Institution: Lancaster University

Unit of Assessment: UoA 10: Mathematical Sciences

Title of case study:
Accurate statistical methods for detecting the source of human campylobacteriosis cases in New Zealand leads to an annual reduction of around 90,000 cases per year.

1. Summary of the impact (indicative maximum 100 words)

Research at Lancaster led to a novel approach to detect the source of cases of campylobacteriosis (a bacterial foodborne disease). The application of this method to data from New Zealand pin-pointed that New-Zealand's high rate of cases was linked to the eating of contaminated poultry. These results were a key part of the evidence used by New Zealand's Food Safety Authority to introduce a new code of practice for the poultry industry. The impact of this code of practice has been a halving of the number of reported cases of campylobacteriosis in New Zealand (from around 16,000 cases in 2006 to less than 7,000 in 2008). With notification rates estimated as 1 in 10, this corresponds to around 90,000 fewer actual cases per year. The saving for the New Zealand economy during the REF census period has been independently estimated as between £100M and £150M.

2. Underpinning research (indicative maximum 500 words)

Research Team at Lancaster

The methodological research was led by Wilson, Fearnhead and Diggle as part of a Veterinary Training and Research Initiative grant to Liverpool and Lancaster, funded by DEFRA and HEFCE. Wilson was a PDRA funded by this grant. He was based in the Department of Mathematics and Statistics at Lancaster, and was supervised by Fearnhead.

Methodological Research (2005-2007)

The underpinning research involved developing a new method for detecting the source of human cases of campylobacteriosis, motivated by interest in source detection by collaborators from the Vet School at Liverpool. This method (Wilson et al. 2008) uses as input genetic data of Campylobacter isolates from both human cases and from different potential animal and environmental source populations. Comparing how similar the genetic type of isolates from human cases are to the genetic type of isolates from the different source population enables one to estimate the relative contribution of each source to the total number of human cases. The key to doing this accurately is obtaining good estimates of the population frequency of different genetic types in each of the animal and environmental sources, which requires a form of density estimation over the high-dimensional space of possible genetic types. The novelty of our method was in constructing a model-based approach to the density estimation, using tractable approximations to well-developed population genetic models. This builds on earlier work developing similar approximations for estimating recombination (Fearnhead and Donnelly 2001, Li and Stephens 2003). The final method is substantially more accurate than cruder alternatives, which often have to throw away information in the data.

Application to New Zealand Data (2007)

During 2007, this method was applied to data from New Zealand, in collaboration with Nigel French's veterinary epidemiologist group at Massey University, New Zealand. This collaboration came out of close links between Lancaster and Massey, with French aware at an early stage of our research on detecting the source of human campylobacteriosis cases, a problem his group were also interested in. Lancaster supported this application of the research, with Wilson collaborating directly in the research of the group in New Zealand. Wilson was the sole statistical geneticist involved in this research, applying the method developed at Lancaster to analyse the data. The results of this analysis appeared later in Mullner et al (2009). This work was carried out while

Wilson was at Lancaster, but the paper was published later, after Wilson had moved to Chicago.

Results of Source Attribution in New Zealand

The results of the analysis showed that ~75% of human campylobacter cases in New Zealand were due to poultry sources. This was a much higher proportion than for other developed countries. In 2006 New Zealand had the highest rate of Campylobacteriosis cases in the developed world. The results from the source attribution were evidence that poor standards in the poultry industry were responsible for this high rate of Campylobacteriosis cases in New Zealand.

The importance of the methodological work developed at Lancaster, and of the input of Wilson to the analysis of the New Zealand data, is attested to by Nigel French. In a letter of support, he states "*Source attribution models developed by Dr Wilson […] helped us to identify that poultry, and one particular supplier, was responsible for the majority of human cases in our sentinel site. The highly cited paper published by Dr Wilson [et al.] in 2008 in PloS Genetics provided a new tool that could be applied to multilocus sequence typing data in New Zealand. He made the models readily available to us and was a highly effective collaborator, enabling us to rapidly adopt the method and communicate the findings to the New Zealand Food Safety Authority. Informed by the model outputs, the Campylobacter risk management policy was developed and implemented, and the public health response was rapid. The models provided the most convincing evidence to date of the importance of poultry as a source infection, enabling interventions to be mandated.*"

3. References to the research (indicative maximum of six references)

Key References

Mullner, Spencer, Wilson, Jones, Noble, Midwinter, Collins-Emerson, Carter, Hathaway and French (2009) Assigning the source of human campylobacteriosis in New Zealand: A comparative genetic and epidemiological approach. *Infection, Genetics and Evolution.* 9(6) 1311-1319 doi:10.1016/j.meegid.2009.09.0003

Wilson, Gabriel, Leatherbarrow, Cheesbrough, Gee, Bolton, Fox, Fearnhead, Hart and Diggle (2008) Tracing the source of campylobacteriosis. PLoS Genetics 4(9):e1000203. doi:10.1371/journal.pgen.1000203

Other References

Li and Stephens (2003) Modeling Linkage Disequilibrium and Identifying Recombination Hotspots Using Single-Nucleotide Polymorphism Data. Genetics, 165(4), 2213-2233.

Fearnhead and Donnelly (2001) Estimating recombination rates from population genetic data. Genetics 159: 1299–1318.

4. Details of the impact (indicative maximum 750 words)

Background

Campylobacteriosis is the most common cause of human bacterial gastroenteritis in the developed world. In most cases the effect on humans is limited to fever, diarrhoea, and abdominal pain, with the illness lasting between 2 and 10 days. However more serious complications, including occasional deaths, can occur, particularly in young babies and the elderly. The mortality rate has been estimated as 0.1% of reported cases.

Introduction of Code of Practice for the New Zealand Poultry Industry (Oct 2007)

The New Zealand Food Safety Authority (NZFSA) has close links with French's group at Massey, and both they and the poultry industry were made aware of the findings of the joint Massey-

Lancaster research on source attribution as they were happening. The research led to public health professionals advocating more rigorous controls on foodborne pathways of campylobacteriosis, particularly for poultry, and in turn to the introduction of a new code of practice for the poultry industry.

Impact of the Code of Practice (Nov 2007 onwards)

This code of practice rapidly led to over a 50 percent reduction in the number of reported cases of campylobacter infection caused by food (from roughly 17,000 cases in 2006 to 8,000 in 2008 with an initial reduction noted as early as November 2007). This has been maintained to the present data. With notification rates often estimated at around 1 in 10 (Duncan 2011), this corresponds to around 90,000 fewer actual cases per year, and given estimated mortality rates, to a saving of about 50 lives during the census period.

The annual economic saving, including direct health costs and loss of output, has been estimated to be in the region of NZ$36M (http://www.foodsafety.govt.nz/elibrary/industry/Zealand_Leads-Efforts_Drastically.htm) to NZ$50M (Duncan 2011). Over the REF census period this corresponds to a total saving in region of £100M to £150M.

The method for source attribution is still used in New Zealand to monitor the effectiveness of the change of policy in an ongoing surveillance programme (French 2013).

Evidence of the Role of the Underpinning Research on Impact

The role the underpinning research had on the introduction of the new code of practice is evidenced by a number of sources. Firstly, Mullner et al. (2009) state "*The evidence provided by our approach has supported national policy making by providing an important contribution to the NZFSA Campylobacter Risk Management Strategy*". The introduction to the NZFSA Campylobacter Risk Management Strategy states "*It has been scientifically established that poultry meat is a primary exposure pathway in New Zealand*", a conclusion that comes from the Massey-Lancaster research. And this fact is used to motivate the resulting strategy for reducing campylobacter levels in poultry.

Two editorials (Dixon 2009a,b) also highlight that the Massey-Lancaster research led by French, and in particular that the use of the modelling methodology of Wilson, was central to change in policy. For example, Dixon 2009b states that this "*modelling methodology provided the clinching evidence to influence an industry highly resistant to any suggestions that chickens were the major source of campylobacteriosis in the country*." Dixon (2009a) adds *"..in New Zealand .... cases of campylobacteriosis have halved over the past year. This has been done by the adoption of new hygiene measures by a poultry industry initially hostile to the idea that it was the major source of the problem – after their necessity had been established by sophisticated computer modelling of the infection.*" A recent presentation at the NZAE Annual Conference (Duncan 2011) also states "*It was this study conducted by Massey University for NZFSA … that motivated the poultry industry to begin investing to reduce the Campylobacter loading on product for sale for human consumption.*"

The work of the group at Massey, to which Wilson contributed, is cited in NZFSA reports on risk management strategies for campylobacter. (For example, French 2009 is cited by in the NZFSA's Campylobacter Risk Management Strategies 2010-2013). French himself writes that "*The contribution to public health made by Dr Wilson and colleagues at Lancaster University should not be underestimated."*

5. Sources to corroborate the impact (indicative maximum of 10 references)

Dixon (2009a) Editorial, The Lancet Infectious Diseases, 9, p.527.

Dixon (2009b) Editorial, Microbe, 4, p.394-395.

French (2009) Enhancing Surveillance of Potentially Foodborne Enteric Diseases in New Zealand:

Human Campylobacteriosis in the Manawatu: Project extension incorporating additional poultry sources. Final Report FDI /236/2005. http://www.foodsafety.govt.nz/elibrary/industry/enhancing-surveillance-potentially-research-projects/finalreportducketc2009.pdf

Mullner P, Spencer S.E.F, Wilson D.J, Jones G, Noble A.D., Midwinter A.C., Collins-Emerson J.M., Carter P., Hathaway S. and French N.P. (2009) Assigning the source of human campylobacteriosis in New Zealand: A comparative genetic and epidemiological approach. Infection, Genetics and Evolution. 9(6) p. 1311-1319.

Duncan (2011) Food safety in the poultry industry: An estimate of the health benefits. 52nd NZAE Annual Conference.

Letter of Support from the Director, mEpiLab, Institute of Veterinary, Animal and Biomedical Sciences, Massey University, New Zealand.

Campylobacter Risk Management Strategies 2008-2011, NZFSA.

Articles detailing the reduction in cases, and resulting economic savings:
http://www.foodsafety.govt.nz/elibrary/industry/Zealand_Leads-Efforts_Drastically.htm

Data on reduction of human campylobacter cases appears in:
Campylobacter Risk Management Strategies 2013-2014, NZFSA, (Figure 2, page 10)
http://www.foodsafety.govt.nz/elibrary/industry/Campylobacter_Risk-Comprehensive_Aimed.pdf

The economic savings are also reported in
http://foodsafety.govt.nz/elibrary/industry/economic-cost-foodborne-disease/sis.pdf