A Comprehensive Study of the Epidemiology of Haematological Malignancies in North Queensland

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Abstract

Background: There is an absence of clinically relevant epidemiological data in regional Australia pertaining to haematological malignancies. ***Aim*:** To determine the incidence and geographical variation of haematological malignancies in North Queensland using a clinically appropriate disease classification. ***Methods***: Retrospective, observational study of individual patient data records of all adults diagnosed with a haematological malignancy between 2005-2014 and residing within The Townsville Hospital Haematology catchment region. We report descriptive summaries, incidence rates and incidence-rate ratios of haematologic malignancies by geographic regions. ***Results***: 1581 haematological malignancies (69% lymphoid, 31% myeloid) were diagnosed over the 10-year study period. Descriptive data is presented for 58 major subtypes as per the WHO diagnostic classification of tumours of haematopoietic and lymphoid tissues. The overall median age at diagnosis was 66 years with a male predominance (60%). We demonstrate a temporal increase in the incidence of haematologic malignancies over the study period. We observed geographical variations in the age-standardised incidence rates per 100,000 ranging from 0.5 to 233.5. Our data suggests an increased incidence rate ratio for haematological malignancies in some postcodes within the Mackay area compared to other regions. ***Conclusion***: This study successfully reports on the incidence of

haematological malignancies in regional Queensland using a clinically meaningful diagnostic classification system and identifies potential geographic hotspots. We advocate for such contemporary, comprehensive, and clinically meaningful epidemiological data reporting of blood cancer diagnoses in wider Australia. Such an approach will have significant implications toward developing appropriate data-driven management strategies and public health responses for haematological malignancies.

Keywords

Haematologic malignancies, epidemiology, public health, classification, regional health planning

Introduction

Haematological malignancies account for approximately 7% of all cancers and are collectively the fourth most frequently diagnosed cancer in the western world (1). In Australia, there are over 17,000 newly diagnosed cases of a haematological malignancy each year with an ongoing increase in disease incidence (2). Haematological neoplasms are derived from myeloid or lymphoid cells, and broadly categorised as non-Hodgkin lymphoma, Hodgkin lymphoma, acute leukaemia, and multiple myeloma. Indeed, the Australian Institute of Health and Welfare reports on blood cancer statistics using this broad classification (3). However, clinicians and

pathologists use the World Health Organisation (WHO) classification of tumours of haematopoietic and lymphoid tissues as a standard for diagnostic classification and reporting (4, 5). The WHO classification is an extensive and detailed diagnostic classification system, and is recurrently updated to incorporate new clinical, prognostic, immunophenotypic and genetic data to discriminate between the vastly heterogenous haematological malignancies. The range and depth of data derived from the WHO classification makes it difficult to use in public cancer registries. Consequently, there is a paucity in detailed epidemiological data of blood cancers in Australia using such a clinically appropriate disease classification system. To respond to similar challenges in the United Kingdom, the Haematological Malignancy Research Network (HRMN) was established and provides informative data on two out of the thirty-seven cancer networks in the UK National Health Service (6).

In addition to incorporating a clinically meaningful classification system, it is equally important to consider geographic regions and changing trends over time (7). The identification of high incidence regions may provide potential aetiological clues for disease, and impact policies relating to access to cancer care (8). Observational studies have suggested that broad-spectrum herbicide use in agriculture may be associated with an increased risk of non-Hodgkin lymphoma. This has been recently highlighted in the lay media with high-profile lawsuits in the United States (9, 10). However, it must be noted that causality has not been established, and there is indeed considerable inconsistency regarding such an association in the current literature. Nonetheless, this avenue has not been explored in Australia, and nor has the question of whether there is increased blood cancer incidence in regions in proximity to mining installations.

In this study, we sought to comprehensively evaluate the incidence of haematological malignancies in North Queensland using the clinically appropriate WHO disease classification system and provide the most comprehensive statistics for haematological malignancies within this region. Potential blood cancer 'hotspots' and contributing factors were also investigated. Such a thorough, high-quality evaluation of the blood cancer burden in North Queensland will benefit numerous stakeholders, including regulators, funding agencies, public health bodies, clinicians, and patients. It will assist prioritisation around cancer care in regional Australia - from prevention, early detection, access to care and treatment.

Methods

Data on all haematologic cancers diagnosed in individuals ≥ 18 years of age and residing within the Townsville Hospital haematology catchment area between January 2005 to December 2014 were obtained from the Queensland Cancer Registry (QCR). The QCR is a population-based register that captures all cancers diagnosed in Queensland. It is a statutory requirement for all public and private hospitals, nursing homes and pathology services to notify QCR of cancer diagnoses. All validated neoplasm related specimens (including peripheral blood) are required to

be notified. The Townsville Hospital catchment for haematology services extends west to the districts around Mt Isa, north to include communities up to Cardwell and south to include the large, regional Central Queensland city of Mackay and surrounding areas (**Figure 1**). Approval by the institutional regulatory boards (Townsville Hospital) was in concordance with the Declaration of Helsinki.

A total of 1705 cases were identified through the QCR. In addition to the blood cancer diagnosis (as per the International Statistical Classification of Diseases [ICD], version 3), each patient's date of birth, date of diagnosis, address at the time of diagnosis, and occupation was also available through the QCR. An extensive and comprehensive review of the blood cancer diagnosis for each case was then undertaken. Using patient medical and pathology records, diagnoses were recoded and updated to ensure an accurate and clinically relevant, contemporary diagnosis based upon the 2017 WHO classification of tumours of haematopoietic and lymphoid tissues (e.g., 'malignant lymphoma' updated to the specific histological subtype, 'refractory anaemia' updated to 'myelodysplastic syndrome (MDS) with multilineage dysplasia', 'mature T-cell lymphoma, NOS' updated to 'angioimmunoblastic T-cell lymphoma'). All cancer diagnoses were also categorised more broadly into either a myeloid or lymphoid neoplasm, followed by a major lymphoid/myeloid subtype.

The updated WHO classification incorporates cytogenetic and molecular characteristics for diseases such as acute leukaemia but given as a subset of cases from our study period did not have such tests performed, it was not possible to recode the existing data using these descriptors. Therefore, detailed subtyping of acute leukaemia was not performed. A minor subset of QCR cases had an incorrect blood cancer diagnosis and these were reclassified. Additionally, a minority of

patients with a solid-organ malignancy (e.g., breast cancer) were incorrectly diagnosed as having a haematologic malignancy and such cases were removed.

We captured diagnoses of subsequent blood cancers within the same patient due to disease transformation (if the 2nd diagnosis was within the study period). Transformation typically included individuals with (MDS)/myeloproliferative neoplasm (MPN) who then progressed to acute leukaemia, or patients with an indolent lymphoproliferative disorder that transformed to an aggressive lymphoma. Likewise, those having a therapy related myeloid neoplasm (tr-MN) diagnosed within the study period were also captured.

After limiting cases to first haematologic diagnoses, removal of non-haematologic malignant diagnoses, and exclusion of patient's postcodes not served by THHS, a total 1581 cases were identified (**Figure 2**). Population data within age groups and postcodes were obtained from the Australian Bureau of Statistics and Queensland Government Statistician's office to allow for the assessment of incidence rates. One-hundred individual occupation codes from the QCR dataset were harmonised into 18 distinct occupation clusters, based on similarities in occupational exposures (supplementary **Table S1**).

Statistical Analysis

Descriptive summaries are presented as frequencies and percentages for categorical variables and median, interquartile range, and range for continuous variables. We estimated the crude incidence rates, age-standardised incidence rates (ASRs) and incidence rate ratios (IRRs) per 100,000 population for each postcode per year and the entire study period. The Australian population of 2001 was used to

generate the ASRs with a 95% confidence interval (CI) by direct standardisation and visualised on the map. We also investigated the effect of trend (year diagnosed), place of usual residence (postcode) and age, on counts of haematologic cancers via Poisson regression incidence rate ratio (IRR) with 95% CI.

Statistical analyses were conducted in Stata Statistical Software (Release 16.1, College Station, TX: StataCorp LLC) and R version 3.6.2 package 'epiR' for direct standardisation (https://CRAN.R-project.org/package=epiR) The visualisation was implemented using R package 'ggplot' and qgis version 3.16 (http://qgis.org).

Results

A total of 1581 adults were diagnosed with a haematological malignancy over the 10 years from January 2005 to December 2014. The median age of diagnosis in the entire cohort was 66 years (range, 18-100 years), with 946 males and 635 females (**Table 1**). There was a higher representation of males in both lymphoid and myeloid disorders compared to females. The median age of diagnosis for lymphoid disorders was 64 years (IQR 55-74 years), and 71 years (IQR 59-80 years) for myeloid disorders. The age distribution of lymphoid and myeloid subtypes is shown in **Table 2** and illustrates that the likelihood of being diagnosed with a haematologic malignancy is higher in the elderly population (defined as ≥ 65 years). There was an

increase in the incidence of haematologic diagnoses over the study period, with increases in both lymphoid and myeloid malignancies (**Figure 3**).

Lymphoid malignancies accounted for 1088 cases, and myeloid malignancies accounted for 493 diagnoses. Data on 58 subtypes of haematological malignant diagnoses are presented in **Table 2 and supplementary Figure S1**. Chronic lymphocytic leukaemia (CLL) was the most common lymphoid disorder, and this was followed by plasma cell myeloma/monoclonal gammopathy of undetermined significance (MGUS). Diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma were the third and fourth most common lymphoproliferative disorders respectively. MPNs were the most common major subtype of myeloid disorder, followed by MDS and acute myeloid leukaemia (AML) respectively.

Twenty-five individuals with MDS or MPN progressed to AML, whilst 20 individuals with a low-grade lymphoma had subsequent high-grade histological transformation within the study period. Twenty-five individuals were diagnosed with a subsequent tr-MN within the study period.

Overall counts, crude incidence rates and age-standardised incidence rates (ASR) (2005-2014) varied geographically across the study region (**Table 3, Figure 4,** and **Figure S2)**. The number of blood cancer cases ranged from one (postcodes 4721, 4738, 4742, 4850 and 4879) to 365 (postcode 4740). Postcodes 4746 (233.5) and 4879 (Cairns region - 0.5) recorded the highest and lowest ASR per 100,000 people respectively. Postcodes 4740 and 4746 are in the Mackay region, and the high ASR is due to the adjustment of different age groups. Supplementary **Table S2** and **Figure S3** presents the yearly ASR across the study region. Persistently high ASR were observed in postcodes 4739, 4799 and 4809.

Using postcode 4879 as the reference category (as it had the lowest ASR and crude incidence rate), we found postcode 4739 (Carmila, within the Mackay region) presented with the highest IRR (152.7, 95% CI:17.8, 1306.7)), and postcode 4850 (Ingham region) had the lowest (0.8, 95% CI: 0.1, 13.3). Other notably high IRR included 4746 (German Creek/May Downs/Middlemount - 118.9), 4750 (Bucasia/Shoal Point - 100.8), 4799 (Bloomsbury/Midge Point - 100.7) – which are all in the Mackay region, and 4819 (96.5), which is Magnetic Island, off Townsville.

The potential geographical disparities in haematologic malignancies were assessed by postcodes within the study region. **Figure 4A** presents the ASR for aggregated data, 2004-2015 and yearly maps were shown in **Figure S3**. The counts, crude rates and ASR of haematologic malignancies demonstrated geographical variations of cancer risk across the study region. The areas of highest cancer incidence were all in the Mackay region. Finally, we investigated the occupational risk of blood cancer diagnoses. There was no significant association between any of the 18 occupation clusters and blood cancers (results not presented).

Discussion

Comprehensive epidemiological data on the underlying incidence of clinically meaningful subtypes of haematological malignancies is currently limited in Australia (11). In this study, we examined the incidence of haematological malignancies in North Queensland using the 2017 WHO disease classification system.

We report a progressive increase in blood cancer incidence (both lymphoid and myeloid) over the study period. This temporal increase may relate to improved diagnostic workup, wider availability of newer ancillary diagnostic tests, and an ever-increasing elderly population. Indeed, this temporal increase in blood cancer diagnoses is in keeping with national data (3). As expected, we report enrichment of haematologic malignancies in the elderly population, with the median age of diagnosis in our cohort at 66 years. Despite this, many interventional studies in

haematology have primarily focused on younger patients with only a modest representation of the elderly cohort (12). This can often lead to the omission of certain therapeutic interventions in the older population. To ensure an appropriate and 'real-world' representation of patients, this work further emphasises the need to incorporate geriatric assessment tools (in place of arbitrary age cut-offs) into prospective clinical trials (13).

Non-Hodgkin lymphoma comprised the most common major subtype of haematological cancer, with the mature B-cell malignancies dominating. However, we report a higher representation of CLL within lymphoid malignancies as compared with malignancy statistics from the United States and United Kingdom, where DLBCL was reported to be the common lymphoid subtype (6, 14). The most common myeloid subtype was MPNs, followed by MDS and then AML. Notably, given as our primary data source was the QCR, it is possible that individuals with blood cancer diagnoses that were not captured by this registry may have been missed.

Our data suggests a higher blood cancer incidence in individuals residing in some postcodes within the Mackay area during 2005-2014. Subgroup analyses to assess for potential enrichment of specific cancer subtypes within the Mackay region was not performed due to sample size limitations. The cause for this observation is unclear and this geographical disparity warrants further study and confirmation. The Mackay region is known for agriculture (referred as the 'sugar capital' of Australia) and mining with the area having vast coal deposits. Though purely speculative, whether such environmental risk factors play a contributory role warrants consideration. However, it must be noted that the duration of the residential status of study subjects was unavailable for analysis.

Geographic isolation from tertiary cancer centres is another barrier to the provision of optimal therapy in regional and remote Australia. Our data underscores the need for adequate access to high-quality cancer care in regional Australia. There continues to be less specialist haematology services in regional Queensland compared with the capital, Brisbane. Consideration to health-care policies that prioritize such shortages in the health professional workforce and increase speciality care for underserved regional and remote populations is encouraged. Another model for consideration is telehealth, which can enhance rural service capabilities(15).

There remains much uncertainty regarding potential modifiable risk factors for lymphoproliferative disorders. A pooled analysis of case-control studies demonstrated an increased risk of multiple myeloma in gardeners and nursery workers, and the authors postulated whether this related to increased generic pesticide exposure (16). We sought to evaluate for any potential associations between occupation and the incidence of multiple myeloma and non-Hodgkin's lymphoma. Although it may be postulated that environmental risk factors may be contributing to the increasing incidence of blood cancers, we could not demonstrate any association between specific occupation clusters and blood cancer incidence in our study.

Our study has some limitations. It is assumed that the data on haematologic malignancies in the study area is exhaustive. Direct standardisation can be sensitive to small counts and, as some postcodes have a small population size, it is difficult to draw firm conclusions regarding geographic disparities. As the ASRs would be subject to random errors, this makes for at times, wide confidence intervals, which were observed in some postcodes. Additionally, our coding of occupational history merged distinct occupations into major classes, and there may have been some

heterogeneity in exposure to occupational hazards using this grouping. Finally, we did not account for other potential confounders such as medical comorbidities, some of which could affect the risk of blood cancers.

Population-based cancer registries provide pivotal data for numerous stakeholders. Data collection of haematologic malignancies is however challenging given the marked number of subtypes, each with distinct pathologies, outcomes, and treatments. To ensure high quality accurate and clinically relevant data, we propose consideration of reporting practices that align with the WHO classification of haematologic neoplasms. Although it is appreciated that such a strategy would be difficult to implement, population-based cancer data provides fundamental information for disease monitoring, epidemiology, and healthcare policy, and clinically appropriate high-quality data is essential. In the UK, the Haematological Malignancy Research Network successfully provides robust data, with centralised coding using the latest WHO classification. A similar model would be of benefit in Australia, and perhaps more so in the regions (17).

Conclusion

High-quality epidemiological data is integral to blood cancer management and remains an unmet need in regional Australia. This study demonstrates that it is possible to collect clinically relevant and accurate data for haematological malignancies, which also provides further insights into potential aetiologic risk factors, and geographic hotspots. Extrapolating such a study to larger regions and nationally will have major implications for improved healthcare, both in healthcare policy and clinical management.

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Figure legends

Figure 1. Major catchments of the Townsville and Mackay Hospital and Health Services, with inclusion of postcodes

Figure 2. Consort diagram of study participants

Figure 3. Incidence of haematologic diagnoses, by major subtype, from 2005-2014

Figure 4. Overall counts (**figure 4A**), crude incidence rates (**figure 4B**) and age-standardised incidence rates (ASR) (**figure 4C**), across the study region from 2005-2014

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Table 1. Characteristics of patients diagnosed with lymphoid or myeloid disorders at Townsville Hospital (2005-2014) (n=1581).

Characteristic	Overall, N = 1,581[1]	Lymphoid, N = 1,088[1]	Myeloid, N = 493[1]
Age (years)	66 (56, 76)	64 (55, 74)	71 (59, 80)
Missing±	1	0	1
Age group (years)			
18-24	35 (2.2%)	24 (2.2%)	11 (2.2%)
25-34	41 (2.6%)	33 (3.0%)	8 (1.6%)
35-44	98 (6.2%)	74 (6.8%)	24 (4.9%)
45-54	172 (11%)	130 (12%)	42 (8.5%)
55-64	373 (24%)	293 (27%)	80 (16%)
65-74	401 (25%)	278 (26%)	123 (25%)
75-84	352 (22%)	202 (19%)	150 (30%)
85 plus	109 (6.9%)	54 (5.0%)	55 (11%)

Characteristic	Overall, N = 1,581[1]	Lymphoid, N = 1,088[1]	Myeloid, N = 493[1]
Ethnicity			
Indigenous (ABTSI)	34 (2.2%)	23 (2.2%)	11 (2.3%)
Non-Indigenous	1,518 (98%)	1,044 (98%)	474 (98%)
Missing	29	21	8
Gender			
Female	635 (40%)	440 (40%)	195 (40%)
Male	946 (60%)	648 (60%)	298 (60%)

[1]Median (IQR); n (%)

± 1 person with unknown exact age, but part of the 25-34 age group.

Table 2. Haematological diagnoses by subtype. Frequency, median and range of age (years) and proportion of male patients.

Subtypes	Total N=1581	Median age, years (range)	Male (%)
Lymphoid disorders			
Mature B-cell neoplasms			
Chronic lymphocytic leukaemia	233	67 (31-96)	64.4
Plasma cell myeloma	189	66 (37-95)	64
Diffuse large B-cell lymphoma	177	65 (24-100)	56.5
Follicular lymphoma	154	60 (35-98)	59.7
Mature B-cell lymphoma, unspecified	46	71 (52-89)	43.5
Mantle cell lymphoma	29	72 (35-86)	72.4
Lymphoplasmacytic lymphoma	24	71 (41-94)	54.2
Extranodal marginal zone lymphoma of the MALT	20	68 (38-87)	35
Hairy cell leukaemia	17	54 (35-92)	94.1
Monoclonal B-cell lymphocytosis	13	62 (50-83)	61.5
Burkitt lymphoma	10	54 (22-75)	70
Splenic marginal zone lymphoma	6	68.5 (55-83)	33.3
High-grade B-cell lymphoma	5	76 (43-78)	60
Plasmacytoma	3	58 (40-61)	33.3
Primary mediastinal B-cell lymphoma	2	28.5 (20-37)	50
Nodal marginal zone lymphoma	2	59.5 (57-62)	100
Post-transplant-lymphoproliferative disorder	2	59.5 (55-64)	100
B-cell lymphoblastic leukaemia			
B-lymphoblastic leukaemia, BCR-ABL1	4	51.5 (44-75)	75
B-lymphoblastic leukaemia, not otherwise specified	19	59 (18-82)	52.6
Hodgkin lymphoma			
Nodular Sclerosis	47	30 (18-82)	40.4
Hodgkin Lymphoma, not otherwise specified	12	53 (22-66)	58.3
Nodular Lymphocyte predominant	9	31 (20-56)	88.9
Mixed Cellularity	8	44.5 (21-80)	62.5
Lymphocyte Rich	5	57 (34-60)	60
T- and NK-cell lymphomas			
Peripheral T-cell lymphoma	8	54 (25-89)	50
Mature T/NK cell, not otherwise specified	7	75 (26-81)	57.1
Anaplastic large cell lymphoma, Alk –	4	63.5 (63-71)	25
Anaplastic large cell lymphoma, Alk+	5	42 (21-75)	80
Angioimmunoblastic T-cell lymphoma	3	70 (68-76)	33.3
Mycosis Fungoides	3	48 (36-77)	33.3
T-cell large granular lymphocytic leukaemia	2	55 (49-61)	50
T-Prolymphocytic leukaemia	1	88 (88-88)	0

Subtypes	Total N=1581	Median age, years (range)	Male (%)
T-cell lymphoblastic leukaemia	6	49.5 (23-64)	83.3
Histiocystic/Dendritic cell	1	36 (36-36)	100
Lymphoid disorder, not classified	12	77.5 (58-90)	41.7
Myeloid disorders			
Acute myeloid leukaemia			
AML, not otherwise specified	65	65 (25-94)	60
AML with MDS related changes	19	78 (37-88)	52.6
Acute Promyelocytic leukaemia	11	47 (23-70)	54.5
Other AML	11	60 (28-82)	54.5
Pure erythroid leukaemia	5	63 (24-89)	100
AML (Monoblastic)	4	69.5 (45-78)	75
AML w' 8:21	2	34 (23-45)	0
Therapy related myeloid neoplasm	2	66 (57-75)	50
Myelodysplastic syndrome			
Multilineage dysplasia	66	77.5 (23-89)	65.2
Excess blasts	38	70 (53-95)	71.1
Ringed sideroblasts	23	75 (63-93)	47.8
Unclassifiable MDS	22	82.5 (55-92)	72.7
Single lineage dysplasia	9	79 (67-87)	66.7
Deletion 5q	5	62 (41-80)	20
Blastic plasmacytoid dendritic cell neoplasm	1	66 (66-66)	100
Myeloproliferative neoplasms			
Essential thrombocythaemia	63	65 (19-91)	54
Polycythaemia vera	40	72 (30-90)	65
Chronic myelomonocytic leukaemia	36	77.5 (50-96)	66.7
Chronic myeloid leukaemia	36	59.5 (19-91)	52.8
Primary myelofibrosis	23	71 (48-86)	60.9
Myeloproliferative neoplasm, other	5	76 (21-87)	40
MDS/MPN	4	75 (65-87)	50
Mastocytosis	3	59 (45-70)	66.7

MALT = mucosa associated lymphoid tissue, Alk= anaplastic lymphoma kinase, MDS= myelodysplastic syndrome; MPN= myeloproliferative neoplasm, NK= natural killer

Table 3A. Crude rate, directly age-standardised incidence rate (ASR) and incidence rate ration (IRR) per 100,000 with 95% confidence intervals by year and age-groups for the period 2005-2014.

Variables	Cases, n (%)	Crude	ASR (95% CI)	IRR (95% CI)
Year				
2005	134 (8.5)	35.2	39.7 (32.9,46.5)	1 (Ref group)
2006	121 (7.7)	30.9	34.6 (28.4,40.9)	0.9 (0.7,1.1)
2007	146 (9.2)	36.4	40.9 (34.2,47.6)	1.0 (0.8,1.3)
2008	157 (9.9)	38.1	43.2 (36.4,50.1)	1.1 (0.8,1.3)
2009	139 (8.8)	32.9	35.9 (29.8,41.9)	0.9 (0.7,1.2)
2010	142 (9.0)	33	36.0 (30.0,42.0)	0.9 (0.7,1.2)
2011	170 (10.8)	38.8	42.4 (35.9,48.8)	1.1 (0.8,1.3)
2012	166 (10.5)	37.3	39.2 (33.2,45.3)	1.0 (0.8,1.2)
2013	209 (13.2)	46.5	48.3 (41.7,55.0)	1.2 (1.0,1.5)
2014	197 (12.5)	43.6	43.8 (37.6,50.0)	1.1 (0.9,1.4)
Age				
<17	0 (0)	0	NA	0.0 (0.0,0.0)
18-24	35 (2.2)	8.2	NA	0.0 (0.0,0.0)
25-34	41 (2.6)	6.7	NA	0.0 (0.0,0.0)
35-44	98 (6.2)	15.8	NA	0.1 (0.1,0.1)
45-54	172 (10.9)	29.0	NA	0.1 (0.1,0.2)
55-64	373 (23.6)	82.8	NA	0.4 (0.3,0.4)
65-74	401 (25.4)	153.7	NA	0.7 (0.5,0.8)
75-84	352 (22.3)	253.5	NA	1.1 (0.9,1.4)
85 plus	109 (6.9)	234.7	NA	1 (Ref group)

NA= Not applicable for this variable.

Table 3B. Crude rate, directly age-standardised incidence rate (ASR) and incidence rate ration (IRR) per 100,000 with 95% confidence intervals per postcode for the period 2005-2014.

Postcode	Cases, n (%)	Crude	ASR (95% CI)	IRR (95% CI)
4721	1 (0.1)	2.7	3.3 (0.0,9.7)	4.4 (0.3,70.0)
4737	47 (3.0)	59.9	57.8 (41,74.5)	84.6 (11.7,613.4)
4738	1 (0.1)	8.2	11.2 (0.0,33.0)	11.3 (0.7,180.4)
4739	5 (0.3)	134.3	108 (9.4,206.6)	152.6 (17.8,1306.7)
4740	365 (23.1)	46.4	48.8 (43.8,53.8)	72.5 (10.2,516.0)
4741	31 (2.0)	40.8	46.1 (28.4,63.7)	60.2 (8.2,440.7)
4742	1 (0.1)	8.8	8.4 (0.0,24.7)	17.6 (1.1,280.9)
4743	2 (0.1)	16.1	124.4 (0.0,296)	57.4 (5.2,633.0)
4744	9 (0.6)	10.6	17.1 (0.7,33.6)	38.0 (4.8,300.1)
4745	8 (0.5	23.6	84.2 (0.0,180.7)	71.2 (8.9,569.7)
4746	7 (0.4)	31.4	233.5 (0.0,631.8)	118.9 (14.6,966.9)
4750	25 (1.6)	48.1	61.7 (35.7,87.8)	100.8 (13.7,743.7)
4751	15 (0.9)	34.6	43.5 (21.1,66.0)	62.6 (8.3,473.8)
4753	13 (0.8)	44.3	54.2 (24.3,84.1)	98.4 (12.9,752.5)
4754	9 (0.6)	45	45.2 (15.4,74.9)	67.7 (8.6,534.5)
4756	4 (0.3)	60.3	67.2 (0.0,140.2)	84.1 (9.4,752.6)

4757	2 (0.1)	58.1	36.9 (0.0,88.0)	83.4 (7.6,920.0)
4798	4 (0.3)	53.6	43.1 (0.6,85.5)	58.8 (6.6,525.8)
4799	8 (0.5)	81.8	90.1 (21.7,158.5)	100.7 (12.6,805.2)
4800	40 (2.5)	45.8	41.2 (28.2,54.3)	61.1 (8.4,444.2)
4802	25 (1.6)	24.4	36.2 (19.5,52.9)	51.1 (6.9,377.0)
4804	6 (0.4)	26.3	23.6 (4.4,42.8)	33.4 (4.0,277.5)
4805	55 (3.5)	50.9	43.5 (31.9,55.2)	64.5 (8.9,465.9)
4806	28 (1.8)	68.4	53.2 (33.1,73.2)	75.3 (10.2,553.3)
4807	49 (3.1)	43.5	34.1 (24.4,43.9)	49.5 (6.8,358.2)
4808	9 (0.6)	75.4	59.2 (20.1,98.2)	96.9 (12.3,764.8)
4809	5 (0.3)	46.5	74.8 (0.0,151.1)	66.4 (7.8,568.2)
4810	101 (6.4)	46.3	45.1 (36.2,53.9)	66.4 (9.3,476.2)
4811	45 (2.8)	38.8	46.0 (32.1,59.9)	69.5 (9.6,504.5)
4812	111 (7.0)	56.1	49.1 (39.9,58.3)	72.2 (10.1,517.0)
4814	173 (10.9)	39	46.5 (39.5,53.4)	69.4 (9.7,495.6)
4815	87 (5.5)	42.6	56.9 (44.6,69.3)	82.8 (11.5,594.2)
4816	31 (2.0)	35.1	38.4 (24,52.8)	51.7 (7.1,378.5)
4817	113 (7.1)	38.5	57.7 (46.5,68.9)	79.8 (11.1,571.6)
4818	60 (3.8)	31.8	44.2 (31.4,56.9)	69.6 (9.6,502.1)
4819	20 (1.3)	87.8	70.9 (38.5,103.3)	96.5 (13.0,719.2)
4820	53 (3.4)	48.4	43.4 (31.6,55.3)	64.3 (8.9,464.8)
4821	9 (0.6)	51.6	41.9 (14.4,69.5)	68.2 (8.6,538.2)
4850	1 (0.1)	0.8	0.6 (0.0,1.7)	0.8 (0.1,13.3)
4868	2 (0.1)	0.9	0.9 (0.0,2.1)	1.6 (0.1,18.1)
4879	1 (0.1)	0.6	0.5 (0.0,1.4)	1 (Ref group)

Supplementary Figure Legends

Figure S1. Overall new blood cancer diagnosis by age in the study region over the period 2005-2014

Figure S2. Direct age-standardised incidence rate (per 100,000 pop) with 95% confidence intervals per postcode for the period 2005-2014. The y-axis was fixed to an upper limit of 350 cases/100,000 pop.

Figure S3. Geographical distribution of yearly age-standardised incidence rates of haematological cancer in the study region over the period 2005-2014

Figure 1

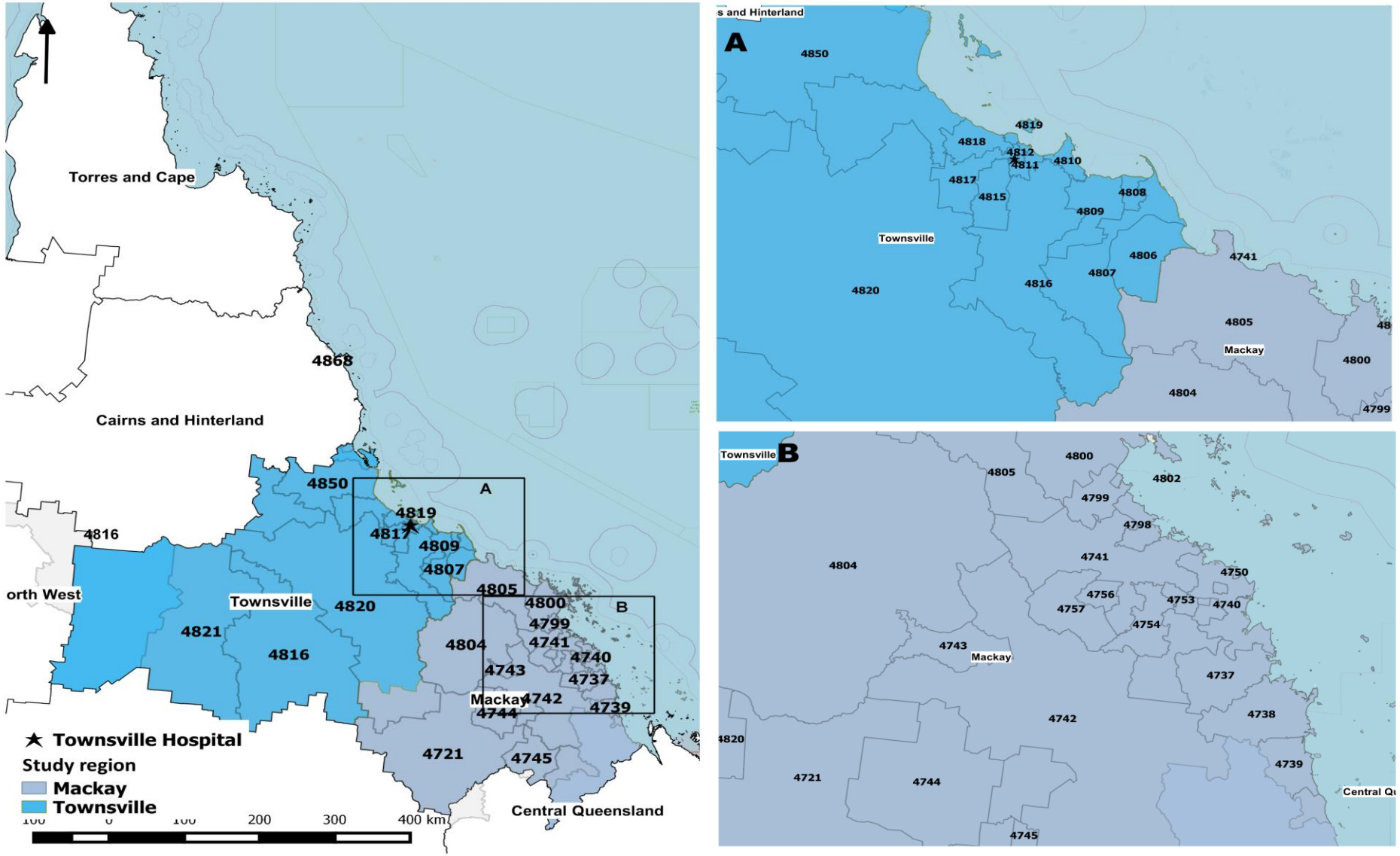

Figure 2

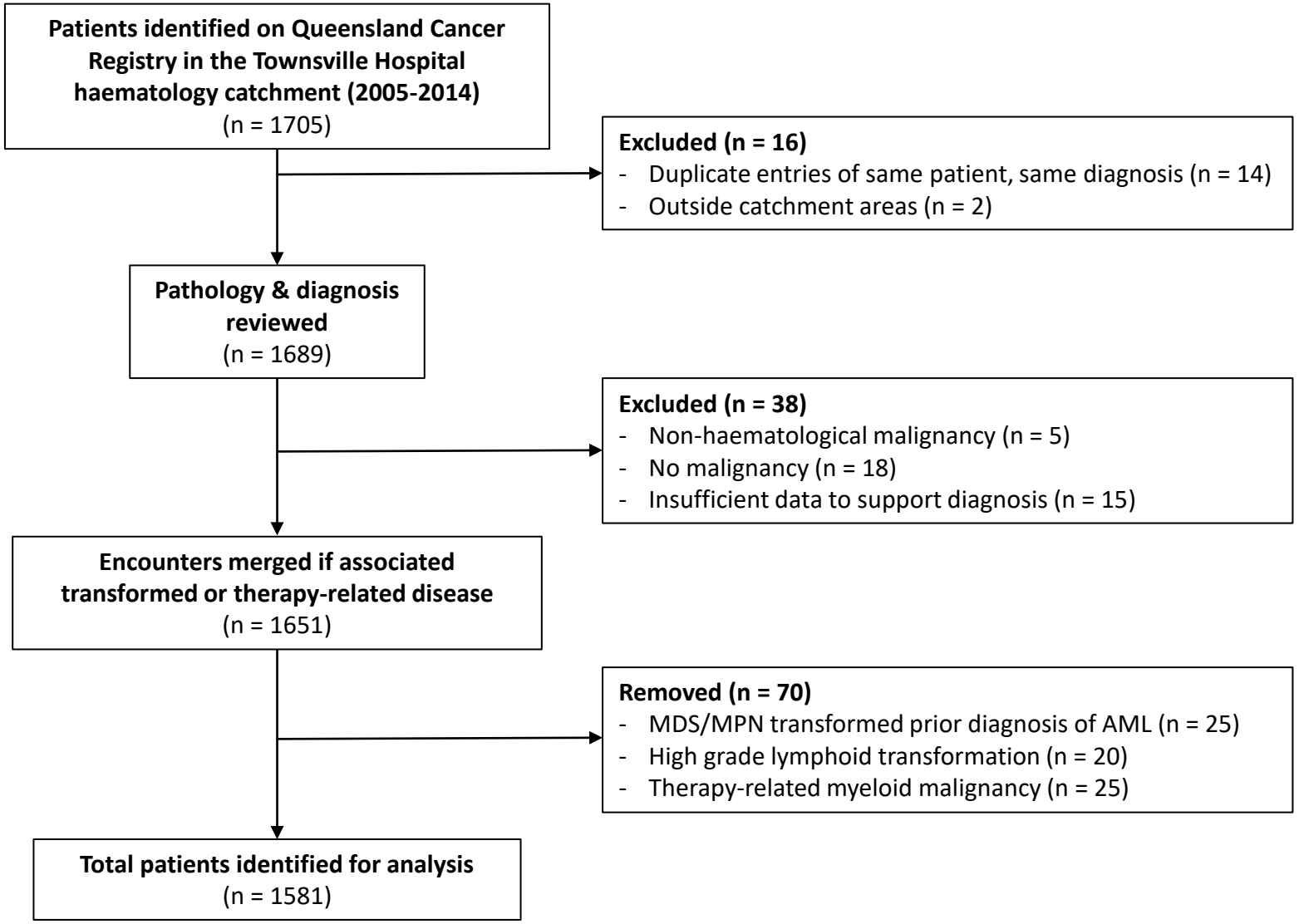

Figure 3

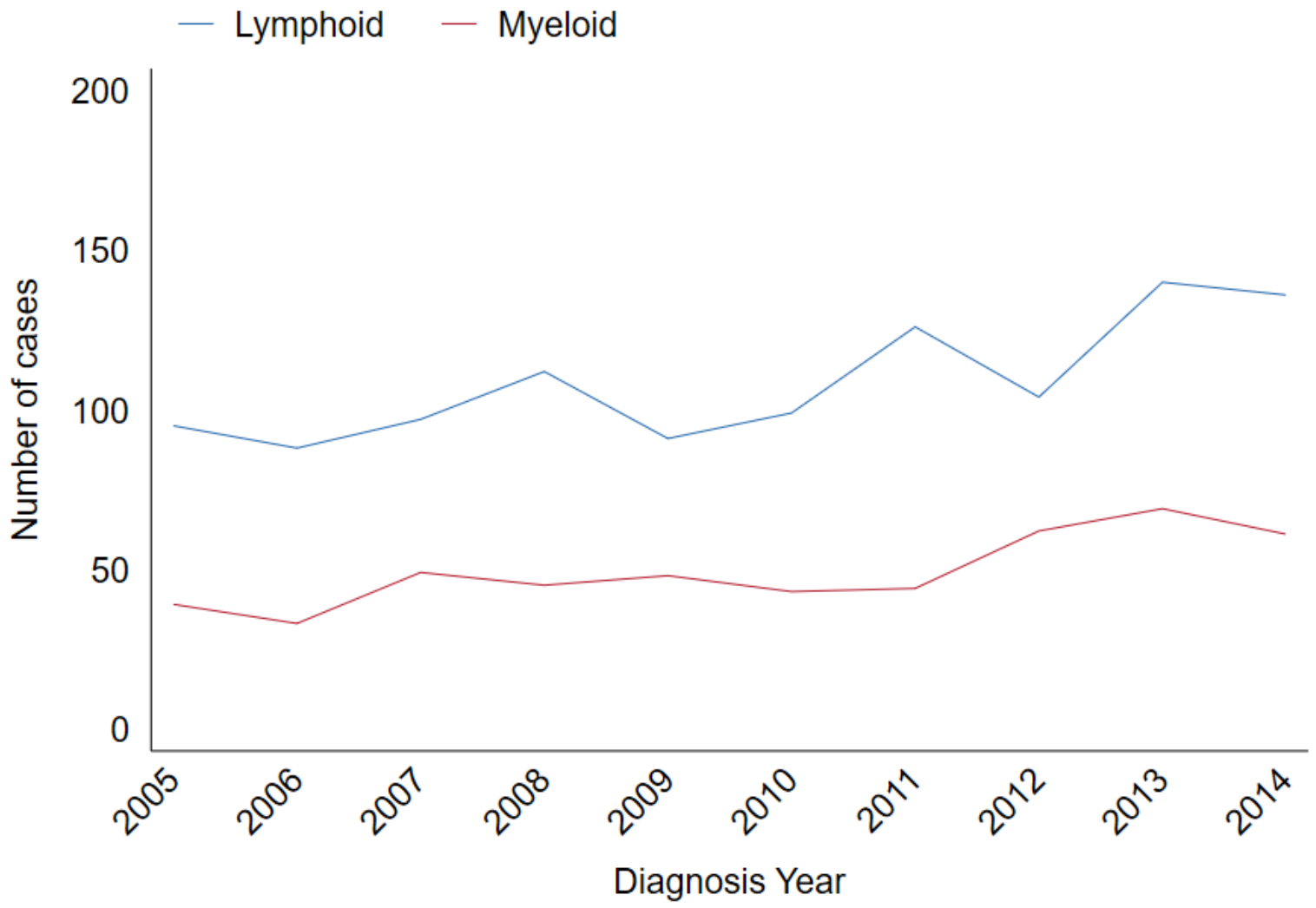

Figure 4A

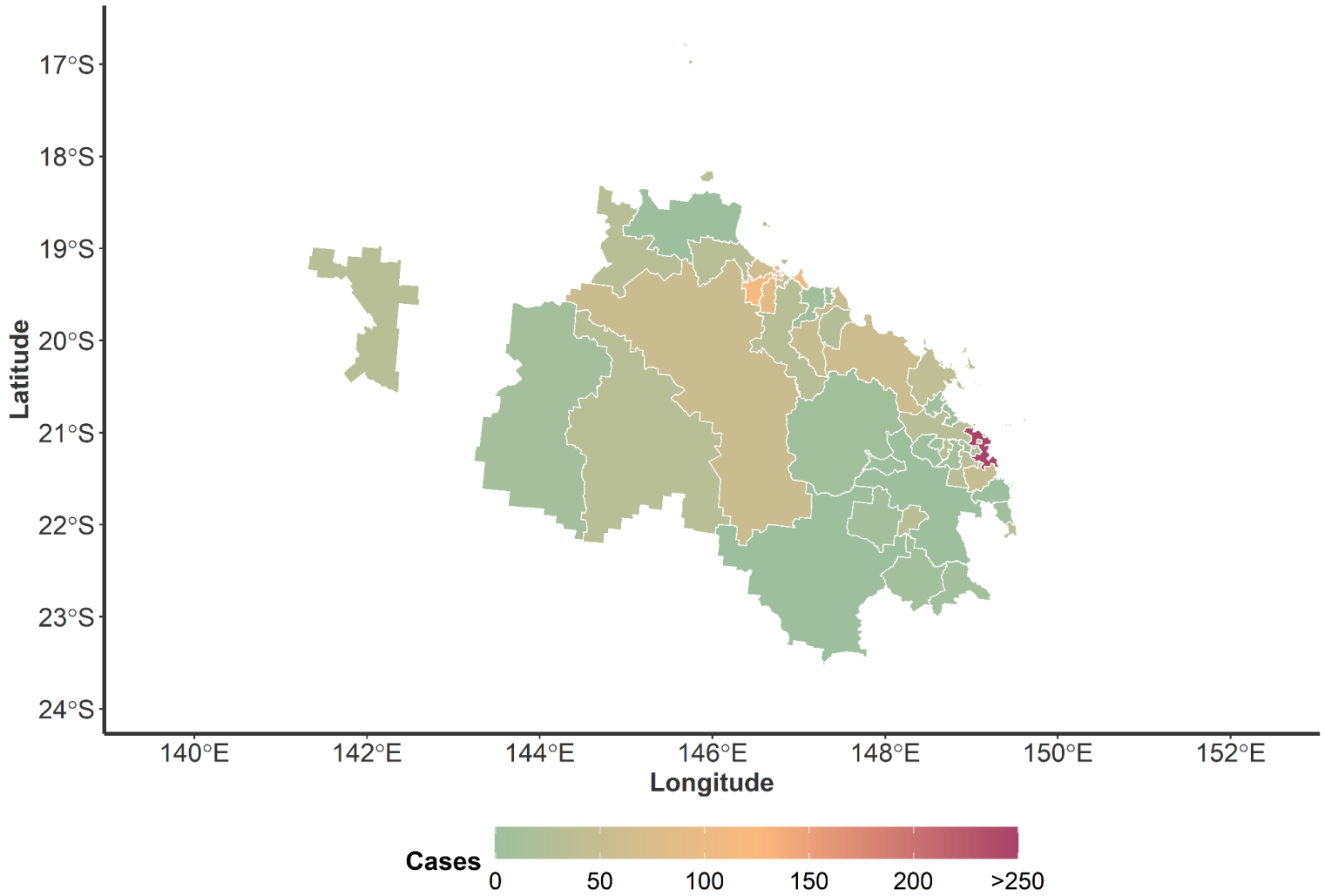

Figure 4B

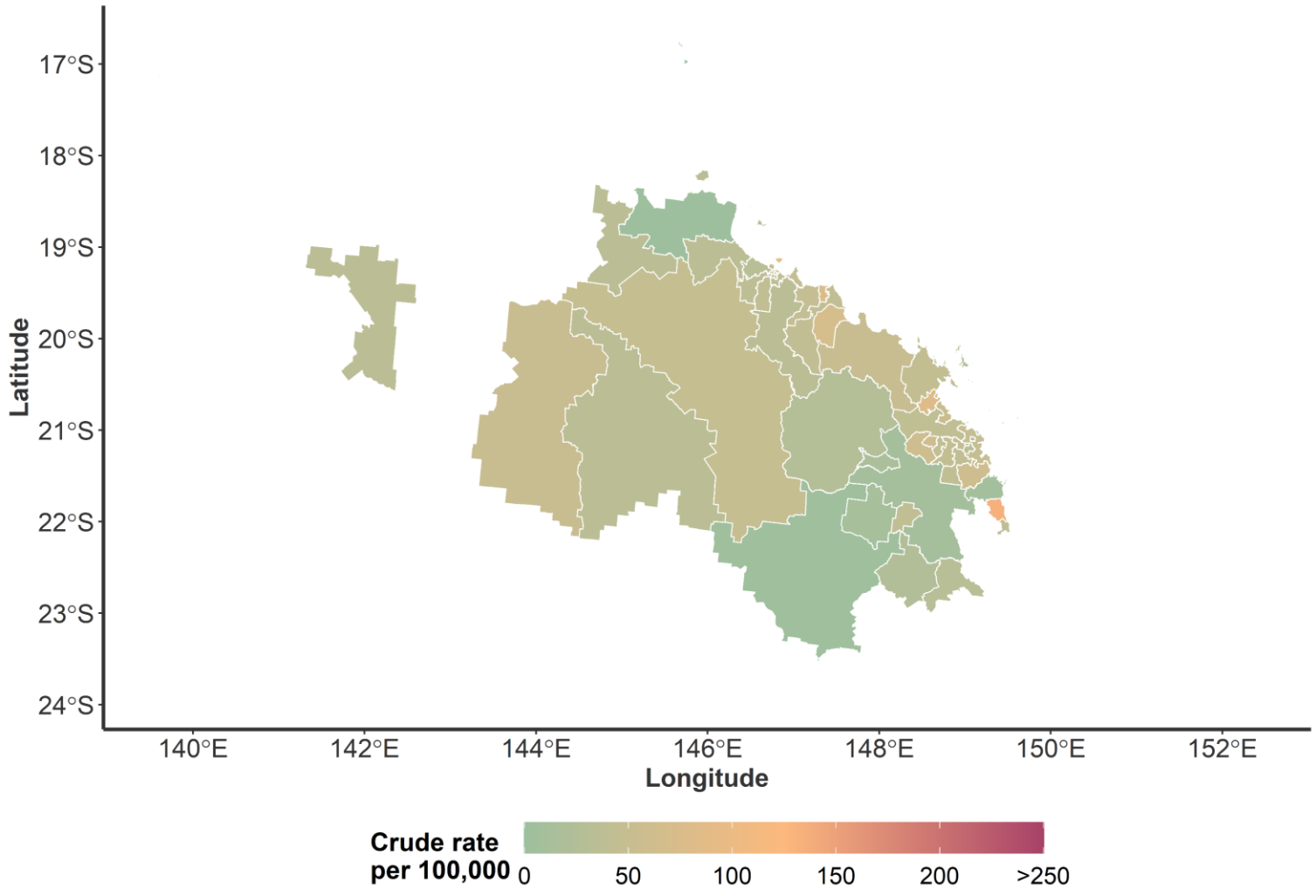

Figure 4C