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Investigating locally-relevant risk factors for Campylobacter infection in Australia: protocol for a case-control study and genomic analysis

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SCHOLARONE[™] Manuscripts

Investigating locally-relevant risk factors for *Campylobacter* infection in Australia: protocol for a case-control study and genomic analysis

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ABSTRACT

Introduction:

The CampySource project aims to identify risk factors for human *Campylobacter* infection in Australia. We will investigate locally-relevant risk factors and those significant in international studies in a case-control study. Case isolates and contemporaneous isolates from food and animal sources will be sequenced to conduct source attribution modelling, and findings will be combined with the case-control study in a source-assigned analysis.

Methods and analysis:

The case-control study will include 1,200 participants (600 cases and 600 controls) across three regions in Australia. Cases will be recruited from campylobacteriosis notifications to health departments. Only those with a pure and viable *Campylobacter* isolate will be eligible for selection to allow for whole genome sequencing of isolates. Controls will be recruited from notified cases of influenza, frequency matched by sex, age group and geographical area of residence. All participants will be interviewed by trained telephone interviewers using a piloted questionnaire.

We will collect *Campylobacter* isolates from retail meats and companion animals (specifically dogs), and all food, animal and human isolates will undergo whole genome sequencing. We will use sequence data to estimate the proportion of human infections that can be attributed to animal and food reservoirs (source attribution modelling), and to identify spatial clusters and temporal trends. Source-assigned analysis of the case-control study data will also be conducted where cases are grouped according to attributed sources.

Ethics and dissemination:

Human and animal ethics have been approved. Genomic data will be published in online archives accompanied by basic metadata. We anticipate several publications to come from this study.

KEYWORDS

Campylobacter, case-control study, risk factors, Australia, whole genome sequencing, source attribution, source-assigned analysis

ARTICLE SUMMARY

Strengths and limitations of this study

- Case-control study is well-powered to identify locally-relevant risk factors.
- Linking genomic data to the case-control study strengthens the analysis by enabling source attribution and source-assigned analyses to be conducted.
- Case-control questionnaire questions are being validated in a separate study, demonstrating the reliability of participant recall.
- Potential reporting bias due to inaccurate recall of study participants.
- Case-control study lacks efficiency for risk factors with high levels of exposure in the study population.

INTRODUCTION

Campylobacter infection is the most commonly notified cause of foodborne gastroenteritis in Australia,¹⁻³ as well as a leading cause of bacterial gastroenteritis world-wide.⁴ At the introduction of Australia's National Notifiable Diseases Surveillance System (NNDSS) in 1991 the incidence rate of notified campylobacteriosis cases was 79.1/100,000 population,⁵ and despite notification rates plateauing in recent years, incidence had risen to 139.7/100,000 population in Australia in 2015,⁵ with an estimated 10 cases for every notified case within the community.⁶ By comparison, the incidence rate of campylobacteriosis in New Zealand in 2014 was 150.3/100,000 population,⁷ with an estimated 10-30 cases in the community for every notified case.⁸ *Campylobacter* notification rates in Australia and New Zealand are still among the highest in the world across high-income countries. Most countries in the European Union consistently report annual campylobacteriosis notification rates below 100/100,000 population.²

Two species of *Campylobacter—Campylobacter jejuni* and *C. coli*—contribute to approximately 95% of human campylobacteriosis.⁹ These *Campylobacter* species are commonly detected in sewage and surface water,¹⁰ reside in the gastrointestinal tract of birds and animals,¹¹ and are frequently found in raw meat, particularly poultry, and raw milk.^{12 13} Campylobacteriosis is mostly foodborne, with an estimated 77% of cases transmitted via food consumption in Australia.^{14 15} Direct and indirect zoonotic transmission can occur via animal contact (direct) or faecally-contaminated water or environments (indirect). Person-to-person transmission is considered rare.¹⁶ The majority of cases are thought to be sporadic, with outbreaks less commonly detected.¹⁷ Most outbreaks are linked to the consumption of poultry, raw milk, or contaminated water.^{17 18}

Targeted control of foodborne bacterial pathogens generally depends on identification of sources and routes of transmission. Since *Campylobacter* are ubiquitous in the environment and most cases are sporadic, identifying sources is difficult. Source attribution methods require isolation of strains from reservoirs to compare *Campylobacter* strain diversity in foods and animals to that in human infections. Beef, sheep and pig meat have a lower prevalence of *Campylobacter* contamination than chicken meat (<5% to 14%),¹⁹⁻²¹ but a higher prevalence is found in animal offal such as liver,²² thus making offal a valuable source of host-associated strains of *Campylobacter* in low-prevalence meats.

STUDY RATIONALE

In the United States, evidence from case-control studies have led to policy change, including changes to chicken slaughtering techniques. The incidence of human *Campylobacter* infection has declined in the US since this policy was introduced in 1997.²³ More recently, evidence from source attribution analyses in New Zealand has led to the development of poultry production policies and practices aimed at reducing the risk of *Campylobacter* transmission via poultry food products.²⁴ New Zealand has seen a 74% reduction in the number of campylobacteriosis cases attributed to poultry in the region, as well as a 54% reduction in cases overall.²⁵

Source attribution modelling enables us to determine which foods and animals are the most likely sources of infection with each *Campylobacter* strain type, and the proportion of cases attributed to each source. This can be done with simple proportional similarity index (PSI) calculations, or by using more complex models.²⁴ Source attribution also allows for human campylobacteriosis cases to be grouped by potential source, increasing the specificity of risk factor analyses. These source-assigned analyses combine the epidemiological information gained through the traditional case-control study with source attribution modelling to provide greater explanatory power to investigate locally-relevant risk factors.

OBJECTIVES

This study aims to:

- Identify dietary, environmental and behavioural risk factors for *Campylobacter* infection in Australia
- 2. Strengthen the epidemiological evidence for previously identified risk factors in Australia
- 3. Identify strain-specific risk factors for infection using Whole Genome Sequencing (WGS) data from case isolates

HYPOTHESES

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We will test several hypotheses regarding specific risk factors for *Campylobacter* infection in Australia. The hypotheses are based on exposures which have previously been identified as risk factors for *Campylobacter* infection in Australia as well as internationally.

We hypothesise that:

- 1. Persons who consume undercooked meats, particularly chicken, are at increased risk of infection.
- 2. Persons who consume offal are at increased risk of infection.
- 3. Persons who own companion animals (especially puppies) are at increased risk of infection.
- 4. Poor food hygiene and handling practices in the home increase the risk of infection.
- 5. Most human infections will be attributed to consumption of chicken meat.
- 6. There will be a high level of genetic diversity amongst *Campylobacter* strains.

STUDY DESIGN

We will conduct a case-control study including genomic testing over a two-year period in three sentinel sites: the state of Queensland (QLD), the Australian Capital Territory (ACT), and Hunter New England (HNE) region of New South Wales (Figure 1). Sporadic cases of culture-positive *Campylobacter* infection will be identified either through state notifiable disease registers, from local pathology service databases or local notification databases. An isolate from each case will be paired with epidemiological data from the case interview. One control will be recruited for each case who participates in the study, with trained interviewers conducting telephone interviews with both cases and controls. Participants will be interviewed using a questionnaire that has been specifically designed to collect information on known potential risk factors. This questionnaire will include a selection of questions being validated in a separate study (Liana Varrone, Validation of questions designed for gastroenteritis investigation). For cases, the questions will cover the seven days prior to the onset of illness, while controls will be questioned on the seven days prior to interview. Meanwhile, *Campylobacter* isolates will also be collected from food and animal samples. All human and non-human isolates will undergo whole genome sequencing for comparison in source attribution modelling. Data for this study will be collected from 1st March 2017 to 1st March 2019.

Figure 1. Map of Australian states and territories, showing the Hunter New England region. (Adapted from figure 1 in Eastwood *et al.* 2010)²⁶

Patient and public involvement

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To develop the study, we engaged state and territory health departments, food safety agencies and industry to establish research questions and methods. The process involved a dedicated workshop, followed by teleconferences and an iterative process of drafting study documentation. We also established a reference panel, which includes representatives from senior levels of government and industry bodies. No patients or other members of the public were involved in the development of this study.

STUDY POPULATION

The three sentinel sites cover a population of approximately 6.1 million people. Based on notification and diagnostic pathology data, we expect approximately 8,650 *Campylobacter* cases to be notified across these sites during the study period.

DEFINITION AND SELECTION OF CASES

Case definition

We define a case as a person from any of the three participating sites with a recent history of acute diarrhoea and a culture-positive stool result for *Campylobacter*.

SAMPLE SIZE

We used risk factor prevalence data from a previous national *Campylobacter* case-control study in 2001/2002 to estimate sample size for this study.²⁷ For example, the prevalence of chicken consumption among controls in 2001/2002 was 80%. A sample size of approximately 1,040 subjects (520 cases; 520 controls) would enable the study to detect an association between chicken consumption and illness with an odds ratio of 1.6, at 80% power and α = 0.05, as reported in the previous study. Sample size estimates for other potential risk factors are listed in Table 1.

Table 1.	Sample size	estimates fo	r an unmatched	case-control study
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Risk factor	Prevalence of exposure among controls (%)	Prevalence of exposure among cases (%)	Odds ratio	No. of required study subjects
Beef	78	85	1.6	960
Pork	52	60	1.4	1130
Lamb	42	50	1.4	1120
Chicken	80	87	1.6	1040
Offal	2.0	5.0	2.6	1154
Puppies	2.1	5.4	2.7	1040

80% power and α = 0.05

From these calculations, we estimate that a study of 1,200 subjects (600 cases; 600 controls) will adequately detect significant associations of these magnitudes for potential risk factors of interest.

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Queensland and Hunter New England sites will each enrol at least 250 cases into the study, while ACT will enrol at least 100 cases. Based on the previous Australian case-control study,²⁷ we expect approximately 80% of selected notified cases to be eligible and participate in the study (Table 2).

State	Expected number of notified cases during study period	Estimated cases from participating pathology laboratory	Culture +ve cases	Sequential sampling of notified cases	Total no. of cases	Expected no. to be recruited (~ 80% participation rate)
QLD	7000	2800 (40%)	1260 (45% in QLD)	Select every 4 th case	315	250
ACT	600	130	130	Include all notified cases	130	100
NSW (Hunter New England)	~1050	313	313	Include all notified cases	313	250
Total	8650	3243	1703		758	600

In Queensland, we will obtain cases from one private pathology provider reporting approximately 40% of the state's *Campylobacter* notifications. We estimate that this provider will notify 2,800 cases during the study period with an estimated 45% of these being culture-positive (1,260 notified cases). In ACT, approximately 600 *Campylobacter* notifications are expected during the study period; 130 are expected from the participating pathology laboratory. In Hunter New England, approximately 1,050 *Campylobacter* notifications are expected during the study period; 313 of these notifications will be from the participating pathology laboratory.

Enrolment of Cases

We will enrol all cases who meet the eligibility criteria (Table 3). Each site will check for new notifications of culture-positive *Campylobacter* infection daily, with only culture-positive *Campylobacter* cases eligible for this study. If a case refuses to participate in the study, we will select a subsequent case for inclusion. Enrolment of cases will depend on consent from the patient, or in the event of a child aged less than 18 years, consent from either one of the parents or the child's guardian. We will interview cases as soon as possible by telephone, preferably within two weeks of notification from the laboratory. It will be at the parent's or guardian's discretion as to whether a

child aged between 15 and 17 years is interviewed directly. The parent or guardian will be interviewed for cases aged less than 15 years.

Table 3.	Eligibility criteria	for cases and controls
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Criteria	Cases	Controls
Had diarrhoea (≥3 loose bowel movements in	Include	Exclude
24hrs)		
Known date of illness onset	Include	N/A
Household members positive for Campylobacter	Exclude	Exclude (4 weeks prior to
in 4 weeks prior to onset of illness		interview date)
Household members experiencing diarrhoea in 4	Exclude	Exclude (4 weeks prior to
weeks prior to onset of illness		interview date)
Travelled outside of Australia in 2 weeks prior to	Exclude	Exclude (2 weeks prior to
onset of illness		interview date)
Travelled interstate for the entire 2 weeks prior	Exclude	Exclude (2 weeks prior to
to onset of illness		interview date)
Can't speak English	Exclude	Exclude
Not able to answer questions for some other	Exclude	Exclude
reason (e.g. intellectually disabled)	4.	
Not contactable after 6 telephone attempts	Exclude	Exclude
Live outside the catchment areas	Exclude	Exclude
Do not have a telephone number available for	Exclude	Exclude
their primary residence, or a mobile phone	0	
An enteric pathogen other than Campylobacter	Exclude	N/A
was isolated/detected in their stool (excluding		
Blastocystis hominis and Dientamoeba fragilis)		

DEFINITION AND SELECTION OF CONTROLS

We will recruit controls from notified cases of influenza, frequency matched by sex, age group and geographical area of residence by Statistical Area Level 4 (SA4). These controls will be selected with a delay of at least six months from their influenza infection to ensure that controls have returned to eating their customary diet.

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Each participating site (QLD, ACT or HNE) will establish a database of controls (previous influenza cases). All cases of influenza notified to the health department in each site between 1st January and 31st December 2017 will be entered into this control database. The age bands are 0-4 years, 5-14 years, 15-34 years, 35-54 years, 55-74 years, and ≥75 years. An appropriate control will be randomly selected from the database within 30 days of interview of the notified case.

Case and control recruitment

Interviewers trained in computer-assisted telephone interviewing (CATI) will conduct telephone interviews. A maximum of six attempts will be made to contact any one case or control, with no more than three attempts in any one day. Three calls will be attempted between 9:00am and 3:59pm, and three attempts between 4:00pm and 8:00pm. A text message will be sent to the potential participant after three failed call attempts, indicating that Public Health is trying to contact them. This protocol will be continued until the person is enrolled or excluded.

QUESTIONNAIRES

We will use specific case and control questionnaires for all participants (see Appendix 1). Cases will be asked additional questions about the clinical course of their illness and treatment. Interviewers will ask identical questions regarding exposures such as foods consumed, dining locations, water sources, domestic food handling techniques and exposure to animals of cases and controls. Questions on foods consumed, dining locations, water consumed, animal and pet exposures will be asked based on a seven-day history. Questions on international travel will be asked based on a twoweek history. Antibiotic and antacid consumption, immunosuppressive treatment and household history of diarrhoea will be based on a four-week history. Questions on food handling and general kitchen practices will be based on usual practices rather than recent history. Demographic information will be collected from cases and controls. Contact information required to conduct interviews will be stored in a password-protected Excel document with only those needing to contact individuals given access. Piloted questionnaires were modified to remove repetitions, improve clarity, and to ensure that interviews could be conducted within 20 minutes.

DATA HANDLING & RISK FACTOR ANALYSIS

We will undertake descriptive reporting of campylobacteriosis incidence by person, place and time. We will also describe the severity of symptoms, treatment, and burden of illness.

Risk factor analysis will involve the examination of two-by-two contingency tables with chi square or exact tests to determine the presence of univariable associations between variables and disease. To measure the strength of an association, we will estimate odds ratios and calculate 95% confidence

intervals in a univariable analysis, followed by multivariable logistic regression modelling to adjust for potential confounders. Risk factors selected for inclusion in the regression model will include age, season and geographic area, variables with a significant univariable association with disease, and variables with a P-value ≤ 0.25 that are biologically plausible and of interest to the research team.

LABORATORY ANALYSES

Human samples

As outlined in Table 2, it is expected that 250 human isolates from Hunter New England, 250 from Queensland, 100 from Victoria and 100 from ACT will be sequenced. The initial isolation and confirmation of *Campylobacter* infection will be performed locally in each State/Territory. Only samples with a pure and viable culture will undergo WGS.

Animal and food samples

We will collect samples from chicken meat (covering the two production methods of continually housed and free range/housed), beef, lamb, pork, and from pet dogs. Given low prevalence of *Campylobacter* in meats other than chicken, samples will be collected from offal (preferably liver) from bovine, ovine and porcine sources to ensure sufficient positive samples are obtained for the study. Given the rising importance of chicken liver pate as a source of outbreaks in Australia,²⁸ chicken offal will also be sampled. Sample sizes by source are based on data from two states to ensure 50 positive samples per food source, and 30 samples in companion animals (Table 4). We will also contact veterinary clinics and teaching hospitals to ensure sufficient *Campylobacter*-positive samples from dogs. Water samples have been omitted from the genomic aspect of this study due to logistical constraints in sampling untreated water sources across the large geographical area involved in this study, and the complexity of designing an appropriate sampling frame. As there is a lack of evidence implicating municipal drinking water as sources of *Campylobacter* infection in Australia¹²⁷ we excluded water sampling from this study.

	Foods						Animals	
	Chicken			Beef	Lamb	Pork	Dogs	Total
	Continually	Free-	Offal	Offal	Offal	Offal		
	housed	range						
Assumed	0.7	0.7	0.7	0.14	0.6	0.22	0.2	
prevalence								
Samples	72	72	72	286	100	272	150	1041
required								
Positive	50	50	50	40	60	60	30	330
isolates								

The initial isolation and confirmation of *Campylobacter* will be performed locally at laboratories in each State/Territory, with isolates forwarded to the Microbiological Diagnostic Unit Public Health Laboratory for WGS, except Queensland isolates which will be sequenced at Queensland Health. To detect seasonal and temporal variation in *Campylobacter* genetic types, 1041 non-human samples (estimated to produce 330 *Campylobacter* isolates) will be collected over a period of one year in Queensland, and two years in New South Wales. To assess latitudinal variation in chicken meat samples across eastern Australia, 105 chicken samples (70 chicken meat and 35 chicken offal) will be collected over a six-month period in Victoria. Food samples will be collected monthly from retail premises, using protocols from surveys undertaken in 2014 by partner organisations, with a pilot of 30 isolates in Queensland.

We will also collect an additional 20-30 human isolates from four additional Australian jurisdictions not participating in this case-control study to undergo WGS. This will be done over a two-month period that overlaps with the case-control study sample collection, and is planned to help inform the generalisability of the case-control study.

SEQUENCING AND SEQUENCE DATA PROCESSING

Campylobacter isolates selected for sequencing will be repurified on solid medium and a single colony selected for preparation of genomic DNA. A sequencing library will be prepared from the genomic DNA for sequencing on the Illumina sequencing platform (MiSeg or NextSeg). A sample of the selected colony will be regrown and cryopreserved (resuspended in liquid medium supplemented with 10% Glycerol and stored at -80°C). In some cases, *Campylobacter* enrichment cultures will be cryopreserved to enable future investigation of the genetic diversity of Campylobacters present. The short-read, paired end dataset produced by the Illumina Instrument from the genomic DNA of each isolate will be processed to produce a draft genome sequence for the isolate using a *de novo* assembler such as MEGAHIT.²⁹ The draft genome sequence will be annotated using Prokka.³⁰ We will use the draft genome sequence to perform the initial sub-species classification by deriving a multilocus sequence type (MLST) using the "Campylobacter jejuni/coli" typing scheme (pubmlst.org). Again, using the draft genome sequence, further typing e.g. virulence factors (http://www.mgc.ac.cn/VFs/) or antimicrobial resistance genotype (https://cge.cbs.dtu.dk/services/ResFinder/) will be performed using Abricate (https://github.com/tseemann/abricate). We will perform comparative genomics to examine the genetic relationships between selected subgroups of isolates in more detail using Nullarbor (https://github.com/tseemann/nullarbor).

SOURCE ATTRIBUTION MODELLING

We will analyse the epidemiological data within designated MLST groups or other typing groups derived from the genomic sequence data. Source attribution modelling and source-assigned analyses will be conducted.

Source attribution models combine typing data from isolates from food, animal and humans to estimate the proportion of human infections that can be attributed to animal and food reservoirs.³¹ ³² Once inferred MLSTs have been ascertained, the proportional similarity index²⁵ will be used to assess similarities by source. We will then undertake source attribution analyses by adapting the asymmetric island model which has previously been applied to MLST data^{25 33} using Markov Chain Monte Carlo (MCMC) methods³⁴ implemented using the free software WinBUGS.³⁵ These methods will first be applied to MLST data extracted from whole genome sequences (the aforementioned "inferred MLSTs"), and then compared to structured phylogenetic modelling approaches^{36 37} that provide scope to infer inter-host transmission.

We will then group cases according to putative source based on these source attribution methods.³⁸ For example, all isolates attributed to chicken will be grouped together, regardless of differing strains. These cases attributed to chicken will then be compared to all controls in a risk factor analysis to produce a source-assigned analysis.

SPATIAL CLUSTERS AND TEMPORAL TRENDS

We will use newly-designated WGS-based MLSTs to assess heterogeneity in isolates from food sources and companion animals in Queensland and New South Wales, and in isolates from chicken meat and humans across Queensland, New South Wales, Victoria and ACT. A two-year sampling framework in New South Wales, one year of sampling in Queensland, and previous survey work in these states will allow us to assess the extent of seasonal and temporal trends. Postcode-level data associated with human illnesses will be used to detect space-time clusters using a scan statistic implemented in the free software SaTScan, at the Statistical Area 1 level.³⁹ We will use a retrospective space-time permutation model to detect high risk clusters by comparing the observed number of illnesses to the expected number in that geographic zone and time-period.⁴⁰

STUDY LINKAGES AND COLLABORATIONS

The CampySource Project Team comprises three working groups and a reference panel. The working groups focus on: food and animal sampling, epidemiology and modelling, and genomics. The reference panel includes expert representatives from government and industry.

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The study is supported by the following partner organisations: the Australian National University, Massey University, University of Melbourne, Queensland Health, Queensland Health Forensic and Scientific Services, New South Wales Health, Hunter New England Health, Victorian Department of Health and Human Services, Food Standards Australia New Zealand, Commonwealth Department of Health and AgriFutures Australia – Chicken Meat Program.

CampySource is also supported by collaboration with the following organisations: ACT Health, Sullivan Nicolaides Pathology, University of Queensland, Primary Industries and Regions South Australia, Department of Health and Human Services Tasmania, Meat and Livestock Australia, and New Zealand Ministry for Primary Industries.

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The CampySource Project Team consists of: Nigel P. French, Massey University, New Zealand; Mary Valcanis, The University of Melbourne; Dieter Bulach, The University of Melbourne; Emily Fearnley, The Australian National University; Russell Stafford, Queensland Health; John Bates, Queensland Health; Trudy Graham, Queensland Health; Keira Glasgow, Health Protection NSW; Kirsty Hope, Health Protection NSW; Arie H. Havelaar, The University of Florida, USA; Joy Gregory, Department of Health and Human Services, Victoria; James Flint, Hunter New England Health; Simon Firestone, The University of Melbourne; James Conlan, Food Standards Australia New Zealand; James J. Smith, Queensland Health; Sally Symes, Department of Health and Human Services, Victoria; Barbara Butow, Food Standards Australia New Zealand; Liana Varrone, The University of Queensland; Linda Selvey, The University of Queensland; Deborah Denehy, ACT Health; Radomir Krsteski, ACT Health; Natasha Waters, ACT Health; Kim Lilly, Hunter New England Health; Julie Collins, Hunter New England Health; Tony Merritt, Hunter New England Health; Joanne Barfield, Hunter New England Health; Ben Howden, The University of Melbourne; Kylie Hewson, AgriFutures Australia – Chicken Meat Program; Laura Ford, The Australian National University; Liz Walker, The Australian National University; Cameron Moffatt, The Australian National University; Martyn Kirk, The Australian National University; and Kathryn Glass, The Australian National University.

While undertaking studies, LV is supported through an Australian Government Research Training Program (RTP) Scholarship.

DECLARATIONS

Ethics approval and consent to participate

Informed Consent

A suitably trained interviewer will inform potential participants about the purpose, methods and demands of the study. We will obtain verbal consent from all study participants or their guardians.

Persons aged 18 years and older will be interviewed following informed consent. It will be at the parent's or guardian's discretion as to whether a child aged between 15 and 18 years is interviewed directly, following informed parental/guardian consent. Parents/guardians will be interviewed for cases aged less than 15 years, after informed consent is obtained.

Confidentiality

All information and identifiers will be kept confidential. Names and personal identifiers will be collected and entered into computer records but will be password protected. No personal identifiers will be included in any published materials relating to this study. All hard copy questionnaires containing patient identifiers will be stored in locked filing cabinets in a secure location to which only study investigators and interviewers will have access.

Risks and Benefits

Participants will be informed there are no individual benefits associated with the study and that participation is voluntary. Failure to participate or a withdrawal of participation will not affect any future treatment. There is also no risk to the patient, and the only cost is time spent – approximately 20 minutes – being interviewed. They may refuse to answer any of the questions or stop at any time.

Animal Ethics

All procedures involving live animals will be performed in accordance with a protocol approved by the University of Melbourne's Animal Ethics Committee (ethics ID: 1714156).

Consent for publication

Not applicable.

Availability of data and materials

The Illumina read sets produced as part of this study will be published at INSDC (Sequence Read Archive (DDJB/NCBI) or the European Nucleotide Archive (EMBL-EBI))

Competing interests

No authors have any competing interests to declare.

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Author contributions

MDK conceived the original idea for this study. All authors contributed to the study design and analysis plan. LV and RJS wrote the first draft with contributions from all authors. LV, RJS, LS, MDK and KG were involved in multiple revisions. The final version of the manuscript was approved by all authors.

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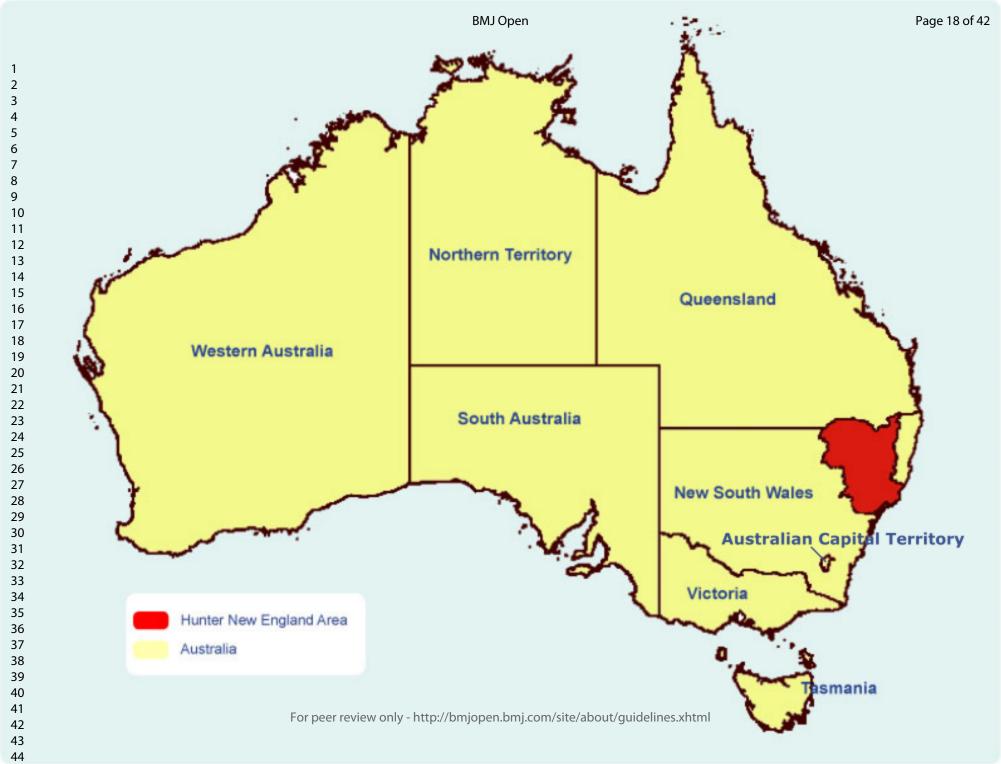
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RefusalIneligible
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Source Attribution of Campylobacter in Australia Study

Case Questionnaire

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

INTRODUCTIO	ON	
Interviewer Note:	If case is less than 15 years of age you will n familiar with the eating habits of the child.	eed to speak to parent or guardian
	If case is aged between 15–17 years you will consent prior to interview.	need to obtain parent or guardian
	Please note that for subjects under the age of not the person being interviewed unless spec	
"Hello, my name	e is <interviewers name=""> and I am calling on</interviewers>	behalf of [Queensland Health / A
	New England Public Health Unit]." beak with <name case="" of=""> or <name case's<="" of="" td=""><td>mother/father>?"</td></name></name>	mother/father>?"
	star with shalle of cases of shalle of case s	
Interviewer Note:	When the case comes to the phone then repe explanatory statement.	at the introduction and proceed wit
	If the case is unavailable then arrange an alte	mative time for the interview
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If NO, arrange an alternative time to phone back to conduct the interview If YES, continue

				e time of your illness, it may be helpful need a few minutes to get these?"
	Vec I will a	et one no		
	No. Lalready	have one with me	·····	
		ccess to a calendar		
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	The first few a	uestions we'll be asking you a	re about s	some symptoms that are associated
	with [your/thei		i c about	some symptoms that are associated
	,, in [, our, mer			
1.	For the pur	poses of this study, we define	diarrhoea	as 3 or more loose stools or bowel
				ur <i>Campylobacter</i> infection, did you
	have diarrh		-	
	Ves		\Box .	Go to Q2
				Check ineligible box then END INTER
		Not sure		Check ineligible box then END INTER
	Don't know		·····	
1 a	During this dia	rrhoeal illness, what was the ma	ximum nu	mber of stools or bowel movements
		ny 24 hour period?		
	0-2	······		Check ineligible box then END INTER
	3-5		2	(If response = $(0-2)$, then recode Q.1 as
	6-10	·····	3	
		0		
	Don't know/	Not sure	7	
2.	For how ma	ny days did your diarrhoea last	?	DAYS
_,				
	Don't know/	Not sure	77	
	CALCULA	TE PRIOR TO INTERVIEW		
	Date sto	ool specimen collected		
			Day	Month Year
3.	Could you	please let me know what th	e date wa	as when your diarrhoea began?
				v G
	Day	Month Year		
		sure of date then prompt with date of stoe	ol specimen)	
	Don't know	Not sure	7	Check ineligible box then END INTER
			······ /	
	I will now just en	ter a couple of other dates that w	e will be ta	llking about throughout the interview.
	I won't be a mor			-
Inte	erviewer Note:			terval from DATE 4 WEEKS BEFORE
		DIARRHOFA REGAN to DA	TEINAV	BEFORE DIARRHOEA BEGAN.

		sehold test positive for Campyloba	icter?	RRHOEA BEGAN>, did anyone else
				Check ineligible box then END INTER
		Not sure		
5.	DIARRHOI <u>household</u> h	ave diarrhoea?	FORE DIA	DATE 4 WEEKS BEFORE ARRHOEA BEGAN>, did anyone else in
				Check ineligible box then END INTER
		Not sure		
	Don't know/	Not sure		
Interv	viewer Note:			erval from DATE 2 WEEKS BEFORE BEFORE DIARRHOEA BEGAN.
_		DIARRIOLA BLOAN & DAI		BEFORE DIARRITOLA BEGAN.
6	In 46 - 2	la hofono vora illa de la d	in france -	NATE 2 WEEVS DEFODE
6.	DIARRHOI	ks before your illness began, that EA> through <date 1="" bei<br="" day="">eas or interstate?</date>		
	INTERVIEV	VER NOTE:		
		t answers "yes",		
		the travel was overseas or interstate		
	2. If travel w			1 1
	Clarify the le	ength of time spent interstate in the	time perio	a just mentioned
	Options to se	elect:		
	A. If the part			ole two weeks interstate: (Select option Yes on of the time: (Select option No)
	Ves		\Box	Check ineligible box then END INTERV
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7.	During this illness, did you have any of the following symptoms?
	Yes No DK/NS
a.	Fever
b.	Vomiting 1 2 7
c.	Stomach cramps \Box_1 \Box_2 \Box_7
d.	Blood in your stool
e.	Nausea
f.	Headache
g.	Muscle/body aches \Box_1 \Box_2 \Box_7
0	
8.	Did you take any antibiotics as a result of this illness?
	Yes
	No \Box
	Don't know/Not sure
9.	What antibiotic(s) were you taking? [Ask person to get tablet bottle, if possible]
	Azithromycin
	Ciprofloxacin
	Norfloxacin
	Erythromycin
	Doxycycline (also known as Doxy or Vibramycin.
	Other (please specify) Specify(
	Don't know/Not sure
10.	Were you admitted to hospital overnight because of this illness?
	Yes
	No Go to Q. 12
	Don't know/Not sure
11.	If yes, for how many nights were you hospitalised? NIGHTS
	Don't know/Not sure
Intervi	ewer Note: Refer to your calendar to determine the interval from DATE 4 WEEKS BE DIARRHOEA BEGAN to DATE 1 DAY BEFORE DIARRHOEA BEGA
	DIAKKHUEA BEGAN TO DATE I DAY BEFURE DIAKKHUEA BEGA

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Intervi	ewer Note: If person can't remember the leave the space blank.	he name of the an	ntibiotic(s), check the DK/NS box and
13.	What antibiotic(s) were you taking? [As	k person to get ta	blet bottle, if possible]
		DK/NS	What date did you stop taking these?
a.	Antibiotic 1	7	(DD/MM) _ 7 DK/NS
b.	Antibiotic 2	7	(DD/MM) _ 7 DK/NS
c.	Antibiotic 3	7	(DD/MM) _ 7 DK/NS
d.	Antibiotic 4	7	(DD/MM) _ 7 DK/NS
14.	In those 4 weeks, were you taking any re	egular medicatio	on that decreases stomach acid?
	Yes No Don't know/Not sure	2	Go to Q. 16 Go to Q. 16
15.	Did you take any of the following in the	4 weeks prior to) illness?
<u>ר</u>	<u> Histamine-2 (H₂) Receptor blocker</u>	Yes	<u>No</u> D <u>K/NS</u>
a.	Zantac (Ranitidine)		2 7
b.	Tagamet (Cimetidine)		2 7
с. d.	Pepcid (Famotidine) Axid (Nizatidine)		
<u>P</u>	Proton Pump Inhibitor		
a.	Losec (Omeprazole)		
b.	Nexium (Esomeprazole)		
c.	Somac (Pantoprazole)		
d.	Pariet (Rabeprazole)		2 7
e.	Zoton (Lansoprazole)	1	
16.	Have you ever been told by a doctor t chronic illness in which diarrhoea or vo irritable bowel syndrome, ulcerative col	miting is a majo	r symptom? (e.g. Crohn's disease,
	Yes	🔲 1 Sp	ecify(
	No		
	Don't know/Not sure		

1					
2	17.	In the 4 weeks before onset of illness, did you	take or rece	ive any of t	the following?
3		•		•	0
4		INTERVIEWER NOTE:			
5		Cyclosporine ("it's an immunosuppressant")			
6			N	NT	DIZAIO
7	0	Prednisone	Yes	No	DK/NS
8	a.				
9		or other steroids <u>not</u> used on your skin		2	7
10	b.	Cyclosporine	1	2	7
11	с.	Chemotherapy	1	2	7
12	d.	Radiation therapy	1	2	7
13					
14					
15					
16					
17					
18					
19					
20					
21		ChemotherapyRadiation therapy.			
22					
23					
24					
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56					
57					
58					
59					

Intervie	ewer Note: Refer to your calendar to determine the interval from the DATE 7 DAYS BEFORE DIARRHOEA BEGAN to the DATE 1 DAY BEFORE DIARRHOEA BEGAN				
	A. WATER				
1					
	m now going to ask you some questions about water that you consumed in the <u>7 days before your</u>				
<u>dia</u>	<u>urrhoea began, t</u> hat is from [diarr_7_days_prior] to [diarr_1_day_prior].				
8.	What is your main source of drinking water at home? (select one only)				
	INTERVIEWER NOTE:				
	Only read out options if they're unsure				
a.	A rainwater tank				
b.	A river or stream				
c.	A private well, bore hole, or spearpoint				
d.	A carrier or tank truck				
e.	Municipal water supply (tap water)				
f.					
g.	Other water supply				
h.	Don't know/Unsure				
	E.				
	E.				
ntervie	ewer Note: If person answered "Yes" to "Municipal water supply" or "Purchased bottle water",				
ntervie	ewer Note: If person answered "Yes" to "Municipal water supply" or "Purchased bottle water", skip to Q.21				
	skip to Q.21				
	1 11 2 /				
	skip to Q.21				
	skip to Q.21 Do you usually treat your <u>main</u> source of drinking water before drinking?				
	skip to Q.21 Do you usually treat your main source of drinking water before drinking? If Required PROMPT: Some examples are chlorination, filtration, boiling and UV treatment of the water before drinking.				
	skip to Q.21 Do you usually treat your main source of drinking water before drinking? If Required PROMPT: Some examples are chlorination, filtration, boiling and UV treatment of the way Yes				
9.	skip to Q.21 Do you usually treat your main source of drinking water before drinking? If Required PROMPT: Some examples are chlorination, filtration, boiling and UV treatment of the way Yes No Don't know/Not sure				
9.	skip to Q.21 Do you usually treat your main source of drinking water before drinking? If Required PROMPT: Some examples are chlorination, filtration, boiling and UV treatment of the way Yes				
9.	skip to Q.21 Do you usually treat your main source of drinking water before drinking? If Required PROMPT: Some examples are chlorination, filtration, boiling and UV treatment of the way Yes 1 No. 2 Go to Q. 21 Which of the following treatments are in place? (select all that apply) Yes No Description Yes Yes No Description Description				
9. 0. a.	skip to Q.21 Do you usually treat your main source of drinking water before drinking? If Required PROMPT: Some examples are chlorination, filtration, boiling and UV treatment of the way Yes				
9. 0. a. b.	skip to Q.21 Image: Property of the second seco				
2 0. a.	skip to Q.21 Image: Property of the second system of the second syst				
20. a. b. c.	skip to Q.21 If I				
20. a. b. c. d.	skip to Q.21 If I				

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15	21. a. b. c. d. e. f. g.	Did you drink water from any of the following sources in the 7 days before onset of diarrhoea? (Select all that apply) A rainwater tank A river or stream A private well, bore hole, or spearpoint A carrier or tank truck Municipal water supply (tap water) Purchased bottle water Other water supply Specify ()
16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 23		Specify ()
 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 		
49 50 51 52 53 54 55 56 57 58 59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

D D	
B. DI	NING LOCATIONS
"Т	he next few questions ask about places where you may have eaten food in the <u>7 days</u>
illr	<u>ness began</u> . So that is from [diarr_7_days_prior] to through [diarr_1_day_prior]"
22.	During this time, did you eat any food prepared outside your home, for example takeaway, restaurant, someone else's home?
	Ves
	No Go to Q 24
	Don't know/Not sure
23.	Did you eat any food from the following places?
	Yes No DK/NS
a.	Café or restaurant
и. b.	
с.	
d.	Other fast food/take away outlet
u.	
23a	How many meals prepared outside of your home, were eaten during this 7 day
	period?
	1-2 meals
	3-4 meals
	\geq 5 meals
	Don't know/Unsure
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	ror peer review only - http://binjopen.binj.com/site/about/guidelines.xhtml

	I would now like to ask you about the dairy products you may have eaten in the <u>7 da</u>
<u>d</u> 24.	<u>iarrhoea began</u> ." Did you drink any raw/unpasteurised milk or eat any products made from raw/unpasteurised milk?
	INTERVIEWER NOTE: Cold-pressed milk is pasteurised and is not to be included as "raw/unpasteurised".
a b	

D MEAT	AND	POULTRY
D. WILLIN	1110	LOODIKI

"I will now ask you some questions about meat and poultry that you may have eaten in the 7 days
before your diarrhoea began, that is from <date 7="" before="" began="" days="" diarrhoea=""></date>
through <date 1="" before="" began="" day="" diarrhoea="">."</date>

25. During these 7 days, did you eat any of the following deli meats or cold cuts?

		Yes	No	DK/NS	
а	Salami/mettwurst			7	
	. Cabanossi/cabana/twiggy sticks				
	. Ham/chicken/turkey/beef			7	
d	. Devon/frankfurts/cheerios	1	2	7	
e	Liverwurst		2	7	
f.	Other	1	2	7	
	Specify ()			
26.	During these 7 days, did you eat any pate?				
	Yes				
	No	2	Go to Q.29		
	Don't know/Not sure	7			
27.	Was the pate eaten,				
21.	-				
	Chicken pate				
	Duck pate				
	Pork pate Another type of pate		Specify ()
	Don't know/Not sure	4	Speeny ()
		<i>,</i>			
28.	Was this pate homemade or purchased from	a store?			
	Homemade	🗌 1			
	Store	2			
	Don't know/Not sure	. 7			
29.	During these 7 days, did you eat any other m	leat or nou	ltrv? Like be	ef, lamb, chicken etc	
->.	During these 7 days, and you cut any other h	icat of pou	intry. Line be		
	INTERVIEWER NOTE:				
	This does not include eggs				
		_			

Yes	1	
No	2	Go to Q.49
Don't know/Not sure	7	

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1 2	ргг	
2 3	BEE	EF / VEAL
4		
5	30.	During these 7 days, did you eat any beef or veal?
6		Yes
7		No Go to Q. 32
8 9		
9 10		
11		
12	31.	During the 7 days prior, did you eat any of the following beef or veal?
13		
14		7
15		DK/N DK/N
16		
17	a.	Minced beef dishes $\Box_1 \Box_2 \Box_7$
18	u.	(eg. bolognese sauce, pie, pastie, lasagne, hamburger patties, sausages)
19 20	b.	Kebabs/souvlaki
20 21		$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
21	c.	(eg. tripe, liver, tongue)
23	d.	Other $\Box_1 \Box_2 \Box_7$
24		(eg. casserole, stir fry, steak, fillet, roast, beef strips)
25		
26	POR	2K
27		
28	22	During these 7 days did you get any node?
29	32.	During these 7 days, did you eat any pork?
30		Yes
31		No 2 Go to Q. 34
32		Don't know/Not sure
33		
34 35		
36	33.	During the 7 days prior, did you eat any of the following pork?
37		
38		Z
39		Ves No
40		
41	a.	Minced pork dishes $\Box_1 \Box_2 \Box_7$
42		(eg. bolognese sauce, pie, pastie, lasagne, hamburger patties, sausages)
43	b.	Kebabs/souvlaki
44	c.	Offal $\Box_1 = 2$ \Box_7 Specify (
45		(eg. tripe, liver, tongue)
46	d.	Other
47 48		(eg. casserole, stir fry, steak, fillet, roast, pork strips)
48 49		
49 50	LAM	ЛВ
51		
52		
53	34.	During these 7 days, did you eat any lamb/mutton?
54		Yes Specify (
55		No
56		Don't know/Not sure
57		
58		
59		

)

)

_)

_)

	Yes No DK/N
a.	Minced lamb/mutton dishes $1_1 2_2 7$ (eg. bolognese sauce, pie, pastie, lasagne, hamburger patties, sausages)
b.	
c.	(eg. tripe, liver, tongue)
d.	Other
GA	ME MEAT
36.	During these 7 days, did you eat any game meat like kangaroo, wallaby, venison or similar?
	Yes Specify (
	No Don't know/Not sure
PO	ULTRY
37.	How often do you <u>usually</u> consume chicken/poultry meat?
	3 or more days per week
	1-2 days per week ² Once per fortnight ²
	Less often than once per fortnight
	Never 5 Go to Q.46
	Don't know/Not sure
38.	During the 7 days before your illness began, did you eat any chicken or other poultry?
	Yes
	No 2 Go to Q.46 Don't know/Not sure
39.	How many meals did you eat that contained chicken or other poultry in the 7 days prior to onset of diarrhoea?
	1-2 meals
	3-4 meals
	\geq 5 meals
	Don't know/Not sure

1		
2	40.	Did you consume any chicken or poultry at home?
3		
4		Yes
5		No 2 Go to Q.43
6		Don't know/Not sure
7		
8		
9	41.	Was the chicken or poultry purchased?
10		(Select all that apply)
11		
12		Raw and fresh
13		Raw and frozen 2
14		Pre-cooked 3
15		Don't know/Not sure
16		
17		
18	42.	How was it stored before consumption?
19		(Select all that apply)
20		
21		INTERVIEWER NOTE: 🔼
22		(On the bench)
23		This is only to be used if they STORE their meat on the bench, this does not include defrosting their meat on
24		the bench.
25		
26		
20		In the freezer
28		In the fridge 2
		On the bench 3
29		Don't know/Not sure
30		
31		
32	12	
33	43.	Prior to cooking, was the chicken rinsed or washed under running water?
34		Yes
35		No
36		
37		
38		
39	44.	During this did time you eat any of the following cooked meats?
40		but mg tins the time you cat any of the following cooked meats
41		
42		Ves No
43		DK No Ye
44	0	Chicken mince \Box_1 \Box_2 \Box_7
45	a.	(including hamburger patties, sausages)
46	b.	
47	с.	Chicken pieces with bones
48	U.	(i.e. wings, drumsticks, whole chicken)
49	d.	Chicken pieces without bones. \Box_1 \Box_2 \Box_7
50	u.	(i.e. breast, tenderloins)
51	e.	Offal
52		specify: liver other
53	f.	
54		
55	g.	
56		
57		

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g.

h.

45.		During this time, on how many days did you eat poultry?
		INTERVIEWER NOTE: 1. A pate is included 2. Eggs are excluded
		Days:
46.		During this time, on how many days did you eat meat (including poultry)?
		INTERVIEWER NOTE: Pate is included
		Days:
47.		During the 7 days prior to illness, did [you/they] eat any meat product, which was raw, rare or appeared undercooked?
		Yes No Don't know/Not sure
48.		Which of the following meats did [you/they] eat that was undercooked?
	a. b. c. d. e.	VesNoDK/NSBeef or veal127Pork127Lamb/mutton127Game meat127
	f. (eg.	Minced meat items 1 2 7 including sausages, hamburger patties) 1 1 1 7

Offal (specify type)_____

Specify (_____

Other meat.....

.

2	49.	How do you <i>prefer</i> the following meat to be cooked?
3		
4 5		INTERVIEWER NOTE:
5 6		Raw: Not cooked at all
6 7		Rare: Mostly red
		Medium: Pink through out
8 9		Well done: Brown through out
9 10		
10 11		INTERVIEWER NOTE:
11		If participant answers Medium/Rare
12		select the rarer option e.g Rare
13		
15		Raw Rare Medium Well done
15	a.	Chicken/Poultry
10	b.	Beef/Veal
17	c.	Pork 1 2 3 4
18	d.	Lamb 1 2 3 4
20	e.	Hamburgers \Box_1 \Box_2 \Box_3 \Box_4
20	f.	Minced meat \square_1 \square_2 \square_3 \square_4
22		
22		
23 24		
24 25		
25 26		
20		
27 28		
28 29		
30 31		Hamburgers
32		
33 34		
35		
36		
37		
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R	will now ask you several questions about the way food is usually prepared in your hon emember, your participation is voluntary and you do not have to answer any of the questions u don't want to."			
50.	How many times per week do you cook for members of your household? INTERVIEWER NOTE: This section around food prepared in the home refers to the person answering the survey (not necessarily the case or control)			
	0 1-5 >5 Don't know/Not sure 0 I Go to Q.63 2 3 7			
51.	Did you handle or prepare any raw meats in the kitchen in the <u>7 days before your</u> <u>diarrhoea began?</u> INTERVIEWER NOTE: Refers to the person answering the survey			
	Yes No Don't know/Not sure			
52.	Did you handle or prepare raw chicken meat or chicken offal in the <u>7 days before your</u> <u>diarrhoea began?</u> INTERVIEWER NOTE: Refers to the person answering the survey Yes No Don't know/Not sure			
Intervi	ewer Note: If person answered "No" to both Q.51 and Q.52 then skip to Q.57			
53.	After a knife is used to cut raw meat or poultry, which of the following options do you usually do? INTERVIEWER NOTE: Refers to the person answering the survey			
	Continue using the knife as is 1 Rinse the knife before continuing to cook 2 Wipe the knife before continuing to cook 3 Wash the knife with detergent before continuing 4 Change to another knife 5 Other 6 Specify (
	No one prepares meat Go to Q. 57			

54.	After a cutting board is used to cut raw meat or poultry, which of the following options do you us do?
	INTERVIEWER NOTE:
	1. Does not matter if water is hot or cold
	2. Refers to the person answering the survey
	Continue using the cutting board as is
	Rinse the cutting board before continuing to cook 2 Wipe the cutting board before continuing to cook
	_
	Specify (
Don't read	Don't know/Not sure
55.	After handling raw meat or poultry in the kitchen, which of the following would you
	usually do before continuing to cook? INTERVIEWER NOTE:
	Refers to the person answering the survey
	Refers to the person answering the survey
	Wipe hands
	Quickly rinse hands under a running tap
	Specify (
	Don't do anything about hands
Don't read	Don't know/not sure
56.	After washing hands during food preparation, what would you usually dry
50.	your hands on?
	INTERVIEWER NOTE:
	Refers to the person answering the survey
	Paper towel
	Sponge/cloth
	Tea-towel /hand towel
	Apron 13
	Don't dry hands
	Other 15
	Specify (
Don't read	Don't know/Not sure
57.	In the past 3 months, has anyone in the household cook meat on a BBQ?
	Yes
	No Go to Q. 59
	Don't know/Not sure

2	58.	After cooking on the BBQ, where would the cooked meat most likely be placed?	
3 4		Back on the same container	
5		Back on the same container after it has been	
6 7		rinsed with water	
8		Back on the same container after it has been	
9		wiped off with a towel	
10 11		Back on the same container, after the container	
12		has been washed with soap and water	
13 14		On a different container 5	
15		Other)
16	Don't read	Don't know/not sure	
17 18		On a different container	
19			
20			
21 22			
23			
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60		. e. peer tertert only intepr/sinjopenionij.com/site/usou(/guidelines/fittill	20

	questions are about contact with animals in the 7 days before your diarrh	oca Degali.
59.	During this time, did you keep or care for any of the following animals as	pets?
	INTERVIEWER NOTE:	
	Not to include one off contact	
		Is any pet less 6 months old
	Yes No DK/NS	Yes No D
a. b		1 2
b. c.	Dog 1 2 7 Chickens 1 2 7	
d.		
и. е.	Other 1 2 7 Other 1 2 7	Specify (
с. f.	Do not keep any pets	
Intomic	wer Note: If person answered No/Don't know to Cat then skip to questio	n 62
Intervie	wer Note: If person answered No/Don't know to Cat then skip to questio	01 02
60.	Do you feed your cat raw meat or bones?	
00.		
	Yes	
	No	(eg. chicken, beef, ka
	Don't know/Not sure \Box_7 Go to Q. 62	
61.	How often does your cat get fed raw meat or bones?	
	Daily	
	Weekly	
	Monthly	
	Less often	
	Don't know/Unsure	
Intervie	wer Note: If person answered No/Don't know to Dog then skip to question	on 65
62.	Do you feed your dog raw meat?	
	Yes D 1 Specify (
		ken, beef, kangaroo, lamb
	Don't know/Not sure	
63.	Do you feed your dog raw bones?	
	Don't know/Not sure	

64.	How often does your dog get fed raw meat or bone	5.
	Daily	
	Weekly	2
	Monthly	3
	Less often	
	Don't know/Not sure	7
65.	Did you get any of your pets in the 4 weeks before	your diarrhoea began?
	Yes	1 Pet(s) (
	No	2
	Don't know/Not sure	7
		_
66.	Were any of your own pets ill with diarrhoea in the	e <u>7 days before your diarrhoea began</u> ?
		1 Pet(s) (
	No	2
	Don't know/Not sure	7
67.	In the <u>7 days before your diarrhoea began</u> , did you faeces or manure (eg. changing litter boxes or pick bag)?	
67.	faeces or manure (eg. changing litter boxes or pick	ing up pet faeces with a plastic
67.	faeces or manure (eg. changing litter boxes or pick bag)?	ing up pet faeces with a plastic
67.	faeces or manure (eg. changing litter boxes or pickbag)? Yes	ing up pet faeces with a plastic
67.	faeces or manure (eg. changing litter boxes or pick bag)? Yes No	ing up pet faeces with a plastic
67. 68.	faeces or manure (eg. changing litter boxes or pick bag)? Yes No Don't know/Not sure Do you live on a farm/hobby farm including a prop	<pre>ing up pet faeces with a plastic 1 Pet(s) (</pre>
	faeces or manure (eg. changing litter boxes or pick bag)? Yes No Don't know/Not sure Do you live on a farm/hobby farm including a prop Yes	<pre>ing up pet faeces with a plastic 1 Pet(s) (</pre>
	faeces or manure (eg. changing litter boxes or pickibag)? Yes No Don't know/Not sure Do you live on a farm/hobby farm including a propyes No	Pet(s) (
	faeces or manure (eg. changing litter boxes or pick bag)? Yes No Don't know/Not sure Do you live on a farm/hobby farm including a prop Yes	Pet(s) (
	faeces or manure (eg. changing litter boxes or pickibag)? Yes No Don't know/Not sure Do you live on a farm/hobby farm including a propyes No	Pet(s) (
	faeces or manure (eg. changing litter boxes or pickibag)? Yes No Don't know/Not sure Do you live on a farm/hobby farm including a propyes No	<pre>ing up pet faeces with a plastic 1 Pet(s) (</pre>
68.	faeces or manure (eg. changing litter boxes or pickibag)? Yes. No. Don't know/Not sure. Do you live on a farm/hobby farm including a propyes. No. Don't know/Not sure. In the 7 days before your diarrhoea began, did you Yes.	<pre>ing up pet faeces with a plastic 1 Pet(s) (</pre>
68.	faeces or manure (eg. changing litter boxes or pickibag)? Yes No Do you live on a farm/hobby farm including a propyes No Don't know/Not sure In the 7 days before your diarrhoea began, did you	<pre>ing up pet faeces with a plastic Pet(s) (perty on acreage 5 acres or over? visit a farm or petting zoo?</pre>

" T	would now like to ask you a faw final guardiang. Damamkan your participation is valuntary and
	would now like to ask you a few final questions. Remember, your participation is voluntary and u do not have to answer any of the questions if you don't want to."
70.	Is any language other than English spoken in your household?
	Yes D 1 Specify (
	No
Don't read	Don't know/Not sure
Don't read	Refused
71.	Are you of Aboriginal or Torres Strait Islander origin?
	No
	Tomas Charit Labor day
	Both
Don't read	
Don't read	Refused
Jon i redu	
72.	Which of the following places best describe where you live?
	Inner city or urban area
	Suburban area
	Town
	Rural or remote area community
	Rural or remote area farm or property
Don't read	Don't know/Not sure
Don't read	Refused
Intervi	ewer Note: See definitions below.
	<u>area:</u>
<u>Suburba</u>	<u>area:</u> housing area further from the centre of the city, which is charact
т	the region being primarily a self-contained residential district.
	remote area farm or property
<u>Kurar or</u>	
	Does your occupation involve any of the following?
73.	
73.	<u> </u>
73.	Working with raw meat
73.	(eg. restaurants, butchery, abattoir etc.)
73.	Working with raw meat 11 (eg. restaurants, butchery, abattoir etc.) 11 Working with animals 12 (eg. farmer, zookeeper, vet/nurse etc.) 12

Retired. CASE not of working age.....

Don't know/Unsure.....

74. What is the highest level of of ducation reached by <u>anyone</u> in your household? Schooling to year 10 or below	2			
s Schooling to year 10 or below		74.	What is the highest level of education reached by <u>anyone</u> in your household?	
Secondary school, above year 10			Schooling to year 10 or below	
7 Technical or further educational institution				
Inversity degree—Undergraduate is Don't read University degree—Orsignaduate (Masters, doctorate). is Don't read Refused. is "Now I am going to read you a list of income categories. Please stop me when a category best describes your total household income, before taxes, in the last financial year? That is the total figure for all household members." 75. Last year the total income for your household was? Less than \$25,000. \$25,000 and \$150,000. Hetween \$50,000 and \$150,000. i More than \$150,000. i Between \$100,000 and \$150,000. i More than \$150,000. i Poor't read Refused. 76. As part of this research we are planning to do a follow-up study. Would you be happy for us to contact you in -6 months' time?" Yes No No if person answered No to Q 76 then skip to the end of the questionnaire Details required: imate: No imate: Phone number: if person answered No to Q 76 then skip to the end of the questionnaire Details required: imate: Name: imate: Phone number: imate: Phone number: imate: <				
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Investigating locally-relevant risk factors for *Campylobacter* infection in Australia: protocol for a case-control study and genomic analysis

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ABSTRACT

Introduction:

The CampySource project aims to identify risk factors for human *Campylobacter* infection in Australia. We will investigate locally-relevant risk factors and those significant in international studies in a case-control study. Case isolates and contemporaneous isolates from food and animal sources will be sequenced to conduct source attribution modelling, and findings will be combined with the case-control study in a source-assigned analysis.

Methods and analysis:

The case-control study will include 1,200 participants (600 cases and 600 controls) across three regions in Australia. Cases will be recruited from campylobacteriosis notifications to health departments. Only those with a pure and viable *Campylobacter* isolate will be eligible for selection to allow for whole genome sequencing of isolates. Controls will be recruited from notified cases of influenza, frequency matched by sex, age group and geographical area of residence. All participants will be interviewed by trained telephone interviewers using a piloted questionnaire.

We will collect *Campylobacter* isolates from retail meats and companion animals (specifically dogs), and all food, animal and human isolates will undergo whole genome sequencing. We will use sequence data to estimate the proportion of human infections that can be attributed to animal and food reservoirs (source attribution modelling), and to identify spatial clusters and temporal trends. Source-assigned analysis of the case-control study data will also be conducted where cases are grouped according to attributed sources.

Ethics and dissemination:

Human and animal ethics have been approved. Genomic data will be published in online archives accompanied by basic metadata. We anticipate several publications to come from this study.

KEYWORDS

Campylobacter, case-control study, risk factors, Australia, whole genome sequencing, source attribution, source-assigned analysis

ARTICLE SUMMARY

Strengths and limitations of this study

- Case-control study is well-powered to identify locally-relevant risk factors.
- Linking genomic data to the case-control study strengthens the analysis by enabling source attribution and source-assigned analyses to be conducted.
- Case-control questionnaire questions are being validated in a separate study, demonstrating the reliability of participant recall.
- Potential reporting bias due to inaccurate recall of study participants.
- Case-control study lacks efficiency for risk factors with high levels of exposure in the study population.

INTRODUCTION

Campylobacter infection is the most commonly notified cause of foodborne gastroenteritis in Australia,¹⁻³ as well as a leading cause of bacterial gastroenteritis world-wide.⁴ At the introduction of Australia's National Notifiable Diseases Surveillance System (NNDSS) in 1991 the incidence rate of notified campylobacteriosis cases was 79.1/100,000 population,⁵ and despite notification rates plateauing in recent years, incidence had risen to 139.7/100,000 population in Australia in 2015,⁵ with an estimated 10 cases for every notified case within the community.⁶ By comparison, the incidence rate of campylobacteriosis in New Zealand in 2014 was 150.3/100,000 population,⁷ with an estimated 10-30 cases in the community for every notified case.⁸ *Campylobacter* notification rates in Australia and New Zealand are still among the highest in the world across high-income countries. Most countries in the European Union consistently report annual campylobacteriosis notification rates below 100/100,000 population.²

Two species of *Campylobacter—Campylobacter jejuni* and *C. coli*—contribute to approximately 95% of human campylobacteriosis.⁹ These *Campylobacter* species are commonly detected in sewage and surface water,¹⁰ reside in the gastrointestinal tract of birds and animals,¹¹ and are frequently found in raw meat, particularly poultry, and raw milk.^{12 13} Campylobacteriosis is mostly foodborne, with an estimated 77% of cases transmitted via food consumption in Australia.^{14 15} Direct and indirect zoonotic transmission can occur via animal contact (direct) or faecally-contaminated water or environments (indirect). Person-to-person transmission is considered rare.¹⁶ The majority of cases are thought to be sporadic, with outbreaks less commonly detected.¹⁷ Most outbreaks are linked to the consumption of poultry, raw milk, or contaminated water.^{17 18}

Targeted control of foodborne bacterial pathogens generally depends on identification of sources and routes of transmission. Since *Campylobacter* are ubiquitous in the environment and most cases are sporadic, identifying sources is difficult. Source attribution methods require isolation of strains from reservoirs to compare *Campylobacter* strain diversity in foods and animals to that in human infections. Beef, sheep and pig meat have a lower prevalence of *Campylobacter* contamination than chicken meat (<5% to 14%),¹⁹⁻²¹ but a higher prevalence is found in animal offal such as liver,²² thus making offal a valuable source of host-associated strains of *Campylobacter* in low-prevalence meats.

STUDY RATIONALE

In the United States, evidence from case-control studies have led to policy change, including changes to chicken slaughtering techniques. The incidence of human *Campylobacter* infection has declined in the US since this policy was introduced in 1997.²³ More recently, evidence from source attribution analyses in New Zealand has led to the development of poultry production policies and practices aimed at reducing the risk of *Campylobacter* transmission via poultry food products.²⁴ New Zealand has seen a 74% reduction in the number of campylobacteriosis cases attributed to poultry in the region, as well as a 54% reduction in cases overall.²⁵

Source attribution modelling enables us to determine which foods and animals are the most likely sources of infection with each *Campylobacter* strain type, and the proportion of cases attributed to each source. This can be done with simple proportional similarity index (PSI) calculations, or by using more complex models.²⁴ Source attribution also allows for human campylobacteriosis cases to be grouped by potential source, increasing the specificity of risk factor analyses. These source-assigned analyses combine the epidemiological information gained through the traditional case-control study with source attribution modelling to provide greater explanatory power to investigate locally-relevant risk factors.

OBJECTIVES

This study aims to:

- Identify dietary, environmental and behavioural risk factors for *Campylobacter* infection in Australia
- 2. Strengthen the epidemiological evidence for previously identified risk factors in Australia
- 3. Identify strain-specific risk factors for infection using Whole Genome Sequencing (WGS) data from case isolates

HYPOTHESES

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We will test several hypotheses regarding specific risk factors for *Campylobacter* infection in Australia. The hypotheses are based on exposures which have previously been identified as risk factors for *Campylobacter* infection in Australia as well as internationally.

We hypothesise that:

- 1. Persons who consume undercooked meats, particularly chicken, are at increased risk of infection.
- 2. Persons who consume offal are at increased risk of infection.
- 3. Persons who own companion animals (especially puppies) are at increased risk of infection.
- 4. Poor food hygiene and handling practices in the home increase the risk of infection.
- 5. Most human infections will be attributed to consumption of chicken meat.
- 6. There will be a high level of genetic diversity amongst *Campylobacter* strains.

STUDY DESIGN

We will conduct a case-control study including genomic testing over a two-year period in three sentinel sites: the state of Queensland (QLD), the Australian Capital Territory (ACT), and Hunter New England (HNE) region of New South Wales (Figure 1). Sporadic cases of culture-positive *Campylobacter* infection will be identified either through state notifiable disease registers, from local pathology service databases or local notification databases. An isolate from each case will be paired with epidemiological data from the case interview. One control will be recruited for each case who participates in the study, with trained interviewers conducting telephone interviews with both cases and controls. Participants will be interviewed using a questionnaire that has been specifically designed to collect information on known potential risk factors. This questionnaire will include a selection of questions being validated in a separate study (Liana Varrone, Validation of questions designed for gastroenteritis investigation). For cases, the questions will cover the seven days prior to the onset of illness, while controls will be questioned on the seven days prior to interview. Meanwhile, *Campylobacter* isolates will also be collected from food and animal samples. All human and non-human isolates will undergo whole genome sequencing for comparison in source attribution modelling. Data for this study will be collected from 1st March 2017 to 1st March 2019.

Figure 1. Map of Australian states and territories, showing the Hunter New England region.

Patient and public involvement

To develop the study, we engaged state and territory health departments, food safety agencies and industry to establish research questions and methods. The process involved a dedicated workshop, followed by teleconferences and an iterative process of drafting study documentation. We also established a reference panel, which includes representatives from senior levels of government and industry bodies. No patients or other members of the public were involved in the development of this study.

STUDY POPULATION

The three sentinel sites cover a population of approximately 6.1 million people. Based on notification and diagnostic pathology data, we expect approximately 8,650 *Campylobacter* cases to be notified across these sites during the study period.

DEFINITION AND SELECTION OF CASES

Case definition

We define a case as a person from any of the three participating sites with a recent history of acute diarrhoea and a culture-positive stool result for *Campylobacter*.

SAMPLE SIZE

We used risk factor prevalence data from a previous national *Campylobacter* case-control study in 2001/2002 to estimate sample size for this study.²⁶ For example, the prevalence of chicken consumption among controls in 2001/2002 was 80%. A sample size of approximately 1,040 subjects (520 cases; 520 controls) would enable the study to detect an association between chicken consumption and illness with an odds ratio of 1.6, at 80% power and α = 0.05, as reported in the previous study. Sample size estimates for other potential risk factors are listed in Table 1.

Table 1.	Sample size	estimates for	r an unmatched	case-control study
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Risk factor	Prevalence of exposure among controls (%)	Prevalence of exposure among cases (%)	Odds ratio	No. of required study subjects
Beef	78	85	1.6	960
Pork	52	60	1.4	1130
Lamb	42	50	1.4	1120
Chicken	80	87	1.6	1040
Offal	2.0	5.0	2.6	1154
Puppies	2.1	5.4	2.7	1040

80% power and α = 0.05

From these calculations, we estimate that a study of 1,200 subjects (600 cases; 600 controls) will adequately detect significant associations of these magnitudes for potential risk factors of interest.

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Queensland and Hunter New England sites will each enrol at least 250 cases into the study, while ACT will enrol at least 100 cases. Based on the previous Australian case-control study,²⁶ we expect approximately 80% of selected notified cases to be eligible and participate in the study (Table 2).

State	Expected number of notified cases during study period	Estimated cases from participating pathology laboratory	Culture +ve cases	Sequential sampling of notified cases	Total no. of cases	Expected no. to be recruited (~ 80% participation rate)
QLD	7000	2800 (40%)	1260 (45% in QLD)	Select every 4 th case	315	250
ACT	600	130	130	Include all notified cases	130	100
NSW (Hunter New England)	~1050 <	313	313	Include all notified cases	313	250
Total	8650	3243	1703		758	600

Table 2.	Sampling	method for	· cases in	each site
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In Queensland, we will obtain cases from one private pathology provider reporting approximately 40% of the state's *Campylobacter* notifications. We estimate that this provider will notify 2,800 cases during the study period with an estimated 45% of these being culture-positive (1,260 notified cases). In ACT, approximately 600 *Campylobacter* notifications are expected during the study period; 130 are expected from the participating pathology laboratory. In Hunter New England, approximately 1,050 *Campylobacter* notifications are expected during the study period; 313 of these notifications will be from the participating pathology laboratory.

Enrolment of Cases

We will enrol all cases who meet the eligibility criteria (Table 3). Each site will check for new notifications of culture-positive *Campylobacter* infection daily, with only culture-positive *Campylobacter* cases eligible for this study. If a case refuses to participate in the study, we will select a subsequent case for inclusion. Enrolment of cases will depend on consent from the patient, or in the event of a child aged less than 18 years, consent from either one of the parents or the child's guardian. We will interview cases as soon as possible by telephone, preferably within two weeks of notification from the laboratory. It will be at the parent's or guardian's discretion as to whether a

child aged between 15 and 17 years is interviewed directly. The parent or guardian will be interviewed for cases aged less than 15 years.

Table 3.	Eligibility criteria	for cases and controls
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Criteria	Cases	Controls
Had diarrhoea (≥3 loose bowel movements in	Include	Exclude
24hrs)		
Known date of illness onset	Include	N/A
Household members positive for Campylobacter	Exclude	Exclude (4 weeks prior to
in 4 weeks prior to onset of illness		interview date)
Household members experiencing diarrhoea in 4	Exclude	Exclude (4 weeks prior to
weeks prior to onset of illness		interview date)
Travelled outside of Australia in 2 weeks prior to	Exclude	Exclude (2 weeks prior to
onset of illness		interview date)
Travelled interstate for the entire 2 weeks prior	Exclude	Exclude (2 weeks prior to
to onset of illness		interview date)
Can't speak English	Exclude	Exclude
Not able to answer questions for some other	Exclude	Exclude
reason (e.g. intellectually disabled)	4.	
Not contactable after 6 telephone attempts	Exclude	Exclude
Live outside the catchment areas	Exclude	Exclude
Do not have a telephone number available for	Exclude	Exclude
their primary residence, or a mobile phone	0	
An enteric pathogen other than Campylobacter	Exclude	N/A
was isolated/detected in their stool (excluding		
Blastocystis hominis and Dientamoeba fragilis)		

DEFINITION AND SELECTION OF CONTROLS

We will recruit controls from notified cases of influenza, frequency matched by sex, age group and geographical area of residence by Statistical Area Level 4 (SA4). These controls will be selected with a delay of at least six months from their influenza infection to ensure that controls have returned to eating their customary diet.

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Each participating site (QLD, ACT or HNE) will establish a database of controls (previous influenza cases). All cases of influenza notified to the health department in each site between 1st January and 31st December 2017 will be entered into this control database. The age bands are 0-4 years, 5-14 years, 15-34 years, 35-54 years, 55-74 years, and ≥75 years. An appropriate control will be randomly selected from the database within 30 days of interview of the notified case.

Case and control recruitment

Interviewers trained in computer-assisted telephone interviewing (CATI) will conduct telephone interviews. A maximum of six attempts will be made to contact any one case or control, with no more than three attempts in any one day. Three calls will be attempted between 9:00am and 3:59pm, and three attempts between 4:00pm and 8:00pm. A text message will be sent to the potential participant after three failed call attempts, indicating that Public Health is trying to contact them. This protocol will be continued until the person is enrolled or excluded.

QUESTIONNAIRES

We will use specific case and control questionnaires for all participants (see Appendix 1). Cases will be asked additional questions about the clinical course of their illness and treatment. Interviewers will ask identical questions regarding exposures such as foods consumed, dining locations, water sources, domestic food handling techniques and exposure to animals of cases and controls. Questions on foods consumed, dining locations, water consumed, animal and pet exposures will be asked based on a seven-day history. Questions on international travel will be asked based on a twoweek history. Antibiotic and antacid consumption, immunosuppressive treatment and household history of diarrhoea will be based on a four-week history. Questions on food handling and general kitchen practices will be based on usual practices rather than recent history. Demographic information will be collected from cases and controls. Contact information required to conduct interviews will be stored in a password-protected Excel document with only those needing to contact individuals given access. Piloted questionnaires were modified to remove repetitions, improve clarity, and to ensure that interviews could be conducted within 20 minutes.

DATA HANDLING & RISK FACTOR ANALYSIS

We will undertake descriptive reporting of campylobacteriosis incidence by person, place and time. We will also describe the severity of symptoms, treatment, and burden of illness.

Risk factor analysis will involve the examination of two-by-two contingency tables with chi square or exact tests to determine the presence of univariable associations between variables and disease. To measure the strength of an association, we will estimate odds ratios and calculate 95% confidence

intervals in a univariable analysis, followed by multivariable logistic regression modelling to adjust for potential confounders. Risk factors selected for inclusion in the regression model will include age, season and geographic area, variables with a significant univariable association with disease, and variables with a P-value ≤ 0.25 that are biologically plausible and of interest to the research team.

LABORATORY ANALYSES

Human samples

As outlined in Table 2, it is expected that 250 human isolates from Hunter New England, 250 from Queensland, 100 from Victoria and 100 from ACT will be sequenced. The initial isolation and confirmation of *Campylobacter* infection will be performed locally in each State/Territory. Only samples with a pure and viable culture will undergo WGS.

Animal and food samples

We will collect samples from chicken meat (covering the two production methods of continually housed and free range/housed), beef, lamb, pork, and from pet dogs. Given low prevalence of *Campylobacter* in meats other than chicken, samples will be collected from offal (preferably liver) from bovine, ovine and porcine sources to ensure sufficient positive samples are obtained for the study. Given the rising importance of chicken liver pate as a source of outbreaks in Australia,²⁷ chicken offal will also be sampled. Sample sizes by source are based on data from two states to ensure 50 positive samples per food source, and 30 samples in companion animals (Table 4). We will also contact veterinary clinics and teaching hospitals to ensure sufficient *Campylobacter*-positive samples from dogs. Water samples have been omitted from the genomic aspect of this study due to logistical constraints in sampling untreated water sources across the large geographical area involved in this study, and the complexity of designing an appropriate sampling frame. As there is a lack of evidence implicating municipal drinking water as sources of *Campylobacter* infection in Australia¹²⁶ we excluded water sampling from this study.

			Food	ls			Anima	als
		Chicken		Beef	Lamb	Pork	Dogs	Total
	Continually	Free-	Offal	Offal	Offal	Offal		
	housed	range						
Assumed	0.7	0.7	0.7	0.14	0.6	0.22	0.2	
prevalence								
Samples	72	72	72	286	100	272	150	1041
required								
Positive	50	50	50	40	60	60	30	330
isolates								

The initial isolation and confirmation of *Campylobacter* will be performed locally at laboratories in each State/Territory, with isolates forwarded to the Microbiological Diagnostic Unit Public Health Laboratory for WGS, except Queensland isolates which will be sequenced at Queensland Health. To detect seasonal and temporal variation in *Campylobacter* genetic types, 1041 non-human samples (estimated to produce 330 *Campylobacter* isolates) will be collected over a period of one year in Queensland, and two years in New South Wales. To assess latitudinal variation in chicken meat samples across eastern Australia, 105 chicken samples (70 chicken meat and 35 chicken offal) will be collected over a six-month period in Victoria. Food samples will be collected monthly from retail premises, using protocols from surveys undertaken in 2014 by partner organisations, with a pilot of 30 isolates in Queensland.

We will also collect an additional 20-30 human isolates from four additional Australian jurisdictions not participating in this case-control study to undergo WGS. This will be done over a two-month period that overlaps with the case-control study sample collection, and is planned to help inform the generalisability of the case-control study.

SEQUENCING AND SEQUENCE DATA PROCESSING

Campylobacter isolates selected for sequencing will be repurified on solid medium and a single colony selected for preparation of genomic DNA. A sequencing library will be prepared from the genomic DNA for sequencing on the Illumina sequencing platform (MiSeg or NextSeg). A sample of the selected colony will be regrown and cryopreserved (resuspended in liquid medium supplemented with 10% Glycerol and stored at -80°C). In some cases, *Campylobacter* enrichment cultures will be cryopreserved to enable future investigation of the genetic diversity of Campylobacters present. The short-read, paired end dataset produced by the Illumina Instrument from the genomic DNA of each isolate will be processed to produce a draft genome sequence for the isolate using a *de novo* assembler such as MEGAHIT.²⁸ The draft genome sequence will be annotated using Prokka.²⁹ We will use the draft genome sequence to perform the initial sub-species classification by deriving a multilocus sequence type (MLST) using the "Campylobacter jejuni/coli" typing scheme (pubmlst.org). Again, using the draft genome sequence, further typing e.g. virulence factors (http://www.mgc.ac.cn/VFs/) or antimicrobial resistance genotype (https://cge.cbs.dtu.dk/services/ResFinder/) will be performed using Abricate (https://github.com/tseemann/abricate). We will perform comparative genomics to examine the genetic relationships between selected subgroups of isolates in more detail using Nullarbor (https://github.com/tseemann/nullarbor).

SOURCE ATTRIBUTION MODELLING

We will analyse the epidemiological data within designated MLST groups or other typing groups derived from the genomic sequence data. Source attribution modelling and source-assigned analyses will be conducted.

Source attribution models combine typing data from isolates from food, animal and humans to estimate the proportion of human infections that can be attributed to animal and food reservoirs.³⁰ ³¹ Once inferred MLSTs have been ascertained, the proportional similarity index²⁵ will be used to assess similarities by source. We will then undertake source attribution analyses by adapting the asymmetric island model which has previously been applied to MLST data^{25 32} using Markov Chain Monte Carlo (MCMC) methods³³ implemented using the free software WinBUGS.³⁴ These methods will first be applied to MLST data extracted from whole genome sequences (the aforementioned "inferred MLSTs"), and then compared to structured phylogenetic modelling approaches^{35 36} that provide scope to infer inter-host transmission.

We will then group cases according to putative source based on these source attribution methods.³⁷ For example, all isolates attributed to chicken will be grouped together, regardless of differing strains. These cases attributed to chicken will then be compared to all controls in a risk factor analysis to produce a source-assigned analysis.

SPATIAL CLUSTERS AND TEMPORAL TRENDS

We will use newly-designated WGS-based MLSTs to assess heterogeneity in isolates from food sources and companion animals in Queensland and New South Wales, and in isolates from chicken meat and humans across Queensland, New South Wales, Victoria and ACT. A two-year sampling framework in New South Wales, one year of sampling in Queensland, and previous survey work in these states will allow us to assess the extent of seasonal and temporal trends. Postcode-level data associated with human illnesses will be used to detect space-time clusters using a scan statistic implemented in the free software SaTScan, at the Statistical Area 1 level.³⁸ We will use a retrospective space-time permutation model to detect high risk clusters by comparing the observed number of illnesses to the expected number in that geographic zone and time-period.³⁹

STUDY LINKAGES AND COLLABORATIONS

The CampySource Project Team comprises three working groups and a reference panel. The working groups focus on: food and animal sampling, epidemiology and modelling, and genomics. The reference panel includes expert representatives from government and industry.

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The study is supported by the following partner organisations: the Australian National University, Massey University, University of Melbourne, Queensland Health, Queensland Health Forensic and Scientific Services, New South Wales Health, Hunter New England Health, Victorian Department of Health and Human Services, Food Standards Australia New Zealand, Commonwealth Department of Health and AgriFutures Australia – Chicken Meat Program.

CampySource is also supported by collaboration with the following organisations: ACT Health, Sullivan Nicolaides Pathology, University of Queensland, Primary Industries and Regions South Australia, Department of Health and Human Services Tasmania, Meat and Livestock Australia, and New Zealand Ministry for Primary Industries.

ACKNOWLEDGEMENTS

The CampySource Project Team consists of: Nigel P. French, Massey University, New Zealand; Mary Valcanis, The University of Melbourne; Dieter Bulach, The University of Melbourne; Emily Fearnley, The Australian National University; Russell Stafford, Queensland Health; John Bates, Queensland Health; Trudy Graham, Queensland Health; Keira Glasgow, Health Protection NSW; Kirsty Hope, Health Protection NSW; Arie H. Havelaar, The University of Florida, USA; Joy Gregory, Department of Health and Human Services, Victoria; James Flint, Hunter New England Health; Simon Firestone, The University of Melbourne; James Conlan, Food Standards Australia New Zealand; James J. Smith, Queensland Health; Sally Symes, Department of Health and Human Services, Victoria; Barbara Butow, Food Standards Australia New Zealand; Liana Varrone, The University of Queensland; Linda Selvey, The University of Queensland; Deborah Denehy, ACT Health; Radomir Krsteski, ACT Health; Natasha Waters, ACT Health; Kim Lilly, Hunter New England Health; Julie Collins, Hunter New England Health; Tony Merritt, Hunter New England Health; Joanne Barfield, Hunter New England Health; Ben Howden, The University of Melbourne; Kylie Hewson, AgriFutures Australia – Chicken Meat Program; Laura Ford, The Australian National University; Liz Walker, The Australian National University; Cameron Moffatt, The Australian National University; Martyn Kirk, The Australian National University; and Kathryn Glass, The Australian National University.

While undertaking studies, LV is supported through an Australian Government Research Training Program (RTP) Scholarship.

DECLARATIONS

Ethics approval and consent to participate

Informed Consent

A suitably trained interviewer will inform potential participants about the purpose, methods and demands of the study. We will obtain verbal consent from all study participants or their guardians.

Persons aged 18 years and older will be interviewed following informed consent. It will be at the parent's or guardian's discretion as to whether a child aged between 15 and 18 years is interviewed directly, following informed parental/guardian consent. Parents/guardians will be interviewed for cases aged less than 15 years, after informed consent is obtained.

Confidentiality

All information and identifiers will be kept confidential. Names and personal identifiers will be collected and entered into computer records but will be password protected. No personal identifiers will be included in any published materials relating to this study. All hard copy questionnaires containing patient identifiers will be stored in locked filing cabinets in a secure location to which only study investigators and interviewers will have access.

Risks and Benefits

Participants will be informed there are no individual benefits associated with the study and that participation is voluntary. Failure to participate or a withdrawal of participation will not affect any future treatment. There is also no risk to the patient, and the only cost is time spent – approximately 20 minutes – being interviewed. They may refuse to answer any of the questions or stop at any time.

Animal Ethics

All procedures involving live animals will be performed in accordance with a protocol approved by the University of Melbourne's Animal Ethics Committee (ethics ID: 1714156).

Consent for publication

Not applicable.

Availability of data and materials

The Illumina read sets produced as part of this study will be published at INSDC (Sequence Read Archive (DDJB/NCBI) or the European Nucleotide Archive (EMBL-EBI))

Competing interests

No authors have any competing interests to declare.

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MDK is supported by a National Health and Medical Research Council Fellowship (GNT1145997).

Author contributions

MDK conceived the original idea for this study. All authors contributed to the study design and analysis plan. LV and RJS wrote the first draft with contributions from all authors. LF was heavily involved in determining timing and logistics in and between all sites. KL assisted in questionnaire design and flow. DB developed the bioinformatics analysis protocol. LV, RJS, LS, MDK and KG were involved in multiple revisions. The final version of the manuscript was approved by all authors.

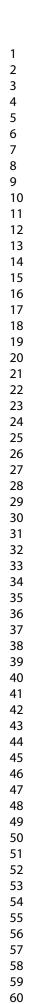
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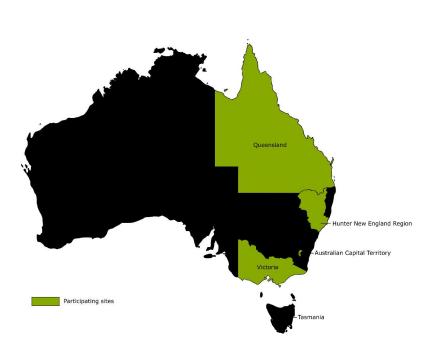


Figure 1. Map of Australian states and territories, showing the Hunter New England region.

Refusal Ineligible	
ID Number	
Interview Date Interview Start Tin	me
Data entered Date Data checked Date	

Source Attribution of Campylobacter in Australia Study

Case Questionnaire

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erviewer Note:	If case is less than 15 years of age you will need to speak to parent or guardian most familiar with the eating habits of the child.
	If case is aged between 15–17 years you will need to obtain parent or guardian consent prior to interview.
	Please note that for subjects under the age of 15 years, questions relate to the case, not the person being interviewed unless specified in the body of the questionnaire.
Health / Hunter	ne is <interviewers name=""> and I am calling on behalf of [Queensland Health / ACT r New England Public Health Unit]." speak with <name case="" of=""> or <name case's="" father="" mother="" of="">?"</name></name></interviewers>
erviewer Note:	When the case comes to the phone then repeat the introduction and proceed with the explanatory statement.
	If the case is unavailable then arrange an alternative time for the interview
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If NO, arrange an alternative time to phone back to conduct the interview If YES, continue

	1. ELIGIBILITY QUESTIONS
	"Because I will be asking about specific dates around the time of your illness, it may be helpful for you to have a calendar or diary in front of you. Do you need a few minutes to get these?"
	Yes, I will get one no
	No, I already have one with me
	Don't have access to a calendar
	The first few questions we'll be asking you are about some symptoms that are associated with [your/their] illness.
1.	For the purposes of this study, we define diarrhoea as 3 or more loose stools or bowel movements in any 24-hour period. When you had your <i>Campylobacter</i> infection, did you have diarrhoea?
	Yes
	No
	Don't know/Not sure
1 a	During this diarrhoeal illness, what was the maximum number of stools or bowel movements
	you had in any 24 hour period? 0-2 Check ineligible box then END INTERVI
	3-5
	6-10
	11-20
	More than 20 5
	Don't know/Not sure
2.	For how many days did your diarrhoea last? DAYS
	Don't know/Not sure
	CALCULATE PRIOR TO INTERVIEW
	Date stool specimen collected
	Day Month Year
	Day Monul Tea
3.	Could you please let me know what the date was when your diarrhoea began?
	(If person is unsure of date then prompt with date of stool specimen)
	Don't know/Not sure
	I will now just enter a couple of other dates that we will be talking about throughout the interview.
	I won't be a moment
	erviewer Note: Refer to your calendar to determine the interval from DATE 4 WEEKS BEFORE
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2	4.	In the 4 weeks before your illness began, that is from <date 4="" before<="" td="" weeks=""></date>
3	••	DIARRHOEA> through <date 1="" before="" began="" day="" diarrhoea="">, did anyone else</date>
4		in your <u>household</u> test positive for <i>Campylobacter</i> ?
5		Yes
6		
7		No 2
8		Don't know/Not sure 7
9 10		
10	5.	In the 4 weeks before your illness began, that is from a DATE 4 WEEKS REFORE
12	5.	In the 4 weeks before your illness began, that is from <date 4="" before<="" td="" weeks=""></date>
13		DIARRHOEA> through <date 1="" before="" began="" day="" diarrhoea="">, did anyone else in your</date>
14		household have diarrhoea?
15		Yes 1 Check ineligible box then END INTERVIEW
16		No 2
17		Don't know/Not sure
18		
19		
20		
21	Intervi	ewer Note: Refer to your calendar to determine the interval from DATE 2 WEEKS BEFORE
22		DIARRHOEA BEGAN to DATE 1 DAY BEFORE DIARRHOEA BEGAN.
23		
24		
25		
26	6.	In the 2 weeks before your illness began, that is from <date 2="" before<="" td="" weeks=""></date>
27		DIARRHOEA> through <date 1="" before="" began="" day="" diarrhoea="">, did you</date>
28		travel overseas or interstate?
29		
30 21		INTERVIEWER NOTE:
31 32		IF participant answers "yes",
33		1. Clarify if the travel was overseas or interstate
33 34		2. If travel was interstate:
35		Clarify the length of time spent interstate in the time period just mentioned
36		
37		Options to select:
38		A. If the participant has travelled overseas or spent the whole two weeks interstate: (Select option Yes)
39		B. If the participant has travelled interstate only for a portion of the time: (Select option No)
40		
41		Yes 1 Check ineligible box then END INTERVIEW
42		No 2
43		Don't know/Not sure
44		_
45		
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	CALTH QUESTIONS
7.	During this illness, did you have any of the following symptoms?
	Yes No DK/NS
a.	Fever 1 2 7
b.	Vomiting 1 2 7
c.	Stomach cramps 1 2 7
d.	Blood in your stool 1 2 7
e.	Nausea 1 2 7
f.	Headache 1 2 7
g.	Muscle/body aches 1 2 7
8.	Did you take any antibiotics as a result of this illness?
	Yes
	No 2 Go to Q. 10
	Don't know/Not sure
9.	What antibiotic(s) were you taking? [Ask person to get tablet bottle, if possible]
	Azithromycin
	Ciprofloxacin
	Norfloxacin
	Erythromycin
	Doxycycline (also known as Doxy or Vibramycin.
	Other (please specify)
	Don't know/Not sure
10.	Were you admitted to hospital overnight because of this illness?
	Yes
	No 2 Go to Q. 12 Don't know/Not sure 7 Go to Q. 12
11.	If yes, for how many nights were you hospitalised? NIGHTS
	Don't know/Not sure
Intervie	wer Note: Refer to your calendar to determine the interval from DATE 4 WEEKS BEFO
	DIARRHOEA BEGAN to DATE 1 DAY BEFORE DIARRHOEA BEGAN.
"F	or the next few questions, I would like to ask you about events which may have occurred in t
	eks before your illness began, so again that's from <date 4="" before="" diarrho<="" td="" weeks=""></date>
	GAN> to <date 1="" before="" began="" day="" diarrhoea="">."</date>
12.	In those 4 weeks, were you taking any antibiotics?
	Yes
	No

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Intervie	The wer Note: If person can't remember the name leave the space blank.	e of the an	tibiotic(s), check the DK/NS box and
13.	What antibiotic(s) were you taking? [Ask person	to get tab	let bottle, if possible]
	D	K/NS	What date did you stop taking these?
a.	Antibiotic 1 [7	(DD/MM) 7 DK/NS
b.	Antibiotic 2 [7	(DD/MM) 7 DK/NS
c.	Antibiotic 3 [7	(DD/MM) 7 DK/NS
d.	Antibiotic 4 [7	(DD/MM) 7 DK/NS
14.	In those 4 weeks, were you taking any regular n	nedication	n that decreases stomach acid?
	Yes[No Don't know/Not sure	1 2 7	Go to Q. 16 Go to Q. 16
15. Н	Did you take any of the following in the 4 weeks Histamine-2 (H ₂) Receptor blocker	s prior to	illness?
a. b. c. d.		1	No DK/NS 2 7 2 7 2 7 2 7 2 7 2 7 2 7 2 7
<u>P</u>	Proton Pump Inhibitor		
a. b. c. d. e.	Losec (Omeprazole) Nexium (Esomeprazole) Somac (Pantoprazole) Pariet (Rabeprazole) Zoton (Lansoprazole)	1 1 1 1	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$
16.	Have you ever been told by a doctor that you chronic illness in which diarrhoea or vomiting i irritable bowel syndrome, ulcerative colitis, or s	s a major	symptom? (e.g. Crohn's disease,
	Yes No Don't know/Not sure	1 Spe	cify(

2 3	17.	In the 4 weeks before onset of illness, did you	take or rec	ceive any of	the following?
4 5		INTERVIEWER NOTE: Cyclosporine ("it's an immunosuppressant")			
6 7			Yes	No	DK/NS
8	a.	Prednisone	105	110	DIMING
9 10		or other steroids not used on your skin	1	2	7
10	b.	Cyclosporine		2	7
12	c.	Chemotherapy	1	2	7
13	d.	Radiation therapy	1	2	7
14 15					
16					
17 18					
18					
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21 22					
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24					
25 26					
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29 30					
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48 49					
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Interviev	ver Note:	Refer to your calendar to determine the interval from the DATE 7 DAYS BEFORI
		DIARRHOEA BEGAN to the DATE 1 DAY BEFORE DIARRHOEA BEGAN
А.	WATER	
"I'n	1 now going to a	ask you some questions about water that you consumed in the <u>7 days before you</u>
	0 0	hat is from [diarr_7_days_prior] to [diarr_1_day_prior].
18.	What is your n	main source of drinking water at home? (select one only)
	INTERVIEWI	ER NOTE: options if they're unsure
	Only read out	options if they re unsure
a.	A rainwater tanl	ık
b.	A river or stream	m 1
		bore hole, or spearpoint
d.	A carrier or tank	ık truck 1
e.	Municipal water	er supply (tap water)
f.		le water
	-	pply 1 Specify (
h.	Don't know/Un	
Interviev		If person answered "Yes" to "Municipal water supply" or "Purchased bottle water"
		skip to Q.21
	Do vou usually	y treat your main source of drinking water before drinking?
19.		y treat your <u>main</u> source of drinking water before drinking?
19.		y treat your <u>main</u> source of drinking water before drinking? OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the
19.	If Required PRO	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the
19.	If Required PRO Yes No	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the
19.	If Required PRO Yes No	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the
	If Required PRO Yes No Don't know/Not	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the
	If Required PRO Yes No Don't know/Not	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the
20.	If Required PRO Yes No Don't know/Nor Which of the fo	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the
20. a.	If Required PRO Yes No Don't know/Not Which of the for Chlorination	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the 1 Specify (
20.	If Required PRO Yes No Don't know/Not Which of the for Chlorination Filtration	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the 1 Specify (
20. a. b.	If Required PRO Yes No Don't know/Not Which of the for Chlorination Filtration Boiling	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the Specify (
20. a. b. c.	If Required PRO Yes No Don't know/Nor Which of the for Chlorination Filtration Boiling UV treatment	OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the Specify (
20. a. b. c. d. e.	If Required PRO Yes No Don't know/Not Which of the for Chlorination Filtration Boiling UV treatment Other Specify (OMPT: Some examples are chlorination, filtration, boiling and UV treatment of the Specify (

1		
2 3	21.	Did you <u>drink</u> water from any of the following sources in the 7 days before onset of diarrhoea?
4		(Select all that apply) Yes No DK/NS
5 6	a.	A rainwater tank
7	b.	A river or stream
8	с.	A private well, bore hole, or spearpoint $\Box_1 = 2 = 7$
9	d.	A carrier or tank truck
10	e.	Municipal water supply (tap water)
11 12	f.	Purchased bottle water
13	g.	Other water supply $\Box_1 \Box_2 \Box_7$
14		Specify ()
15		
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B. DI	NING LOCATIONS
	he next few questions ask about places where you may have eaten food in the <u>7 days b</u> ess began. So that is from [diarr_7_days_prior] to through [diarr_1_day_prior]"
22.	During this time, did you eat any food prepared outside your home, for example takeaway, restaurant, someone else's home?
	Yes 1 No 2 Go to Q 24 Don't know/Not sure 7 Go to Q 24
23.	Did you eat any food from the following places?
a. b. c. d.	Café or restaurant Home cooked meal at someone else's home Kebab shop Other fast food/take away outletYesNoDK/NS127127127127127127127127
23a	How many meals prepared outside of your home, were eaten during this 7 day period?
	1-2 meals
	3-4 meals
	\geq 5 meals
	Don't know/Unsure

	l would now like to a iarrhoea began."	ask you about the dain	ry products you ma	ay have eaten in	the <u>7 days b</u>
4.	Did you drink aı raw/unpasteuris	ny raw/unpasteurised sed milk?	l milk or eat any p	roducts made f	rom
	INTERVIEWER Cold-pressed mill	NOTE: k is pasteurised and is	not to be included a	s "raw/unpasteu	rised".
a b	Unpasteurised mi Other products Specify (ilk	Yes	No 2 2	DK/NS 7 7 7

25.	During these 7 days, did you eat any of the fol	lowing de	eli meats or c	old cuts?
		Yes	No	DK/NS
a	. Salami/mettwurst		2	7
b	. Cabanossi/cabana/twiggy sticks	1	2	7
c	. Ham/chicken/turkey/beef	1	2	7
d	. Devon/frankfurts/cheerios	1	2	7
	. Liverwurst	1	2	7
f.	Other	1	2	7
	Specify ()			
26.	During these 7 days, did you eat any pate?			
	Yes			
	No		Go to Q.29	
	Don't know/Not sure	7		
27.	Was the pate eaten,			
	Chicken pate			
	Duck pate			
	Pork pate			
	Another type of pate		Specify (
	Don't know/Not sure	7		
28.	Was this pate homemade or purchased from a	store?		
	Homemade			
	Store	2		
	Don't know/Not sure	7		
29.	During these 7 days, did you eat any other me	at or pou	ltry? Like be	ef, lamb, chicken etc.
	INTERVIEWER NOTE:			
	This does not include eggs			
	Yes			
	No	1	Go to Q.49	
			00000	

	EF / VEAL	
30.	During these 7 days, did you eat any beef or veal?	
	Yes	
	No	
	Don't know/Not sure 7	
31.	During the 7 days prior, did you eat any of the following beef or veal?	
	Yes DK/N	
	Yes DK	
a.	Minced beef dishes I 1 2 7 (eg. bolognese sauce, pie, pastie, lasagne, hamburger patties, sausages)	
b.	Kebabs/souvlaki	
c.	Offal	
	(eg. tripe, liver, tongue)	
d.	Other	
POR	RK C	
32.	During these 7 days, did you eat any pork?	
	Yes	
	No	
	Don't know/Not sure	
33.	Don't know/Not sure	
33.	During the 7 days prior, did you eat any of the following pork?	
33.	During the 7 days prior, did you eat any of the following pork?	
33. a.	During the 7 days prior, did you eat any of the following pork?	
	During the 7 days prior, did you eat any of the following pork? $ \begin{array}{c} $	
a.	During the 7 days prior, did you eat any of the following pork?	
a. b. c.	During the 7 days prior, did you eat any of the following pork? S Q Minced pork dishes. (eg. bolognese sauce, pie, pastie, lasagne, hamburger patties, sausages) Kebabs/souvlaki. I <td< td=""><td></td></td<>	
a. b.	During the 7 days prior, did you eat any of the following pork? S S Minced pork dishes 1 (eg. bolognese sauce, pie, pastie, lasagne, hamburger patties, sausages) 7 Kebabs/souvlaki 1 2 7 Offal 1 2 7	
a. b. c.	Signed pork dishes Signed pork Signed por	
a. b. c. d.	Signed pork dishes Signed pork Signed por	
a. b. c. d. <i>LAM</i>	During the 7 days prior, did you eat any of the following pork?	
a. b. c. d. <i>LAM</i>	During the 7 days prior, did you eat any of the following pork? Image: Second State S	

35.	During the 7 days prior, did you eat any of the following lamb/mutton?
	Z
	DK/N DK/N
a.	Minced lamb/mutton dishes $\Box_1 \Box_2 \Box_7$
	(eg. bolognese sauce, pie, pastie, lasagne, hamburger patties, sausages)
b.	Kebabs/souvlaki
	Nebabs/souviaki 1 2 7 Offal 1 2 7 1 2 7 1 2 7 1 2 7 1 2 7 1 2 7 1 2 7 1 2 7 1 2 7 7 Specify (
c.	(<i>eg. tripe, liver, tongue</i>)
d.	Other $\Box_1 \Box_2 \Box_7$
	(eg. casserole, stir fry, steak, fillet, roast, lamb strips)
GAN	IE MEAT
0/10	
36.	During these 7 days, did you eat any game meat like kangaroo, wallaby, venison or similar?
	Yes
	No
	Don't know/Not sure
DOI	
POL	
37.	How often do you <u>usually</u> consume chicken/poultry meat?
	3 or more days per week
	1-2 days per week
	Once per fortnight
	Less often than once per fortnight
	Never
	Don't know/Not sure
38.	During the 7 days before your illness began, did you eat any chicken or other poultry?
	Yes
	No 2 Go to Q.46
	Don't know/Not sure
39.	How many meals did you eat that contained chicken or other poultry in the 7 days prior to
57.	onset of diarrhoea?
	1-2 meals
	3-4 meals 2
	3-4 meals

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1		
2	40.	Did you consume any chicken or poultry at home?
3		—
4 5		
6		No
7		Don't know/Not sure 7
8		
9	41.	Was the chicken or poultry purchased?
10 11		(Select all that apply)
12		
13		Raw and fresh
14		Raw and frozen 2
15		Pre-cooked 3
16		Don't know/Not sure
17		
18 19	42.	How was it stand before consumption 2
20	42.	How was it stored before consumption? (Select all that apply)
21		(Select all that apply)
22		INTERVIEWER NOTE:
23		(On the bench)
24		This is only to be used if they STORE their meat on the bench, this does not include defrosting their meat on
25		the bench.
26		
27 28		
28 29		In the freezer
30		In the fridge 2
31		On the bench 3
32		Don't know/Not sure
33		
34		
35	43.	Prior to cooking, was the chicken rinsed or washed under running water?
36 37		Yes
38		
39		No 2 Don't know/Not sure
40		
41		
42	44.	During this did time you eat any of the following cooked meats?
43		
44 45		Ves Vo
46		DK No
47		
48	a.	Chicken mince 1 2 7
49	1-	(including hamburger patties, sausages)
50	b.	Chicken kebabs
51	c.	Chicken pieces with bones 1 2 7 (<i>i.e.</i> wings, drumsticks, whole chicken)
52	b	Chicken pieces without bones. 1 2 7
53 54	u.	(i.e. breast, tenderloins)
55	e.	Offal 1 2 7
56		specify: liver other
57	f.	Duck
58	g.	Turkey 1 2 7
59	0	

2 3	45.		During this time, on how many days did you eat poultry?
4			INTERVIEWER NOTE:
5			
6			1. A pate is included
7			2. Eggs are excluded
8			
9			Days:
10			
11 12 13	46.		During this time, on how many days did you eat meat (including poultry)?
13			
15			INTERVIEWER NOTE:
16			Pate is included
17			
18			Days:
19			
20			
21 22	47.		During the 7 days prior to illness, did [you/they] eat any meat product, which was raw, rare or appeared undercooked?
23			Yes
24			No
25			
26			
27			
28	40		
29	48.		Which of the following meats did [you/they] eat that was undercooked?
30			
31			Yes No DK/NS
32		a.	Chicken/poultry 1 2 7
33 34		b.	Beef or veal 7
34 35		c.	Pork 2 7
36		d.	Lamb/mutton
37		e.	Game meat
38		f.	Minced meat items
39			including sausages, hamburger patties)
40		~	
41		g.	Offal (specify type) 1 2 7
42		h.	Other meat $\Box_1 \qquad \Box_2 \qquad \Box_7$
43			Specify ()
44			
45			
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50 51			
51 52			
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54 55			
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2 3	49.	How do you <i>prefer</i> the following meat to be cooked?
4		
5		INTERVIEWER NOTE: Raw: Not cooked at all
6		
7		Rare: Mostly red
8		Medium: Pink through out
9		Well done: Brown through out
10 11		INTERVIENTED NOTE.
12		INTERVIEWER NOTE:
12		If participant answers Medium/Rare
14		select the rarer option e.g Rare
15		Dom Done Modium Well done
16		Chieleer (Devilter)
17	a.	Chicken/Poultry 1 2 3 4
18	b.	Beef/Veal 1 2 3 4
19	с.	Pork 1 2 3 4
20	d.	Lamb 1 2 3 4
21	e.	Hamburgers 1 2 3 4
22	f.	Minced meat 1 2 3 4
23		
24		
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28 29		
29 30		
30		
32		Minced meat
33		
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F	GENERAL	KITCHEN PRACTICES	
Ľ.	ULNERAL	KITCHEN I KACHCES	

"I will now ask you several questions about the way food is usually prepared in your home. Remember, your participation is voluntary and you do not have to answer any of the questions if you don't want to."

10 50. 11	How many times per week do you cook for members of your household? INTERVIEWER NOTE:			
12	This section around food prepared in the home refers to the person answering the survey (not			
13	necessarily the case or control)			
14	necessarily the case of control)			
15				
16	0 1 Go to Q.63			
17	1-5 2			
18	>5 3			
19	Don't know/Not sure			
20				
21				
22 51.	Did you handle or prepare any raw meats in the kitchen in the <u>7 days before your</u>			
23	diarrhoea began?			
24	INTERVIEWER NOTE:			
25	Refers to the person answering the survey			
26	V			
27	Yes			
28	No 2 Go to Q.57			
29	Don't know/Not sure			
30				
31				
³² 52.	Did you handle or prepare raw chicken meat or chicken offal in the <u>7 days before your</u>			
33 34	diarrhoea began?			
35	INTERVIEWER NOTE:			
36	Refers to the person answering the survey			
37	Yes			
38	No			
39				
40	Don't know/Not sure			
41				
42				
43				
44 Inter	viewer Note: If person answered "No" to both Q.51 and Q.52 then skip to Q.57			
45				
46				
47				
48 53.	After a knife is used to cut raw meat or poultry, which of the following options do you			
49	usually do?			
50	INTERVIEWER NOTE:			
51	Refers to the person answering the survey			
52				
53	Continue using the knife as is			
54	Rinse the knife before continuing to cook			
55	Wipe the knife before continuing to cook			
56 57				
57 58				
58 59	Change to another knife			
60	Other			
	No one prepares meat Go to Q. 57			
Don't read	Don't know/Not sure 8			

3						
4 54.	After a cutting board is used to cut raw meat or poultry, which of the following options do you usually					
5	do?					
6						
7	INTERVIEWER NOTE:					
8	1. Does not matter if water is hot or cold					
9	2. Refers to the person answering the survey					
10						
11	Continue using the cutting board as is					
12	Rinse the cutting board before continuing to cook					
13	Wipe the cutting board before continuing to cook					
14	We do the construction of an effective construction of the formation of th					
15						
16						
17	Other 6					
18	Specify ()					
19 Don't read	Don't know/Not sure					
20						
21						
²² 55. 23	After handling raw meat or poultry in the kitchen, which of the following would you					
24	usually do before continuing to cook?					
25	INTERVIEWER NOTE:					
26	Refers to the person answering the survey					
27						
28	Wipe hands					
28	Quickly rinse hands under a running tap					
30						
31	Wash hands with soap and water					
32	Other 4					
	Specify ()					
33 34						
	Don't do anything about hands					
³⁵ Don't read 36	Don't know/not sure 7					
37						
38 _						
³⁰ ₃₉ 56.	After washing hands during food preparation, what would you usually dry					
40	your hands on?					
40	INTERVIEWER NOTE:					
42	Refers to the person answering the survey					
43						
44	Paper towel					
45						
46	Sponge/cloth					
47	Tea-towel /hand towel					
48	Apron 13					
49	Don't dry hands					
50	Other					
51	Specify ()					
52 Don't read	Don't know/Not sure					
53 <i>Don i redu</i>						
54						
55						
	In the next 2 menths has annous in the branched state and an DDOO					
56 57. 57	In the past 3 months, has anyone in the household cook meat on a BBQ?					
58	Yes					
59						
60						
00	Don't know/Not sure					

² 58.	After cooking on the BBQ, where would the cooked meat most likely be placed?
4 5 6 7	Back on the same container 1 Back on the same container after it has been rinsed with water 2
8 9 10	Back on the same container after it has been wiped off with a towel
11 12 13	Back on the same container, after the container has been washed with soap and water
14 15 16 17 Don't read	On a different container 5 Other 6 Don't know/not sure 7
18 19 20 21	Don't know/not sure
22 23 24	
25 26 27	
28 29 30	
31 32 33	
34 35 36 37	
37 38 39 40	
41 42 43	
44 45 46	
47 48 49	
50 51 52	
53 54 55	
56 57 58	
59 60	

next fev	questions are about contact with animals in the 7 days before your diarrho	bea began."
59.	During this time, did you keep or care for any of the following animals as	pets?
	INTERVIEWER NOTE:	
	Not to include one off contact	
		Is any pet less tha 6 months old?
_	Yes No DK/NS	Yes No DK/N
a. h		
b.	Dog 1 2 7	
C.		
d.	Other birds 1 2 7	
e.		Specify (
f.	Do not keep any pets	
Intervio	wer Note: If person answered No/Don't know to Cat then skip to question	n 62
60.	Do you feed your cat raw meat or bones?	
JU.		
	Yes Specify (
	No 2 Go to Q. 62	(eg. chicken, beef, kangaroo
	Don't know/Not sure Go to Q. 62	
61.	How often does your cat get fed raw meat or bones?	
	Daily	
	Weekly	
	Monthly	
	Less often	
	Don't know/Unsure	
ntervi	wer Note: If person answered No/Don't know to Dog then skip to question	on 65
52.	Do you feed your dog raw meat?	
	Yes Specify (
		en, beef, kangaroo, lamb etc.)
	Don't know/Not sure	,,,
53.	Do you feed your dog raw bones?	
	No 2 Don't know/Not sure 7	

BMJ Open

64.	How often does your dog get fed raw meat or bones?			
	Daily			
	Weekly			
	Monthly 3			
	Less often			
	Don't know/Not sure			
65.	Did you get any of your pets in the 4 weeks before your diarrhoea began?			
	Yes Pet(s) (
	No			
	Don't know/Not sure			
66.	Were any of your own pets ill with diarrhoea in the <u>7 days before your diarrhoea began</u> ?			
	Yes 1 Pet(s) (
	No 2			
	Don't know/Not sure			
67.	In the <u>7 days before your diarrhoea began,</u> did you have contact with household pet			
	faeces or manure (eg. changing litter boxes or picking up pet faeces with a plastic			
	bag)?			
	Yes Pet(s) (
	No			
	Don't know/Not sure			
68.	Do you live on a farm/hobby farm including a property on acreage 5 acres or over?			
	Yes			
	No.			
	No 2 Don't know/Not sure			
	No Don't know/Not sure			
69.				
69.	Don't know/Not sure 7			
69.	Don't know/Not sure			
69.	Don't know/Not sure 7 In the 7 days before your diarrhoea began, did you visit a farm or petting zoo? Yes 1			
69.	Don't know/Not sure 7 In the 7 days before your diarrhoea began, did you visit a farm or petting zoo? Yes 1 No 2 (eg. private farm, commercial farm, petting commerc			
69.	Don't know/Not sure 7 In the 7 days before your diarrhoea began, did you visit a farm or petting zoo? Yes 1 No 2 (eg. private farm, commercial farm, petting commerc			
69.	Don't know/Not sure 7 In the 7 days before your diarrhoea began, did you visit a farm or petting zoo? Yes 1 No 2 (eg. private farm, commercial farm, petting commerc			
69.	Don't know/Not sure 7 In the 7 days before your diarrhoea began, did you visit a farm or petting zoo? Yes 1 No 2 (eg. private farm, commercial farm, petting commerc			
69.	Don't know/Not sure 7 In the 7 days before your diarrhoea began, did you visit a farm or petting zoo? Yes 1 No 2 (eg. private farm, commercial farm, petting commerc			
69.	Don't know/Not sure 7 In the 7 days before your diarrhoea began, did you visit a farm or petting zoo? Yes 1 No 2 (eg. private farm, commercial farm, petting commerc			
69.	Don't know/Not sure 7 In the 7 days before your diarrhoea began, did you visit a farm or petting zoo? Yes 1 No 2 (eg. private farm, commercial farm, petting commerc			

4.	DEMOGRAPHICS
"	I would now like to ask you a few final questions. Remember, your participation is voluntary and
	ou do not have to answer any of the questions if you don't want to."
-	
70.	Is any language other than English spoken in your household?
	Yes
	No
Don't read	Don't know/Not sure
Don't read	Refused
71	
71.	Are you of Aboriginal or Torres Strait Islander origin?
	No 1
	Aboriginal 2
	Torres Strait Islander 3
	Both 4
Don't read	Don't know/Not sure
Don't read	Refused
70	
72.	Which of the following places best describe where you live?
	Inner city or urban area
	Suburban area 2
	Town 3
	Rural or remote area community
	Rural or remote area farm or property
Don't read	Don't know/Not sure
Don't read	Refused
	-7
T (
Interv	iewer Note: See definitions below.
Inner cit	ty area:
	in area:
	the region being primarily a self-contained residential district.
	community over 2000 people
	remote area community:
Rural or	remote area farm or property
73.	Does your occupation involve any of the following?
	Working with raw meat
	(eg. restaurants, butchery, abattoir etc.)
	Working with animals
	(eg. farmer, zookeeper, vet/nurse etc.)
	Disting d
	Retired.

2				
3	74.	What is the highest level of education reached by an	yone in your household?	
4 5		Schooling to year 10 or below		
6		Secondary school, above year 10		
7		Technical or further educational institution		
8 9		(eg. TAFE, apprenticeship, college etc.)	14	
9 10		University degree—Undergraduate	15	
11		University degree—Postgraduate (Masters, doctorate).		
12 Don't	read	Don't know/not sure	7	
¹³ <i>Don't</i>		Refused	9	
14 15				
16	()	· · · · · · · · · · · · · · · · · · ·		
17		low I am going to read you a list of income categoric		
18		scribes your total household income, before taxes, in the r all household members."	last linancial year? I hat is the total ligure	
19 20	75.	Last year the total income for your household was	.?	
21		Less than \$25,000		
22		\$25,000 to \$50,000		
23		Between \$50,000 and \$100,000	2	
24 25		Between \$100,000 and \$150,000	3	
26		More than \$150,000		
27 <i>Don't</i>	read	Don't know/Not sure		
28 29 <i>Don't</i>		Refused		
29 30				
31				
32	76.	As part of this research we are planning to do a follo	ow-up study. Would you be happy for us to contact	
33		you in ~6 months' time?"		
34 35		Yes		
36		No 2	Skip to end of questionnaire	
37				
38 39	Intorvi	ewer Note: If person answered No to Q 76 then ski	n to the end of the questionnaire	
40			p to the end of the questionnane	
41		Details required:		
42		Name:		
43 44		Phone number:		
44 45				
46		Email address:		
47	"Т	That's my last question. Thank you very much for you	r time and cooperation."	
48 49	r		· · · · · · · · · · · · · · · · · · ·	
49 50		COMPLETE AFTER INTERVIEW		
51				
52		Interviewer initials		
53 54		Interview stop time		
54 55		Interview stop time		
56		Length of interviewMINUTES		
57				
58		Respondent recall:		
59 60		Poor 1		
		Fair 2		
		Average 3		
		Good		
		Excellent review only http://bmjopen.bmj.com	/site/about/guidelines.xhtml	