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# A review of listeriosis notifications and co-existing conditions in New South Wales, 2010-2015

Kit Leung, Kirsty Hope and Vicky Sheppard

## Abstract

### Aim

To describe the distribution of known risk factors for listeria infection, including co-existing conditions, among listeriosis notifications in NSW between 2010 and 2015.

### Methods

Data from all notifications of invasive listeriosis in NSW between 1 January 2010 and 31 December 2015 were extracted from the NSW Notifiable Conditions Information Management System (NCIMS). OzFoodNet Listeria Case Questionnaires for each notification were reviewed. Descriptive analyses of notification data were undertaken.

### Results

Between 2010 and 2015, there were 158 listeriosis notifications in NSW with an average of 26.3 notifications a year. Persons over 65 years represented 71.5% of all notifications. A total of 4.4% notifications were among pregnant women, while 79.1% and 64.6% were among persons with a *condition* and on *treatment*, respectively, known to suppress the immune response or increase the risk of infection. Specifically, cancer patients and persons on cancer treatment (chemotherapy, radiotherapy) represented 31.0% and 13.9%, respectively, of all listeriosis notifications. Information on *foods to avoid in preventing listeria* from a healthcare worker prior to infection was received by 7.2% of notifications with a known risk condition and 5.9% of notifications on medication; 41.6% and 46.1% respectively had visited a hospital in the four weeks prior to notification.

### Conclusion

The prevalence of known risk factors for listeriosis among notified cases remains significant in NSW. Improved risk communication resources for this population have been developed, which may be beneficial in reducing the burden of listeriosis in known vulnerable groups.

Key words: *Listeria monocytogenes*, listeriosis, immunocompromised conditions, immunosuppressant medications, cancer, risk factors, patient information, Australia

## Introduction

Listeriosis is a rare food-borne illness associated with high hospitalisation and fatality rates among those infected, particularly in the elderly, pregnant women and persons with weakened immune systems. The average case fatality rate among hospitalisations is estimated to be between 20%–30%<sup>1-3</sup>, with studies showing patients with an underlying condition having higher case fatality rates of up to 40%.<sup>4-6</sup> Listeriosis which is caused by the gram-positive bacterium *Listeria monocytogenes* can be transmitted from person to person, but is commonly transmitted through the consumption of contaminated food including meat, poultry and dairy products, and through utero/placental transmission in infected pregnant women.<sup>7</sup> The incubation period can be up to 70 days and will vary depending on the form of listeriosis.<sup>8,9</sup> Invasive listeriosis is determined by the presence of *L. monocytogenes* in the blood, in the fluid of the central nervous system or infection of the uterus in the case of pregnancy, with a clinical presentation of septicaemia, meningitis and miscarriage.<sup>3</sup> Main risk factors for infection are age, a weakened immune system (due to underlying medical conditions or the use of immunosuppressant therapies), pregnancy and exposure to a high dose or a highly-virulent strain.<sup>10</sup> In the general population, most infections of *L. monocytogenes* are without symptoms or manifest as a mild gastroenteritis illness, often remaining unsuspected or unreported.<sup>1,11</sup>

Increased risk of listeriosis has been associated with: immunocompromising conditions such as HIV, leukaemia, and autoimmune diseases; immunosuppressing treatments, such as those used to treat malignancies (chemotherapy, radiotherapy) or prepare patients for organ transplants (systemic steroids); certain chronic medical conditions such as heart disease, diabetes, liver disease, renal disease, cancer, and alcohol dependency; and persons on medication associated with gastrointestinal tract infection (gastric acid inhibitors).<sup>11-14</sup> A number of studies estimate that immunocompromised persons are between 100 - 2,500 times more likely to develop listeriosis, when compared to 'healthy' adults.<sup>14</sup>

Since standardised reporting of listeriosis in 1991, rates of notification have stabilised over the last decade across Australia. With an average of 80.4 cases reported per year (2009-2014), Australia has a notification rate of 0.3 per 100,000 population.<sup>15</sup> New South Wales (NSW) state accounts for a significant proportion of notifications and has with a mean notification rate of 0.4 per 100,000 (2009-2014).<sup>15</sup>

In Australia, few studies have examined the distribution of persons with immunocompromising conditions or receiving immunosuppressing treatments among listeriosis notifications. Studies to date, including that done by Popovic and authors, have analysed general epidemiological trends such as age, sex, pregnancy status, links to outbreaks, exposures and distribution across jurisdictional boundaries.<sup>16</sup> A case-control study by Dalton and authors identified prior hospitalisation, use of gastric acid inhibitors and consumption of camembert to have been associated with an increased risk of listeriosis among non-perinatal notifications.<sup>17</sup> Australia is expected to have similar epidemiological trends as other high-income countries, where persons with co-existing conditions, in particular those that affect the immune system, present at higher rates than the general population. A study in the UK found that among listeriosis notifications for a 10 year period, patients with co-existing malignancies accounted for more than one third of notifications and cancer patients had a 5 fold-increased risk for developing listeriosis.<sup>18</sup> In Israel, a retrospective study showed 74% of non-perinatal infections involved immunocompromised patients with malignancies, chronic liver disease, chronic renal failure, or diabetes mellitus.<sup>19</sup>

In Australia, education and communication campaigns on the risks of listeriosis and preventative measures for pregnant women and maternal healthcare providers are well established and notification rates among this population remain low.<sup>20</sup> There is a need to better understand the incidence of other risk groups, namely immunocompromised persons, among cases of listeriosis to better target risk reduction efforts in the future.

The aim of this study is to describe the distribution of patients with co-existing conditions and other known risk factors among known cases of listeriosis by examining the demographic and clinical characteristics, and risk factors for infection of notified cases between 2010 and 2015 in NSW, Australia.

## Methods

### Data sources

Listeriosis notification data were extracted from the NSW Notifiable Conditions Information Management System (NCIMS). Under the authority of the NSW Public Health Act 2010, all listed conditions, including invasive listeriosis, must be reported to public health units from general practitioners (GPs), hospitals, and pathology laboratories. Data were included in the study when the year of diagnosis (defined as symptom onset or in lieu of this, the specimen collection date) was between 1 January 2010 and 31 December 2015. The Australian enhanced foodborne disease surveillance network (OzFoodNet) Listeria Case Questionnaires for each case were reviewed where key data of interest was missing in the NCIMS database including whether the patient had cancer or was receiving immunosuppressant medications or treatment at the time of listeriosis diagnosis. OzFoodnet standardised Listeria Case Questionnaires are administered to all invasive listeriosis cases in NSW by public health units, capturing information on case demographics, risk factors, food history and laboratory data.

Responses in the questionnaire of both the attending clinician and the patient/caregiver themselves were included for analysis. Where there was an affirmative response from either treating clinician or patient/caregiver, a record was counted as affirmative, where there was no response recorded by either respondent, it was assumed negative.

Descriptive analyses of notification data were undertaken. Results were compared across demographics (age, gender, pregnancy status), known risk factors (co-existing conditions,

treatments, medications and foods consumed) and previous exposure to healthcare resources (visits and admissions to hospital, information received from healthcare workers) for the study period.

### Definitions (Case definition)

For the purpose of this study, a case is defined as a NSW resident with invasive listeriosis; confirmed by isolation or detection of *L. monocytogenes* from a site that is normally sterile, including fetal gastrointestinal contents, and whose symptom onset or specimen collection date was between 1 January 2010 and 31 December 2015. Only data for NSW was included and linked notifications (where both mother and neonate were both infected) were removed and the data for the mother only included.

Grouped response categories were created for study variables, treatments and food exposures, in order to analyse trends in risk. Response categories for treatments administered at the time of illness were created using responses to the question in the Listeria Case Questionnaire: *in the 4 weeks prior to illness, were you taking any of the following treatments?* (Table 1). Response categories for food exposures with a known high risk of *Listeria monocytogenes* transmission in Australia were created using the responses to the question: *in the 4 weeks prior to illness, did you consume any of the following?* (Table 1). Where 'other' or 'comments' were recorded for treatment and co-existing conditions in the questionnaire, data were reviewed by a medical registrar for inclusion in available categories where relevant to reduce measurement bias. In total, 32 conditions and 11 treatment responses recorded as 'other' were redistributed to available categories after review. Remaining 'other' medications and treatments were not included for analysis as they were not related to impeding the immune system or having a known risk associated with listeriosis.<sup>1</sup>

**Table 1. Definition of study variables**

Risk category	Study variable	Data included*
Treatments administered at the time of illness	systemic steroids	corticosteroids (eg. prednisone)
	immunosuppressants	cyclosporine other drugs that affect the immune system
	cancer treatments	chemotherapy radiation therapy
	antibiotics, antidiarrhoeals, antacids or other medication which reduces stomach acid	antidiarrhoeal medication (eg. Llomitol, Imodium) antacids (eg. Mylanta, Mucaine) medications that reduce stomach acid (e.g. Zantac, Tagamet, Somac, Losec) antibiotics other
Food exposure with a known high risk of <i>Listeria monocytogenes</i> transmission in Australia	pre-prepared fruit	fruit salad self-service salad bar, fruit salad delicatessen
	soft cheeses	brie, camembert, blue veined, fetta, ricotta, mozzarella, other soft cheese
	unpasteurised cheese/milk	unpasteurised cheese, unpasteurised milk
	cold cooked chicken	cold cooked chicken
	deli bought meat	BBQ chicken, luncheon/sandwich meat, ham, salami, chicken/turkey slices, silverside, liverwurst, frankfurts
	pate	pate
	pre-prepared salad	pre-prepared potato salad, pre-prepared coleslaw, pre-prepared pasta salad
	cold/uncooked seafood	mussels, crab, prawns purchased cooked, prawns purchased cold, oysters, smoked salmon, other smoked fish/salmon, sushi/sashimi, other seafood
sandwich fillings	sandwiches/burgers/rolls containing ham, beef, bacon/lettuce/tomato, chicken, turkey, other meat, salad, cheese	

\* OzFoodNet *Listeria* Case Questionnaire response categories

## Descriptive analysis

Descriptive analyses of notification data were undertaken using SAS<sup>®</sup> Enterprise Guide<sup>®</sup> (version 4.3, SAS Institute, Cary, NC, USA) and EXCEL (Microsoft, version 2010).

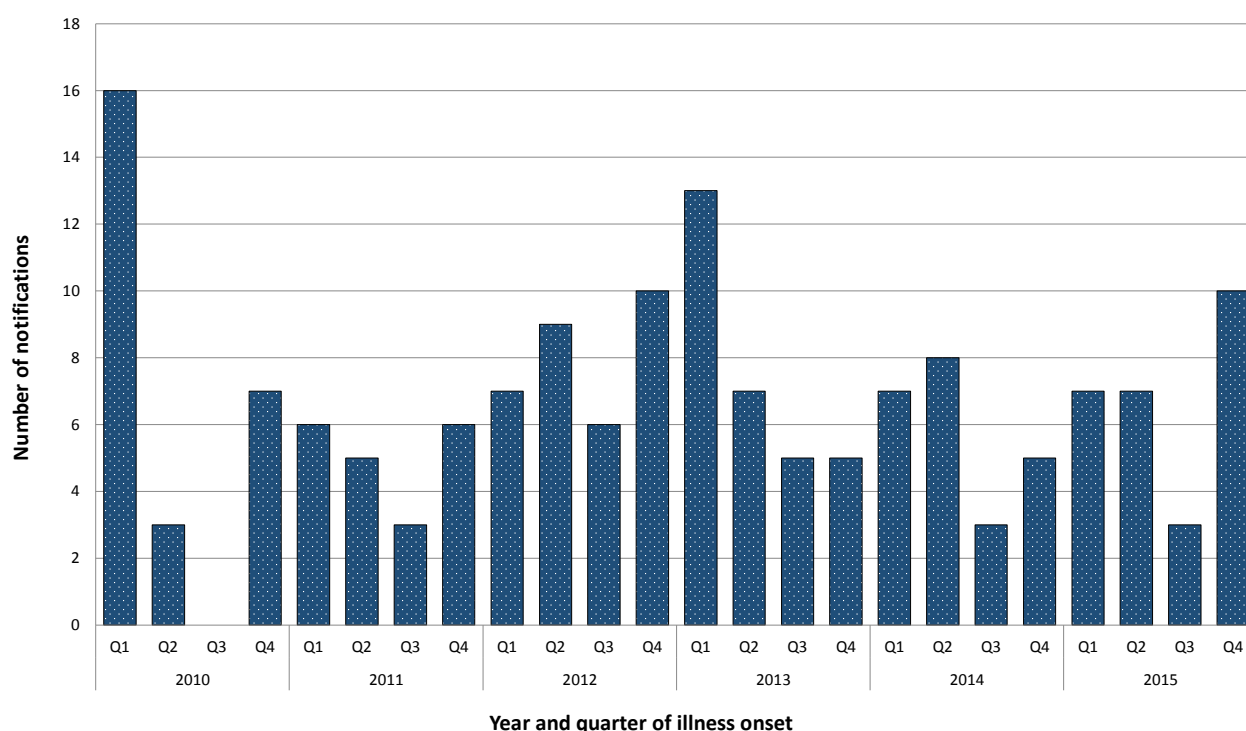
## Results

Between 2010 and 2015, there were 158 listeriosis notifications in NSW with an average of 26.3 notifications a year. Notifications were notably higher in 2012 and 2013, with 32 and 30 notifications, respectively (Figure). There was equal distribution between males and females (79 females, 79 males) with a high proportion of notifications over 65 years, representing 71.5% (n=113) of all notifications. A total of 4.4% (n=7) of notifica-

tions were among pregnant women, while 79.1% (n=125) and 64.6% (n=102) were among persons with a condition or on treatment, respectively, known to suppress the immune response or increase the risk of infection (Table 2).

Underlying conditions known to suppress the immune response or increase the risk of infection included cancer (31.0% of all notifications), heart disease (30.4%), rheumatological conditions (19.0%), blood disorders (18.4%), and liver disease (17.7%) (Table 2). Treatments or medication known to suppress the immune response or increase the risk of listeriosis in the 4 weeks prior to notification included antidiarrhoeal, antacids and antibiotics (taken by 50.0% of all notifications) and systemic steroids (31.7%). At lower

Figure. Number of listeriosis notifications in NSW between 1 January 2010 to 31 December 2015, by quarter and year of illness onset



rates, cancer drugs and immunosuppressants were taken by 13.9% and 13.3% of notifications, respectively (Table 2).

Consumption of high risk foods was frequently reported in the 4 weeks prior to infection; consumption of deli meats, cold seafood, and soft cheeses were reported by 69.6%, 60.8% and 47.5% of respondents, respectively (Table 3). Similar levels of exposure were reported when controlling for having at least one co-existing condition (72.0%, 62.4% and 48.8% respectively), and being on at least one treatment (73.3%, 62.7% and 50.0% respectively).

Contact with a healthcare professional prior to notification was relatively high among all notifications; 38.6% of all notifications visited a hospital (day visit) in the 4 weeks prior to onset of symptoms, and 28.5% were admitted to hospital during the same period. This was observed at slightly higher rates for notifications with a co-existing condition known to suppress the immune response or increase the risk of infection; 41.6% and 31.2% of notifications had visited and were admitted to a hospital prior to illness, respectively. Persons on at least one treatment known to suppress the immune

response or increase the risk of infection also showed similar results; 46.1% and 35.3% had visited and were admitted to a hospital prior to illness, respectively (Table 4).

Receiving information from a healthcare worker about foods to avoid prior to illness was relatively low among all notifications; only 7.0% (n=11) of all notifications reported receiving information on foods to avoid from a healthcare worker. Among notifications with at least one condition or on medications known to suppress the immune response or increase the risk of infection, 7.2% and 5.9%, respectively, had received such information (Table 4).

## Discussion

This paper provides recent data on the prevalence of conditions and treatments known to increase risk of listeria infection among residents of NSW, indicating potential areas for improved clinical management and risk reduction strategies. Between 2010 and 2015, persons with a co-existing condition or on treatment known to suppress the immune response or increase the risk of infection, represented a considerable proportion of listeriosis notifications; 79.1% (125)

**Table 2. Characteristics of listeriosis notifications in NSW between 1 January 2010 to 31 December 2015**

<b>Year of notification</b>	<b>No. (%) notifications</b>
2010	26 (16.5%)
2011	20 (12.7%)
2012	32 (20.3%)
2013	30 (19.0%)
2014	23 (14.6%)
2015	27 (17.1%)
<b>Total</b>	<b>158 (100.0%)</b>
<b>Sex</b>	
Female	79 (50.0%)
Male	79 (50.0%)
<b>Age group</b>	
0-4	1 (0.6%)
25-29	2 (1.3%)
30-34	5 (3.2%)
35-39	2 (1.3%)
40-44	4 (2.5%)
45-49	4 (2.5%)
50-54	6 (3.8%)
55-59	5 (3.2%)
60-64	6 (10.1%)
≥ 65 years	45 (28.5%)
<b>Pregnancy status</b>	
Pregnant	7 (4.4%)
Not pregnant	150 (94.9%)
Unknown	1 (0.6%)
<b>Co-existing conditions*</b>	
≥ 1 co-existing condition	131 (82.9%)
≥ 1 co-existing condition known to suppress the immune response or increase the risk of infection	125 (79.1%)
Cancer	49 (31.0%)
Heart disease	48 (30.4%)
Rheumatological condition	30 (19.0%)
Blood disorder	29 (18.4%)
Liver disease	28 (17.7%)
Diabetes (insulin)	25 (15.8%)
Chronic lung disease (excluding asthma)	18 (11.4%)
Renal or kidney disease requiring dialysis	17 (10.8%)
Other renal disease	14 (8.9%)
Diabetes (non-insulin)	9 (5.7%)
Organ transplant	9 (5.7%)
Other condition	56 (35.4%)
<b>Medications or treatments*</b>	
≥1 medication or treatment known to suppress the immune response or increase the risk of infection	102 (64.6%)
≥1 immunosuppressant medication	62 (39.2%)
Systematic steroids	50 (31.6%)
Cyclosporine or other drugs affecting the immune system	21 (13.3%)
Cancer drugs (radiotherapy or chemotherapy)	22 (13.9%)
Antibiotics, antidiarrhoeals, antacids or other medication which reduces stomach acid	79 (50.0%)
Antidiarrhoeal medication	9 (5.7%)
Antacids	27 (17.1%)
Medications that reduce stomach acid	45 (28.5%)
Antibiotics	42 (41.2%)

\* percentage of all notifications

**Table 3. Consumption of high risk foods among listeriosis notifications in NSW between 1 January 2010 to 31 December 2015**

Consumption in the 4 weeks prior to illness	Notifications					
	All		≥ 1 co-existing condition*		≥1 medication or treatment*	
	n	%	n	%	n	%
Deli meats	110	69.6%	90	72.0%	75	73.5%
Cold or uncooked seafood	96	60.8%	78	62.4%	64	62.7%
Soft cheeses	75	47.5%	61	48.8%	51	50.0%
Sandwich fillings	65	41.1%	53	42.4%	42	41.2%
Cold cooked chicken	35	22.2%	25	20.0%	18	17.6%
Pre-prepared salad	35	22.2%	29	23.2%	24	23.5%
Pre-prepared fruit	17	10.8%	15	12.0%	14	13.7%
Pate	17	10.8%	13	10.4%	9	8.8%
Unpasteurised cheese or milk	13	8.2%	9	7.2%	6	5.9%
Total respondents	158	100.0%	125	100.0%	102	100.0%

\* known to suppress the immune response or increase risk of infection

and 64.6% (102) of all notifications, respectively. Malignancies, heart disease, rheumatological conditions and blood diseases, and antidiarrhoeal, antacids and antibiotics drugs, systemic steroids and cancer drugs specifically, were all frequently reported in persons with *Listeria* infection. Cancer patients accounted for a third of all listeriosis notifications in the reporting period. This is compared to other known risk factors including aged over 65 years (71.5%) and pregnancy (4.3%). Information on foods to avoid to prevent listeriosis provided by a healthcare worker prior to illness was received by relatively few notifications with a known risk factor: 7.2% of notifications with a known risk condition and 5.9% of notifications on medication reported receiving information reporting receiving such information. This was found despite relatively high levels of contact with health professionals prior to infection: 56.8% and 63.7% respectively had visited or been admitted to a hospital in the four weeks prior to illness.

This study is one of few studies to look at the distribution of immunocompromised persons among listeriosis notifications in Australia<sup>17</sup>, and the first to look at distribution in NSW over a 5-year period. Data extracted from notification records and a standardised questionnaire (OzFoodNet *Listeria* Case Questionnaire) was

utilised throughout the study period, making it an appropriate data source for presenting long term trends. The limitations of this study include the use of self-reported data provided in the questionnaire on exposures and treatment regimens from patients and their caregivers prior to illness, potentially leading to recall bias, and the use of pre-fixed categories for treatments and conditions in the standardised questionnaire, which may have led to measurement bias depending on the person collecting the data. Further the questionnaire does not include separate disease categories for autoimmune diseases and HIV, which are associated with increased risk of infection, leading to potential underreporting of trends in these specific vulnerable populations. Incomplete recording of data by surveillance officers due to time constraints or data entry errors may have also occurred, leading to underreporting of certain conditions or exposures. Where possible this study compared both patient and treating clinician responses to the standardised questionnaire and reviewed conditions and treatment responses to ensure they had not been incorrectly categorised during data collection, adjusting where possible for measurement bias. It is also likely that perinatal cases are underreported, due to under recognition and subsequent testing of early stage mis-carriages due to listeriosis not being suspected

**Table 4. Contact with a healthcare professional prior to illness among listeriosis notifications in NSW between 1 January 2010 to 31 December 2015**

	Notifications					
	All (158)		≥ 1 co-existing condition* (125)		≥1 medication or treatment* (102)	
	n	%	n	%	n	%
Contact with a health care professional in the 4 weeks prior to illness						
Day visit to hospital	61	38.6%	52	41.6%	47	46.1%
Admitted to hospital	45	28.5%	39	31.2%	36	35.3%
Information received from healthcare professional on foods to avoid to prevent listeria	11	7.0%	9	7.2%	6	5.9%

\*known to suppress the immune response or increase risk of infection

in the event of an adverse maternal outcome. Fatality outcomes were not used in this study due to incomplete data collection, however might be a useful variable in future analysis. Outbreak data during the study period were not examined and variation between variables in sporadic versus outbreak cases may also be considered in future research in cases among this population group.

Our findings suggest that, similar to studies in other industrialised countries<sup>5,18-19</sup>; immunocompromised persons, either with a primary immunodeficiency (a chronic condition suppressing the immune response) or receiving treatment or therapy that temporarily suppresses the immune system (chemotherapy, radiotherapy, systematic steroids), represents a significant proportion of listeriosis notifications. Findings are also consistent with those in a national case-control study, where cancer and use of antibiotics, systematic steroids and antibiotics were associated with risk of infection and were also found in significant proportion of cases<sup>17</sup>. These results identify specific patient groups in NSW who could benefit from targeted food safety messages to reduce further infections.

Reducing the risk and subsequent burden in susceptible populations has long been the focus of listeriosis control measures in Australia as well as a number of industrialised countries. With the decline of listeriosis notifications among pregnant women over the years, there is encouraging evidence to suggest that targeted strategies in food safety in the food industry, enhanced surveillance and the adoption of protective behaviours by consumers have worked to reduce the incidence of listeriosis in this specific group. Understanding trends of listeriosis among persons with identifiable risk factors can provide useful information to further reduce the disease burden in the population. The significant burden of cancer among Australians<sup>21</sup> and the associated risk of listeriosis with cancer and commonly used cancer treatments and therapies<sup>17</sup>, raises a concern regarding current risk reduction measures targeted at cancer patients. Currently in Australia, food safety information is generally incorporated into consultations by dietitians and nurses on admission to hospital. The extent to which such advice is routinely provided by general practitioners and other primary healthcare providers who may provide long term care for cancer patients and other immunocompromised persons, is not well understood. This

study shows that few immunocompromised persons who developed listeriosis, could recall receiving any information, suggesting room for improvement. Food Standards Australia New Zealand, in collaboration with state and territory food regulators, have developed new food safety advice and resources on listeriosis risk for immunocompromised and other vulnerable persons which may assist clinicians and health facilities to provide food safety advice to their patients.

Communication of the significant proportion of immunocompromised persons among listeriosis notifications and development of key risk reduction messages for use by clinicians may also assist to reduce the burden of the disease. Healthcare professionals, including those working in primary healthcare and key facilities frequented by immunocompromised patients including departments of oncology, haematology, aged-care and in-patient wards should be prioritised for targeted information and resources based on their frequent contact with the group at risk. Risk communication materials for clinicians of immunocompromised patients, including cancer patients, have been developed in other countries including the US.

There are a number of challenges in delivering food safety information to immunocompromised groups that should not be overlooked, such as the personal choice to prioritise food safety among persons with a terminal illness and the positioning of such information at a time when persons undergoing treatment or have been newly diagnosed are provided with large volumes of information.

Further research into clinicians' understanding of associated risk factors, current trends in risk, relevant communication channels and barriers to adopting preventative behaviours by patients and their caregivers could be explored to better understand which risk communication strategies would be best suited for immunocompromised persons.

## Conclusion

The prevalence of known risk factors for listeriosis among notified cases remains significant in NSW. Improved risk communication for this population, supported by information from healthcare professionals, may be beneficial in reducing the burden of listeriosis in known vulnerable groups who have regular contact with the health system.

## Ethics considerations

Data has been de-identified for the use of this report. Data was collected under the NSW Public Health Act 2010.

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