

# Estimating cancer survival in small areas: **possible and useful**

Susanna Cramb, Kerrie Mengersen and Peter Baade

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# Survival

- The proportion who survive a given length of time after diagnosis



A topographic map of Australia showing the state of Queensland highlighted in green. The rest of the continent is shown in shades of brown and tan, representing elevation. The surrounding oceans are dark blue. The text 'Queensland' is overlaid on the left side of the map.

# Queensland

1.73 million km<sup>2</sup>

4.4 million people (2012)

# Queensland

Most dispersed population of any  
State/Territory in Australia



# Queensland

Most dispersed population of any  
State/Territory in Australia

Centralised health services



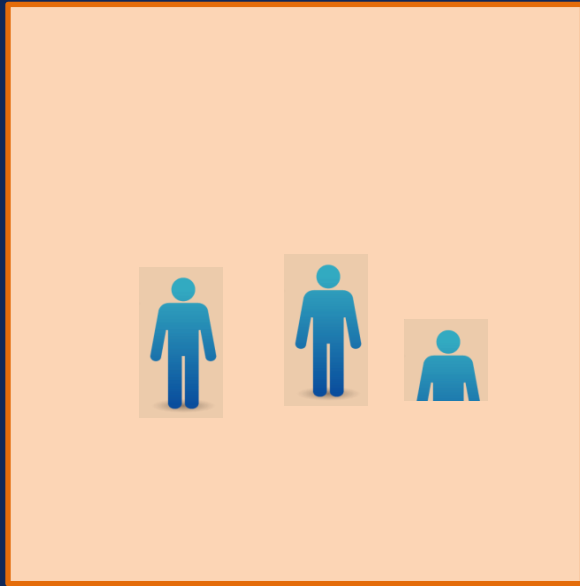
# Queensland:Thailand ratios



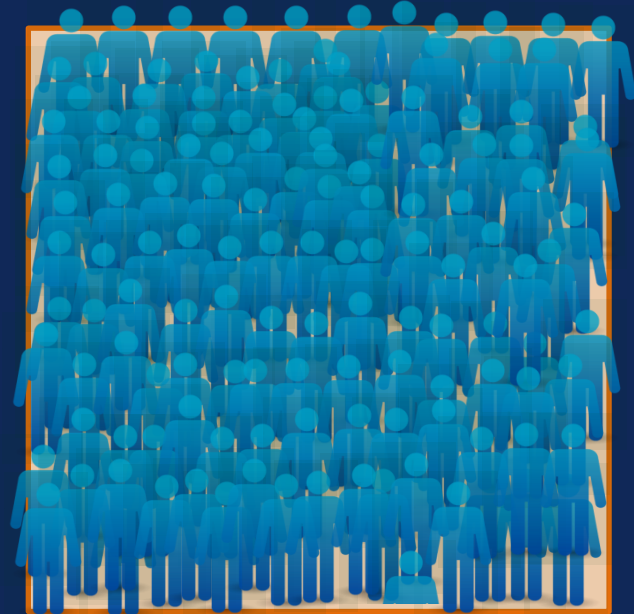
Land area: 3.4 times

Population: 0.06 times

# Queensland



# Thailand



**54 times!**



**Large area + Small population**

**= Sparse data**

**Small area estimation challenge**



# Survival

- Key measure of cancer patient care
- Allows monitoring and evaluation of health services



# Estimating Net Survival



Cause-specific



Relative

# Estimating Net Survival



Cause-specific

Relative



Based on death certificate

# Estimating Net Survival



Cause-specific

Relative



Based on death certificate

Compares against population mortality

# Estimating Net Survival



Cause-specific

Relative



Based on death certificate

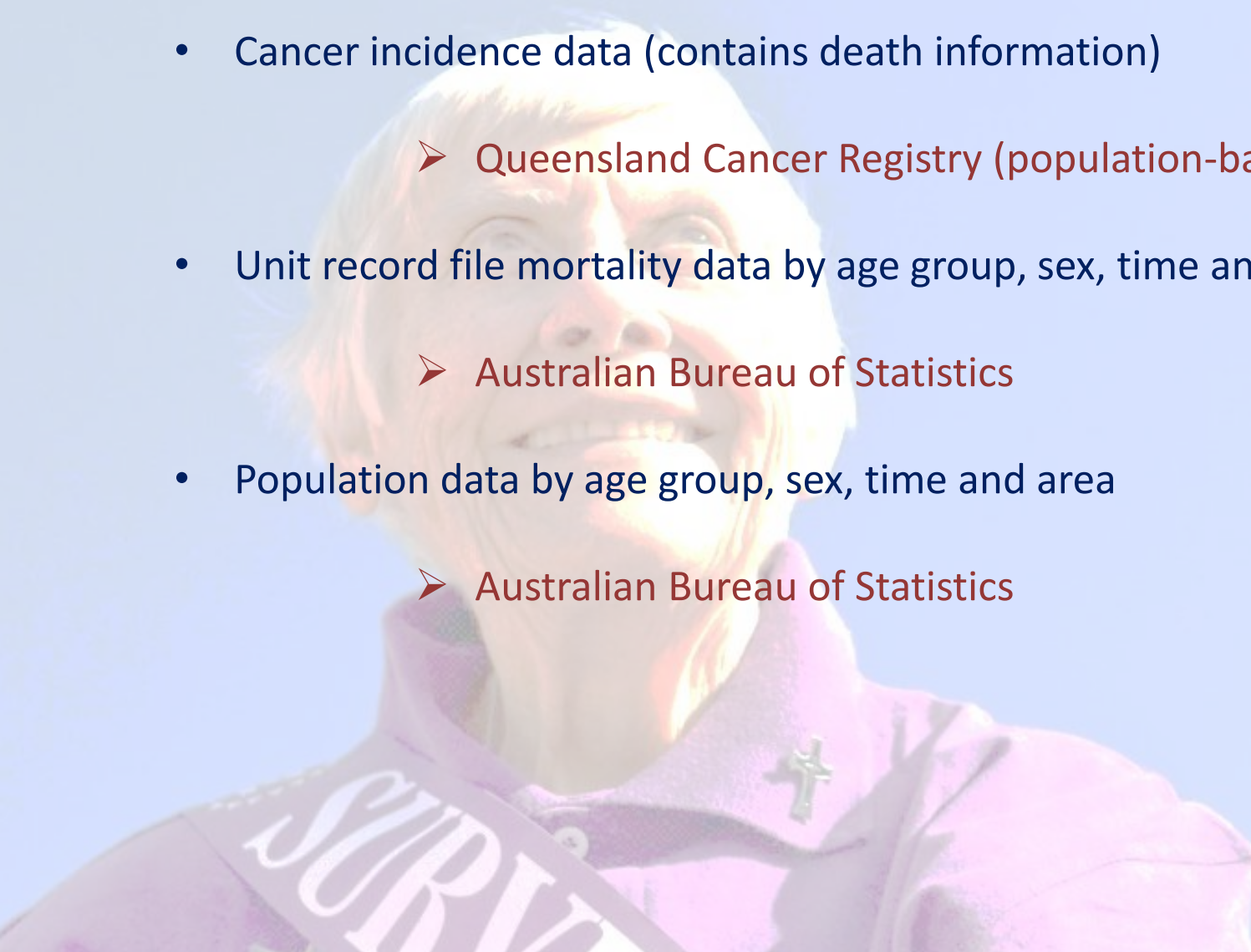


Compares against population mortality



# Data sources

- Cancer incidence data (contains death information)
  - Queensland Cancer Registry (population-based)
- Unit record file mortality data by age group, sex, time and area
  - Australian Bureau of Statistics
- Population data by age group, sex, time and area
  - Australian Bureau of Statistics



# Queensland

478 Statistical Local Areas  
(SLAs) in 2006



# Data preparation

## 1. Population mortality data

- Create lifetables by SLA, sex and year group (e.g. 2003-2007).

_px	_lx	_Lx	_Tx	_ExpYL	_Surv
0.99907	100000	99918	7960372	79.6	1
0.99907	99907	99855	7860454	78.68	0.999074
0.99907	99815	99764	7760599	77.75	0.998148
0.99907	99722	99673	7660835	76.82	0.997223
0.99907	99630	99584	7561162	75.89	0.996299
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0.99988	99526	99520	7362047	73.97	0.995259
0.99988	99514	99508	7262527	72.98	0.995143

## 2. Cancer incidence data

- Calculate the person-time at risk, and the expected deaths using the lifetable data.

## 3. Neighbourhood adjacency matrix file



# Data preparation

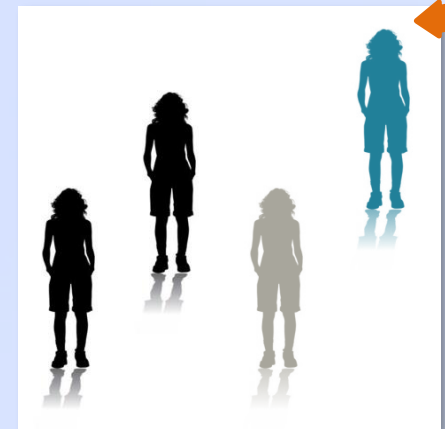
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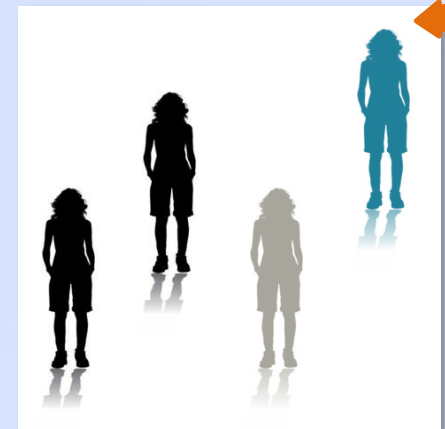
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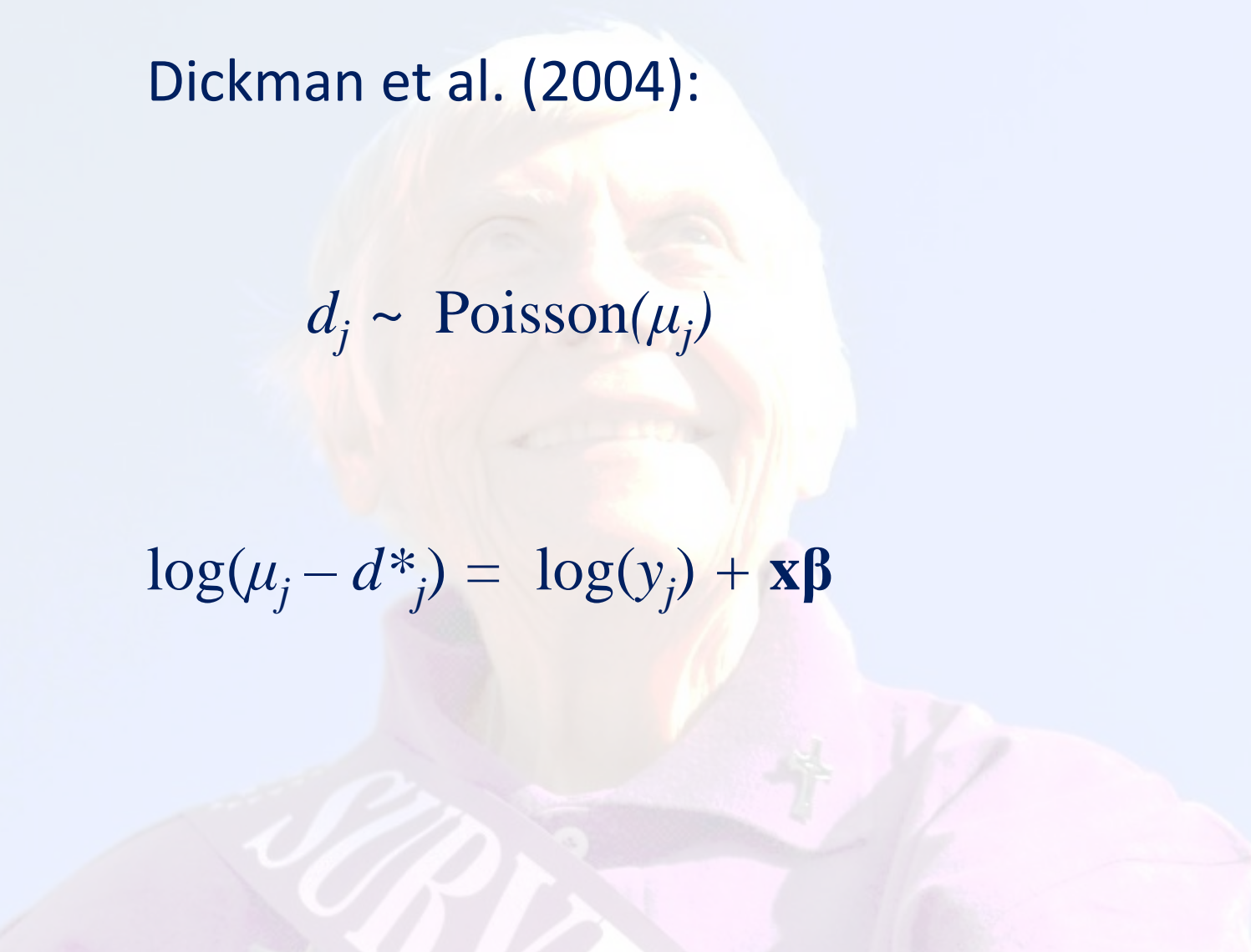


# Relative survival model

Dickman et al. (2004):

$$d_j \sim \text{Poisson}(\mu_j)$$

$$\log(\mu_j - d_j^*) = \log(y_j) + \mathbf{x}\boldsymbol{\beta}$$



# Relative survival model

Dickman et al. (2004):

Observed deaths

$$d_j \sim \text{Poisson}(\mu_j)$$

Covariate parameters

$$\log(\mu_j - d^*_j) = \log(y_j) + \mathbf{x}\boldsymbol{\beta}$$

Excess deaths

Person-time at risk

# Bayesian relative survival model

Based on Fairley *et al* (2008):

$$d_{kji} \sim \text{Poisson}(\mu_{kji})$$

$$\log(\mu_{kji} - d_{kji}^*) = \log(y_{kji}) + \alpha_j + x\beta_k + u_i + v_i$$

where  $k$  = broad age groups

$j = 1, 2, \dots, 5$  follow-up years

$i = 1, 2, \dots, 478$  SLAs

# Bayesian relative survival model

Based on Fairley *et al* (2008):

$$d_{kji} \sim \text{Poisson}(\mu_{kji})$$

Intercept

Unobserved and unstructured

$$\log(\mu_{kji} - d_{kji}^*) = \log(y_{kji}) + \alpha_j + x\beta_k + u_i + v_i$$

Unobserved with spatial structure

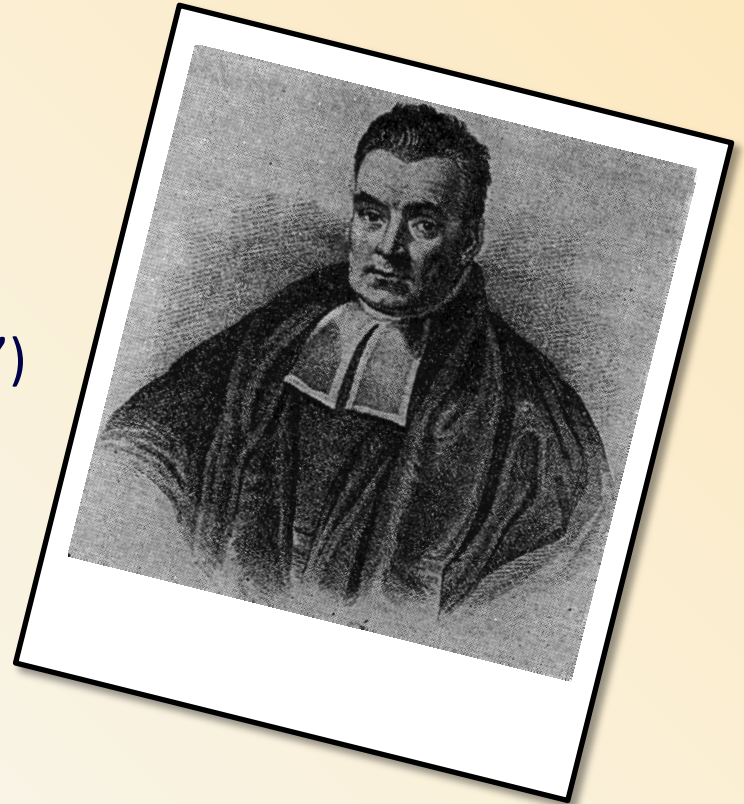
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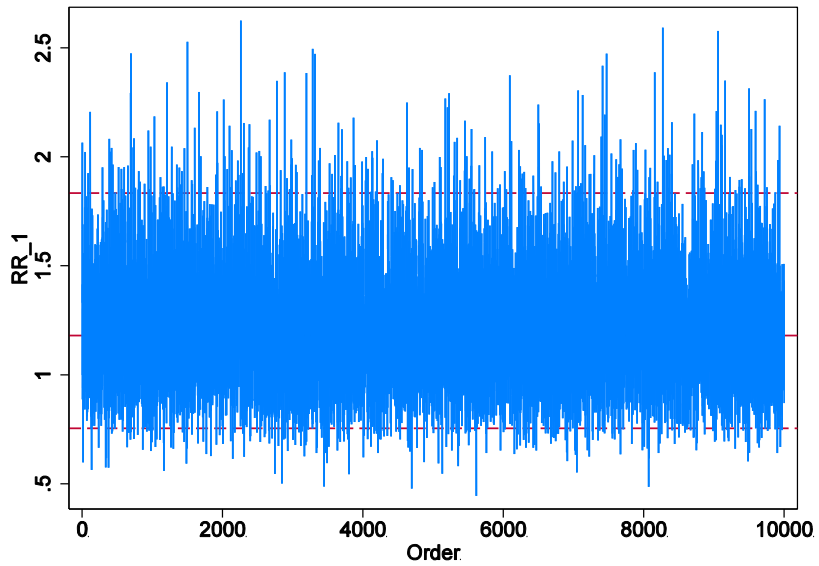
# The Bayesian difference

- Parameters considered to arise from underlying distribution (“stochastic”)
- Use probability distributions (“priors”)
- Simplifies inclusion of spatial relationships
- Posterior distributions for output parameters
- Posterior proportional to Likelihood x Prior

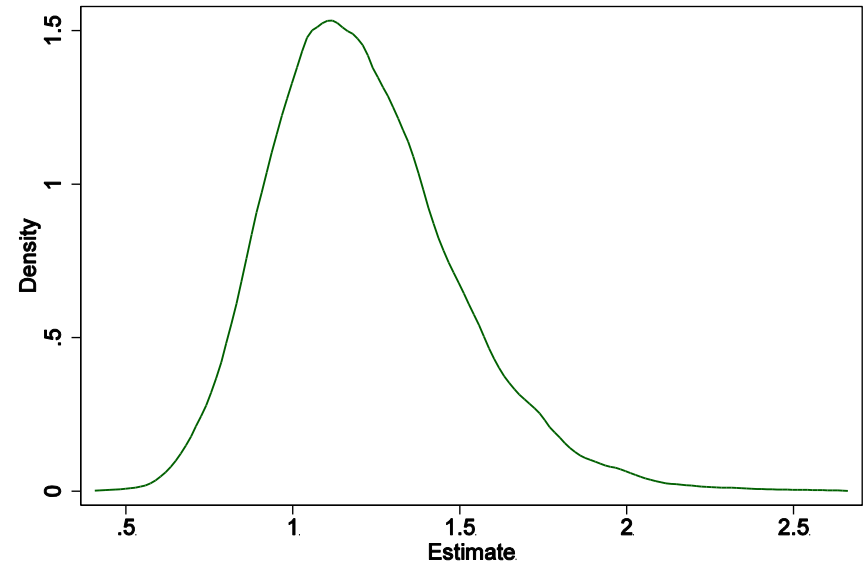


# Posterior distributions

Trace plot



Density plot





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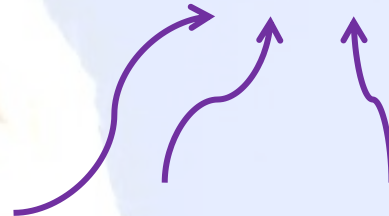
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e.g.  $\sim \text{Normal}(0,1000)$



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e.g.  $\sim \text{Normal}(0,1000)$

CAR prior

where  $k$  = broad age groups

$j = 1, 2, \dots, 5$  follow-up years

$i = 1, 2, \dots, 478$  SLAs

# The Conditional AutoRegressive (CAR) distribution

Area full conditional distributions:

$$p(u_i | u_j, i \neq j, \sigma^2) \sim N \left( \bar{\mu}_i, \frac{\sigma^2}{n_{\delta_i}} \right)$$



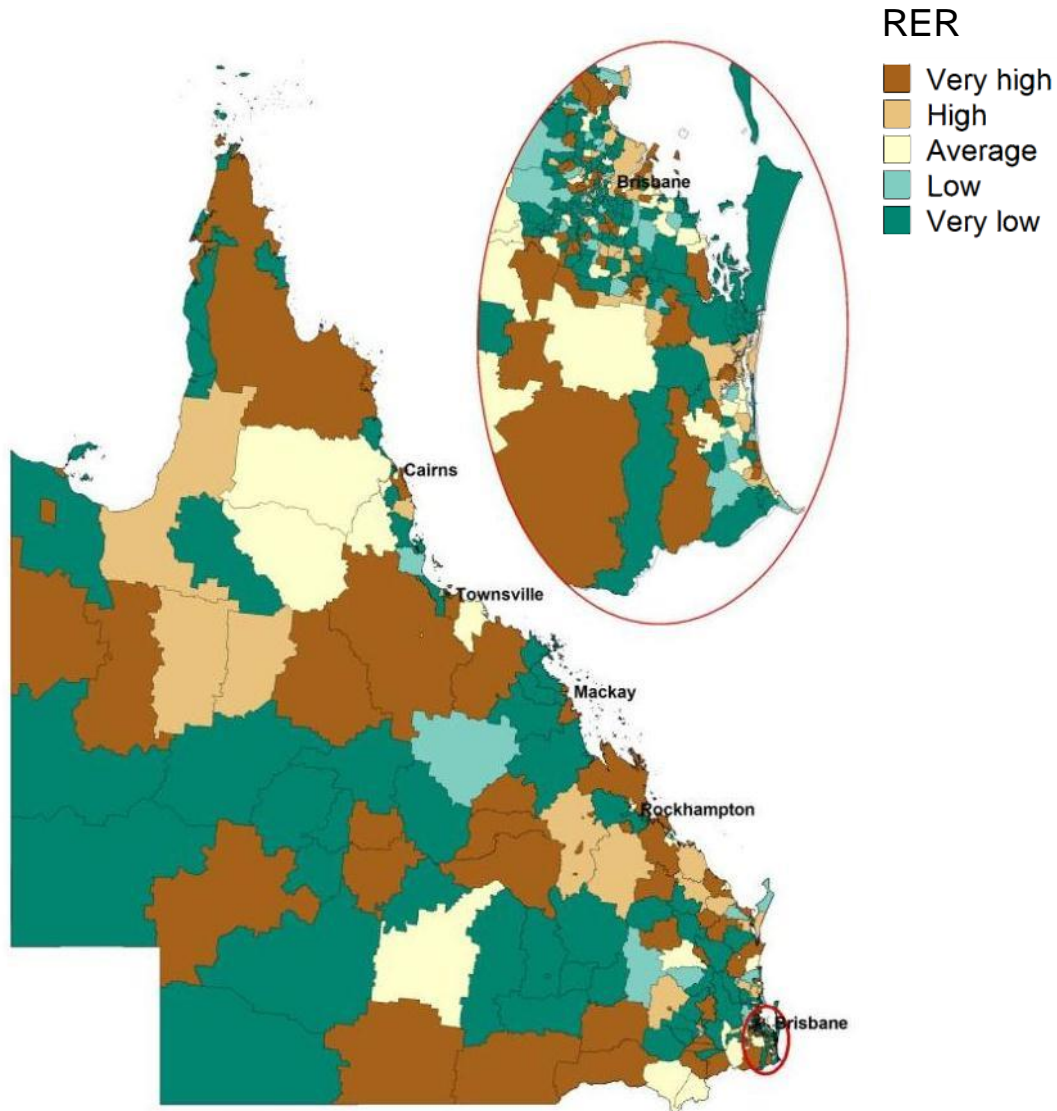
$$\bar{\mu}_i = \sum_{j \in \delta_i} \frac{u_j}{n_{\delta_i}}$$

$n_{\delta_i}$  = number of neighbours

$\sigma^2$  = variance

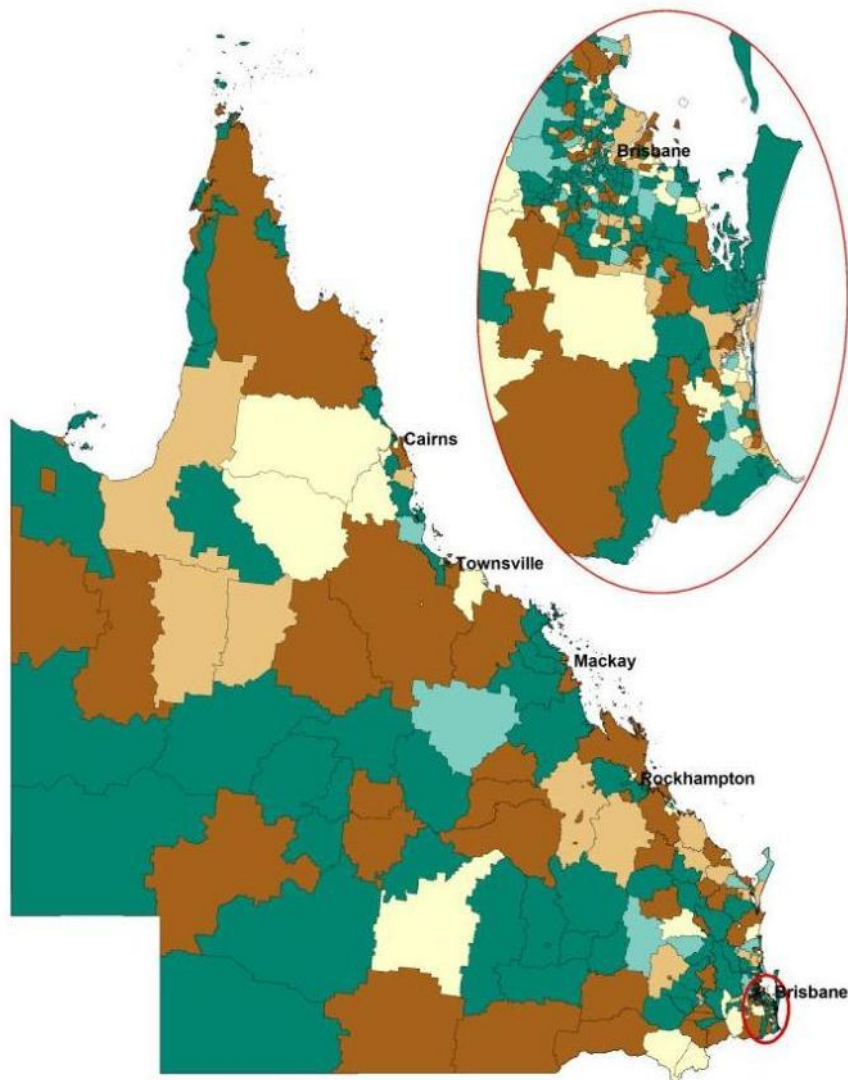
# Breast cancer survival (risk of death within 5 years)

Raw estimates



# Breast cancer survival (risk of death within 5 years)

## Raw estimates



### RER

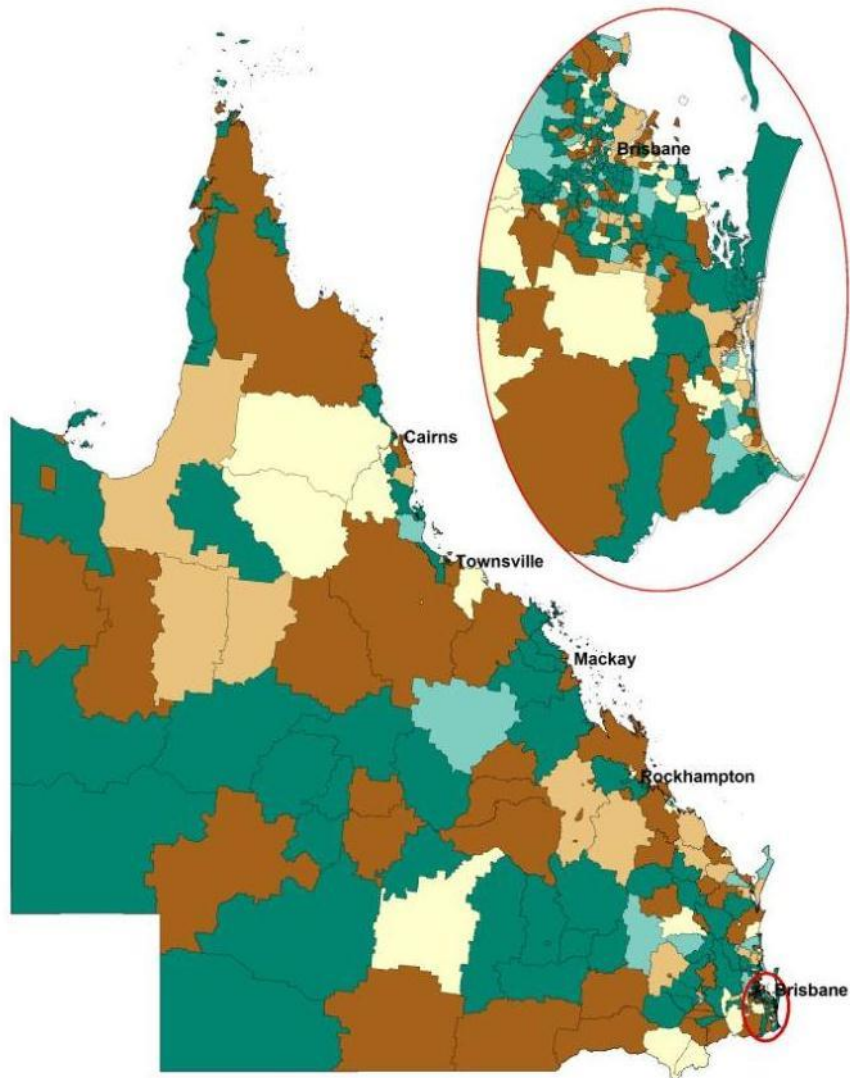
- Very high
- High
- Average
- Low
- Very low

## Problems

- Many large areas have small populations (and vice versa)
- Excessive random variation – obscures the true geographic pattern

# Breast cancer survival (risk of death within 5 years)

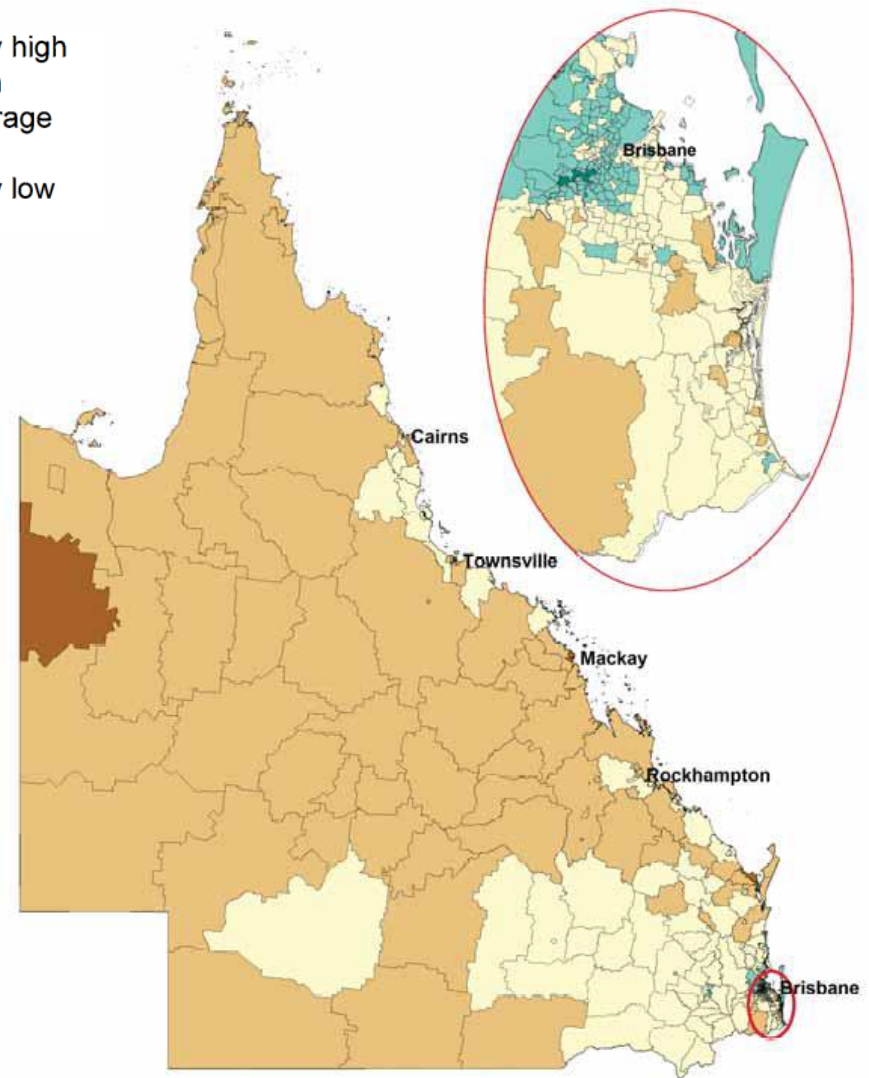
Raw estimates



Smoothed estimates

RER

- Very high
- High
- Average
- Low
- Very low



# Results and Benefits

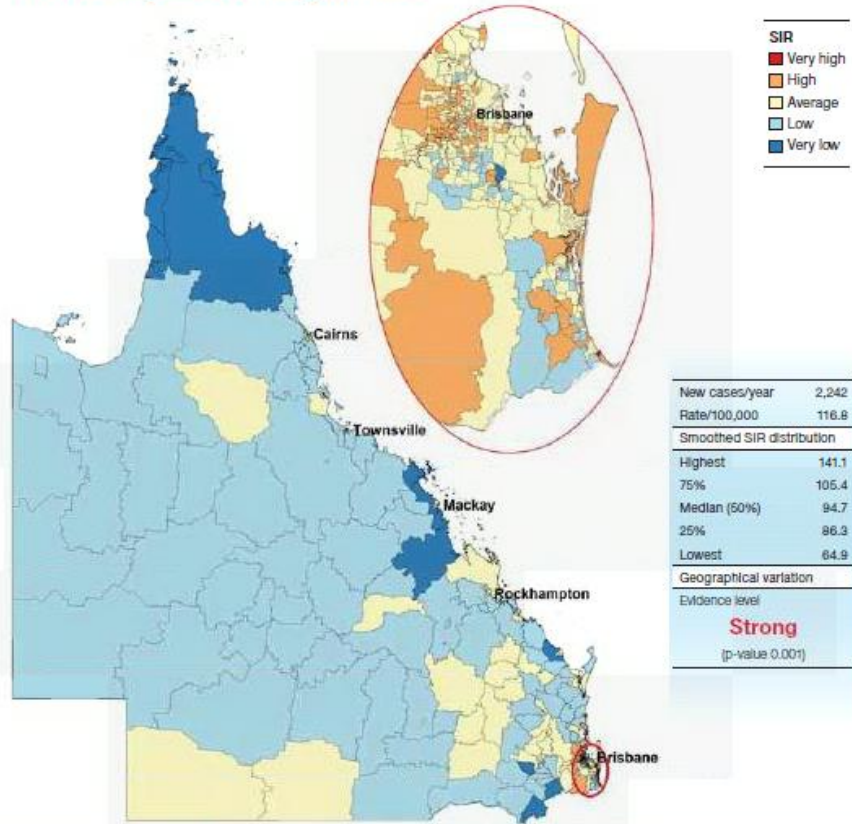
This model allows us to determine:

- Robust small area estimates with uncertainty
- Influence of important covariates
- Probabilities (e.g. probability  $RER > 1$ )
- Ranking
- Number of deaths resulting from spatial inequalities



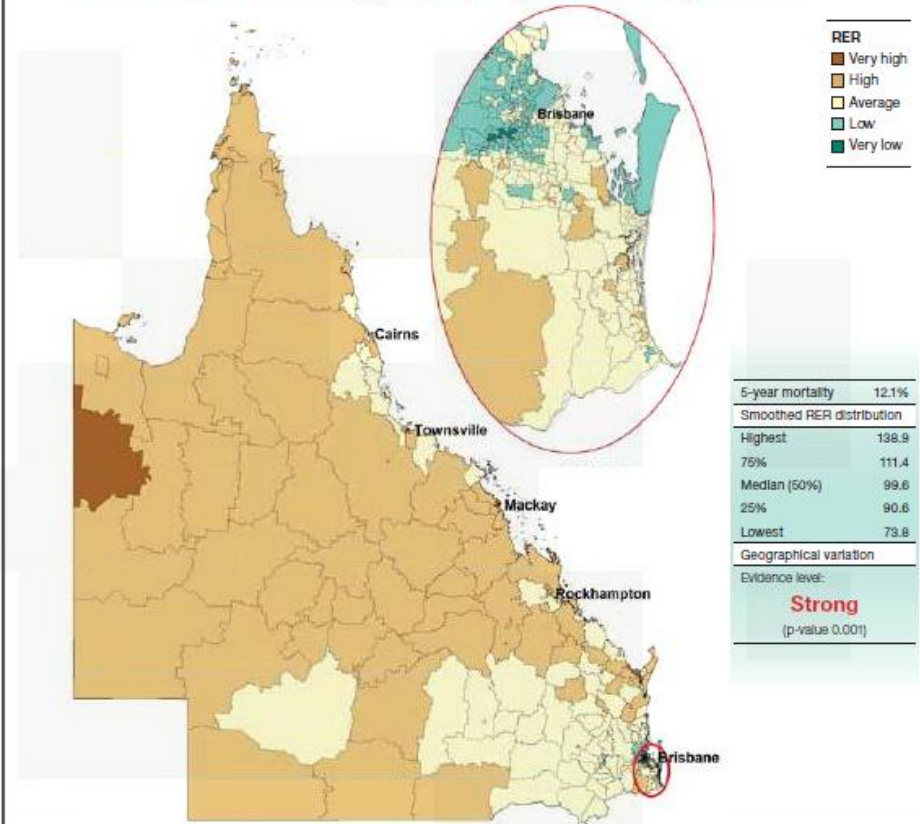
# Breast cancer

## Risk of diagnosis among females

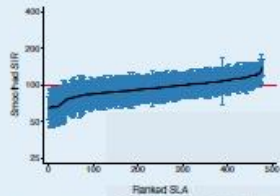


# Breast cancer

## Risk of death within five years of diagnosis among females

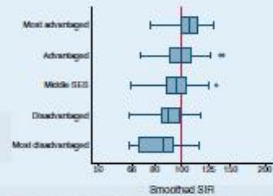


### Level of Uncertainty

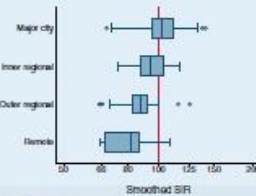


### Distribution of smoothed SIR estimates according to:

#### (a) Socioeconomic status

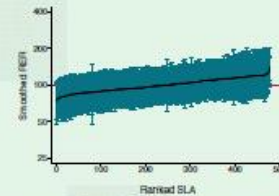


#### (b) Rurality



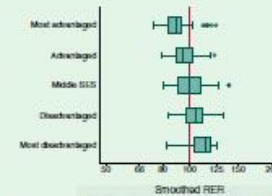
Notes: Smoothed SIR (Standardised Incidence Ratio) estimates are in comparison to the Queensland average (red line on graphs), and should not be directly compared between SLAs (Statistical Local Areas). Data are for cases diagnosed between 1998 and 2007.

### Level of Uncertainty

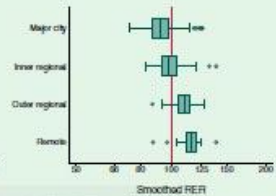


### Distribution of smoothed REER estimates according to:

#### (a) Socioeconomic status



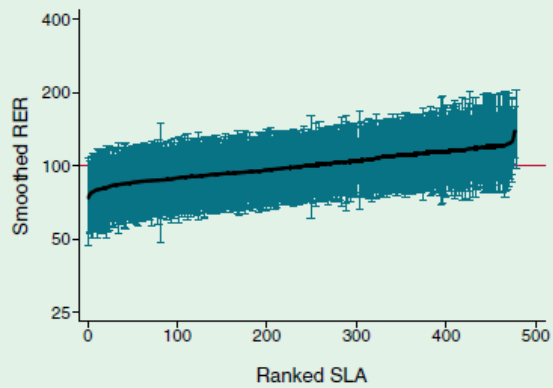
#### (b) Rurality



Notes: Smoothed REER (Relative Excess Risk) estimates are in comparison to the Queensland average (red line on graphs), and should not be directly compared between SLAs (Statistical Local Areas). Data are for 'at risk' cases in the period 1998 and 2007.

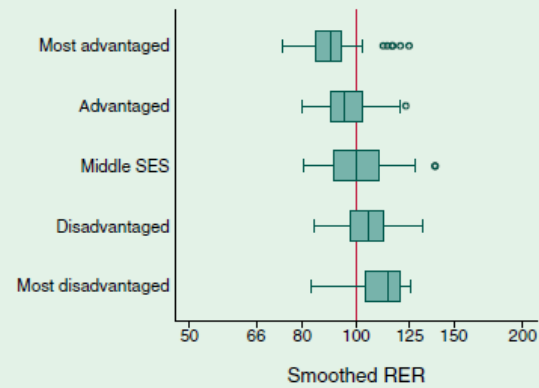
# Graphs

## Level of Uncertainty

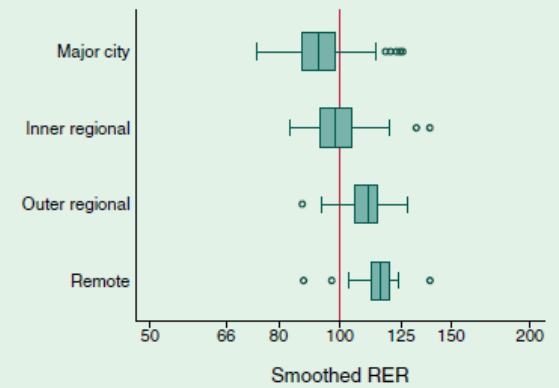


## Distribution of smoothed RER estimates according to:

### (a) Socioeconomic status



### (b) Rurality



# Bayesian relative survival model

Breast and colorectal cancers

$$d_{kji} \sim \text{Poisson}(\mu_{kji})$$

$$\log(\mu_{kji} - d_{kji}^*) = \log(y_{kji}) + \alpha_j + x\beta_k + v_i + u_i$$

where  $k$  = broad age groups/SES/remoteness/stage/gender

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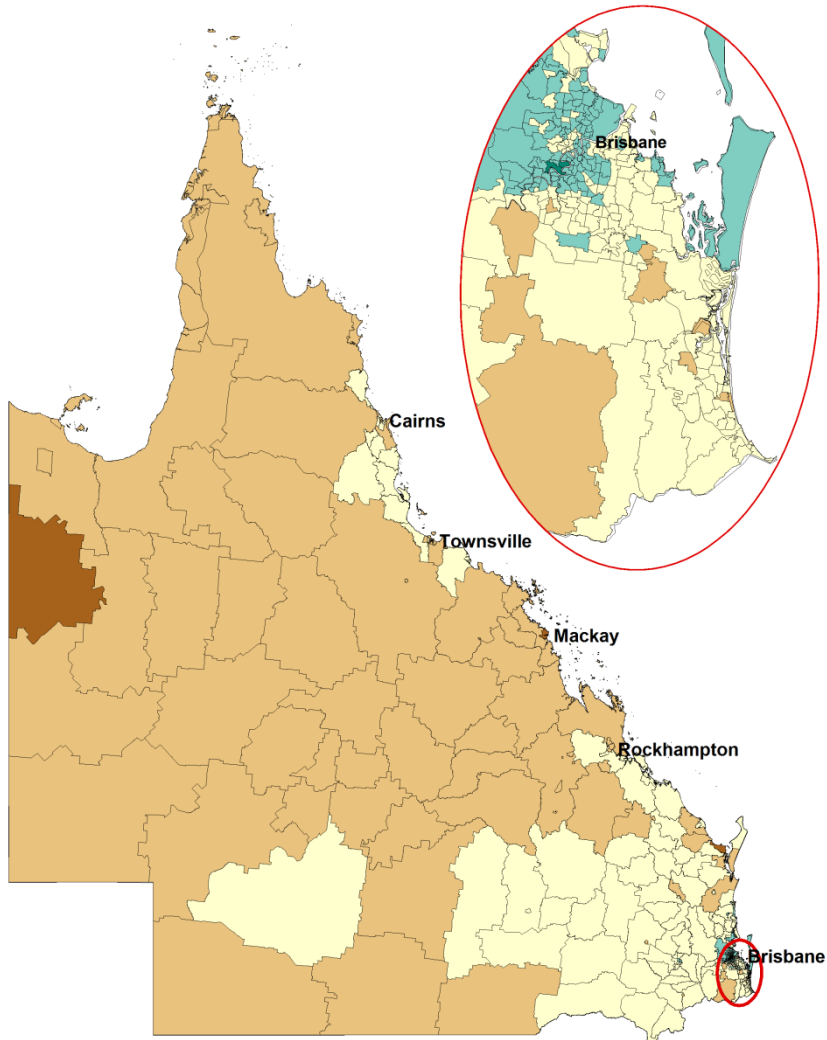
$j$  = 1,2,...5 follow-up years

$i$  = 1,2,...478 SLAs

# Breast cancer survival (risk of death within 5 years)

Adjusted for age

Spatial variation p-value=0.001

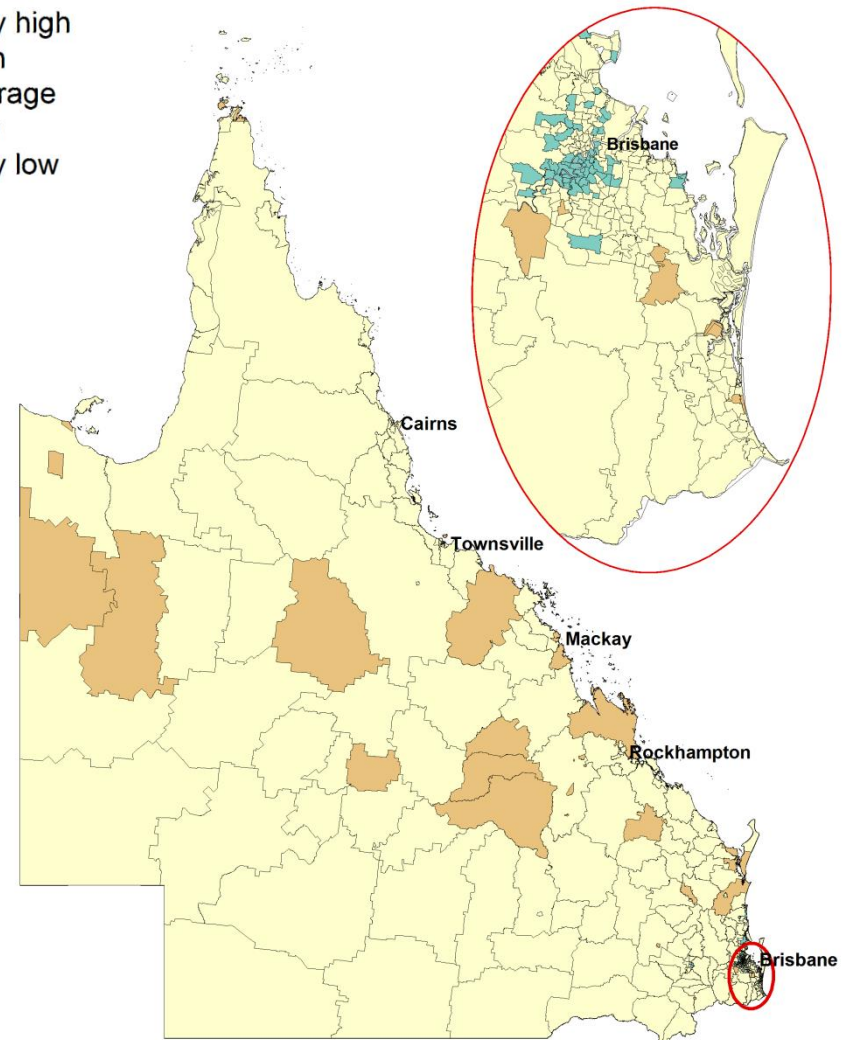


Adjusted for age & stage

Spatial variation p-value=0.042

RER

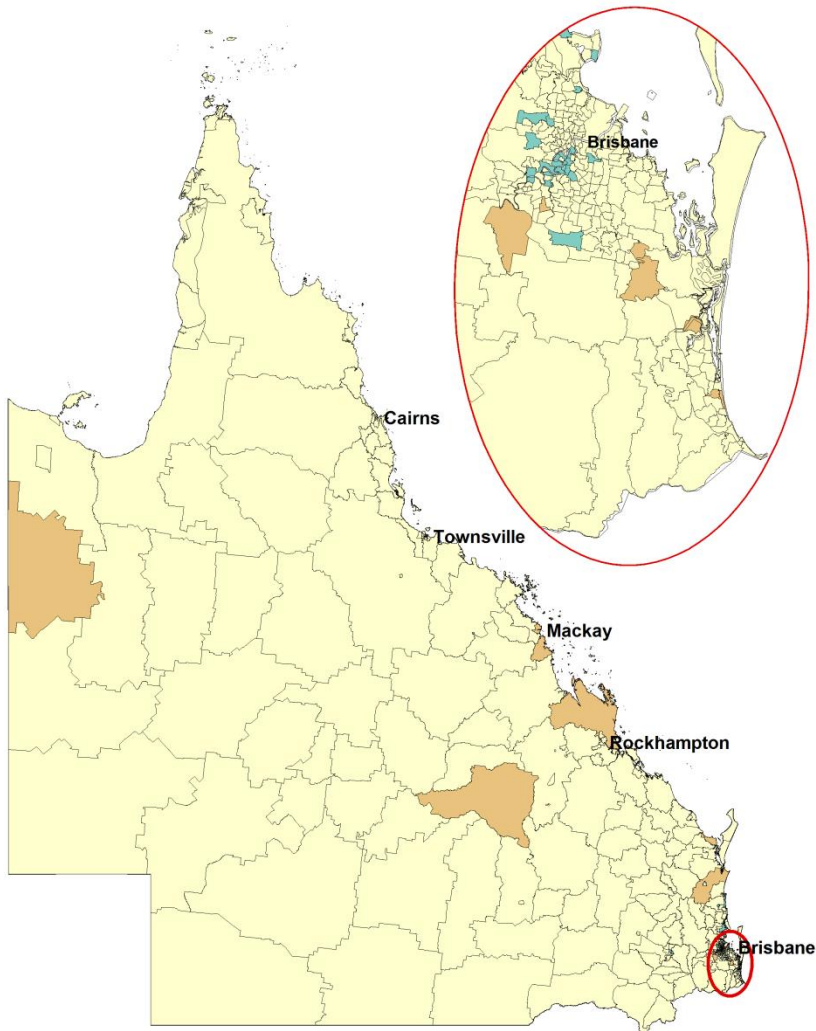
- Very high
- High
- Average
- Low
- Very low



# Breast cancer survival (risk of death within 5 years)

Adjusted for age, stage & SES

Spatial variation p-value=0.452

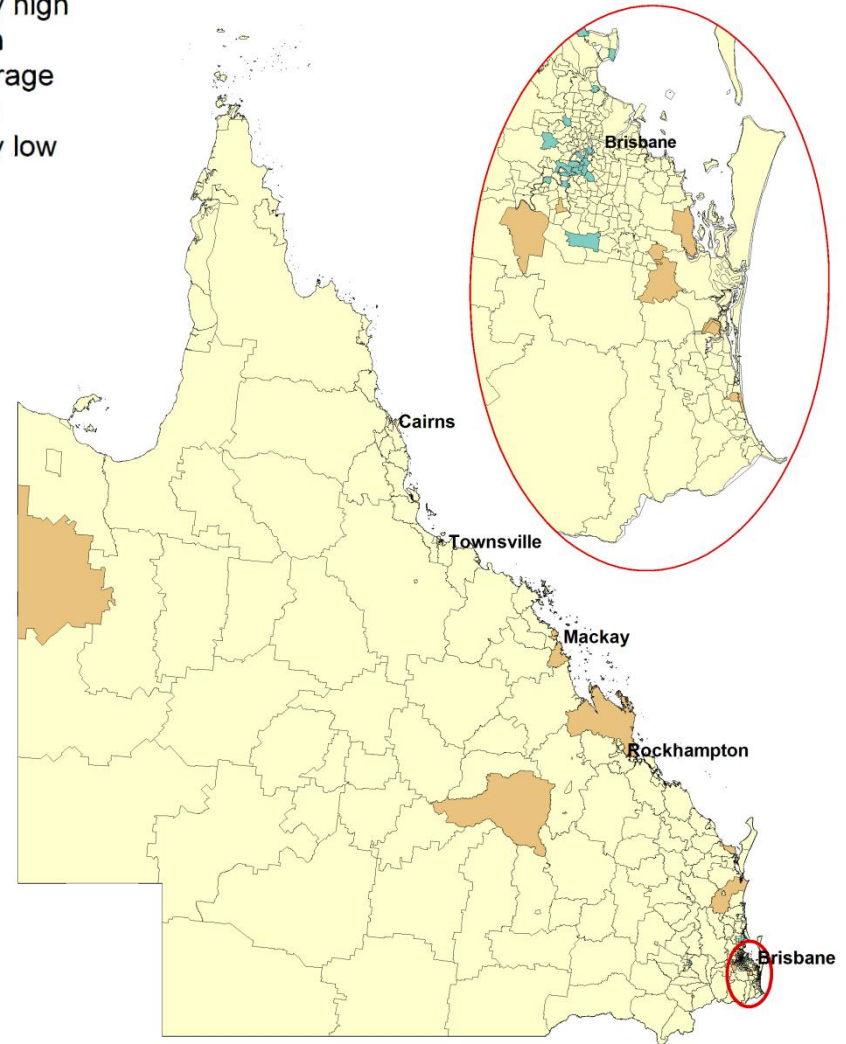


Adjusted for age, stage, SES & distance

Spatial variation p-value=0.631

RER

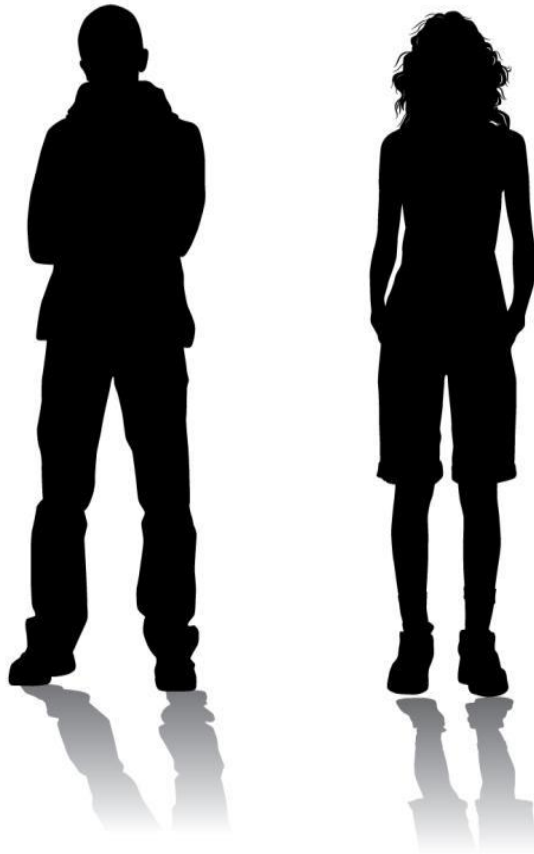
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# How many deaths could be prevented if no spatial inequalities?

Number of deaths within 5 years from diagnosis due to non-diagnostic spatial inequalities (1997-2008):

Colorectal cancer:



Breast cancer:



# How many deaths could be prevented if no spatial inequalities?

Number of deaths within 5 years from diagnosis due to non-diagnostic spatial inequalities (1997-2008):

Colorectal cancer: **470** (7.8%)

Breast cancer: **170** (7.1%)

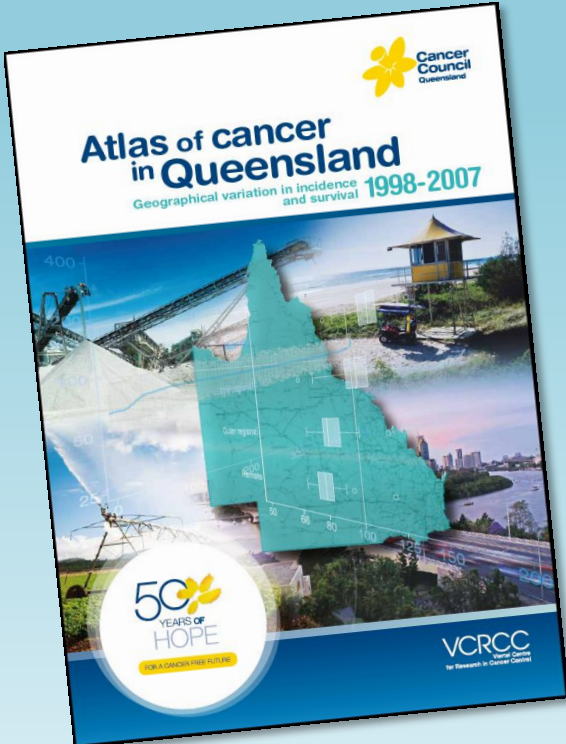




# Implementation

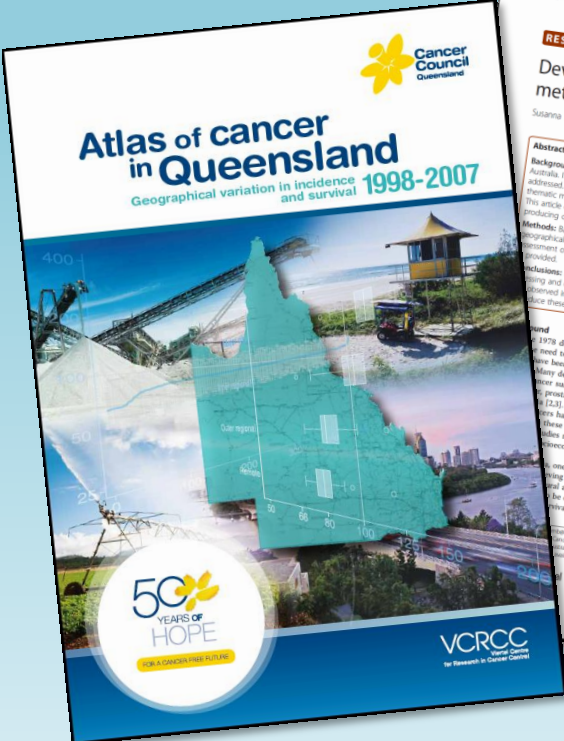
- Neighbourhood matrix created in GeoDa (<https://geodacenter.asu.edu/>)
- Ran in WinBUGS (Bayesian inference Using Gibbs Sampling) interfaced with Stata
  - Freely available at: [www.mrc-bsu.cam.ac.uk/bugs](http://www.mrc-bsu.cam.ac.uk/bugs)
  - 250,000 iterations discarded, 100,000 iterations monitored (kept every 10th)
  - Time taken: 3 hours 15 minutes+
- On a dedicated server:
  - Dual CPU Quad Core Xeon E5520's: 8 Cores and 16 Threads, large 8MB Cache
  - Quick Path Interconnect: fast memory access

Cramb SM, Mengersen KL, Baade PD. 2011. The Atlas of Cancer in Queensland: Geographical variation in incidence and survival, 1998-2007. Cancer Council Queensland: Brisbane.



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Cramb et al. *International Journal of Health Geographics* 2011, 10:9  
<http://www.ij-healthgeographics.com/content/10/1/9>

INTERNATIONAL JOURNAL OF HEALTH GEOGRAPHICS

RESEARCH  
Developing the atlas of cancer in Queensland: methodological issues  
Open Access

Susanna M Cramb<sup>1,2\*</sup>, Kerrie L Mengersen<sup>1</sup>, Peter D Baade<sup>1,3</sup>

**Abstract**  
**Background:** Achieving health equity has been identified as a major challenge, both internationally and within Australia. Inequalities in cancer outcomes are well documented, and must be quantified before they can be addressed. One method of portraying geographical variation in data sets maps. Recently we have produced thematic maps showing the geographical variation in cancer incidence and survival across Queensland, Australia. This article documents the decisions and rationale used in producing these maps, with the aim to assist others in producing chronic disease atlases.  
**Methods:** Bayesian hierarchical models were used to produce the estimates. Justification for the cancers chosen, geographical areas used, modelling method, outcome measure missed, production of the adjacency matrix, agreement of convergence, sensitivity analyses performed and determination of significant geographical variation is provided.  
**Conclusions:** Although careful consideration of many issues is required, chronic disease atlases are a useful tool for identifying and quantifying geographical inequalities. In addition they help focus research efforts to investigate why observed inequalities exist, which in turn inform advocacy, policy, support and education programs designed to reduce these inequalities.

**Keywords:** Health equity, cancer outcomes, geographical variation, thematic maps, Queensland, Australia, chronic disease atlases, Bayesian hierarchical models, adjacency matrix, convergence, sensitivity analyses, advocacy, policy, support and education programs.

**Background:** The 1978 declaration of Alma-Ata which highlighted the need to address inequalities in health status of less developed nations has seen improvements in cancer survival, notably for colorectal cancer, prostate cancer, non-Hodgkin lymphoma and breast cancer [1]. However, incidence and mortality rates for these outcomes persist, with numerous studies reporting disparities in cancer outcomes by socioeconomic status or urban/rural categories. One of the greatest recognized health inequities is the lack of health equity for all [2]. Cancer incidence and mortality rates in disadvantaged areas are generally higher than in advantaged areas [3]. Cancer outcomes are generally poorer in disadvantaged areas [4]. Often these areas have a higher prevalence of risk factors such as smoking, obesity and lower levels of physical activity [11,12]. Distance is also important, with cancer patients in rural areas having reduced access to cancer care services [13-15].

Inequalities need to be quantified before they can be addressed. Maps have been used to portray geographical variation in cancer incidence and survival [16]. By providing a visual representation of cancer outcomes, geographic patterns of disease are able to be identified and effectively addressed [17]. For example, cancer mortality maps showed high mortality from cancer in the south-eastern United States of America which led to the identification of snuff dipping as a risk factor [18]. Similarly, mammography screening efforts were intensified after finding low in-situ breast cancer incidence rates from mapped data in north-western Connecticut [19].

We recently developed thematic maps showing the geographical variation in cancer incidence and survival across Queensland, Australia [20]. With a population of 4.2 million [21] and covering an area of 1.9 million km<sup>2</sup>, Queensland is a large and geographically diverse state. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

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Full list of author information is available at the end of the article

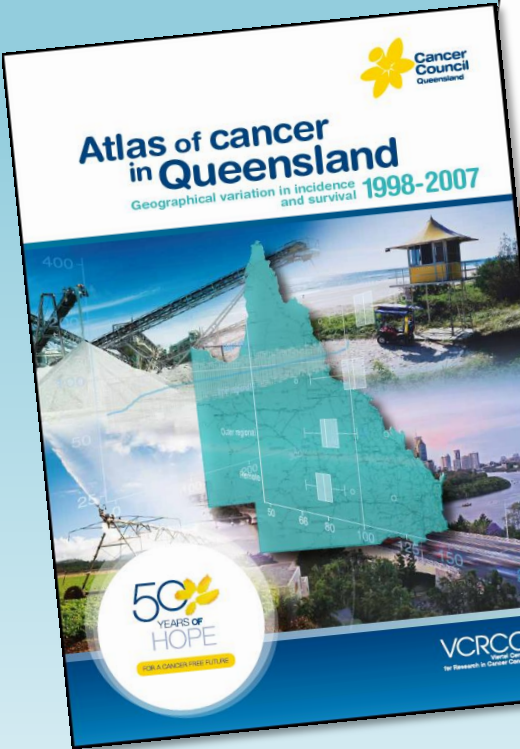
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Cramb SM, Mengersen KL, Turrell G, Baade PD. 2012. Spatial inequalities in colorectal and breast cancer survival: Premature deaths and associated factors. *Health & Place*;18:1412-21.



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**Methods:** Bayesian hierarchical models were used to produce the estimates. Justification for the cancers chosen, the geographical areas used, modelling method, outcome measures measured, production of the adjacency matrix, adjustment of convergence, sensitivity analysis performed and determination of significant geographical variation is provided.  
**Conclusions:** Although careful consideration of many issues is required, chronic disease atlases are a useful tool for identifying and quantifying geographical inequalities. In addition they help focus research efforts to investigate why observed inequalities exist, which in turn inform advocacy, policy support and education programs designed to reduce these inequalities.

**Background:** The 1978 declaration of Alma-Ata which highlighted the need to address inequalities in health status between developed nations has seen improved cancer survival, notably for colorectal cancer, prostate cancer, non-Hodgkin lymphoma and breast cancer [1]. However, notable disparities in cancer outcomes persist, with numerous studies reporting disparities in cancer outcomes across economic status or subnational categories [2,3]. Also, incidence and mortality rates for these outcomes persist, with numerous studies reporting disparities in cancer outcomes across economic status or subnational categories [4].

One of the greatest recognized health inequalities is the disparity in health equity for all [5]. Cancer is the leading cause of death and disability in Australia, with 148,000 people diagnosed with advanced cancer each year [6]. In Queensland, cancer is the leading cause of death and disability, with 148,000 people diagnosed with advanced cancer each year [6]. In Queensland, cancer is the leading cause of death and disability, with 148,000 people diagnosed with advanced cancer each year [6].

We recently developed thematic maps showing the geographical variation in cancer incidence and survival across Queensland, Australia [2]. With a population of 4.2 million [21] and covering an area of 1.9 million

areas have a higher prevalence of risk factors such as smoking, obesity and lower levels of physical activity [11,12]. Distance is also important, with cancer patients in rural areas having reduced access to cancer care services [13,15].

Inequalities need to be quantified before they can be addressed. Maps have been used to portray geographical data for a range of diseases since the mid-1800s, including cancer outcomes, geographic patterns of disease are able to be identified and effectively addressed [17]. For example, cancer mortality maps showed high mortality from lung cancer in south-eastern United States of America factor [18]. Similarly, mammography screening efforts were intensified after finding low in situ breast cancer incidence rates from mapped data in north-western Connecticut [19].

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**Spatial inequalities in colorectal and breast cancer survival: Premature deaths and associated factors**

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**ABSTRACT**

This study examines the influence of cancer stage, distance to treatment facilities and area disadvantage on breast and colorectal cancer spatial survival inequalities. We also estimate the number of premature deaths after adjusting for cancer stage to quantify the impact of spatial survival inequalities. Population-based descriptive study of residents aged <90 years in Queensland, Australia diagnosed with primary invasive breast (23,002 females) or colorectal (14,600 males), 11,706 breast and 6278 colorectal cancer deaths, 1998–2007. Bayesian hierarchical models explored relative survival inequalities across 478 regional cancer stages and disadvantage explained the spatial inequalities in breast cancer survival. However spatial inequalities in colorectal cancer survival persisted after adjustment. Of the 6278 colorectal cancer deaths within 5 years of diagnosis, 476 (8%) were associated with spatial inequalities in socio-demographic factors, 16 factors beyond cancer stage at diagnosis. For breast cancer, of 2412 deaths, 176 (7%) were related to spatial inequalities in socio-demographic factors. Quantifying premature deaths can increase incentive for action to reduce these spatial inequalities.

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**1. Background**

Worldwide, breast cancer is the most common cancer in women, while colorectal cancer is the second most commonly diagnosed among women, and third most common among men (Fitzly et al., 2010). In developed nations, including Australia, survival for both these cancers has improved over recent decades (Australian Institute of Health and Welfare and Cancer Australia, Australian Association of Cancer Registries, 2008), with Australia having one of the highest survival rates in the world (Coleman et al., 2011).

However, the improvement in survival has not been observed equally across all population subgroups. Inequalities for both breast and colorectal cancer survival have been reported for deprivation and differences in health care access (Du et al., 2011; McKenzie et al., 2011). Within Australia, poorer survival has been observed for those in areas of greater socio-economic disadvantage, greater remoteness and, for rectal cancer, for the distance to tertiary-level facilities (Australian Institute of Health and Welfare and Cancer Australia, 2011).

The quality of patient management can be gauged by survival (Yu et al., 2004). The prognosis for breast and colorectal cancer depends in large part on the stage of disease at diagnosis (Schottenfeld and Fraumeni, 2005), which may vary geographically (Tun et al., 2002; Tun et al., 2011). Beyond that, the outcome depends on other non-diagnostic factors such as treatment, rehabilitation, environmental factors such as area disadvantage, and patient characteristics including comorbidities (Yu et al., 2004), all of which could potentially contribute to geographical variation in cancer survival. Throughout this paper we use the term “non-diagnostic” to encompass these other factors.

Since only a few population-based cancer registries collect stage information, not many studies have been able to separate the effect of diagnostic from other factors on geographic inequalities in cancer survival on a population basis. In New South Wales (NSW), Australia, it was found that adjusting for stage did not reduce the survival differential for colorectal cancer (Yu et al., 2005a). However, in Italy, stage at diagnosis explained most of the colorectal cancer survival inequalities between Northern and Southern areas, while treatment had a minimal role (Fusco et al., 2010). In England, stage at diagnosis and deprivation were important causes of breast cancer survival inequalities (Davies et al., 2007).

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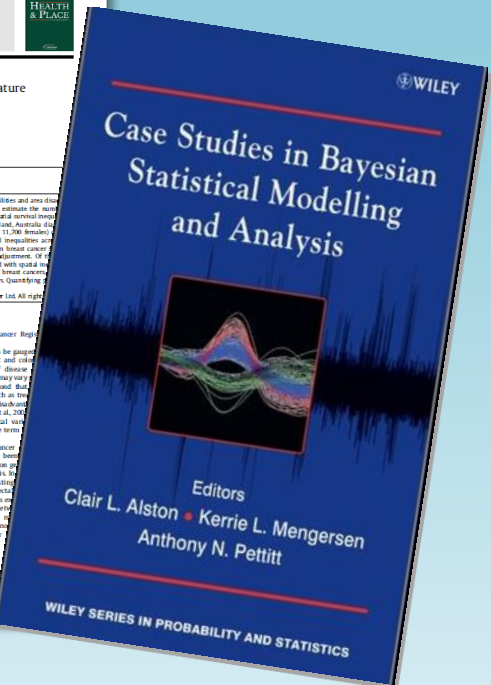
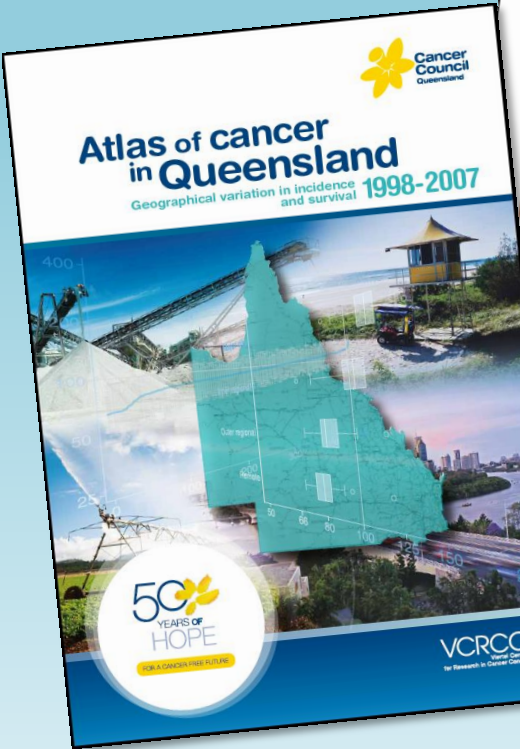
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“By increasing our understanding of the small area inequalities in cancer outcomes, this type of innovative modelling provides us with a better platform to influence government policy, monitor changes, and allocate Cancer Council Queensland resources”

~ Professor Jeff Dunn,  
Cancer Council Queensland CEO

