 moderate and 2 low) finding no variations.

Among 30 299 cases extracted from the National Breast Cancer Audit database, non-metropolitan women were at least five times more likely to have a mastectomy than metropolitan women,<sup>26</sup> whereas another study using this database reported that the proportion of mastectomies progressively increased with increasing remoteness.<sup>72</sup> Various state-specific studies also reported similar patterns.<sup>73–76</sup> Studies using the National Breast Cancer Audit database found that non-metropolitan women were 6% less likely to undergo breast-conserving surgery,<sup>48</sup> and that the proportion who had breast-conserving surgery decreased progressively with increasing remoteness.<sup>72</sup> Similar findings were evident across six other state-level studies.<sup>39 53 73 77–79</sup> Only three studies reported no differences in surgical patterns by residential location.<sup>80–82</sup>

Two studies based on the National Breast Cancer Audit Database reported that non-metropolitan women were up to 20% less likely to receive adjuvant radiotherapy than metropolitan women.<sup>48 72</sup> Moreover, women residing in areas lacking radiotherapy facilities had a higher likelihood (23%) of not receiving radiotherapy than those from regions with such facilities.<sup>72</sup> Three state-based studies also reported similar patterns.<sup>39 53 83</sup> Findings for other treatment modalities were less consistent with no geographical differentials in receipt of either hormonal therapy<sup>83 84</sup> or chemotherapy,<sup>39 79 83</sup> higher uptake of chemotherapy<sup>50</sup> and lower for hormonal therapy among non-metropolitan women<sup>39</sup> being reported.

Non-metropolitan women were consistently (12%–58%) less likely to undergo sentinel node biopsies (SNBs)<sup>85–87</sup> or postmastectomy breast reconstruction<sup>88–91</sup> with only one earlier study reporting no difference in reconstruction rates.<sup>92</sup> They also had a 10% higher risk of unplanned readmissions.<sup>93</sup> However, no geographical variations in axillary node surgery<sup>76 78 82</sup> or access to specialist breast care nurses were evident.<sup>94 95</sup>

Of the seven included studies comprising non-metropolitan women only, one reported that breast care nurses were important in ensuring continuity of care,<sup>96</sup> two found a high level of patient satisfaction with the treatment decision process<sup>97 98</sup> and one found that geographical setting was no impediment to receiving breast-conserving surgery or to accessing multidisciplinary care at a single non-metropolitan treatment centre.<sup>99</sup> Among regional women in the state of New South Wales, breast-conserving surgical rates increased by 9% after a publicly funded radiotherapy service became available in 2013, compared with earlier years when the only options were a local private or publicly funded out-of-areas service.<sup>100</sup> However, regional women who lived  $\geq 100$ –200 km away (vs  $< 100$  km) from a radiotherapy service were twice as likely to have a mastectomy.<sup>101</sup>

The only study examining geographical variations in clinical management for advanced breast cancer found no geographical variations in mastectomy rates among women with metastatic disease.<sup>73</sup>

### Recommended clinical management

Nine (4 high and 5 moderate quality) of 15 included studies reported geographical variations in guideline-concordant care with non-metropolitan women being less likely to undergo adjuvant radiotherapy,<sup>48 53 72 83</sup> hormonal therapy<sup>39</sup> or SNBs<sup>85–87</sup> and more likely to experience longer delays in commencing adjuvant chemotherapy.<sup>55</sup> However, the other six studies (two high, two moderate and two low quality) found no significant geographical variations in receipt of recommended care.<sup>76 78 79 82 84 94</sup>

### Referral

Non-metropolitan women were less likely to be referred to a radiation oncologist<sup>79</sup> and were more likely to experience delays in assessment by a medical oncologist.<sup>55</sup> Further, in a cross-sectional survey of 70 non-metropolitan women, 42% were referred to another health professional before surgery.<sup>98</sup> All studies were of moderate quality.

International studies have consistently shown geographical variations in access to high-volume surgical care<sup>102–104</sup> and provided clear evidence that such care is related to improved breast cancer survival<sup>103 105</sup> and better concordance with clinical care guidelines.<sup>106 107</sup> Hence, eligible studies that described access to high caseload surgeons were also considered for this clinical question. One high-quality study reported that non-metropolitan women were 9% more likely to be treated locally by low caseload surgeons<sup>26</sup> (defined as  $\leq 10$  or  $< 20$  cases/year) with similar findings reported by three other high-quality studies.<sup>39 49 77</sup>

### Treatment completion

Of the two included studies, one found that non-metropolitan women were more likely to complete prescribed chemotherapy than metropolitan women.<sup>55</sup> Another reported that women treated by low caseload surgeons ( $\leq 20$  cases/year) were more likely to decline clinician-recommended surgery, radiotherapy or chemotherapy based on data from the National Breast Cancer Audit.<sup>108</sup><sup>39 49 77</sup>

The review did not identify any studies examining geographical variations in the specific treatment options offered to non-metropolitan and metropolitan Australian female patients with breast cancer or post-treatment follow-up according to current national guidelines.<sup>109</sup>

## DISCUSSION

This review found consistent evidence for variations in survival and clinical management, limited evidence for variations in diagnostic outcomes and inconsistent evidence for variations in tumour characteristics by

residential location of Australian female patients with breast cancer.

While gaps in the literature limited our ability to draw clear links between identified variations and the drivers of these variations, there was good evidence that poorer breast cancer survival (at least up to 5 years after diagnosis) for non-metropolitan women reflects more advanced disease at diagnosis, greater comorbidities, treatment-related factors and area-level disadvantage.<sup>28 32 36 39–43</sup> According to the recent systematic review by the International Agency for Research on Cancer,<sup>110</sup> there is sufficient evidence for the efficacy of mammographic screening in reducing breast cancer mortality for women aged 50 to 69 years. In Australia, increasing participation for groups with low screening rates can be achieved through the existing and well established population-based national mammographic programme (BreastScreen). Targeted strategies are required including thorough engagement and communication with primary care to improve screening participation rates.<sup>59</sup> It is possible that these survival patterns are impacted by the lead time caused by mammographic screening,<sup>111</sup> whereas we found only limited evidence that participation in the publicly funded BreastScreen services varies by geographical area, the lack of data on the number of privately screened women precludes an evaluation of actual population-based screening participation and its impact on the observed survival patterns. Hence, it remains a priority to explore means to combine data on public and private screening to gain more comprehensive information on total rates of breast cancer screening nationally.

The review found a consistent pattern of geographical variations in patterns of care and lower receipt of optimal clinical management for early breast cancer among non-metropolitan women in Australia. Reasons for these variations likely included limited access to oncological services and multidisciplinary care.<sup>112 113</sup> Regional Cancer Centres across Australia and integrated cancer networks were established to improve access to oncological care for regional patients.<sup>14 17</sup> However, overcoming barriers to multidisciplinary care, considered best practice in breast cancer care,<sup>114–116</sup> in regional areas remains a challenge. Multidisciplinary cancer teams (MDTs) are sparse outside metropolitan areas and vary widely in the disciplines represented within existing teams.<sup>113</sup>

The efficacy of MDTs in informed clinical decision making, coordinated care and evidence-based practice for patients with breast cancer has been well documented.<sup>117–120</sup> Several of the included studies in this review identified limited access to MDT care for non-metropolitan women as a possible contributor to lower receipt of guideline concordant care.<sup>26 44 49 86 91 108</sup> It is possible that the major benefits of MDT lie, in part, with greater adherence to standard therapy,<sup>44 108 119</sup> which may indirectly impact clinical outcomes.

The evidence for the impact of MDT on breast cancer survival is more limited, possibly reflecting methodological limitations and heterogeneity in MDT definitions.<sup>119 121</sup>

However, surgical specialisation has been shown to be associated with improved survival,<sup>105</sup> and we found that non-metropolitan women had consistently poorer access to high-volume surgeons<sup>26 39 49 77</sup> which in Australia are predominantly based in major cities.<sup>122</sup>

Australian clinical practice guidelines for the management of early breast cancer recommend postoperative radiotherapy after breast-conserving surgery to reduce the risk of local recurrence, adjuvant endocrine therapy and/or chemotherapy where appropriate based on hormone receptor status,<sup>123</sup> and SNB offered to women with unifocal clinically node negative tumours ( $\leq 30$  mm).<sup>124</sup> However, this review found limited but consistent evidence for geographical variations in receipt of care according to these guidelines. Specifically, non-metropolitan women were less likely to undergo adjuvant radiotherapy,<sup>39 49 53 72 83</sup> hormonal therapy<sup>39</sup> or SNB.<sup>85–87</sup> Lower utilisation of SNB in non-metropolitan areas may reflect inadequate access to necessary resources, less relevant training and experience in performing SNB among general surgeons outside major treatment centres<sup>86 87</sup> and lack of interdisciplinary collaboration required to perform SNBs.<sup>85–87</sup> Surgeon-level interventions may be required to help improve SNB rates and hence quality of care and reduced morbidity.

The finding that non-metropolitan women were less likely to receive adjuvant radiotherapy likely reflects variations in access to such facilities.<sup>72 83 100 101</sup> However, it should be acknowledged that all included studies were published in the period 1 January 1990 to 24 November 2017, and that some earlier studies may not reflect current practice and/or the impact of improved access to radiation services with the development of new radiotherapy infrastructure in regional Australia over the last 5 years.<sup>14 125</sup> Both service affordability and availability impact radiotherapy utilisation<sup>126</sup> with the uptake of breast-conserving surgery among regional women increasing after provision of a publicly funded local radiotherapy service.<sup>100</sup> Similar patterns were also reported for radiotherapy utilisation among all regional patients with cancer.<sup>127 128</sup> The waiting time from radiation oncologist assessment to receiving radiotherapy (for any cancer) has also improved over time.<sup>126</sup> Although implementation of routine reporting of waiting times from diagnosis to commencing radiotherapy by geographical location would help identify when and where delays in referral and commencing treatment occur.

Given the potential survival benefits of adjuvant radiotherapy,<sup>129 130</sup> the lower utilisation of radiotherapy among non-metropolitan women<sup>39 48 53 72</sup> and those with poorer access to radiotherapy facilities<sup>72 83 101</sup> is of concern.

Although some recent Queensland-based studies found limited evidence for a temporal reduction in geographical variations for breast cancer stage<sup>52</sup> and surgical patterns,<sup>77</sup> in practice, these changes were subtle and although the non-metropolitan to metropolitan differential reduced, it was still evident in the most recent time period. Moreover, despite improvements in survival over

all areas in Queensland over time, geographical inequalities remained.<sup>33 35</sup> These studies highlight the importance of ongoing monitoring of measured outcomes along breast cancer continuum to assess whether there has been a definitive change in these variations and to identify key drivers of any changes.

While the review found consistent evidence for variations in breast cancer survival and clinical management, patterns were inconsistent for other outcomes, primarily due to heterogeneity of the included studies or in some cases a lack of studies. These findings emphasise the importance of the work of Cancer Australia (Australia's national cancer control agency) in establishing a national comprehensive system for recording breast cancer stage and clinical management at the population level, thereby enabling accurate monitoring of the effectiveness of strategies and initiatives to improve breast cancer outcomes for non-metropolitan women in Australia.

On an international scale, inequities in access to specialised care<sup>102–104</sup> and geographical variations across the breast cancer continuum including screening,<sup>7</sup> stage at diagnosis<sup>9 131</sup> and patterns of care<sup>8 107 131–136</sup> are well documented. There is widespread consensus that these variations reflect a combination of socioeconomic, demographic and environmental factors including geography, comorbidities, access, treatment and stage at diagnosis that defy easy solutions.<sup>7–9 103 104 131 135</sup> The persistence of such inequities even for universal (publicly funded) healthcare systems<sup>7 103 131 133 136</sup> highlights the complexity of the underlying issues.

## LIMITATIONS

A number of issues made direct comparisons and to some extent interpretation of findings across studies particularly challenging. The assessment of comparability was hampered by the wide variability in study quality, levels of evidence, methodology, data sources, time period and terminology. These issues also prevented meta-analyses being carried out. Many studies were predominantly conducted at the state level, making the generalisation of findings to the national level difficult. The review also highlighted the need to improve and standardise definitions of geographical location to produce more uniform and reliable remoteness classifications. This would improve data comparability in terms of residential location and hence facilitate more definitive conclusions to be drawn on the strength of the available evidence. Similar concerns have been noted by international reviews on area-level variations in other cancer outcomes.<sup>8 137 138</sup>

Moreover, many studies had important limitations including selection bias and inadequate follow-up that impacted their quality. While using registry data allows generalisability of findings, such studies cannot comprehensively control for all potential confounders, especially those related to individual-level socioeconomic status, clinical or treatment factors since Australian cancer registries do not routinely collect information on these

measures.<sup>139</sup> Hence, population-based studies can adjust for area-level socioeconomic status but not between-persons differences. Only cross-sectional studies, although deemed inferior to population-based studies in terms of representativeness, can collect information on individual-level measures.

Considerable efforts were made to conduct a comprehensive search of existing literature on specified clinical questions by searching multiple databases with complex queries and evaluating reference lists of identified articles, published reviews and government reports to find additional articles. However, it is still possible that the search term criteria used could have unintentionally resulted in exclusion of relevant articles. Included articles were also limited to those indexed in the accessed databases.

## CONCLUSIONS

By examining the current evidence relating to geographical variations in breast cancer outcomes across the continuum of care for Australian women, this review has important implications for clinical practice, service delivery and future research. It has highlighted the gap in knowledge of variations in the treatment of advanced breast cancers, patient decision making and post-treatment follow-up.

While addressing the geographical variations in breast cancer survival and clinical management will require a multifaceted approach, initial efforts could include improving access to and participation in breast screening programmes, raising awareness of the benefits of early detection and enabling all women diagnosed with breast cancer to be assessed by a multidisciplinary team that considers all relevant treatment options and have access to best practice treatment. To achieve equitable access for all women, it is crucial to promote coordinated care among non-metropolitan women and initiatives to facilitate the educational diffusion of healthcare changes among clinicians and patients through emerging technologies<sup>140</sup> to overcome barriers of distance. Recognising the heterogeneity of existing studies in terms of geographical coverage and definitions, the establishment of a national comprehensive system for recording breast cancer stage and clinical management would enable accurate monitoring of the success of these initiatives.

Finally, encouraging evidence-based research aimed at better understanding the reasons for geographical variations in breast cancer management and outcomes at each stage of the continuum of care needs to be a priority to inform the development of targeted initiatives to improve survival and quality of life for rural and remote women with breast cancer in Australia.

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