

HEALTH PROTECTION RESEARCH UNIT
IN GASTROINTESTINAL INFECTIONS


*National Institute for
Health Research*

BOOK OF ABSTRACTS AND PRESENTATION OF KEYNOTE SPEAKERS

ANNUAL SCIENTIFIC MEETING
LIVERPOOL – 1 & 2 MARCH 2017



IFR Institute of
Food Research



UNIVERSITY OF
LIVERPOOL



Public Health
England

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KEYNOTE SPEAKERS

Keynote speakers for the 2017 National Institute for Health Research (NIHR) Health Protection Research Unit (HPRU) in Gastrointestinal Infections (GI) annual conference: Professor Anne Murcott, Professor Simon Capewell, Professor Patrick Wall and Professor Sarah O'Brien.



Professor Anne Murcott: 'Good reasons for bad behaviour: a sociological approach to food handling in a domestic kitchen'

Anne Murcott is author of books, articles and papers in sociology on various aspects of health and on food, diet and culture. Trained in social anthropology and in sociology, she taught at the University of Wales then moved to the University of London. She has also taught at Newcastle and Deakin Universities, Australia and the University of Otago, New Zealand. She is now Professorial Research Associate, Food Studies Centre, SOAS, London, Honorary Professor at the University of Nottingham and Professor Emerita London South Bank University. She was Director of the Economic & Social Research Council (UK) Research Programme "'The Nation's Diet" the social science of food choice' in the 1990s and was editor of *Sociology of Health & Illness*, and international editor of *Food, Culture & Society*.

Her current work includes co-editing *Waste matters: new perspectives of food and society* (The Sociological Review Monograph 2013) with David Evans and Hugh Campbell, *The Handbook of Food Research* (Bloomsbury 2013) with Warren Belasco and Peter Jackson *The Craft of Writing* (Manchester forthcoming) with Andrew Balmer. She serves as an expert member of the UK Food Standards Agency's General Advisory Committee on Science. In 2009 she received an honorary doctorate from the University of Uppsala.



Professor Simon Capewell: Working at the Public Health Science/Policy interface: Lessons from Slavery, Rum and Tobacco?

Simon trained in general, respiratory and cardiovascular medicine in Newcastle, Cardiff, and Oxford, then in public health in Edinburgh and Glasgow. He was appointed as the first Professor of Clinical Epidemiology in the University of Liverpool in 1999.

Simon manages a research programme mainly involving cardiovascular disease (CVD) and food policy, with well over three hundred peer-reviewed papers, many in top journals, and funding thus far totalling over £25 million. He enjoys facilitating multidisciplinary research teams, mentoring colleagues and writing papers and grant applications.

His recent research includes programmes funded by MRC, NIH, NIHR, EU & BHF examining:

- why CVD death rates have recently plummeted in the USA, UK, Poland & elsewhere, and why CVD rates are increasing in China and many other developing countries, and
- the development of effective and cost-saving CVD prevention strategies in high, middle and low income countries (majoring on healthy food policies, and using quantitative modelling, policy analyses and empirical evidence).

Simon is Vice President (Policy) for the UK Faculty of Public Health and previous President of the Society for Social Medicine. He is also a Trustee for the FPH, for the UK Health Forum, and for Heart of Mersey regional CVD prevention charity. He enjoys contributing to policy development and service work. He has recently chaired/participated in a dozen national /international policy and prevention committees, including Academy of Medical Royal Colleges (Obesity), American Heart Association, Obesity Health Alliance, British Heart Foundation, NICE (CVD prevention), UK FPH, European Society of Cardiology and WHO.



Professor Patrick Wall: After dinner speaker

Patrick Wall is Associate Professor of Public Health in University College Dublin's School of Public Health and Population Sciences (which hosts the National Nutrition Surveillance Centre). His teaching and research interests include food borne diseases, lifestyle related diseases and health damaging consumer behaviour. He is a co-director of the UCD Centre for Behaviour and Health which is engaged in research on behavioural economics, population health disparities and policy interventions.

He was the first Chief Executive of the Irish Food Safety Authority and contributed to the setting up of this science based consumer protection agency. He was the second Chairperson of the European Food Safety Authority, a pan EU Agency with a remit is to provide comprehensive scientific advice on food safety for the entire food and feed supply chains and issues directly impacting on these such as animal welfare, animal health and plant health.

He was one of seven non-Chinese nationals on the committee advising the

Beijing Food Authority on food safety controls for the 2008 Beijing Olympics. He is the Chairperson of the Mental Health Commission's Research Committee. He is a member of the Food Safety Authority of Ireland's Healthy Eating Guidelines steering committee.

He qualified in Veterinary Medicine in University College Dublin, in Human Medicine in the Royal College of Surgeons of Ireland. He has an MSc in Infectious diseases from the University of London and an MBA from the Michael Smurfit School of Business. He is a Diplomate of the European College of Veterinary Public Health, a Member of the Faculty of Public Health Medicine of Ireland, a Fellow of the Faculty of Public Health Medicine in the UK and is a Member of the Royal College of Veterinary Surgeons.



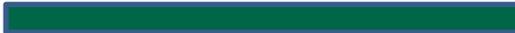
Professor Sarah O'Brien: Modernising diagnosis and surveillance of Gastrointestinal Infections

Sarah O'Brien is Professor of Infection Epidemiology and Zoonoses. Sarah qualified in Medicine in 1996 at Newcastle University and trained in Public Health Medicine in Oxford and Newcastle-upon-Tyne. She held Consultant positions in Health Protection in Birmingham, Glasgow and London before joining the University of Manchester in 2004. She moved to the University of Liverpool in 2011.

Sarah has considerable expertise in the epidemiology of infectious diseases, particularly foodborne disease, and was the Chief investigator for the Second Study of Infectious Intestinal Disease. She is currently Chairman of the government's Advisory Committee on the Microbiological Safety of Food and is a World Health Organisation advisor for the Foodborne Epidemiology Reference Group. Her personal research interests include unravelling the epidemiology of infectious diseases and understanding the contribution of acute infection to chronic illness.



ORAL ABSTRACTS



1

Family income and presentation to primary and secondary care for Diarrhoeal, Respiratory and Ear Infection: evidence from the UK Millennium Cohort Study?

Dr Mara Violato

Research Fellow

Tracking disease in the population theme

Background

Reducing inequity in the use of healthcare services is an objective of many healthcare systems. UK empirical studies show a pro-poor distribution of general practitioner consultations and a pro-rich distribution of hospital care. Diarrhoeal, respiratory, and ear infections are the most common infections among infants, with rates of illness generally higher in lower income populations.

Aims

To investigate the extent to which family income is associated with healthcare utilisation for diarrhoeal, respiratory, and ear infection in British infants of 9 months of age; to identify the main mechanisms that may mediate such relationship; to estimate the economic burden of healthcare use from a NHS perspective.

Methods

The relationship between infants' presentation (1=Yes; 0=No) to primary and secondary care and family income are explored for 19,000 children born in 2000-2002 (Millennium Cohort Study), within the Grossman model of demand for healthcare. The potentially mediating role of a wide range of family, social and environmental factors is investigated through multivariate logit models. Costs associated with healthcare use are estimated.

Results

75% of infants present to primary care; 15% are admitted to hospital. Preliminary results show that infants from families in the highest income quintile are more likely to present to primary care for diarrhoeal (OR: 1.46; 95% CI: 1.21, 1.77) and ear infection (OR: 1.54; 95% CI: 1.28, 1.85) than infants from the lowest income quintile. Opposite results are found for hospital admissions, with richer children being less likely to be admitted to hospital than their poorer counterparts for both gastroenteritis (OR: 0.62; 95% CI: 0.37, 1.04) and respiratory infections (OR: 0.46; 95% CI: 0.34, 0.63). Duration of breastfeeding and other environmental factors appear to mediate the relationship.

Conclusions

This study provides novel evidence on healthcare use by socioeconomic group for common infant infections. The results will help inform policy interventions and health promotion programmes.

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2

Investigating the burden and transmission of acute gastroenteritis in care homes on Merseyside

Thomas Inns

PhD Student

Pathways theme

The main objective of my work so far in this first year has been to organise and set up a study to investigate the burden and transmission of acute gastroenteritis in care homes on Merseyside. The aim of this project is to pilot an enhanced surveillance system for acute gastroenteritis among the elderly in care homes. This will provide data that can then be extrapolated and used in mathematical models to calculate the burden of norovirus infections in the elderly in long-term residential care in the UK, and the potential impact of a norovirus vaccine specifically targeted to this population. The study will take place in care homes in North West England. I have developed a detailed protocol and associated study materials; this has received sponsorship from the university and has received approval from a Research Ethics Committee. Liaising with the Liverpool Community Health Trust to identify potential sites and beginning recruitment to the study is now my priority.

I am also undertaking an analysis of recent care home acute gastroenteritis outbreaks in Cheshire and Merseyside, using data collected by Public Health England. This analysis will produce background epidemiological data and provide context for the main study.

Additionally, I am currently undertaking a systematic review of the literature to provide background and context for this work. The systematic review will look at "Community-based surveillance of acute gastroenteritis".

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3

Relationship between socioeconomic status and gastrointestinal infections in developed countries: A systematic review and meta-analysis

Natalie Adams and
Tanith Rose

PhD Students

People theme

Background

The association between socioeconomic status (SES) and health is well-documented; however limited evidence on the relationship between SES and gastrointestinal (GI) infections exists, with published studies producing conflicting results. This systematic review aims to assess the association between SES and risk of GI infection, exploring possible sources of heterogeneity in effect estimates reported in the literature.

Methods

MEDLINE (Ovid), Scopus and Web of Science and grey literature were searched from 1980 to October 2015 for observational studies reporting a quantitative association between GI infections and SES in a representative population sample from a member-country of the Organisation for Economic Co-operation and Development (OECD). Harvest plots were created for comparison where heterogeneity between studies was high, stratified by age; level of SES variable; GI measurement; and predominant mode of transmission. Meta-analysis was performed on a subset of data.

Results

6,021 studies were identified; 102 met the inclusion criteria. Overall risk of GI infection for low versus high SES was 1.06 (95%CI 0.95-1.19). For children, risk of GI infection was significantly higher for those of low SES versus high (RR 1.51, 95% CI 1.26-1.83), but there was no significant difference for adults (RR 0.84, 95% CI 0.62-1.12).

Conclusions

Disadvantaged children, but not adults, appear to have greater risk of GI infection compared to their more advantaged counterparts. Increased risk may relate to different exposures, risk factors or healthcare-seeking behaviours. Gaining further insight into this relationship will help to inform policies to reduce inequalities in GI illness in children.

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How qualitative research evidence can help to better understand health inequalities in Gastrointestinal Infection (GI) in socially contrasting places

Dr Sarah McGarrol

Postdoctoral Researcher

People theme

There is strong evidence of a social gradient in most health outcomes linked to both causes and consequences of ill health. Socioeconomic and geographical inequalities have been well documented in chronic conditions, such as coronary heart disease but understandings around health inequalities and gastrointestinal infections, is not well known. Previous quantitative studies have shown that around 25% of people in the UK will suffer an episode of infectious intestinal disease (IID) per year. The consequences of this can result in a great number of days lost from school and/or work. Hospital admissions are also shown to be twice as great for those from more disadvantaged areas compared to affluent areas. Other studies investigating risk of GI infections have most often focused on factors influencing risks, rather than examining the influence of differing social and geographical environments in detail.

This research, as part of the 'People' theme, seeks to contribute to understandings of the interactions between people and place. Engagement with the idea that 'place', as well as individual characteristics contributes to health variations, has been recognised. Significant research has applied extensive quantitative methods and techniques and statistical modelling to show a general 'contextual' effect (usually of deprivation), on the health of populations. Qualitative, in-depth methods have been increasingly used to provide insights into how conditions in particular places influence health and health related behaviour. This kind of research is valuable because it can help us understand specific mechanisms through which places affect health and can help identify potential opportunities for intervention (Cummins, et al, 2007).

The paper will outline the value of qualitative 'place-based' research and provide examples from a recent structured review exploring health within socially-contrasting places. The insights from these studies are important for conducting research which seeks to investigate the interacting and complex factors within selected socially contrasting localities for gastro-intestinal infections.

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How are the management and consequences of gastrointestinal infections shaped in the context of households with young children in differing socio-economic and geographical locales?

Suzanne Rotheram

PhD Student

People theme

Background

Gastrointestinal infections are an important cause of UK morbidity with approximately 25% of the population having at least one episode each year.

The patterning of socio-economic inequalities in gastrointestinal infections in high income countries is under-researched and has previously shown inconclusive patterns. Recent research suggests that while more affluent populations have higher reported rates of infection, the consequences of infection are greater in more deprived populations. This inequality is particularly evident in children under five living in areas of deprivation in the United Kingdom who are twice as likely as their more affluent counterparts to be admitted to hospital as a result of a gastrointestinal infection.

This presentation will outline plans for a PhD to examine why socio-economic and geographical differences might shape the uneven distribution of these consequences. It will do this by examining the management and consequences of gastrointestinal infections in households with children under five.

Methods

This presentation will outline plans for a PhD that incorporates multiple methods, data and analyses to provide a greater understanding of how broader policies, social, economic and environmental factors might interact to produce inequalities in this disease.

An ethnographic approach will incorporate a systematic review, observational fieldwork, narrative and ethnographic interviews, geographic information systems (GIS) mapping and geo-ethnography. These methods will be used in two socio-economically contrasting locales to examine how and why the physical and social environment might influence the management and consequences of gastrointestinal infections. Interviews and observations across different settings (households and community) and with different parties (household and community) will provide a multi-faceted understanding of inequalities in these infections.

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Place–Based case studies: Understanding how the local context and environment influences differential exposure, differential vulnerability and differential social, economic and health care consequences of GI infection

Dr Rachael Eastham and
Dr Alexandra Kaley

Postdoctoral Researchers

People theme

Background

The relationship between deprivation and GI infection is not well understood, with literature highlighting conflicting results. Despite limited evidence, extant studies suggest that trends differ between adults and children, with children in more deprived areas having higher risk of infection and hospitalisation. Further work is needed to understand ways in which interactions within the domestic and public social context increase risk of GI.

Aims

To deliver an in-depth understanding of GI infection within the wider social context and within households; and to characterise how these factors influence outcomes for communities living in the North West of England.

Methodology

Using qualitative participatory techniques, we interviewed parents with children aged 0-11 to explore how the material, social and cultural environment (place) influence the consequences of GI infection for families. As part of the interview, study participants undertook an activity using graphic/photo elicitation techniques. A thematic analysis will be carried out on the multiple forms of data for each participant. The final set of themes identified shall be drawn from topics that occurred through the workshop exercise, qualitative interviews and theoretical ideas from the literature review.

Results

Data collection is currently underway and preliminary results will be presented at the scientific meeting. 10 semi-structured interviews have been undertaken out of a minimum of 20 which are expected to be completed by Jan 2017. Thus a range of narrative and visual data will be presented.

Conclusion

Qualitative research allows us to elicit lived experience and the way in which people relate to places and the resources that are available to them locally; this is not a facet of GI infection that has been previously captured. This is important because if we want to reduce the burden of GI infection then we need to design interventions that accurately reflect the reality of people's lives.

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Sequelae of gastrointestinal infections: incidence and risk factors

Oluwaseun Esan

PhD Student

Tracking disease in the population theme

Background

Gastrointestinal (GI) infections are common. Currently, the surveillance of GI infections such as *Campylobacter* and *Salmonella* is primarily based on laboratory data held by Public Health England. Information on symptoms severity, treatment of infection and subsequent complications is not captured by this data source.

The Clinical Practice Research Datalink (CPRD) provides a platform to assemble cohorts for long-term follow-up at relatively low costs. This data resource contains clinical and demographic information on patients of all participating General Practices in the UK. In this study, we describe the baseline characteristics of a cohort assembled using this resource in the study of sequelae following *Campylobacter* and non-typhoidal *Salmonella* (NTS) infections.

Methods

This is an open retrospective cohort study of all patients diagnosed with *Campylobacter* or NTS registered at CPRD practices that are deemed to have “acceptable” patient records between 1st January 2000 and 30 September 2015. Patients not meeting data quality flags before date of first consultation for GI infection were excluded. On receipt of data, standard data quality checks were performed. The final cohort was established using the earliest record of GI consultation.

Results

A total of 53,913 patients from 662 practices representing all regions of the United Kingdom were provided by the CPRD. Patients with a read code for serology, negative culture results and systemic infections only (21,444) or Read codes for both *Campylobacter* and NTS infection on the same date were excluded (85). Overall, 32,469 patients were available for follow-up with a mean (SD) age of 44.0 (22.1) years (49% female).

Conclusions

We have established a cohort of patients with GI infections to study subsequent sequelae and estimate the risk of common sequelae following medication. Linkage to hospitalization, deaths and deprivation data will allow the estimation of the economic burden associated with sequelae of GI infections.

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Development of methods for the analysis of observational studies in systematic reviews and its application to analyses of sample data

Adedoyin Awofisayo-Okuyelu

PhD Student

Tracking disease in the population theme

Systematic reviews of observational studies are increasingly being used as a means of answering research questions especially when they involve measuring parameters. There are reports on the process of undertaking and reporting, and guidelines for meta-analysis of systematic reviews of trials and observational studies. However, these guidelines focus on comparing interventions or risk factors rather than measure parameters such as incubation period.

The authors have undertaken systematic reviews of observational and experimental studies to estimate the incubation period of common gastrointestinal pathogens and have developed methods for assessing, extracting and analyzing combined data. The development of the bespoke method is described.

In RCTs, formal statistical test for heterogeneity is available in the form of chi-squared test included in forest plots and quantifying inconsistency is done by deriving I^2 . In our study, we used Kolmogorov-Smirnov tests (KS test) as a means of identifying and quantifying heterogeneity among the studies, and the hierarchical cluster analysis as a process of defining subsets of studies that do not have evidence of heterogeneity.

We applied our newly developed method to undertake a systematic review and meta-analysis in estimating the incubation period of *Campylobacter*. The outputs of the KS test were the D-statistics which gave an estimation of the effect size (degree of heterogeneity between the studies), and the p-values which showed the statistical strength of evidence for heterogeneity. We evaluated the pattern of heterogeneity by creating a hierarchical cluster to show a graphical representation of the dissimilarities between the studies and identify similar subgroups within the data could be analysed. This is equivalent to the use of a forest plot to show a graphical representation of the effect sizes in RCTs. We identified five clusters with 99.8% probability that studies between clusters are dissimilar; however, there was limited evidence of similarities of studies within clusters.

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Environmental sampling to detect presence of Shiga toxin-producing *E. coli* in the English countryside

Dr Erica Kintz

Postdoctoral Researcher

Pathways theme

Background

Shiga toxin *E. coli* (STEC) cause bloody diarrhoea that can progress to kidney failure. While the public commonly believes that these infections are acquired from consuming contaminated food, the scientific literature illustrates that direct or indirect contact with animal or their environment are also a significant source of STEC illness.

Methods

Three different locations each in the North West and East Anglia were walked at least once a month over the course of sixteen months. Three walkers per walk wore boot socks over their shoes to sample the soil along the walking route. The resulting 720 individual boot socks were screened by multiplex PCR for the presence of *stx1*, *stx2* and *eaeA*.

Results

Overall, 12.36% of the boot socks were positive for either of the *stx* genes. Far more positive samples contained *stx2* (n=66) compared to *stx1* (n=15). A vast majority of the positive *stx* samples, 82%, also encoded *eaeA*. However, if one looked at the two regions included in the study, there were interesting differences in the presence of positive *stx* boot socks. In East Anglia, only 3.6% of the boot socks were positive for *stx*, compared to 21.1% of the boot socks from the walks in the North West. The summer seasonal peak traditionally associated with STEC was also seen in the number of positive boot socks by month for the North West region.

Conclusions

The number of positive boot socks broadly reflects the amount of ruminant livestock in each region, with the North West containing many more cows or sheep than are present in East Anglia. These results suggest that individuals visiting the countryside could acquire STEC from the environment even if ruminant animals are not immediately present.

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Retrospective genomic analyses of *Campylobacter* isolates to investigate long-term trends in human campylobacteriosis in the UK

Clare Barker

PhD Student

Pathogens theme

Campylobacter is the leading cause of gastroenteritis in the United Kingdom, with an estimated 280,000 cases each year. Confirmed isolates belonging to outbreaks and single cases of infection are received by Public Health England for typing and antibiotic susceptibility testing, and are subsequently archived. This project has examined a selection of these archived isolates through the use of whole genome sequencing (WGS) and genomics, bringing new insights into past outbreaks and exploring how isolates have changed over time.

One collection of archived *Campylobacter jejuni* isolates, belonging to the same immunocompromised patient and covering 15 years of recurrent infection, was sequenced. Genomic analysis was then used to enable a detailed, long-term view of microevolution of this single strain within its human host. Genetic mutations predicted to confer antibiotic resistance were seen to be gained and lost over time. These predictions based on the sequenced genomes were supported by laboratory testing. This research reinforces how useful WGS can be in diagnosing and aiding treatment of resistant bacterial infections.

A large number of historic *Campylobacter* outbreak isolates were sequenced in order to explore how WGS could have contributed to outbreak analysis at the time, and what the individual genomes reveal about the outbreaks. In many cases, isolates from the suspected source of contamination were sequenced alongside patient isolates, revealing the origins of the outbreaks. Additionally, genetic antibiotic resistance data from the genomes were compared to phenotypic data from laboratory resistance testing. This analysis displays how powerful the use of WGS can be in public health microbiology, particularly during outbreaks.

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Source attribution of *Campylobacter*

Dr Melissa Jansen van Rensburg

Postdoctoral Researcher

Pathogens theme

Background

The foodborne pathogens *Campylobacter jejuni* and *Campylobacter coli* are a major cause of bacterial gastroenteritis worldwide. Genetic models for the attribution of genotypes to sources of infection, based on multilocus sequence typing (MLST) data, have improved our understanding of *Campylobacter* epidemiology. The aims of this study were to: (i) establish publicly available reference sets of animal and environmental isolates; (ii) implement attribution methods in the *C. jejuni/coli* PubMLST database; and (iii) determine the relative importance of different sources in Oxfordshire, UK.

Methods

Animal and environmental *Campylobacter* isolates with MLST data were identified in the literature and grouped in the *C. jejuni/coli* PubMLST database. Python code was developed to automate attribution analyses using the STRUCTURE algorithm. Human disease isolates recovered between 2003 and 2016 in Oxfordshire were analysed using these resources.

Results

Reference sets of 8,968 *C. jejuni* and 3,967 *C. coli* isolates were established, comprising ten and seven sources, respectively. Analyses of 7,116 *C. jejuni* and 754 *C. coli* human disease isolates indicated that food animals were the major sources of infections, with proportions relatively stable over time. Among *C. jejuni* cases, 46 and 40% were attributed to chicken and ruminants, respectively. Among *C. coli* cases, 64% were attributed to chicken, while pigs and ruminants each accounted for 16% of infections. For both species, the wild birds and/or the environment accounted for <1% of cases.

Conclusions

Chicken has consistently been the principal source of human campylobacteriosis in Oxfordshire, followed by the other major food animals. The results highlight the need for further interventions and monitoring along the farm-to-fork continuum to reduce the incidence of *Campylobacter*. Additionally, the resources developed for use in this study will enable other researchers to rapidly and easily attribute *Campylobacter* isolates to host sources.

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A spatio-temporal analysis of STEC O157 in England

Richard Elson

PhD Student

Pathways theme

Shiga-toxin producing *Escherichia coli* (STEC) O157 is a zoonotic infection that can cause serious illness in humans. The transmission pathway from the ruminant reservoir to humans is complex and infections can be acquired directly from animals or their faeces, or indirectly via contaminated food, water or the environment.

We examined the relationship between the presence of cases and variables related to socio economic factors (rural/urban residence, socio economic status), animal density (cattle, sheep, pigs and horses) and environmental factors (inland water coverage, distance to coast and numbers of private water supplies). Spatial and space time scan statistics were used to test for evidence of localised clustering of sporadic cases.

The occurrence of STEC O157 in England shows distinct geographical and temporal variation, partly explained by residential proximity to the ruminant reservoir. Evidence of space-time clustering suggests that geographically restricted transmission can occur, sometimes for long periods.

Planned work includes a review of spatial methods and further spatial analyses incorporating whole genome sequence data from humans and cattle.

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Study of the burden of infectious intestinal disease associated with school absenteeism and the development of a pilot study for the use of school absence registers as a syndrome surveillance system

Dr Anna Donaldson

Honorary Research Fellow

Pathways theme

Background

Children have the highest incidence of illness due to Infectious Intestinal Disease (IID) and many cases will be managed conservatively at home and will not, therefore, be detected by current surveillance systems. Children are also high transmitters of disease and can introduce IID into the wider community by transmitting pathogens to parents, siblings and other family members. Of particular concern is the introduction of IID, for instance norovirus, into healthcare settings such as hospitals and nursing homes.

It is mandatory for schools to record absences due to illness but school data does not currently record details on the symptoms or cause of illness. If key symptoms, or clusters of symptoms, could provide enough discrimination to indicate a likely causative organism, enhanced school absence data could be used to provide a more accurate estimate of the burden of disease in school-aged children. This data would form the basis of an enhanced surveillance system which could provide an early warning system for outbreaks amongst school-aged children. This would have benefits in terms of preventing and managing outbreaks within schools, as well as reducing onward transmission of disease into the community.

Methods

1. To undertake a literature review of the impact of IID on school absenteeism and the role of school absence data as a form of surveillance.
2. To correlate school absence data with GP data to create an estimate of the causes of absenteeism in children and the burden of disease associated with IID.
3. To explore IID2 Study data to identify probable cases of IID based on symptomology and to use these findings to identify symptoms, or clusters of symptoms, that provide the best discrimination of the causative organism.
4. To develop a pilot study for an enhanced surveillance system within schools based on identification and recording of symptomology.

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Application of metagenomics and metabolomics for the diagnosis of gastroenteritis

Saskia Neuert

PhD Student

The Microbiome theme

Despite a decline in associated mortality, infectious intestinal diseases (IID) and their potential long-term adverse consequences remain a major healthcare problem even in industrialised countries. Routinely used diagnostic methods often are time-consuming and require isolation of pathogens from faecal matter prior to identification. Even the most advanced, rapid approaches fail to detect an aetiological agent of IID in 40% of cases referred for laboratory diagnostics. Improved diagnostics, allowing more targeted treatment, would be greatly beneficial, especially in cases of recurrent, prolonged and severe disease or for patients with underlying co-morbidities.

There is huge potential in exploiting recent advances in –omics technologies in this context and therefore we aim to establish two integrated pipelines based on metagenomic and metabolomic profiling as a novel approach to routine diagnostics of gastroenteritis directly from the stool samples provided. We will make use of clinical faecal samples obtained by Norfolk and Norwich University Hospital from patients presenting with symptoms of gastroenteritis. DNA extracted from these samples will be analysed using 16S rRNA gene and shotgun sequencing and bioinformatics tools will be employed to identify pathogens and changes in microbiota composition associated with a specific infection. Furthermore, ¹H NMR spectroscopy will be performed on faecal water extracts from the same samples to detect changes in metabolite profiles related to the presence of certain pathogens. Finally, we will correlate the profiles obtained and assess the feasibility of using the pipelines in a clinical diagnostic setting and their performance in comparison to the techniques used routinely.

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The impact of Rotavirus vaccination program in England on Emergency department attendances: where are we now?

Helen Hughes

PhD Student

People theme

Background

Rotavirus gastroenteritis is a common childhood disease, estimated to have been the causative agent responsible for high numbers of GP consultations and hospital admissions in children each year. A rotavirus vaccination program, targeted at infants aged 2-3 months, was introduced in the UK in July 2013. Previous work demonstrated an apparent decrease in gastroenteritis in children during what was expected to be the next 'rotavirus season', March-April 2014.

Methods

The Emergency Department Syndromic Surveillance, part of the Public Health England suite of syndromic surveillance, collects anonymised daily data from a sentinel network of emergency departments across England and Northern Ireland. Using the data collected in this system daily attendances with a diagnosis of gastroenteritis will be identified and analysed for 2012 to 2016 (2 years pre and 3 years post vaccination implementation) to estimate any ongoing impact of this new vaccination program, since the initial investigation of the 2014 rotavirus season.

Preliminary Results

The reduction in ED attendances for children under 5 years during 2014 immediately following vaccination implementation, was observed to have continued in following years.

Preliminary Conclusions

Following the introduction of the rotavirus vaccination into the childhood vaccination schedule for infants there has been an apparent ongoing reduction in severe gastroenteritis which would have resulted in attendance at an ED for emergency medical attention.

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Core genome MLST and SNP typing are congruent as seen within a European *Salmonella* Enteritidis outbreak

Madison Pearce

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Pathogens theme

Background

Salmonella enterica serovar Enteritidis is the largest cause of human *Salmonella* infection globally. In 2014 over 350 cases were reported in a large, egg associated, multi-country outbreak of Enteritidis. The outbreak size and complexity and available information of where and when isolates were sourced made it ideal for a comparative analysis of SNPs approaches and novel cgMLST methods.

Materials & Methods

The cgMLST profiles were identified using the Enterobase scheme, these profiles were compared with SNPs and wgMLST using statistical and visual approaches. The spread of the outbreak was analysed via contract tracing and then by plotting the locational and temporal distribution of isolates onto minimal spanning trees generated using cgMLST. Finally, it was possible to put the outbreak into the wider context of Enteritidis as a whole, using cgMLST and a visual comparison was again possible using minimal spanning trees.

Results

This study showed that cgMLST was largely congruent with both SNPs and wgMLST. Analysis of contact tracing found no relationship between wholesalers and restaurants, suggesting diversity was generated at the source. There was no relationship between cgMLST clustering and country of origin. However, when compared temporally, isolates outside the outbreak period clustered separately and bacterial strains appear to replace each other over the course of the outbreak, this is supported by the epidemiology. Placing the outbreak into wider context showed a unique cluster within Enteritidis.

Discussion

As food from a single source is supplied to more countries, global collaboration becomes increasingly necessary to identify the source and spread of an outbreak. While SNPs are capable of fine typing they are difficult to standardise, whereas cgMLST remains constant over time, can be accessed globally and allows users to place isolates into a wider context. Combined these points make cgMLST ideal as an international surveillance scheme.

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Combating *Clostridium difficile* infection through the use of faecal microbiota transplantation

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Postdoctoral Researcher

The Microbiome theme

The incidence and severity of *Clostridium difficile* infection (CDI) is increasing, and the current treatment through the use of antibiotics can be expensive with no guarantee of success. Considering the global problem of increasing occurrences of antibiotic-resistant bacteria, faecal microbiota transplants (FMT) offer a cheaper treatment without the need for long-term antibiotic use. In conjunction with the Norfolk and Norwich University hospital, we are currently studying the effectiveness of FMT to treat patients with recurrent/refractory CDI, and how the bacterial community and metabolomic profiles may differ in faecal samples collected from the patients pre- and post-FMT treatment.

Donors provide faecal and blood samples, which are screened extensively for potentially pathogenic bacteria, parasites, viruses, and transmissible diseases prior to acceptance onto the study. Using sterilized study-specific equipment, fresh faecal samples are homogenized in sterile saline, and loaded into sterile syringes before being transported directly to the hospital. The faecal slurry is administered to the patient by the medical staff via a nasojejunal tube. Faecal samples are collected from the patient prior to the procedure, and within 1-2 weeks and 3-6 months after the procedure for 16S rRNA gene and ¹H NMR analysis.

To date, we have performed 21 FMT procedures with a 90.48% success rate, as determined as cessation of symptoms and a negative *C. difficile* toxin screen. The study is still running, however a subset of 22 donor and patient faecal samples have undergone Illumina paired-end sequencing of the 16S gene, and ¹H NMR, and are currently being analysed. These datasets will be interrogated in order to examine whether the presence of certain bacteria or metabolites can be indicative of a healthy gastrointestinal profile, which may lead to an improvement in treatments for CDI sufferers.

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Re-assessing the total burden of norovirus circulating in the United Kingdom population

Dr John Harris

Lecturer in Health Protection

Norovirus is recognised as the commonest cause of gastrointestinal disease in all age groups worldwide. Surveillance of norovirus disease is challenging, the majority of cases will experience a mild self-limiting illness and are unlikely to contact medical services for a diagnosis. Furthermore, during a medical attendance it unlikely a sample will be taken for diagnosis. The second Infectious Intestinal Diseases study (IID2) estimated the incidence of norovirus in the UK at 47/1000 population, which equates to around three million cases a year, at a cost to cases and the health service of between £63-£106 million. The estimates from the IID2 study, one of only two large population based cohort studies that provide disease estimates derived from detection of norovirus in stool samples using Polymerase Chain Reaction (PCR), norovirus was determined with a cycle threshold (ct) value of 30 or less; a more stringent cut-off than used in diagnostic laboratories. Norovirus can be detected in stool samples above this ct value but are more likely to be representative of asymptomatic carriage or sub-clinical illness. The low infectious dose of norovirus means asymptomatic individuals potentially contribute to ongoing transmission. Using a less stringent but clinically relevant diagnostic threshold increases the estimation of the population burden of norovirus infection by around 26% to 59/1000 person years (95% CI 52.32 - 64.98), equating to 3.7 million norovirus infections annually (3.3 – 4.1 million). With possible vaccines on the horizon for norovirus, having a good estimate of the total burden of norovirus infection, as well as symptomatic disease will be useful in helping to guide vaccination policy when candidate vaccines become available

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POSTER ABSTRACTS



1

Relationship between socioeconomic status and gastrointestinal infections in developed countries: A systematic review and meta-analysis

Natalie Adams and
Tanith Rose

PhD Students

People theme

Background

The association between socioeconomic status (SES) and health is well-documented; however limited evidence on the relationship between SES and gastrointestinal (GI) infections exists, with published studies producing conflicting results. This systematic review aims to assess the association between SES and risk of GI infection, exploring possible sources of heterogeneity in effect estimates reported in the literature.

Methods

MEDLINE (Ovid), Scopus and Web of Science and grey literature were searched from 1980 to October 2015 for observational studies reporting a quantitative association between GI infections and SES in a representative population sample from a member-country of the Organisation for Economic Co-operation and Development (OECD). Harvest plots were created for comparison where heterogeneity between studies was high, stratified by age; level of SES variable; GI measurement; and predominant mode of transmission. Meta-analysis was performed on a subset of data.

Results

6,021 studies were identified; 102 met the inclusion criteria. Overall risk of GI infection for low versus high SES was 1.06 (95%CI 0.95-1.19). For children, risk of GI infection was significantly higher for those of low SES versus high (RR 1.51, 95% CI 1.26-1.83), but there was no significant difference for adults (RR 0.84, 95% CI 0.62-1.12).

Conclusions

Disadvantaged children, but not adults, appear to have greater risk of GI infection compared to their more advantaged counterparts. Increased risk may relate to different exposures, risk factors or healthcare-seeking behaviours. Gaining further insight into this relationship will help to inform policies to reduce inequalities in GI illness in children.

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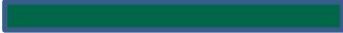
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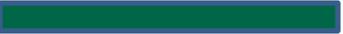
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Retrospective genomic analyses of *Campylobacter* isolates to investigate long-term trends in human campylobacteriosis in the UK


Clare Barker
PhD Student
Pathogens theme

Campylobacter is the leading cause of gastroenteritis in the United Kingdom, with an estimated 280,000 cases each year. Confirmed isolates belonging to outbreaks and single cases of infection are received by Public Health England for typing and antibiotic susceptibility testing, and are subsequently archived. This project has examined a selection of these archived isolates through the use of whole genome sequencing (WGS) and genomics, bringing new insights into past outbreaks and exploring how isolates have changed over time.

One collection of archived *Campylobacter jejuni* isolates, belonging to the same immunocompromised patient and covering 15 years of recurrent infection, was sequenced. Genomic analysis was then used to enable a detailed, long-term view of microevolution of this single strain within its human host. Genetic mutations predicted to confer antibiotic resistance were seen to be gained and lost over time. These predictions based on the sequenced genomes were supported by laboratory testing. This research reinforces how useful WGS can be in diagnosing and aiding treatment of resistant bacterial infections.

A large number of historic *Campylobacter* outbreak isolates were sequenced in order to explore how WGS could have contributed to outbreak analysis at the time, and what the individual genomes reveal about the outbreaks. In many cases, isolates from the suspected source of contamination were sequenced alongside patient isolates, revealing the origins of the outbreaks. Additionally, genetic antibiotic resistance data from the genomes were compared to phenotypic data from laboratory resistance testing. This analysis displays how powerful the use of WGS can be in public health microbiology, particularly during outbreaks.

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Place–Based case studies: Understanding how the local context and environment influences differential exposure, differential vulnerability and differential social, economic and health care consequences of GI infection

Dr Rachael Eastham and
Dr Alexandra Kaley

Postdoctoral Researchers

People theme

Background

The relationship between deprivation and GI infection is not well understood, with literature highlighting conflicting results. Despite limited evidence, extant studies suggest that trends differ between adults and children, with children in more deprived areas having higher risk of infection and hospitalisation. Further work is needed to understand ways in which interactions within the domestic and public social context increase risk of GI.

Aims

To deliver an in-depth understanding of GI infection within the wider social context and within households; and to characterise how these factors influence outcomes for communities living in the North West of England.

Methodology

Using qualitative participatory techniques, we interviewed parents with children aged 0-11 to explore how the material, social and cultural environment (place) influence the consequences of GI infection for families. As part of the interview, study participants undertook an activity using graphic/photo elicitation techniques. A thematic analysis will be carried out on the multiple forms of data for each participant. The final set of themes identified shall be drawn from topics that occurred through the workshop exercise, qualitative interviews and theoretical ideas from the literature review.

Results

Data collection is currently underway and preliminary results will be presented at the scientific meeting. 10 semi-structured interviews have been undertaken out of a minimum of 20 which are expected to be completed by Jan 2017. Thus a range of narrative and visual data will be presented.

Conclusion

Qualitative research allows us to elicit lived experience and the way in which people relate to places and the resources that are available to them locally; this is not a facet of GI infection that has been previously captured. This is important because if we want to reduce the burden of GI infection then we need to design interventions that accurately reflect the reality of people's lives.

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Application of metagenomics and metabolomics for the diagnosis of gastroenteritis

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PhD Student

The Microbiome theme

Despite a decline in associated mortality, infectious intestinal diseases (IID) and their potential long-term adverse consequences remain a major healthcare problem even in industrialised countries. Routinely used diagnostic methods often are time-consuming and require isolation of pathogens from faecal matter prior to identification. Even the most advanced, rapid approaches fail to detect an aetiological agent of IID in 40% of cases referred for laboratory diagnostics. Improved diagnostics, allowing more targeted treatment, would be greatly beneficial, especially in cases of recurrent, prolonged and severe disease or for patients with underlying co-morbidities.

There is huge potential in exploiting recent advances in –omics technologies in this context and therefore we aim to establish two integrated pipelines based on metagenomic and metabolomic profiling as a novel approach to routine diagnostics of gastroenteritis directly from the stool samples provided. We will make use of clinical faecal samples obtained by Norfolk and Norwich University Hospital from patients presenting with symptoms of gastroenteritis. DNA extracted from these samples will be analysed using 16S rRNA gene and shotgun sequencing and bioinformatics tools will be employed to identify pathogens and changes in microbiota composition associated with a specific infection. Furthermore, ¹H NMR spectroscopy will be performed on faecal water extracts from the same samples to detect changes in metabolite profiles related to the presence of certain pathogens. Finally, we will correlate the profiles obtained and assess the feasibility of using the pipelines in a clinical diagnostic setting and their performance in comparison to the techniques used routinely.

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Comparison of MLST, rMLST and wgMLST as global typing schemes for *S. Enterica*

Madison Pearce

PhD Student

Pathogens theme

Background

Salmonella enterica (*S. enterica*) is a zoonotic, foodborne pathogen responsible for millions of cases of acute gastrointestinal disease worldwide, each year. MultiLocus Sequence Typing (MLST) compares sequence similarity across 7 housekeeping genes; ribosomal MLST (rMLST) compares sequence similarity across a maximum of 53 ribosomal genes, whilst whole genome MLST (wgMLST) compares a dataset against an entire reference genome. These varying levels of gene coverage were compared and the utility of each approach, as a global typing scheme for *S. enterica*, was assessed.

Materials | Method

Pairwise comparisons were used to analyse various sets of isolates, from pubMLST's BIGSdb, at all three levels of genetic discrimination and to generate trees and nets using the built-in Genome Comparator tool. These datasets were chosen for depth and variety: an example of every serovar of *S. enterica* found within BIGSdb was used, to ensure that serovars formed distinct genetic lineages; Enteritidis, Gallinarum and Pullorum isolates were used to analyse closely related serovars; Newport isolates were used to examine antigenically identical isolates; and isolates from the phylogenetic grouping lineage 3 were used to analyse a genetically complex group.

Results

Comparisons showed that in general MLST, rMLST and wgMLST all distinguished serovars and previously identified phylogenetic groupings with high congruence. The wgMLST analyses took 24 – 96 hours to perform (compared to 3 – 20 minutes for rMLST) but showed the highest level of resolution. The neighbornets illustrated that possible genetic relationships decreased as number of genes increased. Analyses of serovars within subspecies one, indicated a relatively high level of recombination and horizontal gene transfer.

Conclusion

rMLST for *Salmonella enterica* provides greater discrimination and resolution between lineages than MLST, while taking significantly less time to perform than wgMLST. Furthermore, these results show high congruence between the three methodologies, suggesting high compatibility and scalability for future analyses

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How are the management and consequences of gastrointestinal infections shaped in the context of households with young children in differing socio-economic and geographical locales?

Suzanne Rotheram

PhD Student

People theme

Background

Gastrointestinal infections are an important cause of UK morbidity with approximately 25% of the population having at least one episode each year.

The patterning of socio-economic inequalities in gastrointestinal infections in high income countries is under-researched and has previously shown inconclusive patterns. Recent research suggests that while more affluent populations have higher reported rates of infection, the consequences of infection are greater in more deprived populations. This inequality is particularly evident in children under five living in areas of deprivation in the United Kingdom who are twice as likely as their more affluent counterparts to be admitted to hospital as a result of a gastrointestinal infection.

This presentation will outline plans for a PhD to examine why socio-economic and geographical differences might shape the uneven distribution of these consequences. It will do this by examining the management and consequences of gastrointestinal infections in households with children under five.

Methods

This presentation will outline plans for a PhD that incorporates multiple methods, data and analyses to provide a greater understanding of how broader policies, social, economic and environmental factors might interact to produce inequalities in this disease.

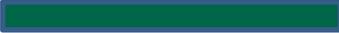
An ethnographic approach will incorporate a systematic review, observational fieldwork, narrative and ethnographic interviews, geographic information systems (GIS) mapping and geo-ethnography. These methods will be used in two socio-economically contrasting locales to examine how and why the physical and social environment might influence the management and consequences of gastrointestinal infections. Interviews and observations across different settings (households and community) and with different parties (household and community) will provide a multi-faceted understanding of inequalities in these infections.

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