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A nested environmental approach to typhoid epidemiology in Central Division, Fiji

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A nested environmental approach to typhoid epidemiology in Central Division, Fiji

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A nested environmental approach to typhoid epidemiology in Central Division, Fiji

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i) Declaration

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ii) Thesis Abstract

Many current disease threats involve interactions within and between nested subsystems of biological organisation. Typhoid fever is a serious disease threat in the South Pacific region, with Fiji reporting the highest annual number of cases, yet risk factors in this setting have been poorly studied. While localised behaviours have dominated perspectives on typhoid transmission, interactions between distal ecological conditions, conditions of the residential environment and localised behaviour deserve greater attention for their potential to influence transmission. This thesis demonstrates a nested approach to typhoid epidemiology using a fivefold methodology to explore how regional, river basin, residential, socio-cultural and behavioural subsystems influence the risk of typhoid transmission in Central Division, Fiji, whereby I: (1) provide a regionally specific literature review examining health consequences of wetland ecosystem service interruption associated with common natural disasters; (2) use quantitative geospatial analysis to evaluate relationships between sub-catchment environmental characteristics and typhoid incidence and recurrence; (3) use a case-control design at a residential level to investigate bacterial contamination and chemical composition of water and soil as vehicles of exposure, complemented with observational analysis of living conditions, spatial analysis of household position and factor analysis to explore multivariate relationships influencing typhoid risk; (4) question 160 typhoid fever cases and 319 control subjects to reveal risky socio-cultural and behavioural practices and; (5) synthesize significant risk factors within and across nested subsystems and test several intervention scenarios using a Bayesian Network approach.

Regional typhoid burden is influenced by climate change induced warming, altered rainfall patterns, increased storm severity and rising seas, coupled with population growth, slow economic growth, urbanisation, environmental change and limited capacity for adaptive management. The most parsimonious models for incidence and recurrence at the sub-catchment scale included total high soil-erosion risk area, percentage area that was highly erodible, connectivity between road and river networks and riparian forest fragmentation as predictor variables. In the residential setting, five factors, related to drainage, housing and condition of water and sanitation were significant in predicting typhoid. Multivariate analysis of household questionnaires indicated the following significant risk factors for typhoid fever: using an unimproved pit latrine, not washing produce (i.e. fruit or vegetables) or hands before eating, bathing outside, water not always accessible, having sand/wood plank floors and attending mass gatherings. The above results suggest that anthropogenic alteration of land cover and hydrology in river basin and residential systems increases risk of exposure where sediment increases following runoff. Localised socio-cultural and behavioural subsystems interact with residential and river basin subsystems to enhance risk of typhoid transmission. Bayesian network analysis suggests combined interventions within a subsystem provides greater exposure reduction than the sum of individual interventions and simultaneous interventions on select risk factors, across multiple nested subsystems, provides greater exposure reduction than elimination of risk factors in any one subsystem. A nested epidemiological approach to studying and interrupting waterborne disease transmission extends the testing of causal assumptions beyond the domestic domain, enhances traditional case-control approaches and provides evidence for multi-scale interventions on both distal and proximal drivers of disease and environmental degradation.

iii) Acknowledgements

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List of Acronyms

ABM	Australian Bureau of Meteorology
ADB	Asian Development Bank
AIC	Akaike Information Criterion
AusAid	Australian Agency for International Development

BCE	Before Common Era
BN	Bayesian Network
CARE	Cooperative for Assistance and Relief Everywhere
CFU	Colony-Forming Unit
CPT	Conditional Probability Table
CSIRO	Commonwealth Science and Industrial Research Organisation
CWMH	Colonial War Memorial Hospital
dbRDA	Distance-based Redundancy Analysis
DISTLM	Distance-based Linear Models
DOE	Department of Environment
DOF	Department of Forestry
DTM	Digital Terrain Model
ECU	Edith Cowan University
EFA	Exploratory Factor Analysis
EHO	Environmental Health Officer
EM	Expectation Maximization
ESRI	Environmental Systems Research Institute
ETM	Enhanced Thematic Mapper
FCCDC	Fiji Centre for Communicable Disease Control
FMOH	Fiji Ministry of Health
FNHRC	Fiji National Health Research Committee
GDP	Gross Domestic Product
GIS	Geographical Information System
GOF	Government of Fiji
GPS	Global Positioning System
IAEH	International Association for Ecology and Health
IIM	Integrated Island Management
IFPRI	International Food Policy Research Institute
IFRC	International Federation of Red Cross and Red Crescent Societies
IPCC	Intergovernmental Panel on Climate Change
LIM	Lysine Indole Motility
LUC	Land Use Categories
MEA	Millennium Ecosystem Assessment
MoHMS	Ministry of Health and Medical Services
MPN	Most Probable Number
MU	Melbourne University

NIWA	National Institute of Water and Atmospheric Research, Ltd (New Zealand)
NG	National Government
NGO	Non-Government Organization
NTCOPD	National Taskforce on Communicable and Outbreak Prone Diseases
OED	Oxford English Dictionary
OR	Odds Ratio
PCO	Principal Coordinate Ordination
PCR	Polymerase Chain Reaction
PDRRDMF	Pacific Disaster Risk Reduction and Disaster Management Framework
PEDRR	Partnership for Environment and Disaster Risk Reduction
PERMANOVA	Permutational Multivariate Analysis of Variance
PRIMER	Plymouth Routines in Multivariate Ecological Research
PTSD	Post-Traumatic Stress Disorder
RBZ	Riparian Buffer Zone
RFU	Relative Fluorescence Units
RMI	Republic of the Marshall Islands
rtPCR	Real Time Polymerase Chain Reaction
SD	Standard Deviation
SDOH	Samoan Department of Health
SIDS	Small Island Developing States
SRDP	Strategy for Disaster and Climate Resilient Development in the Pacific
TSI	Triple Sugar Iron
UN	United Nations
UNDP	United Nations Development Program
UNEP	United Nations Environment Program
UNICEF	United Nations Children's Fund
UNISDR	United Nations International Strategy for Disaster Reduction
ViPS	Vaccine Injectable Polysaccharide
WASH	Water Sanitation and Hygiene
WHO	World Health Organization
WHO-DPS	WHO-Division of Pacific Technical Support

CHAPTER 1. General Introduction

"Shape clay into a vessel; It is the space within that makes it useful."

Lao Tzu quoted in Max-Neef 2005

Daily around 2 billion people use a drinking-water source contaminated with faeces and live without adequate sanitation (UN and WHO 2015). Over a million people die each year from water-related diseases, at least 50% of these deaths are children and attributable to microbial intestinal infections (Kovacs et al. 2015). Economic losses associated with these infections are conservatively estimated at 12 billion US dollars per year, a cost disproportionately borne by the poorest countries (Alhamlan et al. 2015). Climate and landscape changes are predictably exacerbating the threat of infection and economic loss, with some regions becoming more arid while others suffer more frequent and consequential flooding (Barrett et al. 2015). The unavailability of potable water and adequate sanitation continues to play a central role in the transmission of waterborne microbial pathogens and underlies several of the most persistent blights on humanity. A focussed effort to improve stewardship of water resources, sanitation and hygiene can prevent about 10% of the global burden of disease (Prüss-Üstün et al. 2008).

Our most important health and sustainability problems will not be solved by reductionist approaches to public health, conservation and infrastructure development. These important disciplines often combat infectious diseases, biodiversity loss and can improve drinking water quality through reactive, non-intersecting lenses, with singular focus on particular pathogens, species or contaminants. The solutions to critical sustainability problems lie not in controlling the microbe or manatee *per se,* but in the development of interdisciplinary systems thinking, focussing investigation on the interacting processes that drive seemingly disparate problems. A clear and dedicated focus on understanding system complexity can guide improved efficiency of interventions to synchronously reduce burden of disease while improving the quality of habitable space. Re-examining history and broadening the focus of contemporary study of water related diseases, their ecological settings and the interventions to control them can help us understand how interdisciplinary systems approaches can yield elegant, sustainable solutions to our greatest afflictions.

1.1 *Systems approaches*

There is innate understanding that the health of humankind relies on natural systems to provide clean water, nutrition, natural hazard reduction and regulation of infectious disease, among other crucial ecosystem services (MEA 2005). Indigenous cultures, such as Aboriginal and Torres Strait islanders, organised socio-cultural systems along these principles, defining the word "health" as harmony between life and land (Mills 2000). The Greek physician Hippocrates published this notion of human health and ecosystems being contextually and mutually dependent around 2600 years ago (Hippocrates 400 BCE, in 1983 translation). While innately understood, developing an empirical understanding of these relationships is complex and requires interdisciplinary systems approaches to scientific inquiry (Horwitz and Finlayson 2011).

A system can be defined by interrelated components that function together within a defined and explicit boundary, often to advance a common purpose, while a subsystem is a system itself, nested within a larger system (Batterman et al. 2009). The interdisciplinary field of systems science is conceptually grounded in understanding "interrelationships between parts and their relationships to a functioning whole" and improving clarity around system boundaries and their relationships (Trochim et al. 2006). System science seeks to study the often non-linear and dynamic relationships between complex networks of subsystems which create a whole greater than the sum of the parts. Systems scholars contend that whole-system characteristics manifestly 'emerge', through processes of collective self-organisation, adaptation and co-evolution, that cannot be understood from study of individual components (Gu et al. 2009).

Empirical evidence from the study of physical and biological systems, in particular, has revealed emergent and self-organising properties from molecular (Westerhoff and Palsson 2004) to social scales (Luhmann 1995). Recent studies of urban systems offer additional insight into systems behaviour, with cities displaying complex nested coevolution through natural systems, infrastructure, technologies and institutions (Chapman et al. 2016). The study of systems complexity is itself evolving, as multiple disciplines and research streams overlap to form a shared philosophical viewpoint, striving to revise the seeming traditional scientific bias towards reductionism (Chungtai and Blanchet 2017). While systems thinking is usually practised in ecology, it is also highly relevant to the applied field of public health with its historical focus on complex social-scale interventions. The public health literature generally reflects a poor understanding of the use and development of the relatively abstract ideas surrounding the field of systems thinking (Chungtai and Blanchet 2017). Within this field there is clearly a need to identify relevant and applicable interdisciplinary research methods to study complex, system-level environmental determinants of health.

1.2 *Harkening to epidemiological origins*

The notion of a geographically defined subsystem as a determinant of infectious disease has been foundational to public health intervention since John Snow used an environmental map to trace the source of a cholera outbreak in London in 1854 (Feingold et al. 2010). This conception shaped the modern field of epidemiology and led to geographically focussed campaigns of sanitation, hygiene, water infrastructure and housing, leading to vast improvements in public health and longevity (Szreter 1988). The great utility of taking a broad systems focus, and intervening upstream of the problem, was apparent even without advances of germ theory to guide reasoning. Twentieth century growth in understanding of microorganisms gradually shifted focus from the environment as a source of disease, narrowing the emphasis of public health to vaccines, antibiotics, pesticides, and barriers to infection (Eisenberg et al. 2007). While these advances have clearly yielded improvements to the health of humankind, the past several decades have produced a growing body of literature calling for a return to less reductionist origins of public health by re-examining the role of environmental change in infectious disease (Daily and Ehrlich 1996; McMichael 1997; Patz et al. 2004; Eisenberg et al. 2007; Feingold et al. 2010; Remais and Eisenberg 2012) and more broadly for interdisciplinary systems research to guide sustainable development (Weiss and McMichael 2004; Wilcox and Colwell 2005; Corvalan et al. 2005; Parkes et al. 2005, Charron 2012). Ensuring accessibility to potable water and sanitation are among the greatest sustainable development challenges and a major intersection point for the study of environmental change and infectious disease transmission.

1.3 *Typhoid fever*

A persistent blight at this intersection of environmental change and public health is Typhoid fever, an exclusively human, faeco-orally transmitted, systemic disease caused by infection with the bacterium *Salmonella enterica subspecies enterica* serovar Typhi (*S.* Typhi). Typhoid causes an estimated 21 million cases and 223,000 deaths annually, primarily in south Asia and sub-Saharan Africa (Mogasale et al. 2014). While largely controlled in the affluent world, typhoid remains a serious public health issue in much of the developing world, particularly in low income, high-density settings. Also, from 2 to 5 percent of Typhoid fever sufferers will remain long-term asymptomatic "carriers" and excrete the pathogen into the environment from their stool and urine for years (Baker et al. 2011; Watson and Edmunds, 2015). The delivery of potable water, adequate sanitation infrastructure and hygiene promotion (WASH) remain the foundations of typhoid prevention and control, while vaccination is also recommended by WHO for use in endemic and epidemic settings (WHO 2008). Despite a continued history as one of the major water related plagues, much is still unknown about the biology of this bacterial pathogen and the complexity of the disease in endemic areas (Wain et al. 2015).

Our current understanding of *S.* Typhi transmission recognises humans as the only known reservoir and individuals with acute typhoid and carriers as the primary risk for infection to others. Due to a high infectious dose of around 10^4 organisms (Levine et al. 2001), direct transmission of *S.* Typhi without some type of vehicle is thought to be uncommon and has only been rigorously described during oral-anal sexual practices (Reller et al. 2003). Indirect transmission involving vehicles is understood to be the most common form and is further subdivided into "short-cycle" and "long cycle" transmission (González-Guzmán 1989). "Short-cycle" transmission occurs when a household member excreting *S.* Typhi contaminates food or water leading to local transmission, often within the same household. "Long cycle" transmission occurs when infected human faeces or urine makes its way into environmental reservoirs such as water sources or food production systems and infects people through these vehicles. The relative contribution of carriers versus those with acute typhoid to transmission pathways is still poorly understood and context dependent (Saul et al. 2013) and the notion that particular ecological settings could act as sites of carriage has yet to be seriously explored.

1.4 *Typhoid models and epidemiological studies*

The models used for policymaking and economic evaluation of intervention strategies require local parameterisation to determine the relative risk of short and long cycle transmission and the contribution of carriage within that particular setting (Watson and Edmunds, 2015). Few studies have been comprehensive in quantifying the distinctive parameters involved in disease transmission and modellers continue to lack crucial elements such as: mean duration of carriers, mean life of bacteria in the environment and the proportion of short versus long cycle transmission (González-Guzmán 1989; Saul et al. 2013; Pitzer et al. 2014). Even the usefulness of this short versus long cycle dichotomy has not been sufficiently explored from a multi-scalar ecological perspective, where spatial, temporal and organisational system boundaries surrounding the disease are explicitly defined and investigated. Short-cycle transmission could be more clearly ecologically defined as a proximal subsystem relating to an individual person or household, a particular downstream location or occurring over a short duration of time. Whereas long cycle transmission could be characterized as a distal subsystem that manifests at the population or ecosystem level, has upstream origins and acts over the longer term.

At an individual or household level, the classic epidemiological approach of a case-control study is by far the most widely used technique for assessing typhoid risk and testing causal hypotheses (Black et al. 1985; Luby et al. 1998; Vollard et al. 2004; Karkey et al. 2013). In various settings, differential risk is attributed to a multitude of factors, most commonly related to poor food and water hygiene, poor sanitation, low socio-economic status and crowding. A comprehensive review of typhoid case-control studies, including the identified risk factors and suggested interventions to reduce disease, between 1985 and 2016, is presented in Chapter 5. Case-control studies assess the proximal subsystem, though very few simultaneously test potential vehicles of exposure for their physicochemical characteristics, amount of faecal contamination or even for *S.* Typhi specifically (Baker et al. 2011). This broader investigatory approach can both verify and quantify the characteristics of the exposure routes implied by a matching case-control study. While investigating the proximal subsystem is important for questions related primarily to short-cycle transmission or shorter duration outbreaks, case-control risk factor analysis is challenged by its capacity to elucidate root causes, such as social or ecological conditions, or examine distal mechanisms (Eisenberg et al. 2007).

A classic example of long cycle transmission was demonstrated by Sears et al. (1984) in Chile, where using a sewer swab technique, *S.* Typhi was isolated from untreated sewage being applied directly to fields where salad vegetables were cultivated. This provided strong support to the hypothesis that crops irrigated with water contaminated with faeces were important vehicles in the transmission of *S.* Typhi across this endemic setting. Recent clear evidence for distal or long cycle transmission comes from the high-incidence, endemic setting of Kathmandu, Nepal (Karkey et al. 2010; Baker et al. 2011). These studies implicate contaminated public waterspouts using a combination of hospital records, geospatial analysis, molecular and microbiological techniques to demonstrate the spatial risk of a specific public setting where both faecal contamination and *S.* Typhi genomes were found in water samples. A small number of recent studies have also used geospatial tools along with hospital records to demonstrate increased risk, within specific administrative boundaries, correlated to variables that imply long cycle transmission such as rainfall, proximity to major water bodies, polluted farmland and canals (Wang et al. 2012, 2013; Corner et al. 2013; Dewan et al. 2013; Akullian et al. 2015). These studies suggest potential mechanisms by which long cycle transmission could occur, however, only one study combines spatial analysis at a distal municipal scale with microbial and molecular analysis at a proximal household scale to strengthen these causal assumptions (Baker et al. 2011). The social and ecological characteristics of these study settings were poorly described and no studies exist that assess the variable risk associated within an ecological or geomorphological defined subsystem such as a river basin.

Contemporary models of transmission also lack crucial parameters to deal with the persistence and fate of viable S. Typhi in the environment (Watson and Edmunds 2015). The most sophisticated models presented by Saul et al. (2013) and Pitzer et al. (2014), make assumptions regarding a degree of seasonality, that there is a single common source of environmental contamination accessible to all members of the community and that persistence of S. Typhi in the environment is short compared to the period of infection in the individual. While seasonality has been demonstrated (WHO 2011; Wang et al. 2012), assumptions regarding persistence are largely untested. S. Typhi are notoriously difficult to culture from environmental samples, however, recent advances in rtPCR are allowing study of potential viable environmental reservoirs (Baker et al. 2011).

Within particularly nutrient rich media (e.g., cheese), and particular saprophytes, S. Typhi can be viable for almost a year (Mitscherlich and Marth, 2012). Early research on the recovery of S. Typhi from clay loam soil has been reported up to 5.5 months (Grancher and Deschamps 1889) and experimental work suggests S. Typhi may multiply and persist in live oysters (Mitscherlich and Marth, 2012). S. Typhi has also been shown to survive for months in contaminated eggs and frozen oysters (Elsarnagawy 1979; Nishio et al. 1981). Viable, but non-culturable S. Typhi can survive in natural groundwater up to a month and in pond water for up to 20 days (Cho and Kim, 1999). Similar survival results of 29 days are demonstrated in distilled water and 0.9% NaCl at room temp (18-24°C) and extended to 65 days in a refrigerator (4-6° C) (Uyanik et al. 2008). In early epidemiological studies, outbreaks of typhoid lasting over a month have been related to specific food items where lipids, sugars and nutrients were readily available for bacterial growth and persistence, such as cheese, chocolate and ice-cream (Cumming 1917; Rich 1923; Vener et al. 1940).

The environment into which S. Typhi is shed and the physicochemical characteristics of these settings is undoubtedly important in determining the persistence of the bacteria outside of the human host. In a proximal subsystem, the nature of handled food or locally contaminated soil may be important. In a more distal subsystem, nutrient-rich runoff from river basins in which forests are cleared for agriculture and fertilised may provide additional growth and survival resources for the bacteria in waterways and saturated soil. There is a clearly a need to examine S. Typhi ecology across multiple subsystems, including estimations of persistence and transport characteristics, transmission pathways and even refining the basic tools to carry out environmental investigations, such as the ability to detect the pathogen in complex environments (Remais and Eisenberg 2012).

1.5 *Prevention and control strategies for typhoid (and other enteric diseases)*

The foundation of typhoid prevention and control interventions is providing potable water, adequate sanitation and promoting hygienic behaviour (WASH). Intervention strategies must balance the immediate versus long-term economic efficiencies of WASH against other currently recommended measures such as improvement of income distribution, identification and management of carriage and vaccination (Levine et al. 1982; Gasem et al. 2001; Sharma et al. 2009; Karkey et al. 2013; Watson and Edmunds 2015). Research on water-related enteric disease intervention and control shifted focus from the individual host to environmentally centered interventions (WASH) in the late 1970's, influenced by the F-diagram of Kawata (1978) who promoted the notion that enteric disease was transmitted through food, flies, fields, fingers, and fluids. Cairncross et al. (1996) further refined this conceptual diagram by introducing group causation, dividing the domestic (household) and public domains into separate transmission groups with differing politics and intervention strategies. Other refinements include studies on the influence of socio-economics (Stanton and Clemens 1987; Yaeger et al. 1991), gender roles (El Azar et al. 2009; Usfar et al. 2010) and geographic location (Jenkins et al. 1989; Eisenberg et al. 2006), introducing more complex, multi-scalar causal frameworks of transmission and potential upstream points of intervention.

Eisenberg et al. (2007) introduced a dynamic feedback version of the F-diagram recognising the interdependencies of multiple transmission pathways and showed how the efficacy of WASH interventions depends on both household and community-level transmission. Although there have been improved research frameworks for enteric disease epidemiology and control, Eisenberg et al. (2012) note the relatively poor emphasis on multiple transmission pathways and their interdependencies and highlight the need to focus the causal lens on socioeconomics, gender, geography and ecosystem changes. Distal scale sociological phenomena such as the flow of migrants from rural to urban centers and ecological considerations such as forest fragmentation, climate change and the impact of flooding frequency have yet to make it into the modern F-diagram. The most recent and sophisticated model of intervention effectiveness suggests that to eliminate typhoid from a mid-to-high-incidence setting, vaccination alone will be ineffective without a suite of interventions including improved treatment strategies, better detection and treatment of chronic carriers and improvements in WASH (Pitzer et al. 2014).

The field of environmental conservation and management has traditionally focused on habitat and species conservation without sufficient attention to examining specific human health outcomes of environmental change (Myers et al. 2014). Likewise, the field of public health has become heavily reliant on drug treatment alone for control of environmentally mediated diseases and environmental management has an important, yet largely underdeveloped, role to play (Remais and Eisenberg 2012). In the most recent *Global Report for Research on Infectious Diseases of Poverty*, WHO stated that the future of global health depends on innovative, interdisciplinary and action-oriented research that integrates health, environment, and sustainability into the development agenda (WHO 2012). Understanding the non-linear complexity and multi-scalar relationships between typhoid fever transmission and their socio-ecological settings requires precisely such research.

1.6 *EcoHealth: an emerging field of systems research*

EcoHealth is an emerging research field that represents a convergence of the traditional social sciences, environmental science and public health, seeking to explore this dynamic complexity from a balanced systems perspective (Parkes et al. 2003, 2005; Forget and Lebel 2011; Wilcox and Kueffer 2008; Bunch et al. 2008; Charron 2012). Drawing from a series of case studies of ecosystem approaches to health, funded by the Canadian International Development Research Centre, Charron (2012) recently outlined six key principles of ecohealth research practice as: i) systems thinking, ii) transdisiplinary research, iii) stakeholder participation, iv) sustainability, v) gender & social equity and vi) knowledge-to-action. While these principles are seldom applied to infectious disease research projects, some interesting examples exist, including: tackling echinococcosis (a cystic parasitic disease) in the butcher slums of Kathmandu (Waltner-Toews et al. 2005; Neudoerffer et al. 2005); road construction-related diahorreal disease in Ecuador (Eisenberg et al. 2007); and dam construction-related malaria transmission in Sub-Saharan Africa (Kibret et al. 2015). Although there is progress in ecosystem approaches to water-related infectious diseases, research and interventions mostly deal with proximal causes of infection and transmission without sufficient attention to distal causal factors involving both social and ecological processes (Batterman et al. 2009). This narrowed focus undermines the level of transdisciplinarity, sustainability, equity and overall knowledge gain that could be achieved.

Within the study of typhoid transmission and control, system-level transdisciplinary research is lacking in the academic literature.

The river basin is a useful geomorphological boundary in which to undertake systems-level research on the socio-ecological determinants of health (Parkes et al. 2008; Parkes and Horwitz, 2009). Not only is it the geographical space in which water flows but a subsystem in which the forces of population growth, climate change and governance manifest. Parkes et al. (2010) introduced the Watershed Governance Prism, providing a framework to link social, ecological, and health concerns in the river basin context. The vertices of this three dimensional heuristic device present four perspectives on governance with differing emphasis on social-ecological systems, health and the watershed itself (Table 1.1). The prism must be viewed as a whole as there are explicit limitations to any given perspective.

Table 1.1 Perspectives of the Watershed Governance Prism (from Parkes et al. 2010)

Governance Perspective	Emphasis	Limitations
A. Sustainable development **(Watersheds, ecosystems, social systems)**	'Triple-bottom' line of economy, society and environment within a watershed, catchment or river basin*	Fails to recognise the ecological, social and economic factors in watersheds are also 'upstream' drivers of the determinants of health.
B. Ecosystems and well-being **(Watersheds, ecosystems, health/well-being)**	Physical environment and freshwater ecosystem goods and services provided by living systems, including buffering against direct environmental hazards such as contaminants and pathogens.	Tends to overlook social/equity issues, and links between ecosystems and social determinants of health
C. Social determinants of health **(Watersheds, social systems, health/well-being).**	Social equity, livelihoods and the socio-economic determinants of health, valuing equitable, multi-stakeholder processes for water management.	May overlook biophysical processes and ecosystem services that are integral to water resources and health
D. Social-ecological health promotion **(ecosystems, social systems,**	"Double-dividend" from linking sustainable freshwater ecosystem services with equitable social processes and	Tends to overlook the upstream drivers of social and ecosystem change within watersheds as the "causes of

health/well-being)	enhancing social–ecological resilience.	the causes" determining health and well-being

* A river basin or catchment is an extent or area of land where all surface water converges to a single point at a lower elevation. In North America, the term watershed is used synonymously with catchment, although in most English speaking countries it is used to mean the high elevation perimeter of that area, or the drainage divide.

Bunch et al. (2014) recently tested this model to determine the prevalence in peer-reviewed literature of different perspectives relating to river basins and public health between 2000 -2010. The review revealed health is addressed in only 3.5% of academic journals addressing river basin management, and river basin management is virtually absent from public health literature. Environmental management literature, while acknowledging the importance of river basins for health, is nonspecific about the nature of health outcomes and discusses primarily biophysical rather than social determinants. This exhibits a clear lack of integration across fields of river basin management and public health, despite clear potential for synergistic benefits to food and water security and reduction of disease burden. A clear demonstrative opportunity lies in the interdisciplinary examination of basin scale environmental determinants of water-related disease such as typhoid fever.

1.7 Investigating system-level ecological determinants of typhoid in Fiji

Typhoid is mainly studied in large, highly populated continental systems of Southeast Asia and Africa where, in terms of population, disease burden is highest. Pacific Island nations, however, offer a unique opportunity to study the dynamics of the disease in less complex (smaller, less populated, geographically isolated), high-incidence settings. The regional incidence rate of typhoid in the Pacific is among the highest in the world, with greater than 100 cases per 100, 000 people per year (Crump et al. 2004). Serious outbreaks of typhoid fever are commonplace in Nauru, Western Samoa and repeatedly over the last decade in Fiji, which has the highest reported annual number of cases of any country in the region (Olsen 2001; WHO 2010; Thompson et al. 2014). Typhoid is endemic in Fiji and the incidence has risen dramatically since 2005 (Kool and Whippy 2011). While typhoid in Fiji is seasonal, associated with minimum temperature and accentuated by heavy rainfall events that often accompany tropical cyclones, the main modes of transmission are unclear (WHO 2011; Scobie et al. 2014). While local socio-cultural and behavioural factors are likely to play a role in typhoid transmission (Singh 2010), association with rainfall and flooding suggest that environmental factors are also important. Fiji has very heavy rainfall (2-6 metres/year), is particularly susceptible to tropical cyclones and flooding, and was ranked the 16th highest at-risk country globally in 2015 (Garschagen et al. 2015). Populations concentrated along low-lying coastlines and watercourses are particularly sensitive to disaster risk (Chapter 2, Jenkins and Jupiter 2015). About 45% of the national population are in rural areas, with around 70% of the rural population drinking water drawn directly from creeks and rivers and only 12% with access to treated sewerage (Fiji Department of Information, 2014). Water supply and waste management in rural areas and urban settlements remains challenging because of steep volcanic topography and heavy rainfall. Sanitation systems in rural areas are often shallow pit latrines built into permeable soil with high water tables and frequently flood into nearby waterways. Rates of rural to urban migration are high, thus increasing urban poverty and the number of informal settlements with inadequate water, sanitation and hygiene (Barr 2007). Fiji has also experienced an increased frequency and magnitude of flooding over the past few decades, attributable to an interaction of accelerating river basin alteration (deforestation, expanding agriculture, road building, gravel extraction, dams, and waterway diversions) and climate change impacts such as sea level rise and increased frequency and intensity of tropical storms (Lata and Nunn 2012). Recent research has also shown that degraded river basins in Fiji are associated with lower abundance and diversity of aquatic resources of commercial and cultural importance and these effects are further magnified by heavy rainfall (Jenkins et al. 2010; Jenkins and Jupiter 2011), with additional implications for nutrition and cultural wellbeing.

The overarching principles of EcoHealth practice are well suited to study the complex systems surrounding exposure and transmission of typhoid in endemic settings such as Fiji. By taking a nested systems approach to studying the environmental epidemiology over multiple interacting subsystems, this thesis will address several of the current deficiencies in typhoid transmission models and intervention strategies through a focussed investigation based in Central Division. I propose that understanding the determinants of typhoid in an endemic setting will be greatly enhanced by concurrent investigation of regional, river basin and residential subsystems, alongside traditional case-control approaches at the household or individual level. Analyzing a network of multi-level interdisciplinary results will reveal system-level emergent properties unlikely to be predicted by reductionist methods.

1.8 *A general nested systems conceptual model for typhoid exposure in Fiji*

The following conceptual model presents general factors predicted to influence typhoid exposure risk over four nested subsystems of organisation with arrows indicating potential cross-system influences and showing thesis chapters in which factors for each subsystem will be investigated (Figure 1.1). Fiji is positioned within the Pacific Islands region with its particular sensitivity to climate variability and natural disasters, geographic isolation, small developing economy, rapid population growth and environmental change (Chapter 2, Jenkins & Jupiter 2015). The interaction of market and climatological forces and national policy decisions, including the availability and use of typhoid vaccination, effect typhoid risk through numerous pathways on each smaller nested level of organisation. At the river basin level, the hydrological network primarily mediates spatial spread of waterborne pathogens (Bertuzzo et al. 2012). Catchment level patterns of land alteration, combined with changing climate, influence waterborne disease transmission through modification of hydrology (e.g., floods, droughts, landslides), thereby likely facilitating the spread of pathogens (e.g., Bunch et al. 2014; Jenkins and Jupiter 2015). WASH interventions and medical treatment within this level can provide herd protection, with sanitation interventions, in particular, the most likely to provide protection, since they reduce environmental contamination (Fuller et al. 2016). In the broader residential setting, such as village or settlement, factors such as elevation, proximity to altered land and hydrology and the condition of housing, sanitation and waste disposal are thought to influence typhoid risk (e.g., Dewan et al. 2013; Akullian et al. 2015) and are mediated by social dynamics of community cohesion, local leadership, mutual respect and cultural practice (Mehta 2016). At the individual or within household level, consuming contaminated water and food, using inadequate sanitation, poor hygiene behaviour and socio-economic factors are the principal risk factors that have been described (e.g., Sharma et al. 2009; Mbakaya et al. 2015; Alba et al. 2016).

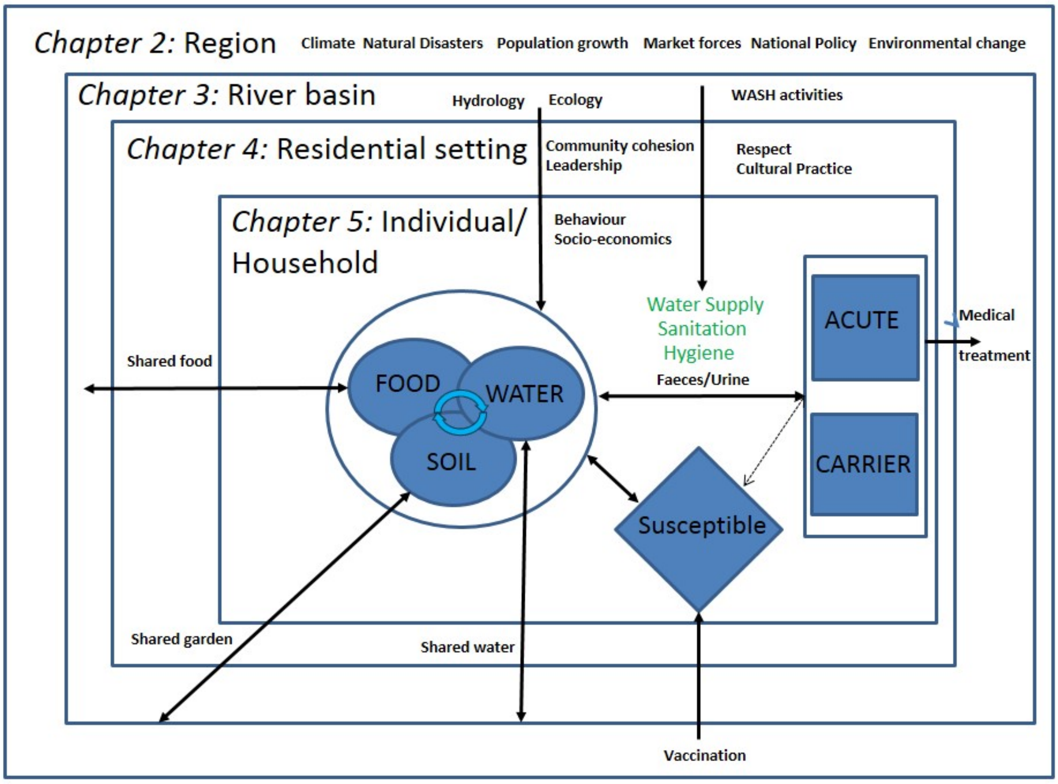

Figure 1.1 General conceptual model of factors influencing typhoid exposure risk over four nested subsystems of organisation with arrows indicating potential cross-subsystem influences.

1.9 *Study approach*

This thesis can be methodologically defined as an interdisciplinary ecosystem approach to health, exploring the nested determinants of typhoid fever in Central Division, Fiji. Although I explore potential determinants acting at global and Pacific island regional levels in Chapter 2, the primary study boundary was the administrative area of Central Division, which was chosen for practical and logistical reasons. In August 2012, national and international typhoid fever experts convened in the capital city (Suva) to discuss options for control and prevention of typhoid fever (Thompson 2012). A case-control study in Central Division was among the primary recommendations of this expert panel. Central Division is the most populous division in Fiji, containing the capital city of Suva, the most extensive road network and the largest and best equipped hospital and laboratory facilities in the country. The division consistently has among the highest number of confirmed typhoid cases, and all health centers in the division are required to send blood samples from suspected cases to the Colonial War Memorial Hospital Microbiological Laboratory in Suva for blood culture confirmation. This central registry of all laboratory confirmed cases provides the only reliable source from which to recruit cases for the entire Central Division study area. The Fiji Centre for Communicable Disease Control (FCCDC), also based in Suva, is where my study was positioned by the Fiji Ministry of Health and Medical Services (MoHMS), and where the primary national water laboratory is based. In addition, I was logistically constrained by locations I could reach by road, collect environmental samples and return to FCCDC to process on the day of collection, which also confined me to Central Division. This work represents a long-term collaboration with a great number of individuals and institutions, many of whom were part of the expert panel called upon by the Fiji MoHMS in 2012 to provide advice for typhoid control and management.

In this thesis a novel synthetic approach to studying the environmental epidemiology of typhoid is presented in the following manner: Chapter 2 (Jenkins and Jupiter 2015) establishes a regional context by providing the first comprehensive literature review of the direct and indirect health consequences of interruptions to Pacific Island wetland ecosystem services associated with increasingly common natural disaster events. Water and food provisioning, physical hazards, psycho-social wellbeing and transmission of infectious diseases (e.g., typhoid) are examined in the Pacific Island context and examples given of how wetland systems can either mitigate or contribute to health outcomes. This chapter also presents an original generalised conceptual model of mechanisms determining health (with *S.* Typhi as an example of bacterial carriage) and livelihood outcomes during cyclones or heavy rainfall in the context of high island river basins. Opportunities for improving management of wetland ecosystems for human health benefits are explored in the context of local to regional-scale management frameworks.

Chapter 3 (Jenkins et al. 2016) presents the first study of typhoid fever to assess variable risks associated with the ecological conditions of a sub-catchment. In this study, we calculate the burden and spatiotemporal nature of enteric fever attributable to S. Typhi in Central Division, Republic of Fiji, and define the level of disease incidence and recurrence at a sub-catchment level. We use quantitative analysis to explore the relationships between sub-catchment environmental characteristics and the incidence and recurrence of typhoid over 30 months (2013–2015). This study explores associations between distal environmental drivers and local transmission patterns at the population level. This chapter will help to identify predictive spatial risks and potential proactive intervention strategies where they lie at the sub-catchment level.

Chapter 4 investigates the influence of the residential setting and microbiological and physicochemical characteristics of the lived environment on the risk of typhoid transmission. Using an overarching case-control design, I use a combination of spatial characteristics, living condition observations and measured biophysical parameters to investigate typhoid risk. I measure bacterial contamination and chemical composition of water and soil as indicators of vehicles of exposure, complemented with a ranked observational analysis of residential living conditions, quantitative spatial analysis of household locations and a factor analysis to explore multivariate relationships. This study seeks to identify unique combinations of environmental determinants related to drainage, housing and the condition of water and sanitation that influence the risk of typhoid transmission. This study also seeks evidence to support the notion that certain types of nutrient enrichment in water and soil may support the persistence of S. Typhi external to the human host. This interdisciplinary study enhances the scope of customary case-control epidemiological approaches by categorizing the residential environments into which *S.* Typhi is shed, extending the testing of causal assumptions beyond the immediate domestic domain, and allowing interventions to be made with greater specificity at the residential level.

Chapter 5 examines the proximal risk factors for typhoid at the individual and within-household level using a classic case-control study approach. In this study, patients with blood culture-confirmed typhoid fever were sought from February 2014 through August 2016 along with two age interval, gender, ethnicity, and residential area matched controls per case, resulting in 479 participants being administered a detailed questionnaire. I use matched univariate and multivariate conditional logistic regression analyses to evaluate associations between exposures and risk of typhoid fever. In this study I explore the specific risk factors for Central Division, Fiji related to consuming contaminated water and food, inadequate sanitation, poor hygiene behaviour and socio-economic factors. I also investigate a unique set of factors, unreported in typhoid case-control literature, related to distal activities in the water catchment.

In the final chapter (Chapter 6), I synthesize significant results from the studies within this thesis, across multiple disciplines and nested subsystems (as presented in Figure 1.1). Here, I examine the interaction between distal ecological conditions, proximal settings of the lived environment and individual behaviour on the risk of typhoid exposure. I also highlight recent molecular microbiology and human gut microbiome approaches to augment this nested systems methodology. I synthesize significant risk factors quantitatively derived from three nested systems of organisation (sub-catchment, residential, individual) within the Central Division, Fiji context, and examine how they interact using a Bayesian Network approach. I use this network model to test potential intervention scenarios and elucidate the relative influences of interventions on typhoid exposure risk. I also examine the intended and incidental outcomes of this research, suggest a multi-level intervention approach and highlight advantages and limitations of this overall research process. This synthesis of results reconceptualises typhoid transmission in this socio-ecological setting and provides important focal points for intervention across arenas of public health and environmental management.

This thesis was written so that Chapters 2, 3, 4 and 5 could be stand-alone pieces of work to be published discretely as a series of related papers. While aspects of these individual works may contain reiteration, the thesis is arranged so the broad study rationale (presented here in Chapter 1) is followed by a chapter-by-chapter exploration of each subsystem (as presented in Figure 1.1), concluding with a synthesis of results that, as a whole, seeks to exemplify an interdisciplinary endeavor of greater utility than the sum of its nested components.

CHAPTER 2

A Pacific Islands regional perspective on natural disasters, health and wetlands

The following chapter, without preamble, is the prepublication version that was published as: Jenkins AP, Jupiter SD. 2015. Natural disasters, health and wetlands: A Pacific small island developing state perspective. In: *Wetlands and Human Health*, Wetlands: Ecology, Conservation and Management 5, Finlayson CM, Horwitz P, Weinstein P (eds). Springer, New York. Pgs. 169 -191

2.1 *Preamble*

The tropical islands of the Pacific are simultaneously blessed with a globally significant natural and cultural tapestry while being uncommonly vulnerable due to geographic isolation, rapid population and economic growth and increasing frequency and intensity of natural disasters associated with climate change (Jupiter et al. 2014). Small island states, such as the Pacific islands, are highly vulnerable to the risk of disaster due to climate change (IPCC, 2007). The landscapes and seascapes supporting the health and well-being, culture and economies of the region are also rapidly being transformed, reducing socio-ecological resilience to both environmental and climate change (Barnett and Campbell 2010). Deforestation and degradation of terrestrial and aquatic biomes is driving loss of abundance and diversity of key resources for livelihoods and cultural practice (e.g., Jenkins et al. 2010). Access to safe water and adequate sanitation is not keeping pace with population growth and ecosystem transformation, with two-thirds of the population continuing to rely on unprotected sources of water and unsanitary means of excreta disposal (WHO/UNICEF, 2016). Infectious diseases are the primary cause of death in the region, with water and sanitation related diseases, including Malaria, Dengue, Leptospirosis and Typhoid among major causes of mortality (WHO 2013). Increased flooding and high surface runoff rates on deforested and agricultural lands compounds the risks for faecal contamination of water sources and bacterial infection and enhances conditions for mosquito vector proliferation. In many Pacific island countries, flooding events following cyclones and prolonged rainfall have been linked to outbreaks of waterborne bacterial disease (e.g., typhoid, leptospirosis) and vector borne diseases (e.g., Malaria, Dengue) resulting in costly disaster response measures (WHO 2010).

Pacific Islanders are also socio-culturally entwined and deeply dependent on wetland systems (freshwater lakes and streams, salt marshes and mudflats, mangrove and coastal littoral forests, seagrass, fringing and offshore coral reefs, deep sea trenches and abyssal plains) and human populations aggregate along coastal areas and floodplains. Given this important relationship to wetlands and particular sensitivity of the region to disaster risk, climate variability and rapid environmental change, it is valuable to study the health consequences of natural disasters in this particular ecosystem context. This aspect of investigation establishes a regional context for this thesis by examining the effects of these critical interacting factors on water and food provisioning, physical hazards, psycho-social wellbeing and transmission of infectious diseases (such as typhoid) along with the documented health consequences. Regional level engagement on ecological determinants of health throughout the production of this thesis helped to catalyze the formation and activities of the Oceania Chapter of the International Association for Ecology and Health (IAEH) and several collaborative research publications, championing regionally specific and integrative approaches to Ecohealth practice (Jupiter et al. 2014, Kingsley et al. 2015, Jenkins and Jupiter 2015). The following chapter is one of these regionally specific works (Jenkins and Jupiter 2015) which was published in the book, *Wetlands and Human Health* (Finlayson et. al. 2015) and presents the original generalised conceptual model of mechanisms determining health (using *S.* Typhi as an example of bacterial carriage) and livelihood outcomes during cyclones or heavy rainfall in the context of high island river basins.

Climate change and natural disasters dominate discourse on sustainable development in the Pacific Island region, particularly with regard to health risks (WHO 2015), although population growth, slow economic progress, urbanization and environmental change all play significant interacting roles in determining regional health outcomes (Chapter 6). Specific regional attributes with the potential to influence waterborne disease transmission will be summarized in the final synthesis chapter (Chapter 6, Table 6.2). Of particular importance to this synthesis, and to the thesis overall, is the significant regional level influence of frequent natural disasters on ecosystem services provided by wetland ecosystems and the consequential health outcomes, which is the principal focus of Chapter 2.

2.2 Abstract

Natural disasters in the context of public health continue to be a challenge for small island developing states (SIDS) of the Pacific. Pacific SIDS are particularly sensitive to disaster risk given geographic isolation, developing economies, lack of adaptive capacity and the interaction of climate variability with rapid environmental change. Health risks are amplified by the high levels of dependence on wetland resources and population concentration along low-lying floodplains and coastal margins. Thus, the health consequences of disasters cannot be considered in

isolation from their wetland ecosystem settings. Wetlands provide protective and essential provisioning services in disasters, yet can also become vehicles for poor health outcomes. In this chapter we review the direct and indirect health consequences of interruptions to wetland ecosystem services associated with disaster events and emphasize how longer-term health effects of natural disasters can be exacerbated when wetland services are lost. We examine patterns of ill health for those populations in Pacific SIDS that are associated with wetlands and provide examples of how wetlands can either mitigate or contribute to these health outcomes. Finally, we identify opportunities and examples of improved management of wetland ecosystems for human health benefits under local to regional-level management frameworks. Greater understanding at the interface of wetland ecology and disaster epidemiology is needed to strengthen existing models of disaster risk management and wetland conservation. We suggest applying principles of Integrated Island Management (IIM) as regionally appropriate means to guide those seeking to build this understanding.

2.3 Introduction

Natural disasters are disruptions to ecological systems that exceed people's capacity to adjust, thereby necessitating external assistance (Lechat 1976). They can be geophysical (earthquake, volcano, mass movement), meteorological (storm), hydrological (flood), climatological (extreme temperature, drought, wildfire), biological (epidemic, infestation, stampede) and extra-terrestrial (asteroid, meteorite) in nature (Below et al. 2009). Natural disasters currently affect over 200 million people annually, are frequently concentrated in and around wetland areas, and cause considerable loss of life and prolonged public health consequences (UNISDR, 2005). Public health impacts of natural disasters are magnified by the interactions of urbanisation, environmental degradation and climate change on floodplains, coastal margins and tectonically active areas (Kouadio et al. 2012). Small island developing states (SIDS) in Oceania, encompassing Melanesia, Micronesia and Polynesia (Figure 2.1), are particularly vulnerable to the impacts of natural disasters (Table 2.1). Five Pacific Island countries rank among the world's top 16 at-risk countries, including Vanuatu, Tonga, Solomon Islands, Papua New Guinea and Fiji (Garschagen et al. 2015). In the context of disaster risk, vulnerability is defined as the state of susceptibility to harm from disturbance (Adger 2006) and is a function of exposure, sensitivity and adaptive capacity (IPCC 2007). Pacific SIDS have high exposure to natural disasters, whose incidence and severity are on the rise (ABM and CSIRO, 2011). Pacific SIDS are also particularly sensitive to disaster risk given the concentration of human populations along low-lying wetland areas (McIvor et al. 2012). Furthermore, the geographic isolation of many island communities results in low adaptive capacity, as they cannot easily access emergency services, freshwater and food following acute disturbance events (Barnett and Campbell 2010).

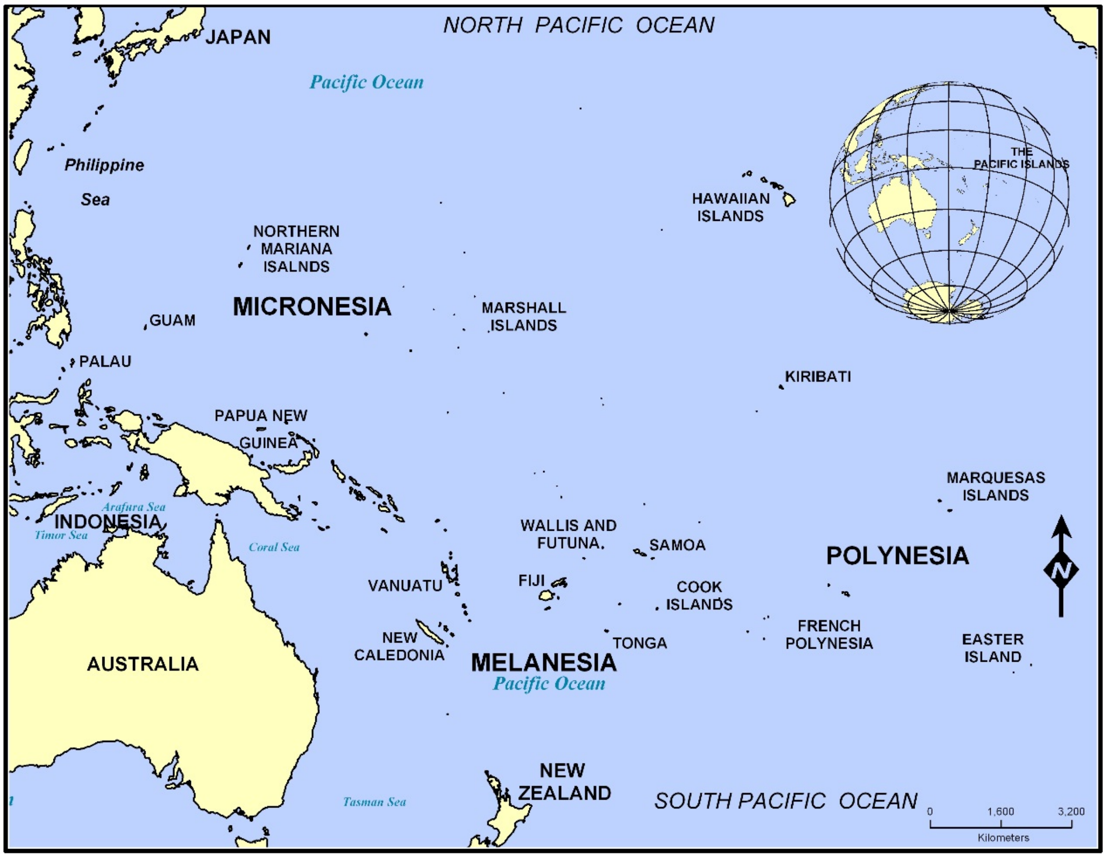

Figure 2.1 Map of the Pacific Islands, showing its sub-regions and the principal island nations. (Source: Jenkins and Jupiter, 2015)

Following natural disasters, there are direct and indirect pathways to poorer health outcomes in wetland systems; those affected cover a broad spectrum of community members including immediate victims, rescue workers, those with lost property or livelihoods, families of the injured and those beyond the vicinity of the disaster (Galea, 2007). The enormous economic costs of disasters also impact on the ability of SIDS to provide adequate recovery services: for example, annual losses from tropical cyclones and earthquakes are estimated to be as high as 6.6 percent of national GDP in Vanuatu (Jha & Stanton-Geddes, 2013). In this chapter we review the direct and indirect health consequences of interruptions to wetland ecosystem services associated with disaster events and emphasize how longer-term health effects of natural disasters can be exacerbated when wetland services are lost. We examine patterns of ill health for those populations in Pacific SIDS that are associated with wetlands and provide examples of how wetlands can either mitigate or contribute to these health impacts. Finally, we identify opportunities for improved management of wetland ecosystems for human health benefits under local to regional-level management frameworks.

Table 2.1. Pacific islands country estimated level of vulnerability to specific natural hazards including interacting effects. Vulnerability is depicted as high (H), medium (M) or low (L) as a function of exposure, sensitivity and adaptive capacity. Dashes indicate where the disaster type has not occurred, is unlikely to occur or cannot occur within the particular country. Adapted from UNDP (2002).

Country	**Tropical Cyclones**	**Storm Surges**	**Coastal Floods**	**River Floods**	**Drought**	**Earthquake**	**Landslide**	**Tsunami**	**Volcanic Eruptions**
Cook Islands	H	H	M	L	H	L	L	M	–
Federated States of Micronesia	M	M	H	H	L	L	M	–	–
Fiji	H	H	H	H	H	H	H	H	L
Kiribati	L	M	H	–	H	L	L	L	–
Republic of the Marshall Islands	H	H	H	–	H	L	L	L	–
Nauru	L	L	L	–	H	L	L	L	–
Niue	H	H	M	–	H	M	L	M	–
Palau	H	H	M	M	H	L	L	M	–
Papua New Guinea	H	H	H	H	H	H	H	H	H
Samoa	H	H	H	M	L	M	H	H	M
Solomon Islands	H	H	H	H	H	H	H	H	H
Tokelau	H	H	H	–	M	L	L	M	–
Tonga	H	H	H	L	H	H	L	H	H
Tuvalu	H	M	H	–	H	L	L	M	–
Vanuatu	H	H	H	H	H	H	H	H	H

2.4 *Impacts on water provisioning*

It is well recognised that wetlands play a key role in the hydrological cycle, influencing both quantity and quality of available fresh water (Costanza et al. 1997; Maltby & Acreman 2011). Wetlands influence groundwater recharge, base flow maintenance, evaporation and flooding. Wetland condition also influences the quality of fresh water available for personal hydration, agriculture and industry through processes of erosion control, water purification, nutrient retention and export (Cherry, 2012). Clean water on many small tropical islands is limited and vulnerable, with heightened susceptibility to contamination from inadequate sanitation and treatment facilities (Falkland, 1999). The occurrence of natural disasters often results in increased contamination of water resources and disruption to water distribution and treatment facilities. Low-lying islands and atolls that rely on shallow and fragile groundwater lenses are often the most seriously affected (Dupon, 1986).

Tropical storms, cyclones and associated flooding are among the most common natural disasters in the region. The Pacific region has the highest frequency of recorded cyclones, with 45% of all cyclones reported from 1980 to 2009 (Doocy et al. 2013). Fiji alone has reported 124 natural disasters in the past 37 years, with tropical cyclones accounting for 50 percent of these events (Lal et al. 2009). There is an average of five to six tropical cyclones annually in the South Pacific (Gupta, 1988), resulting in major consequent impacts on freshwater provisioning and therefore acute and chronic impacts on human health. Impacts arise from direct damage to infrastructure and indirect flood-associated pollution in wetland areas from which people access water for drinking, cooking and bathing (Young et al. 2004; Ellison 2009).

For example, with wind speeds of 80 to 110 knots and rainfall of 300 to 400 mm /day, Cyclone Ami in 2003 had devastating effects on Fiji, in particular on the islands of Vanua Levu, Taveuni and the eastern islands of the Lau Group (Mosley et al. 2004). A month after the cyclone subsided, a study conducted on drinking water quality on the island of Vanua Levu showed nearly 75% of samples did not conform to World Health Organisation (WHO) guideline values for safe drinking water (Mosley et al. 2004). This was most likely from the large amounts of silt and debris entering the water supply sources during the cyclone. Turbidity and total coliform levels had increased by 56 and 62 per cent, respectively, from pre-cyclone levels and poor water treatment led to this contamination being transferred through the reticulation system (Mosley et al. 2004). Communities were unaware that they were drinking water that was inadequately treated. This study also demonstrated that a simple paper strip water-quality test kit (for hydrogen sulphide,

H_2S) correlated well with the lab based tests. WHO has subsequently been distributing these simple kits to remote communities to allow water supply testing post natural disaster.

The impact from storm surges on freshwater provisioning is amplified by sea level rise, which propagates storm damage further inland. While immediate damage is increased by this interaction, the compounding long-term issue of saltwater intrusion into the groundwater supply is serious (Sherif and Singh 1996). The shallow freshwater lens on atolls is the only source of fresh water other than rainwater. After a Category 5 cyclone swept a storm surge across remote Pukapuka Atoll in the Northern Cook Islands, the freshwater lens took 11 months to recover to potable conditions and remnants of the saltwater plume were still present 26 months after the saltwater incursion (Terry and Falkland 2009).

Low-lying atolls are also particularly susceptible to drought as they rely almost entirely on rainfall as a source of freshwater. In the latter part of 2011, Tuvalu declared a state of emergency after receiving less than normal rainfall for six months. Households were rationed two buckets of water a day (40 L) and the state hospital limited admissions to cope with the water rationing (NIWA 2012). The Red Cross declared that drought conditions had also caused contamination of the limited groundwater supplies (IFRC 2013). International aid agencies responded by shipping bottled water, supplying a desalination plant and increasing the number of water storage tanks in the country. This drought was attributed to La Niña, when the cooling of the surface temperature of the sea around Tuvalu leads to reduced rainfall (Salinger and Lefale 2005). A few months later, the atoll country of Tokelau also declared a state of emergency due to drought under similar circumstances of climate and geomorphological vulnerability. The Republic of the Marshall Islands (RMI), another low-lying atoll country, declared a state of disaster due to drought conditions in May 2013, with 6,400 people across 15 atolls facing health, environmental, social and economic hardships due to the dry weather (IFRC 2013). Water supplies in RMI, are primarily generated by reverse osmosis units and rainwater catchments, both generally poorly maintained and limited in number (IFRC 2013).

Minimizing pollutants from reaching toxic levels in groundwater for drinking purposes is invaluable in the context of disaster recovery. Wetlands such as marshes and riparian vegetation contribute to the natural filtration of water and to the improvement of its quality (Norris 1993; Lowrance et al. 1997). The slowing of floodwaters by wetland systems allows for sediments to deposit (trapping metals and organic compounds), pollutants and nutrients to be processed, and pathogens to lose their viability or be consumed by other organisms in the ecosystem (Millennium Ecosystem Assessment, 2005). High levels of nutrients in the water column, commonly associated with agricultural runoff and sewage effluent, such as phosphorus and nitrogen, can be substantially reduced or transformed by assimilation, sedimentation and other biological processes in wetlands (Dillaha et al. 1989; McKergow et al. 2003), though during periods of high flow (i.e., during heavy storms and where basins are more channeled and the gradient is steep), the extent of pollutant storage will be lower (Gaudet, 1978). By contrast, losses of wetland systems can contribute to spread of waterborne bacteria. For example, a recent study in Hawaiian streams demonstrated that reductions in riparian canopy cover were associated with *Enterococcus* increases in stream water where each 1% decrease in riparian vegetation was associated with a 4.6% increase of *Enterococcus* (Ragosta et al. 2010).

Well-managed wetlands in disaster prone island river basins can be relied upon to mitigate some water pollution problems, however every wetland has a finite capacity to assimilate pollutants and may rapidly overload during a cyclone or flooding event (Gaudet 1978). Despite this, wetlands have a key role to play in integrated catchment-based disaster reduction and recovery strategies to address water quality issues.

2.5 *Impacts on transmission of infectious disease*

A number of authors have predicted that climate-induced disasters will increase the incidence of infectious diseases caused by vector-borne and waterborne parasites and pathogens (Patz et al. 1996; Colwell 1996; Harvell et al. 2002; Patz et al. 2004), though this has also been challenged (Ostfeld, 2009; Harper et al. 2012). Wetland alteration and other environmental damage caused by natural disasters can act as persistent drivers of infectious disease. Floods, for example, create conditions that allow mosquitoes to proliferate and increase the amount of human-mosquito contact (Gubler et al. 2001). The condition of wetlands prior to, during and after disaster events can also contribute to the collection of stagnant or slow moving water that favours mosquito breeding and associated vector-borne diseases. River-basin deforestation, river damming and rerouting all have been attributed to enhancing conditions for flooding and vector proliferation (Ahern et al. 2005). Storm surges in combination with sea level rise can also alter predominantly freshwater wetlands into increasingly brackish areas and subsequently increase breeding areas for the salt tolerant malaria vector, *Anopheles sundaicus* (Krishnamoorthy et al. 2005). In the endemic zones of the Pacific, malaria is identified as among the top five causes of non-traumatic death post-disasters (WHO 2013).

There are clear relationships between natural disasters and waterborne diseases when extremes in the hydrologic cycle cause both water shortages and floods, both of which are associated with increased diarrhoeal diseases (Patz et al. 2004). Within periods of water shortage, poor hygiene and the likelihood of multiple uses of the same water source (e.g., cleaning, bathing, and drinking) is a major contributor to disease transmission, while other mechanisms such as concentration of pathogens may also be important (Lipp et al. 2002). The RMI, Tokelau and Tuvalu have all experienced drought disasters since 2011, and both Tokelau and Tuvalu have experienced substantial associated diarrhoea outbreaks as limited water resources became contaminated (WHO 2013).

During periods of flooding and heavy rainfall, faecal matter and associated pathogens flush from the land and contaminate drinking water sources. For example, a typhoon in Chuuk, Federated States of Micronesia, in 1971, prevented the use of the usual groundwater sources. Chuuk communities were forced to use alternative water sources, which were contaminated by pig faeces, leading to an outbreak of balantidiasis (Walzer et al. 1973). In countries like Fiji, clear associations have been made with regard to increased rainfall and diarrhoea cases (Singh et al. 2001) and post cyclone spikes in waterborne diseases such as typhoid have also been documented (Scobie 2011).

Damage to sanitation and sewage infrastructure associated with tropical storms and flooding also imposes serious infectious disease risk. The risks of spread of waterborne infectious diseases magnifies with lack of clean water, poor sanitation, poor nutritional status and population displacement (Dennison and Keim 2009). Outbreaks of diarrhoeal illness are common after floods in low and high-income countries alike, while developing countries with poor water and sanitation infrastructure also commonly suffer from outbreaks of cholera, typhoid and other waterborne microbial diseases (Cabral, 2010). In several Pacific island countries, including Fiji and Samoa, flooding events following cyclones and prolonged rainfall have been linked to outbreaks of several waterborne bacterial diseases (e.g., leptospirosis, shigellosis, typhoid), resulting in costly disaster response measures (Jenkins, 2010). The probability of infectious disease increases following tropical cyclone events in proportion to disruption of public health services and the health-care infrastructure, damage to water and sanitation networks, changes in population density (especially in crowded shelters), population displacement and migration, increased environmental exposure due to damage to dwellings, and ecological changes (Shultz et al. 2005).

As people and animals are driven together in dry areas, increased contact with rodents and livestock often results in outbreaks of the bacterial infection leptospirosis (Gaynor et al. 2007;

Lau et al. 2010; Lau et al. 2012). Leptospirosis, a bacterial disease, can be transmitted by direct contact with contaminated water. Rodents, in particular, shed large amounts of the pathogenic bacteria in their urine, and transmission occurs through contact of the skin and mucous membranes with water, damp soil or vegetation (such as sugar cane), or mud contaminated with rodent urine (Watson et al. 2007). Flooding facilitates spread of bacteria because of the proliferation of rodents and the proximity of rodents to humans on shared high ground. Leptospiral infection in humans causes a range of symptoms, from none to mild such as headaches, muscle pains, and fevers; to severe with bleeding from the lungs or meningitis (McBride et al. 2005). In 2012, Fiji was impacted by flooding from sequential tropical depressions that caused widespread flooding impacting much of Western Viti Levu in January 2012 and again in March 2012. These events resulted in substantial population displacement and significant post-disaster increases in leptospirosis cases three to eight weeks following each of the major flooding episodes (Figure 2.2). Conservative estimates place the number of cases at 300 and the number of deaths at 25 (WHO 2013).

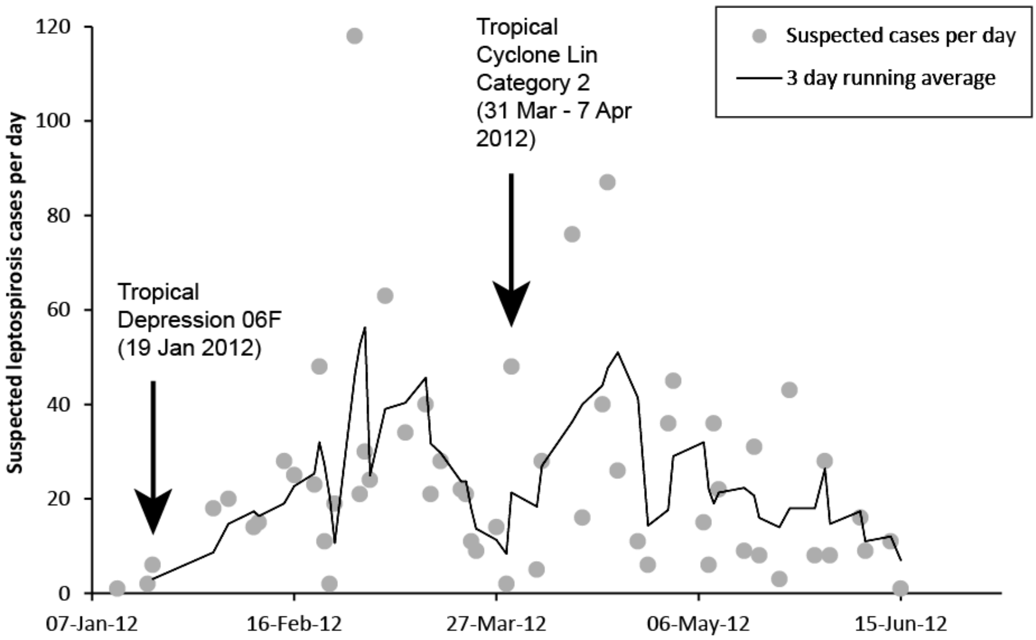

Figure 2.2 Suspected leptospirosis cases after sequential flooding disasters following tropical storm events — Western Division, Fiji, 2012. (Source: Jenkins and Jupiter 2015, adapted from WHO 2013).

In the context of natural disasters such as tropical cyclones and large storms, river basin modification via logging, mining and agriculture can exacerbate the environmental exposure of communities to infectious disease (Patz 2000; Patz et al. 2004; Horwitz et al. 2012; Myers et al. 2013). The combination of increases in the severity of severe storms and rainfall and increased landscape modification is already having a notable impact on disease transmission. Around 3% of forests are lost each year with serious consequences both on land and in adjacent water drainages (Hansen et al. 2010). Change in the diversity and abundance of species, soil dynamics, water chemistry, hydrological cycles and new forest fringe habitats creates new disease exposure dynamics (Myers and Patz 2009). Construction of dams and irrigation systems in river basins also contribute to disease emergence. Dams and irrigation have been associated with rises in schistosomiasis (Malek 1975), Rift Valley fever, filariasis, leishmaniasis, dracunculosis, onchocerciasis, and Japanese encephalitis (Harbin et al. 1993; Jobin 1999). Road building, commonly associated with logging enterprises in Pacific SIDS, has also been linked to increased incidence of dengue fever (Mackenzie et al. 2004) and diarrhoeal disease (Eisenberg et al. 2006).

In the Pacific Islands context, this increased environmental exposure results from interacting processes of flooding and sea level rise as river basin modification acts in concert with a changing global climate (Nicholls et al. 2007). Flooding and erosion rates are often accelerated by forest clearance (e.g., Likens et al. 1970; Costa et al. 2003). Deforestation within river basins is a major cause of flooding and landslide activity during periods of high rainfall and major storms and can prime the basin for future floods through increased sediment deposition (Cockburn et al. 1999). Where land is cleared, grazed or tilled, changes in compaction, infiltration and vegetative cover may lead to increased soil erosion and runoff (Pimentel et al. 1993; Roth 2004). A comprehensive 56 country study of forest cover and flood risk demonstrated that a 10% loss of natural forest cover can result in a 4 to 28% increase in flood frequency and a 4 to 8% increase in flood duration (Bradshaw et al. 2007). The Western Pacific is also experiencing significant sea level rise (Church et al. 2006), and this interaction of river flooding and sea level rise can produce substantial increases in flood risk to populations and infrastructure. Overall, the small islands of the Pacific Ocean are among the most vulnerable to flooding (Nicholls et al. 1999) precisely because of this interaction between deforestation, wetland ecosystem degradation and climate impacts such as sea level rise and increased frequency of tropical storms (Knutson et al. 2010). Fiji, for example, has experienced an increased frequency and magnitude of flooding over the past few decades, attributable to the aforementioned combination of factors and particularly affecting populations living in river deltas and on flood plains (Lata and Nunn 2012).

2.6 *Impacts on food provisioning and livelihoods*

Wetland ecosystems and the resources they provide are central to the food provisioning and livelihoods of Pacific island peoples. These food provisioning services can be severely impacted by various natural disasters. Health issues associated with malnutrition in the wake of disasters occur through reduced caloric, protein or micronutrient intake or ingesting toxic levels of trace elements (Cook et al. 2008). Incidence of under nutrition in Pacific SIDS is predicted to become more prolonged and widespread due to impacts associated with climate change and associated climate-induced disasters (Barnett, 2007). Impaired nutritional intake is also a risk factor for mortality from infectious diseases, such as gastroenteritis and measles, which are often also more common in the post-disaster phase (Cook et al. 2008).

Natural disasters, such as tropical cyclones and severe storms, cause significant loss in agricultural production each year in the Pacific. More than 80% of the population of the Pacific islands is rural and about 67% depend on agriculture for their livelihoods (ADB and IFPRI, 2009). Crop production for subsistence and commercial use is heavily dependent on wetlands, often located on fertile floodplain areas. Cyclone Ami, for example, caused over US$35 million in lost crops in Fiji in 2003 (Mackenzie et al. 2005). In Tuvalu saltwater intrusion from storm surge affected communal crop gardens on six of Tuvalu's eight islands and destroyed 60% of traditional pit gardens (ADB and IFPRI, 2009). High risk of flooding in river catchments also threatens food production. Heavy flooding of the Wainibuka and Rewa rivers in Fiji in April 2004 damaged between 50% and 70% of crops (Fiji Government 2004). During the January 2009 floods in Fiji, crops were destroyed and many did not have another source of income to buy food, medical supplies or send children to school (Lal et al. 2009). Drought also presents problems for agriculture everywhere in the region, particularly given the lack of irrigation (Barnett 2007).

River basin modification also affects the food provisioning services that assist communities in the disaster recovery process. Aspects of the relationships between river basin modifications, natural disasters, infectious disease risk and food provisioning are hypothesized in Figure 2.3. In a recent Fijian study, a dam constructed in the upper catchment of the Nadi River basin as part of a flood mitigation project helped to reduce the frequency of local floods but also resulted in a significant reduction in the availability of fish for local community subsistence (Jenkins and Mailautoka 2011). The dam construction didn't account for the highly migratory nature of insular fish faunas and compounded the long-term nutritional vulnerability of the community.

The highly migratory fish faunas of island systems are disproportionately affected due to a greater probability of encountering obstacles such as dams or other hydrological modifications, predation by non-native species and degraded water quality. These vulnerable species include ones with the greatest socioeconomic value to communities. Jenkins et al. (2010) demonstrated the notable absence from degraded catchments of fishes that traditionally formed staple diets of inland communities. Other notably absent species in heavily modified catchments include many migratory species that form important commercial and cultural fisheries for Pacific islanders. These effects are largely seasonal and magnified in degraded catchments, with pronounced negative impacts during heavy rainfall and severe storms on food-provisioning services and biodiversity (Jenkins and Jupiter 2011). These effects will likely become more severe under predicted future climate scenarios (ABM & CSIRO 2011). Community bans on harvesting and clearing within riparian wetlands can be effective at maintaining fish diversity even in areas where forests have previously been extensively cleared (Jenkins et al. 2010). However, these benefits are rapidly removed once the ban has been lifted and food fish from rivers again become scarce (Jenkins and Jupiter 2011).

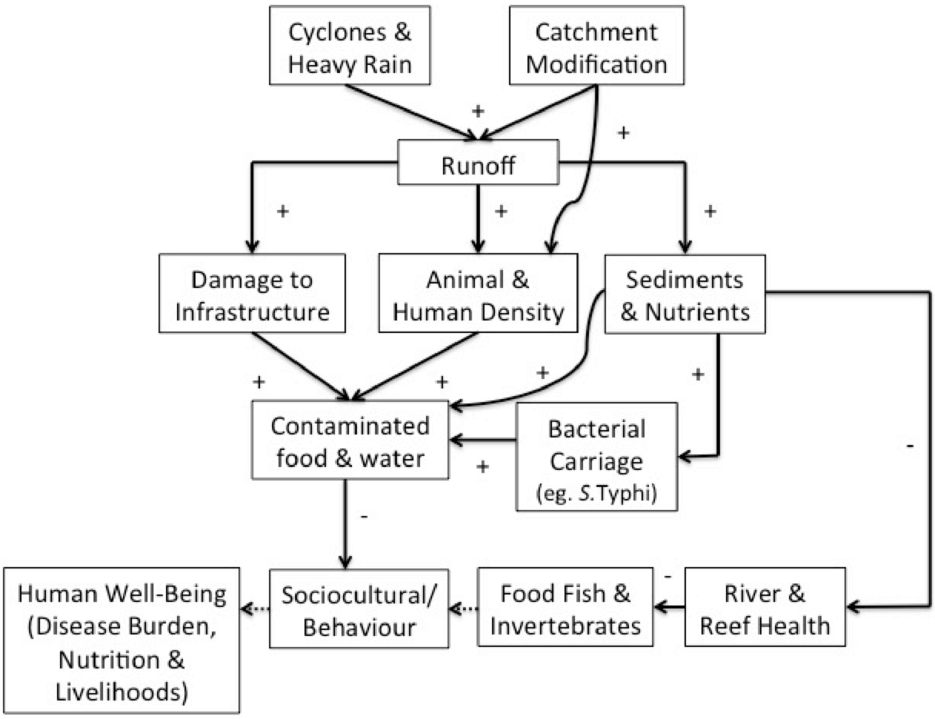

Figure 2.3 Generalised conceptual model of mechanisms determining health and livelihood outcomes during cyclones or heavy rainfall in the context of high island river basins. + and – indicate positive and negative contribution or affect on the following factor and dotted lines show the mediating effect of socio-cultural behaviour.

Managing river basins to minimize runoff and consequent eutrophication downstream will also provide greater availability of aquatic resources of value such as fisheries. This applies to both within river and downstream coral reef ecosystems. Fabricius (2005) reviewed the negative impacts to coastal coral reefs (e.g., increases in downstream macroalgal cover) associated with impacts of reduced water quality from adjacent, highly modified river basins. Letourneur et al. (1998) showed a decrease in commercial reef fish species richness and biomass with increasing exposure to terrestrial runoff from rivers in New Caledonia. While fishing pressure is certainly a mediating factor in availability of fisheries resources from coral reefs, Wilson et al. (2008) noted from a study in Fiji that habitat loss, in part due to changes in water quality, is currently the overriding agent of change.

Dependence on coral reefs and coral reef fisheries is high in most Pacific SIDS, not only for dietary needs but also for both subsistence and market-based economies (Bell et al. 2009; Gillett 2009). Forty-seven percent of coastal households list fishing as the primary or secondary source of income and in rural communities the subsistence fishery accounts for 60 to 90% of all fish caught (Gillett 2009). Direct impact on coral reef habitat that supports coral reef fisheries production can have a devastating impact on food security. For example, in Solomon Islands an 8.1 magnitude earthquake followed by a tsunami in April 2007 resulted in rapid, massive uplift of large sections of coral reefs and mangrove ecosystems in areas of Western Province, and severe damage to reefs of western Choiseul from wave energy. Monitoring data from impacted Choiseul coral reef systems show significant decreases in the availability of food fish and invertebrates, as well as a reduction in hard coral cover (Hamilton et al. 2007).

2.7 *Impacts as sites of physical hazards*

At least 1% of the global coastal wetland estate is lost each year primarily by direct reclamation (Davidson 2014), and these losses may have profound impacts on ecosystem services related to coastal protection. There is a body of evidence suggesting that coastal wetland ecosystems (including mangrove forests, coral reefs and salt marshes) can help to reduce the direct risk of damage and injuries associated with some natural disaster events (e.g., Danielson et al. 2005; Das and Vincent 2009). The immediate injuries recorded during disasters in the proximity of coastal wetland systems include lacerations, blunt trauma, sprains/strains and puncture wounds, often in the feet and lower extremities, which become susceptible to infection (Ahern 2005; Shultz et al. 2005; Hendrikson et al. 1997). However the precise extent to which mangroves and other coastal vegetation ecosystems serve as bio-shields is debated (Bayas et al. 2011), and the role of coastal wetland vegetation in wave impact and storm surge mitigation still remains controversial (Geist et al. 2006; Iverson & Prasad 2007; Kaplan et al. 2009).

Data on the extent of coastal vegetation and impacts on Pacific Islands post-tsunami are limited, yet some lessons can be learned from examples from South East Asia. In the coastal regions of western Aceh in 2004, the potential for mitigating tsunami impacts appeared limited as a result of the massive energy released by waves with heights exceeding 20 m (Cochard 2011). Studies do suggest, however, that coastal wetland vegetation appears to reduce casualties and damage (Kathiresan & Rajendran 2005; Bayas et al. 2011). Bayas et al. (2011) reported loss of life decreased by 3 to 8% behind coastal vegetation, indicating that trees may have slowed and/or diverted the waves, thereby allowing greater opportunity to escape to safety. In contrast, when plantations or forests were situated behind villages there was a 3 to 5% increase in the number of casualties (Bayas et al. 2011). Similarly, 2,100 people were killed and at least 800 were severely injured following a 1998 tsunami in eastern Saundaun Province, Papua New Guinea, where villages were located directly on sand spits in front of the mangroves surrounding the lagoon (Dengler and Preuss 2003). Given these mixed outcomes, mangrove planting as a tsunami mitigation measure has received criticism for failing to control for confounding factors such as distance from shoreline (Kerr and Baird 2007; Baird et al. 2009). One recent review concluded that the value of coastal vegetation as a tsunami buffer is minor (Baird and Kerr 2008), with the authors suggesting that the claim that coastal wetland vegetation can act as a bio-shield gives false hope to vulnerable communities.

Recent experimental studies show that mangroves can reduce the height of wind and swell waves over relatively short distances (McIvor et al. 2012), though these coastal protection services are likely nonlinear and vary with habitat area and width (Barbier et al. 2008). Wave height can be reduced by 13 to 66% over 100 m of mangroves. However, most studies have measured the attenuation of only relatively small waves (wave height < 70 cm) and further research is needed to measure the attenuation of larger wind and swell waves by mangroves. In addition, the ability of mangroves to provide coastal defense services is dependent on their capacity to adapt to projected rates of sea level rise (McIvor et al. 2012). Recent evidence suggests that mangrove surface soils are rising at similar rates to sea level in a number of locations (McIvor et al. 2013). However, data are only available for a small number of sites and mostly over short time periods. To allow for continued mangrove protection, wetland managers need to monitor the conditions allowing mangroves to persist and adapt to changing sea levels. This requires monitoring the maintenance of sediment inputs, protection from degradation and the provision of adequate space for landward migration (McIvor et al. 2012). The removal of coastal wetland vegetation may be a greater short-term threat to other services such as storm surge abatement and fisheries supply than sea level rise. It is important for concerned communities of practitioners to be promoting mangroves and coastal wetland vegetation as more than a bio-shield but also as an important source of livelihood provisioning that can assist in the medium to long-term disaster recovery process (Bayas et al. 2011). Artificial protection structures like seawalls cannot provide the nursery and fisheries benefits of natural systems, such as mangroves and coral reefs that can assist in hastening community recovery.

2.8 *Impacts on psychosocial well-being*

Wetlands are of great cultural and social significance to Pacific Islanders and play a crucial role in mediating psychosocial health and well-being. The use of wetlands and wetland ecosystem services is arguably an important aspect of Pacific cultural identity (Strathern et al. 2002). Pacific authors argue that notions of well-being are linked closely to cultural identity (McMullin 2005), that illness is often seen as an inevitable disruption to life and social systems (Drummond and Va'ai-Wells 2004), and that health gives meaning to an individual's place and actions within a community context (Ewalt and Mokuau 1995). Thus, if Pacific Islanders lose their wetland services, they are at risk of a diminution of cultural identity and social well-being.

Some authors note an ecology driven model of well-being that is based on the vitality and abundance of natural resources relied upon for subsistence and cultural practices (McGregor et al. 2003). Within this ecological model, the collective family unit forms the core social unit within which the individual lives and interacts, which is interdependent upon the lands and associated resources for health (physical, mental and emotional) and social well-being. In both cases, the myriad wetland ecosystems of the Pacific are the settings for health where cultural identity, subsistence life and social systems co-exist (*sensu* Horwitz and Finlayson 2011).

While descriptions of psychosocial issues surrounding disasters in Pacific SIDS are relatively scant, it is well documented that populations exposed to natural disasters are affected by a variety of mental health issues (eg. Cook et al. 2008; Shultz et al. 2005). The exposure to loss of life or loved ones, social displacement and economic loss have wide-ranging health effects and contribute to persistent post-traumatic stress disorder (PTSD) and depression (Cook et al. 2008). Persistent PTSD was documented in New Zealand after Cyclone Bola in 1988 (Eustace et al. 1999). When a succession of five typhoons struck Guam in 1992, persons who had acute stress disorder following the initial typhoon were significantly more likely to have progressed to PTSD or depression after the full series of typhoons (Staab et al. 1996). Increases in the rates of suicide and child abuse have also been reported post-cyclones (Shultz et al. 2005) and significant evidence exists post-flooding that children experience long-term increases in PTSD, depression, and dissatisfaction with life (Ahern et al. 2005). Addressing chronic care injuries and psychosocial well-being in the aftermath of these types of disasters can span several generations. Galea et al. (2005) suggested that over a third of initial cases of post-disaster PTSD can persist for more than a decade. As Pacific SIDS are particularly sensitive to disaster risk given the concentration of people along low-lying, wetland areas (e.g., McIvor et al. 2012), post-disaster mental health issues may also be concentrated in these vulnerable populations.

Well-managed wetlands may help to mitigate the psychosocial stress and mental health issues associated with natural disasters. Damaged wetland systems and the community awareness and perception of this damage may result in pathological mental health outcomes as outlined above. A recent study on Pacific Island families showed that those families located in neighbourhoods with perceived higher levels of environmental pollution (including wetland degradation), noise and reduced safety were more than twice as likely to have psychological morbidity, with mothers 7.3 times more likely to be affected (Carter et al. 2009).

While the loss of loved ones, income, livelihood options and displacement all contribute to mental distress, the loss of a "sense of place" is also emerging as an important mental health consideration. Albrecht (2005) has used the particular term "solastalgia" for the pain or sickness caused by the loss or, or inability to derive, solace connected to the present state of one's home environment. This concept of solastalgia is illuminated in any case where the environment has been negatively affected by forces that undermine a personal and community sense of identity, belonging and control (Horwitz et al. 2012). This concept is of particular relevance in the context of natural disasters and for the Pacific Islands where cultural identity and factors of spiritual significance are closely tied with local environmental conditions (McGregor et al. 2003; McMullin, 2005).

Evidence is also emerging that people actively involved in local conservation projects report better general health and a sense of community belonging than those who were not involved (Moore et al. 2006). Wetlands managers and public health practitioners need to recognise the need to align wetland conservation and restoration efforts with the potential effects on mental health in both the disaster prevention and recovery contexts. Managing wetlands in the wake of natural disasters to minimize the future damage to livelihoods or exposure to pathogens and improve community solidarity in the recovery process are likely to positively contribute to the mental well-being and the speed of recovery in the affected population.

2.9 *Managing wetlands for disaster risk reduction and public health*

The health consequences of disasters cannot be considered in isolation from the wetland ecosystems in which they occur. Wetlands can help to provide protective and essential provisioning services during and following disasters, though in some conditions, they can also become a setting for disease spread and exacerbate harmful conditions. Evidence-based management of wetland conditions surrounding disaster events is important for both disaster response and prevention well beyond the time and place of the disaster itself. The identification and management of short-term health impacts surrounding disasters often captures the attention and financial assistance while many intermediate to long-term impacts are overlooked (Cook et al. 2008). Recovery from disasters such as tropical cyclones, flooding, or tsunamis around wetland areas is commonly a protracted process. Disaster risk reduction strategies must factor in the medium- to longer-term preventative and recovery processes that integrate traditional public health interventions with wetland conservation and restoration, land use planning and climate change adaptation.

2.91 *Opportunities and examples of good practice at regional, national and local levels*

At a global level, following the World Conference for Disaster Reduction, the United Nations General Assembly produced the Hyogo Framework for Action in 2005, a 10-year framework bringing different sectors and actors under a common global system of coordination to reduce disaster losses (UNISDR 2005). In the context of managing wetlands for public health in the face of disasters, the focus of policy makers seeking to integrate wetland management with disaster risk reduction under the Hyogo Framework should focus on Priority Action 4 "*Reducing the underlying risk factors*" by targeting the appropriate sectoral development planning and programmes. Implementing agencies of this framework can act through global alliances such as Partnership for Environment and Disaster Risk Reduction (PEDRR) to advocate the importance of wetland management in achieving health outcomes through Priority Action 4.

At the Pacific regional level, the current policy framework for disaster management is the Pacific Disaster Risk Reduction and Disaster Management Framework (PDRRDMF) for Action 2005 – 2015. The Secretariat of the Pacific Community's Applied Geoscience Commission works to support countries to adapt this framework and implement priorities at a national and sectoral level. This often comes in the form of developing National Action Plans and more recently Joint National Action Plans which seek to address both disaster and climate change risks (SOPAC 2013). Work is underway to develop a new Strategy for Disaster and Climate Resilient Development in the Pacific (SRDP) to succeed the current PDRRDMF and 'Pacific Islands Framework for Action on Climate Change', both due to expire in 2015. The replacement strategy will combine the two inter-related fields of disaster risk reduction and climate change adaptation. Within the implementation of this framework, there will be opportunities for countries to tailor national strategies around managing and restoring wetlands to reduce disaster risk and improve adaptive capacity of coastal communities.

The Ramsar Convention on Wetlands provides another international policy framework for the management of wetlands and their associated services. Aligned with the Ramsar Convention, the Pacific regional framework for wetlands management is the Regional Wetlands Action Plan for the Pacific 2011 - 2013. Goal 1.4 calls for "*Precise linkages between ecosystem health and human health in the Pacific to be investigated*" and "*Improved engagement between wetland decision makers and human health sectors*", but underlying strategies and objectives have not been explicit in this regard. The challenge is for countries and territories to embed specific objectives for wetland management for health outcomes in the implementation of their respective National Biodiversity Strategies and Action Plans, which typically cover commitments under the Ramsar Convention.

Important learning opportunities exist within some local approaches to island wetlands management collated with a handbook of good practice in Pacific Integrated Island Management (IIM) (Jupiter et al. 2013). IIM is an approach that calls for "sustainable and adaptive management of natural resources through coordinated networks of institutions and communities that bridge ecosystems and stakeholders with the common goals of maintaining ecosystem services and securing human health and well-being" (Jupiter et al. 2013). Five of the ten guiding principles of IIM are particularly relevant for those seeking to integrate island wetland management into disaster risk management systems: adopt a long-term integrated approach to ecosystem management; maintain and restore connectivity between complex social and ecological systems; incorporate stakeholders through participatory governance with collective choice arrangements, taking into consideration gender and social equity outcomes; recognise uncertainty and plan for adaptive management through regular monitoring, evaluation and review leading to evidence-based decision-making; and organise management systems in nested layers across sectors, social systems and habitats. Box 2.1 illustrates these principles applied to the management of the Takitumu Lagoon, Cook Islands, for coupled health and environmental outcomes.

Box 2.1 Takimutu Lagoon Health Report Card, Rarotonga

The Takitumu district of the high island of Rarotonga, Cook Islands, has developed an integrated ecosystem-based management plan encompassing high island forests, streams, coastal plains and the coral reef lagoon (Dakers and Evans 2007). Advisory committees were established across several sectors to deliver the components of the management plan including government, donor and local leader steering committees, a technical advisory group for issues surrounding environmental monitoring and an inter-departmental committee for within government coordination. In particular, declining stream and lagoon water quality associated with piggery waste was a focal issue around which environmental and health sector authorities could engage. A Takitumu Lagoon Health Report Card was produced for each village for overall water quality, bacterial load, ciguatera in landed fishes, lagoon faunal abundance, adjacent stream water quality, stream bacterial load and safety of groundwater, and then it was shared widely with communities and relevant stakeholders. As a result of this focused attention on connectivity across wetland systems, new Public Health (Sewage) Regulations and an associated Code of Practice were developed. In addition, improvements were made in the system for assessing and approving changes to existing land use through a tightening of regulations needed for planning consent by the Environment Authority. This example demonstrates how IIM planning across multiple island wetland habitats can successfully bring together a wide range of stakeholders around shared concerns of public health and environmental quality (Jupiter et al. 2013). It also demonstrates that synthesizing high quality technical information around these shared concerns is catalytic in garnering both community support and effecting policy change relevant to both wetlands management and public health, thus strengthening the resilience of the community to environmental exposure to disaster risks.

2.10 *Conclusions and further research needs*

Natural disasters are a continuing and growing threat to public health with particular impact on the small developing nations of the Pacific. Disasters affect human health and the ecological properties of wetlands in ways that are not always obvious or expected in the medium to long-term. While wetlands can mitigate the effects of some disaster related health issues, they can also exacerbate ill health in affected populations. The extent to which specific wetland contexts and types can facilitate disaster mitigation and recovery is generally poorly studied. Building greater understanding at the interface of wetland ecology and disaster-related epidemiology is needed to strengthen existing models of disaster risk management and wetland conservation. Health surveillance systems should incorporate aspects of wetland quality and key provisioning services alongside routine disease surveillance and continue to collect this information in the weeks, months and years following a disaster. This will provide policy makers and managers the tools to monitor and evaluate the longer acting health consequences of interventions in various wetland disaster settings.

A precautionary approach is encouraged for wetland managers to provide careful evidence-based recommendations with regard to the extent of services to expect from wetlands surrounding natural disaster events. While being cautious with advice, wetland managers and scientists must also be proactive in seeking collaboration with public health and disaster risk management arenas to enhance both prevention and recovery strategies. To help manage the impacts of physical hazards, wetland scientists can determine the extent of damage to wetland systems and assist in adapting built and natural infrastructure around wetlands to minimize risks. Wetland ecologists should assist public health authorities in the identification of environmental reservoirs and exposure routes to infectious diseases for humans, livestock and other wildlife. The traditional core work of protecting and restoring important wetland types, such as riparian vegetation and mangroves, can help mitigate community exposure to water contamination and storm surge and also help provide long-term livelihood benefits such as fisheries and psychosocial benefits such as exercise and community engagement.

CHAPTER 3

Health at the sub-catchment scale: typhoid & its environmental determinants in Central Division, Fiji

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3.1 Abstract

The impact of environmental change on transmission patterns of waterborne enteric diseases is a major public health concern. This study concerns the burden and spatial nature of enteric fever, attributable to *Salmonella* Typhi infection in the Central Division, Republic of Fiji at a sub-catchment scale over 30-months (2013-15). Quantitative spatial analysis suggested relationships between environmental conditions of sub-catchments and incidence and recurrence of typhoid fever. Average incidence per inhabited sub-catchment for the Central Division was high at 205.9 /100 000, with cases recurring in each calendar year in 26% of sub-catchments. Though the numbers of cases were highest within dense, urban coastal sub-catchments, incidence was highest in low-density mountainous rural areas. Significant environmental determinants at this scale suggest increased risk of exposure where sediment yields increase following runoff. The study suggests that populations living on large systems that broaden into meandering mid-reaches and floodplains with alluvial deposition are at greater risk compared to small populations living near small, erosional, high-energy headwaters and small streams unconnected to large hydrological networks. This study suggests that anthropogenic alteration of land cover and hydrology (particularly via fragmentation of riparian forest and connectivity between road and river networks) facilitates increased transmission of typhoid fever and that environmental transmission of typhoid fever is important in Fiji.

3.2 Introduction

Typhoid fever is a significant enteric disease, causing an estimated 20.6 million cases and 223,000 deaths annually (Mogasale et al. 2014). While appropriate antibiotic treatment can reduce case fatality to 1%, untreated case fatality can exceed 10% (WHO 2008). The causal agent is the bacterial pathogen *Salmonella enterica* subspecies *enterica* serovar Typhi (S. Typhi), which is transmitted between humans through ingestion of faeces and urine that contaminates food and water. *S.* Typhi is human host adapted and reservoirs of infection only exist within acutely infected individuals and the 1-6% of typhoid fever sufferers who become asymptomatic carriers and excrete the pathogen into the environment for months to years (Levine et al. 1982, Monack

2012).

South central and southeast Asia are generally recognised as exhibiting the highest incidence (> 100 cases per 100 000 per year) and high fatality rates (Crump et al. 2004, Parry 2005) of human typhoid fever. While most epidemiological studies are from south Asia and sub-Saharan Africa, few equivalent studies exist for the Pacific Islands region where a high disease burden is suspected (Crump et al. 2004). Estimating incidence or determining risk factors in resource poor island countries with limited surveillance and substantial underreporting are difficult (Scobie et al. 2014). Accurate compilation of the spatiotemporal nature of laboratory-confirmed typhoid cases is very valuable for establishing disease patterns, predicting risk and prioritising resource allocation. Geographical Information Systems (GIS) and spatial statistics are recognised as powerful tools for mapping disease patterns and modeling causative factors (Dewan et al. 2014). Use of both techniques can enhance surveillance and risk prediction, with spatial models particularly important for examining the influence of scale.

River basins (or catchments) are important for investigating the complex socio-ecological determinants of health (Parkes et al. 2008, Parkes and Horwitz 2009). Waterborne pathogens are directly or indirectly under hydrological control as they are transmitted when contaminated water (or food contaminated by water) is consumed (Gatto et al. 2013). While local scale hygiene and human mobility are important for waterborne disease transmission (Valema et al. 1997), a catchment's hydrological network primarily mediates spatial spread (Bertuzzo et al. 2012). Catchment scale patterns of land alteration, combined with changing climate, influence waterborne disease transmission through modification of hydrology (e.g., floods, droughts, landslides), thereby facilitating the spread of pathogens (see Bunch et al. 2014; Jenkins and Jupiter 2015). While risk of typhoid fever in endemic settings is associated with household scale food and water safety, as well as sanitation and hygiene levels (Valema et al. 1997, Vollard et al. 2004), broader scale geospatial studies suggest environmental condition may also enable more efficient disease transmission (e.g., Akullian et al. 2015, Baker et al. 2011).

Typhoid fever infection risk is highest in environments with poor standards of living and, availability of clean water and sanitation, yet predisposing environmental characteristics in surrounding hydrological networks are not well studied. While socio-cultural and economic factors are important (Valema et al. 1997, Vollard et al. 2004), the environmental context into which S. Typhi is shed also influences transmission at the scale of a slum, city, district or country, with prevalence rates associated with climate variables, elevation, and proximity to altered land and contaminated water (e.g., Mermin et al. 1999, Kelly-Hope et al. 2007, Wang et al. 2013, Akuillan et al. 2015). The question addressed in this study is whether environmental reservoirs contribute to endemic transmission. The research implies waterborne transmission as an important environmental pathway, yet no study of typhoid fever has addressed the variable risks associated with the ecological conditions of a geomorphological unit such as a sub-catchment.

In this study we calculate the burden and spatiotemporal nature of enteric fever attributable to *S.* Typhi in Central Division, Republic of Fiji, and define the level of disease incidence and recurrence at a sub-catchment level. We use quantitative analysis to explore the relationships between sub-catchment environmental characteristics and the incidence and recurrence of typhoid over 30 months (2013-15). This study explores associations between distal environmental drivers and local transmission patterns at the population level. The study outcomes can be used to produce predictive spatial risks and identify proactive intervention strategies where they lie at the sub-catchment level. This paper is one of series that seeks to determine the scaled nature of typhoid prevalence in Fiji; subsequent papers will address risks at the village, household and individual levels.

3.21 *Typhoid in Fiji*

Typhoid fever is endemic in Fiji and its incidence is reported as increasing since the 1990s (WHO 2010), particularly after 2004-05 so that it exceeded 52/100 000 in 2010 (Scobie et al. 2014). The explanations for this sudden increase are individually unconvincing (Thompson et al. 2014) (see Chapter 5, pg 87 for further discussion). At least 17 typhoid outbreaks have occurred in Fiji since 2005 (WHO-Division of Pacific Technical Support [WHO-DPS], unpublished data). While worldwide children under five are most likely to present with the illness, in Fiji young adults from 15-30 years old present most frequently (Thompson et al. 2014). Indigenous Fijians represent 90% of reported cases (Singh 2010).

Typhoid is seasonal in Fiji with case peaks from January to June each year, typically lagging the rainy season (November to April; WHO/FMOH/UNDP 2011; Scobie et al. 2014) by 2 months. Outbreaks associated with cyclones and flooding have been reported (Jenkins 2010). Distribution of cases varies geographically, although surveillance data suggest typhoid is becoming increasingly common in rural areas (Thompson et al. 2014).

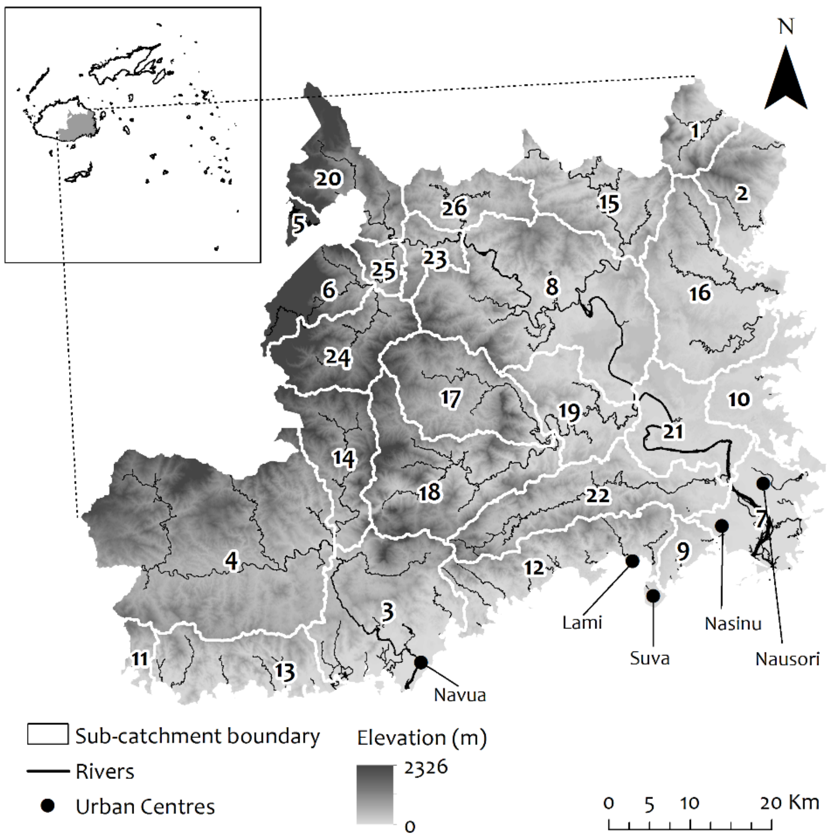


Figure 3.1 Location of Central Division on Viti Levu in the Fiji Islands (inset) showing elevation, river network, sub-catchment boundaries and major urban centres. Sub-catchment numbers relate to data presented in Tables 3.3 and 3.44.

3.3 Methods

3.31 *Study Area*

The Fiji island archipelago, (12-22° S and 176°E-178° W), includes 332 islands with a total land area of 18,270 km^2 (Neall and Trewick, 2008). This study was conducted in the Central Division, one of Fiji's four divisions, located on the south-eastern, wettest and most populous half of the largest island of Viti Levu (10,642 km^2) (Figure 3.1). Viti Levu has complex geological origins (Neall and Trewick, 2008), steep slopes, large rivers and well developed estuaries along coastal floodplains. Mean annual rainfall is very high in the southeast of Viti Levu (>3,200 mm), particularly during the cyclone season (November to May). The northwest portions of Viti Levu fall in rain shadows of the ranges and therefore receive lower mean annual rainfall (< 2,000 mm) (Barker et al. 2006). The Central Division consists of five provinces over a land area of 4,293 km^2. It is the most populous division (370,570 people) and includes the capital city of Suva, which contains approximately 174,000 inhabitants. Approximately 56.8% of inhabitants are indigenous Fijian (iTaukei), 37.5% are Fijians of Indian descent and 5.7% are other ethnicities (Fiji Bureau of Statistics, 2007 census). An urban area, the Suva-Nausori corridor, stretches from Lami, immediately west of Suva, through Nasinu to Nausori in the northeast. While numerically the population is concentrated in this corridor (and Navua), much of Central Division is sparsely populated in small rural villages and settlements proximal to major watercourses within each sub-catchment.

3.32 *Collection of typhoid case location data*

There were 236 confirmed typhoid fever cases between January 2013 and June 2015, confirmed by microbiology conducted at the Colonial War Memorial Hospital (CWMH), Suva, which were included in this study. We defined cases as residents of Central Division who had *S.* Typhi isolated from blood culture at the CWMH. Typhoid cases from the 2013 calendar year were collected retrospectively based on laboratory records of the CWMH clinical microbiology lab (Fiji Ministry of Health) where 168 laboratory-confirmed cases of typhoid fever from the five sub-divisional health centres were reported. Given the approximate two-week incubation period for *S.* Typhi, we located and obtained accurate geospatial data for all case residences during the two-week window prior to onset of fever as the most probable location of the patient coming into contact with the pathogen. 12 retrospective cases found to be residing outside of Central Division during this window were excluded. 80 cases were added from a prospective study beginning in January 2014. Only cases above the age of 18 years were eligible for enrollment in the prospective study until an amendment to ethics approvals, resulting in 6 cases not being enrolled; all age groups were enrolled from May 1st, 2014. All retrospective and prospectively enrolled cases were contacted and interviewed about their place of residence during the two-week window and geo-located by taking the position with a handheld Global Positioning System (GPS) placed one metre from the front door of their residences.

3.33 *Ethics*

Ethics approvals were obtained from the Fiji National Health Research Committee (FNHRC# 201370) and the Human Research Ethics Committee of Edith Cowan University (Proj # 10017). A research permit was obtained from the Fiji Ministry of Education, National Heritage Culture and Arts (Ref: RA 02/14) and permission was sought from provincial administrators and village chiefs before village visits. Verbal and written details of the study were provided in Fijian and/or English according to the participants' preferences, and written informed consent was obtained from all participants. All data were de-identified prior to analysis.

3.34 *Levels of typhoid incidence & recurrence*

A combination of ArcMap v10.2 geo-processing tools and field-based investigation were used to derive data for variables predicted to relate to typhoid incidence and recurrence. We estimated population data to the sub-catchment level by summing 2014 village population census data (from Provincial Offices) for all villages in each sub-catchment and estimating 450 for each settlement (average national value; Mohanty 2006), as settlements are not accounted for in national census data. For urban catchments the national census figures for 2007 were used and apportioned according to location of catchment boundaries. Cumulative incidence per 100 000 people was calculated as the total reported lab-confirmed typhoid cases within the sub-catchment boundary (between January 1st 2013 and June 30, 2015) divided by the population multiplied by 100 000. These rates were further catergorised into incidence levels: level 0=0; level 1= 1-100; level 2 =101-500; and level 3 > 500. The cutoffs for levels were chosen to allow sufficient sample size within each category for statistical comparison. The interpretation of incidence levels as "high", "medium" or "low" follows the global burden literature on typhoid incidence (e.g., Crump et al. 2004, Mogasale et al. 2014) where at a regional scale >100/100 000 is considered "high", 10-100 is "medium" and <10 is "low". As several sub-catchments were >500 we refer to > 100 – 500 as "high" and > 500 as "very high" incidence. If typhoid cases occurred within a sub-catchment boundary within any calendar year this was considered an "occurrence." The level of typhoid recurrence was calculated as the sum of occurrences within any individual sub-catchment over the study duration. Typhoid recurrence was catergorised as level 0 corresponding to no recurrence, level 1 recurrence in one, level 2 in two and, level 3 recurrence in all 2.5 years.

3.35 *Geographical data*

Geographical data were obtained as geospatial data layers and used as inputs for deriving potential environmental predictors of typhoid incidence and recurrence. Table 3.1 describes the layers, their sources and the basic processing performed before predictor variables were derived.

Table 3.1 Geospatial data layers, sources and data processing.

Base layer	Source	Dataset details	Processing details *
Viti Levu coastline	Fiji Department of Lands, National Government (NG)	NA	None
Central Division boundary	iTaukei Lands and Fisheries Commission, NG	NA	Removed small islands off Viti Levu
Road network	Fiji Department of Lands, NG	2015 update (sealed & unsealed)	None
River network	Fiji Department of Lands, NG	Primary network with 2nd order streams	None
Creek network	Fiji Department of Lands, NG	3rd order & higher creeks	Merged creek & river layers to create hydrology network layer
Dense forest cover	Fiji Department of Forestry (DoF), NG	Digitized from 2001 Landsat ETM+ data, verified against DoF vegetation maps of 2010	None
Digital terrain model (DTM)	Secretariat of the Pacific Community, Geoscience Division	25 metre resolution with contour shading	None
River catchment boundary	Wildlife Conservation Society, Suva, Fiji. (Atherton et al. 2005)	Manually digitized using 25 m DTM, hydrology network, 20 m relief contours, Government of Fiji topographic maps (1982–2002).	Small creeks in coastal catchments grouped, containing up to 20 creeks draining into the same embayment or section of coastline.
Sub-catchment boundary	Created in this study (Figure 3.1)	Generated by Watershed Explorer (ArcHydro Tools v 2.0 ESRI) using river catchment layer, river network & 25 m DTM.	Boundary polygons verified & corrected using hydrology network & topographic maps. Polygon slivers from catchments external to Central Division removed.
Climate surfaces	Landcare Research, New Zealand. (Barker et al. 2006)	Derived from Fiji Meteorological Service records (1971-2000) & rainfall data at 5 locations (43 and 91 stations for temperature & rainfall respectively)	Created projection in metres from decimal degrees & converted polygon to raster
Soil resources	Secretariat of the Pacific Community, Fiji (Leslie 2012)	Derived from Twyford & Wright (1965), revised with modern laboratory soil characterization & soil classification of soil series (Seru & Leslie 1986, Leslie & Seru 1998).	None

*All data transformed to UTM zone 60S with WGS 84 datum and processed in ArcMap 10.2 (ESRI).

In this paper we use the term “catchment” to mean the area of land where all surface water converges to a single point at a lower elevation where waters join with another water body.

Catchments drain into other catchments in a hierarchical pattern, with smaller sub-catchments combining into larger catchments.

3.36 *Sub-catchment environmental variables*

Potential environmental predictors of typhoid incidence and occurrence were derived from geospatial input (Table 3.1) at the sub-catchment scale. Descriptions of each variable and processing undertaken in ArcMap 10.2 are in Table 3.2. These data were used to describe the environmental characteristics of the sub-catchments. The hydrological function of rivers was described based on field observations by the first author in each sub-catchment using the classification system of Rosgen (1994).

Table 3.2 Environmental predict0r variables, data inputs and geospatial processing undertaken at the sub-catchment scale. RBZ (Riparian Buffer Zone) = 100 m linear buffer on both sides of river network; Forest fragments = isolated patches of forest within RBZ > 0.5 ha.

Environmental variables	Variable details	Data inputs	Processing undertaken	Processing details
1. Area (ha)	Geodesic area of sub-catchment	Sub-catchment boundary	Geometry calculated	NA
2. Dense forest (%)	Percentage cover of dense forest	Dense forest area (ha), sub – catchment area (ha)	None	Area of dense forest divided by sub-catchment area multiplied by 100
3. RBZ forested (%)	Percentage of RBZ containing dense forest	RBZ (ha), RBZ forested (ha)	None	Area of RBZ forested divided by area of RBZ multiplied by 100
4. RBZ forest fragments /km	Number of forest fragments per km of river in RBZ	RBZ forest fragments, River length (km)	None	RBZ forest fragments divided by river length (km)
5. Road density (km/ha)	Density of roads	Road length (km), Area (ha)	None	Road length (km) divided by Area (ha)
6. Creek crossings	The number of intersections between creeks or rivers and roads within the sub-catchment	Hydrology network, Road network, sub-catchment boundary	Intersected, dissolved, joined, and counted.	Creek intersections resulted in point layer; river intersections resulted in line layer. These layers joined and counted.
7. Creek crossings/km	Creek crossings per kilometre of road	Creek crossings, Road length (km)	None	Creek crossings divided by road length (km)
8. Total High Erosion Area (ha)	Area of surface soil of high and	High Erosion Area (ha), Very	None	Sum of High Erosion Area (ha)

	very high risk of erosion (Leslie 2012)	High Erosion Area (ha)		and Very High Erosion Area (ha)
9. Total High Erosion Area (%)	Percentage of surface soil of high and very high risk of erosion	Total High Erosion Area (ha), Area (ha)	None	Total High Erosion Area (ha) divided by Area (ha) multiplied by 100
10. High Flood Risk Area (ha)	Surface area of high and very high risk of flooding (Leslie 2012)	Soil resource layer, divisional boundary, sub-catchment boundary	Intersected, classified, summed by map unit	LUC categories were identified in Central Division. Classified using soil limitations (Leslie 2012) into low, medium, high and very high risk
11. High Flood Risk Area (%)	Percentage of surface area of high and very high risk of flooding (Leslie 2012)	High Flood Risk Area (ha), Area (ha)	None	High Flood Risk Area (ha) divide by Area (ha) multiplied by 100
12. Rainfall – monthly min (mm)	Average minimum monthly rainfall	Climate surface derived from Barker et al. 2006, sub-catchment boundary	Intersected, zonal statistics, average by sub-catchment	NA
13. Rainfall – annual (mm)	Average annual rainfall	Climate surface derived from Barker et al. 2006, sub-catchment boundary	Intersected, zonal statistics, average by sub-catchment	NA
14. Temperature – monthly min (C°)	Average minimum monthly temperature	Climate surface derived from Barker et al. 2006, sub-catchment boundary	Intersected, zonal statistics, average by sub-catchment	NA

3.37 *Data analysis*

Initially 43 variables were identified as potential environmental risk factors for typhoid fever infection (Appendix 1). Scatterplots were explored to reduce dimensionality of this dataset. Variables that were highly correlated ($r^2 > 0.6$) but had poor data spread were removed, yielding a total of 14 remaining predictors (Table 3.2). To determine the strength of association between remaining variables, a Spearman's rank correlation coefficient (ρ) resemblance matrix was created and significance was determined at $\alpha = 0.05$ and $\alpha = 0.01$ (df =25) (Appendix 2). Distance-based linear models (DISTLM) were applied to assess the combinations of the 14 variables that most parsimoniously predict total typhoid incidence and recurrence using the BEST selection procedure (all possible variable combinations) and Akaike Information Criterion (AIC). BEST selection procedures were chosen over a stepwise procedure to overcome falsely elevated variance due to the order in which variables are processed (Anderson et al. 2008). DISTLM models were run using modified Gower resemblance matrices (log base 10) for all data sets. Issues of collinearity were also reduced through the use of resemblance matrices, which account for this when r values < 0.95. The final selection of model variables balanced parsimony with low AIC values. A distance-based redundancy analysis (dbRDA) was used to visualise the results of the DISTLM. The dbRDA routine is a multivariate multiple regression of principal coordinate (PCO) axes on predictor variables where the routine finds linear combinations of the predictor variables that explain the greatest variation in the data cloud (Anderson et al. 2008). The dbRDA routine was used to perform constrained ordinations of the incidence and recurrence data using the environmental variables selected in the BEST outputs of the DISTLM models. The length and direction of the vectors represent the strength and direction of the relationship. Uninhabited sub-catchments were excluded from the models. DISTLM and dbRDA were performed using the PRIMER 6 and PERMANOVA + packages (PRIMER-E Ltd, Plymouth, UK).

3.4 Results

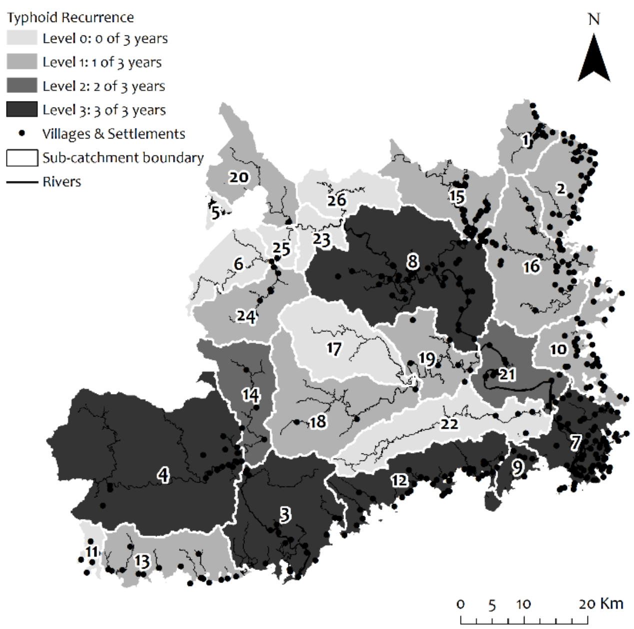
3.41 *Incidence levels*

Of 23 inhabited sub-catchments, 18 had confirmed cases of typhoid fever over the 30-month study period (Figure 3.2, Table 3.3) with four adjacent rural sub-catchments (4,14,18,24) exhibiting very high-incidence (per year range 539 - 976, mean 758; 30 month range 531 - 1197, mean 847). The highest incidence recorded in any one year was 976/100 000 in the Upper Navua River sub-catchment in 2013. Nine sub-catchments were high-incidence settings (> 100 cases/100 000/yr) in any one-year while 11 sub-catchments were high-incidence over 30months. The remaining sub-catchments, in which typhoid had been confirmed, were medium incidence settings (range 11 – 95, mean 40). Average incidence per inhabited sub-catchment over 30 months for Central Division was high at 205.9 /100 000. All five inhabited sub-catchments without confirmed cases had populations below 1500. Three sub-catchments are unpopulated (5, 17, 26) and therefore had no reported cases.

Table 3.3 Typhoid fever incidence (per 100,000) and demographic characters within sub-catchments of Central Division, Fiji. Key: Pop = population; Vil = # of villages; Set = # of settlements; Inc-13 = Incidence in 2013; Inc-14 = Incidence in 2014; Inc-15 = Incidence January to June 2015; CumInc = cumulative incidence January 2013 to June 2015; IncL = Incidence level; RepL = level of recurrence. R indicates river, Ck indicates creek, N = northern, S = southern, low = lower, mid = middle, up = upper.

Name	Pop	Vil	Set	Inc-13	Inc-14	Inc-15	CumInc	IncL	RepL
1. Dawasamu R	3241	5	8	123.4	0.0	0.0	123.4	2	1
2. Londoni Ck	8895	13	22	33.7	0.0	0.0	33.7	1	1
3. Navua R (low)	8217	8	3	133.9	12.2	36.5	182.6	2	3
4. Navua R (mid)	2209	10	8	905.4	90.5	45.3	1041.2	3	3
5. Muaira Ck (N)	0	0	0	0.0	0.0	0.0	0.0	0	0
6. Muaira Ck (S)	456	1	0	0.0	0.0	0.0	0.0	0	0
7. Rewa R (low)	140900	59	13	12.1	7.8	3.5	23.4	1	3
8. Rewa R (mid)	8860	13	26	169.3	33.9	11.3	214.5	1	3
9. Suva Central	56556	5	4	58.3	35.4	12.4	106.1	1	3
10. Savu R	9908	27	10	70.6	0.0	0.0	70.6	1	1
11. Somosomo R	1461	2	4	0.0	0.0	0.0	0.0	0	0
12. Tamavua R	49796	39	34	38.2	44.2	18.1	100.5	2	3
13. Taunovo R	3522	7	10	113.6	0.0	0.0	113.6	2	1
14. Navua R (up)	2254	6	3	976.0	221.8	0.0	1197.8	3	2
15. Wainibuka R (up)	9418	9	31	0.0	21.2	0.0	21.2	1	1
16. Waibula R	8895	13	22	11.2	0.0	0.0	11.2	1	1
17. Waiboa Ck	0	0	0	0.0	0.0	0.0	0.0	0	0
18. Waidina R	564	1	2	0.0	531.9	0.0	531.9	3	1
19. Waidradra R	1238	5	1	80.8	0.0	0.0	80.8	1	1
20. Wailoa R	1050	1	3	0.0	95.2	0.0	95.2	1	1
21. Wainalumu Ck	2967	9	3	134.8	33.7	0.0	168.5	2	2
22. Wainamanu R	1189	3	1	0.0	0.0	0.0	0.0	0	0
23. Wainasavu Ck	250	0	1	0.0	0.0	0.0	0.0	0	0
24. Waininavitilevu Ck	1131	7	1	618.9	0.0	0.0	618.9	3	1
25. Wainula Ck	363	2	2	0.0	0.0	0.0	0.0	0	0
26. Waisomo R	0	0	0	0.0	0.0	0.0	0.0	0	0

a)



b)

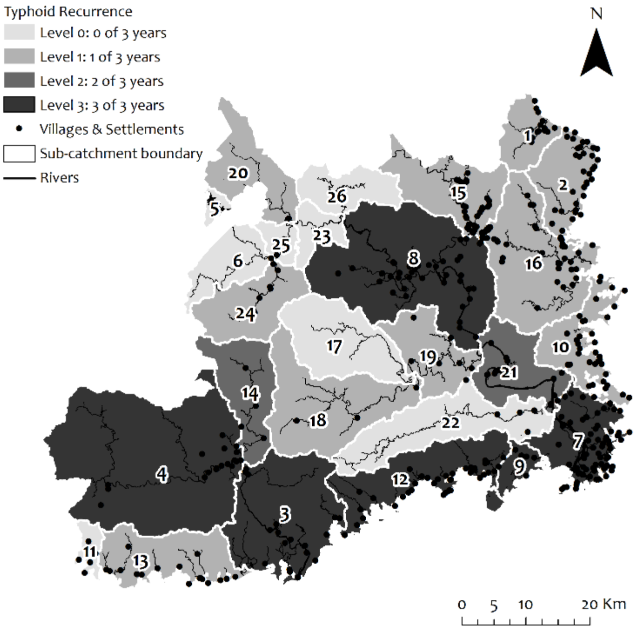


Figure 3.2 Levels of typhoid incidence per 100 000 (a) and typhoid recurrence (b) at a sub-catchment scale over 30 months (2013 -2015) in Central Division, Fiji. Sub-catchment numbers relate to data presented in Tables 3.3 and 3.4.

3.42 *Recurrence levels*

Twenty-six percent of inhabited sub-catchments had recurring cases of typhoid in each calendar year (Figure 3.2, Table 3.3). Recurring typhoid fever occurred in all highly populated urban catchments. Two rural sub-catchments had typhoid fever cases in 2013 and 2014. Ten sub-catchments had typhoid in only one of the three years. For the two full calendar years of the study, the number of cases peaked in May 2013 (24) and June 2014 (57).

3.43 *Demographics* (Appendix 3)

The median age for enrolled cases was 28 years (range: 2-78) and 51.3 % were male. Young adults from 15-30 years old presented most frequently (32.6% of cases) and 97.9 % of cases were indigenous Fijian. These findings are consistent with past studies in Fiji (Singh 2010, Thompson et al 2014). 53.7 % were urban cases and around a third (32.5%) were rural with the rest (13.8%) residing in peri-urban areas. Primary occupation was not collected from retrospective cases, however, unemployed persons (26.3 %), students (25.0%), laborers (16.3%) and housewives (13.7%) made up the majority of prospectively enrolled cases.

3.44 *Sub-catchment environmental characteristics*

There are 26 sub-catchments within the Central Division ranging in area from 57,192 ha to 1626 ha (Mean 16,012, SD 12,482; Table 3.4). Fifteen of 26 sub-catchments are within the Rewa River catchment (290,000 ha), the largest river basin in the tropical South Pacific Islands covering nearly a third of Viti Levu (Terry et al. 2002). Combined with three large sub-catchments of the Navua (Fiji's third largest river), about half the island is drained by these two primary systems. The eight remaining sub-catchments are distinct systems composed of one or more small coastal rivers. Distinct sub-catchments are complete river systems whereas all others are headwater, mid-reach or lower floodplain systems of the two large primary rivers. Smaller sub-catchments are primarily steep, mountainous headwater systems with bedrock and boulder beds, rapid flow, erosional, colluvium deposition and high-energy debris transport functions. With an increase in area, gradient generally becomes less steep with broadening valleys, meandering mid-reaches or lower floodplain systems over alluvial substrate, greater alluvial depositional function and tidal influence. The exceptions to this rule are the large, deeply gorged headwater systems of the Navua and the Waidina sub-catchment. Distinct sub-catchments are small, low gradient, meandering coastal streams, with the exception of Suva Central with narrow valleys that are deeply incised in alluvial or colluvial material with small lower reaches and unstable, high bank erosion rates. Sub-catchment area and surface area are not proportional as small headwater catchments are more topographically complex with higher surface area to geodesic area ratios than larger mid-reach and floodplain sub-catchments.

Table 3.4 Environmental characteristics of sub-catchments in Central Division, Fiji. (Key: Hydro = hydrological function; a = alluvial; c = colluvial; d = depositional; e = erosional; f = large floodplain; h = high energy debris transport; t = tidal; Area = geodesic area of sub-catchment; DF = dense forest; RBZ = forested riparian buffer zone; FF=forest fragments; RL=road length; RD = road density; CC = creek crossings; HEA = High & very high erosion risk areas; HFRA = high and very high flood risk areas; RM = minimum monthly rainfall; RA = annual average rainfall; TM = minimum monthly temperature).

Sub-catchment	Catchment	Reach	Gradient	Geography	Hydro	Area (ha)	DF (%)	RBZ (%)	FF/km	RD (km/ha)	CC(#)	CC/km	HEA (ha)	HEA (%)	HFRA (ha)	HFRA (%)	RM (mm)	RA (mm)	TM (C°)
1. Dawasamu R	distinct	all	low	coastal	ad	7449.6	79	88	2.6	2.3	20	1.2	4962.5	67	1193.9	16	107.4	2949.3	18.5
2. Londoni Ck	distinct	all	low	coastal	ad	11634.9	83	80	3.5	3.7	22	0.5	7428.5	64	4074.3	35	111.7	2897.9	18.8
3. Navua R (low)	Navua	lower	low	coastal	fad	27792.3	79	50	1.2	5.2	33	0.2	13416.9	48	6569.1	24	159.3	3340.9	17.8
4. Navua R (mid)	Navua	mid	steep	montane	ecd	57192.8	99	91	0.3	0.6	6	0.2	34718.6	61	4230.7	7	112.5	3009.1	16.0
5. Muaira Ck (N)	Rewa	head	steep	montane	ecdh	1626.6	82	45	0.6	2.1	0	0.0	629.9	39	16.3	1	173.7	4777.3	11.9
6. Muaira Ck (S)	Rewa	head	steep	montane	ecdh	9604.2	97	95	0.4	0.0	0	0.0	5955.5	62	1724.3	18	158.4	4394.6	13.1
7. Rewa R (low)	Rewa	low	low	coastal	fad	14198.5	40	39	1.6	18.2	62	0.2	6143.4	43	10741.7	76	123.5	2927.0	19.8
8. Rewa R(mid)	Rewa	mid	med	low inland	acd	43734.6	86	47	1.8	4.2	50	0.3	21363.7	49	8878.1	20	120.2	3121.1	18.3
9. Suva Central	distinct	all	high	coastal	ecd	3591.1	22	26	11.1	55.5	70	0.4	2229.7	62	2368.6	66	160.4	3377.8	19.3
10. Savu R	distinct	lower	low	coastal	t	11949.9	77	86	6.4	8.2	7	0.1	3577.8	30	3714.3	31	119.1	2679.5	19.8
11. Somosomo R	distinct	all	steep-med	coastal	cd	2659.0	99	100	2.6	6.3	7	0.4	1518.3	57	235.4	9	97.2	2383.8	17.2
12. Tamavua R	distinct	all	med	coastal	ecad	19516.0	84	63	2.0	11.7	83	0.4	11406.1	58	3295.8	17	179.4	3640.3	18.4
13. Taunovo R	distinct	all	low	coastal	ad	15570.0	93	85	1.1	4.6	26	0.4	9805.0	63	2276.6	15	118.5	2640.8	17.7
14. Navua R	Navua	head	steep	montane	ecd	13895.5	93	69	1.4	1.9	18	0.7	10557.1	76	729.0	5	135.7	3604.1	15.4
15. Wainibuka R	Rewa	head	med	montane	acd	15836.4	93	74	0.6	3.4	24	0.5	8584.2	54	782.4	5	108.6	2861.6	18.7
16. Waibula R	distinct	all	low	coastal	ad	26692.0	84	56	1.8	5.5	40	0.3	9933.8	37	6202.1	23	117.7	2771.1	19.3
17. Waiboa Ck	Rewa	head	steep -med	montane	cdh	17841.4	99	91	0.4	0.1	1	0.7	12596.4	71	1048.4	6	136.8	3544.5	16.9
18. Waidina R	Rewa	head	steep -med	montane	cdh	24722.4	95	73	0.9	2.4	36	0.6	15398.4	62	2303.9	9	151.3	3692.9	16.6
19. Waidradra R	Rewa	mid	med	low inland	acd	12064.2	87	61	1.1	4.2	17	0.3	3306.8	27	2236.3	19	140.9	3253.9	19.0
20. Wailoa R	Rewa	head	steep	montane	ecdh	13222.3	95	77	1.1	1.3	14	0.8	7235.6	55	409.5	3	110.3	3633.6	14.7
21. Wainalumu Ck	Rewa	mid	low	low inland	ad	13579.1	74	18	2.9	7.0	15	0.2	3833.1	28	4489.9	33	136.0	3046.4	19.5
22. Wainamanu R	Rewa	mid	steep	montane	cd	20840.8	92	87	0.8	3.4	21	0.3	11277.0	54	2575.2	12	161.6	3565.4	18.2
23. Wainasavu Ck	Rewa	head	steep	montane	ecdh	5016.6	95	65	1.3	1.5	2	0.3	3484.7	69	153.2	3	103.8	3067.6	17.4
24. Waininavitilevu Ck	Rewa	head	steep	montane	ecdh	13736.0	95	63	1.5	0.3	3	0.9	11625.5	85	664.0	5	138.7	3879.6	14.5
25. Wainula Ck	Rewa	head	steep	montane	ecdh	3266.7	88	53	2.1	3.9	5	0.4	2206.7	68	167.8	5	104.3	3167.5	16.7
26. Waisomo R	Rewa	head	steep	montane	ecdh	9102.4	97	87	0.4	0.0	0	0.0	5735.1	63	487.4	5	99.9	2941.2	17.9

Most (92.3 %) sub-catchments have high cover of dense forest (mean 84.8, SD 17.6), apart from two urban sub-catchments (9, 7) although forest in the 100 metres directly adjacent to the river (Riparian Buffer Zone, RBZ) is reduced in 84.6% of sub-catchments. Thirty one percent of secondary creeks and rivers contain less than half (mean 37.4, SD 12.8) of the RBZ forest, with a mean percentage of 67.1 % over all catchments (SD 21.6). The RBZ is highly fragmented in 69% of sub-catchments, without a single kilometre stretch of continuous riparian forest. Roads contribute significantly to this by bisecting a river every 2.6 km on average. Sub-catchments are highly prone to erosion, with 88% of sub-catchments demonstrating over a third of proportionate area being of "high" or "very high" erosion risk. 84. 3% of the soil within high erosion areas are silty clay loams (Leslie 2012). Around 17.2% of the division is considered high to very high risk of flooding, with floodplains of two large river systems, and the urban catchments of Suva and Navua, accounting for two thirds of this area. The Central Division receives copious amounts of precipitation throughout the year with a mean annual rainfall across all sub-catchments of 3275.7 mm (SD 538.6). Temperatures remain relatively constant throughout the year with an average low of 17.9 °C (SD 2.0).

3.45 *Distance-based linear models (DISTLM)*

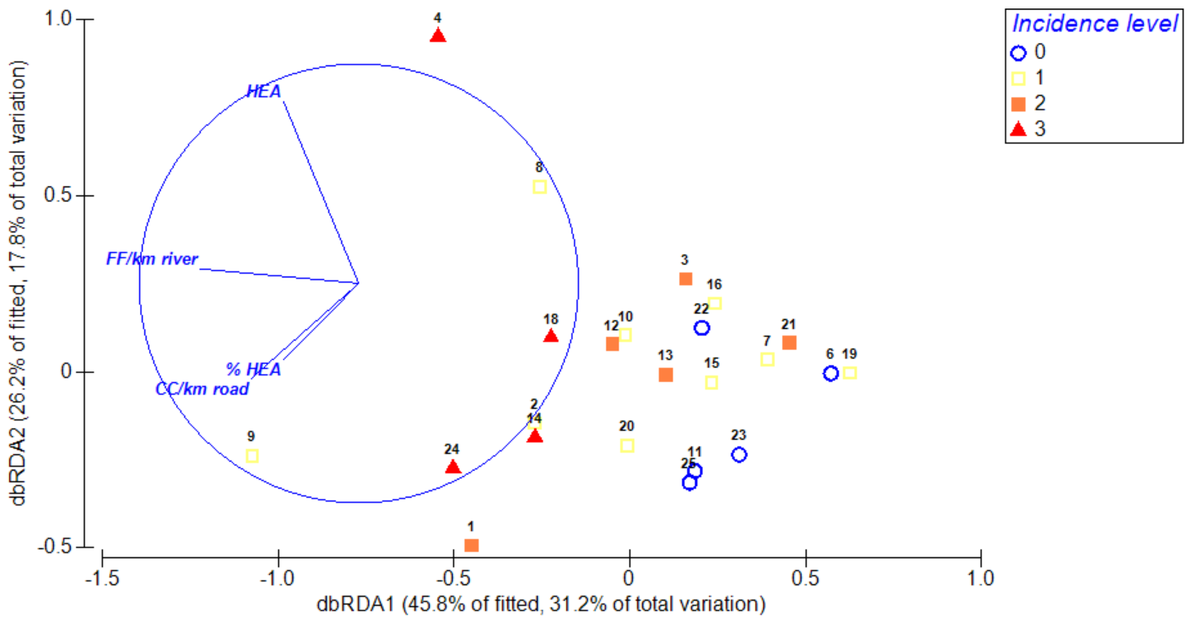
The most parsimonious model for total incidence of typhoid explained 61.0% of the variance and included, in order of importance: total area of high erosion risk, percentage of high erosion risk area, number of creek crossings per kilometre of road, and number of forest fragments within the riparian zone per kilometre of river (Table 3.5a). The most parsimonious model for recurrence explained 36.8% of variance and included, in order of importance: total area of high erosion risk, percentage of high erosion risk area, number of creek crossings per kilometre of road, and number of forest fragments within the riparian zone per kilometre of river (Table 3.5b).

Table 3.5 Results from BEST distance-based linear models (DISTLM) assessing the contributions of environmental predictor variables on (a) total incidence and (b) recurrence of typhoid. Environmental characters are listed in order of % variation attributable to each character added to the model. Only the most parsimonious solutions determined by Akaike Information Criterion are shown. HEA = High & very high erosion risk areas; CC = creek crossings; FF=forest fragments.

Predictor variable	Pseudo-F	P-value	% Variation
(a)	*Total incidence*	(R^2 = 0.61; AIC =2.88)	
HEA	5.71	0.034	21.4
%HEA	5.28	0.028	14.2
CC/km road	3.95	0.063	12.9
FF/km river	5.46	0.026	11.9
(b)	*Recurrence*	(R^2= 0.37; AIC =19.2)	
HEA	2.97	0.05	12.4
%HEA	2.37	0.09	8.7
CC/km road	2.18	0.11	8.6
FF/km river	2.02	0.13	7.1

The dbRDA diagram depicting total incidence (BEST selection procedure DISTLM, *AIC=2.88*, $R^2=0.61$) shows zero incidence sites largely separated from very high-incidence (level 3) sites along the dbRDA1 axis (Figure 3.3 a). The greatest amount of variation in the incidence data along this axis is explained by total and percentage area of high erosion risk (Table 3.5 a). The dbRDA diagram depicting recurrence (BEST selection procedure DISTLM, *AIC=19.2*, $R^2=0.37$) shows zero incidence sites separated largely from very high-incidence (level 3) sites along the dbRDA1 axis (Figure 3.3 b). The greatest amount of variation in the recurrence data along this axis is also explained by total and percentage area of high erosion risk (Table 3.5).

a)



b)

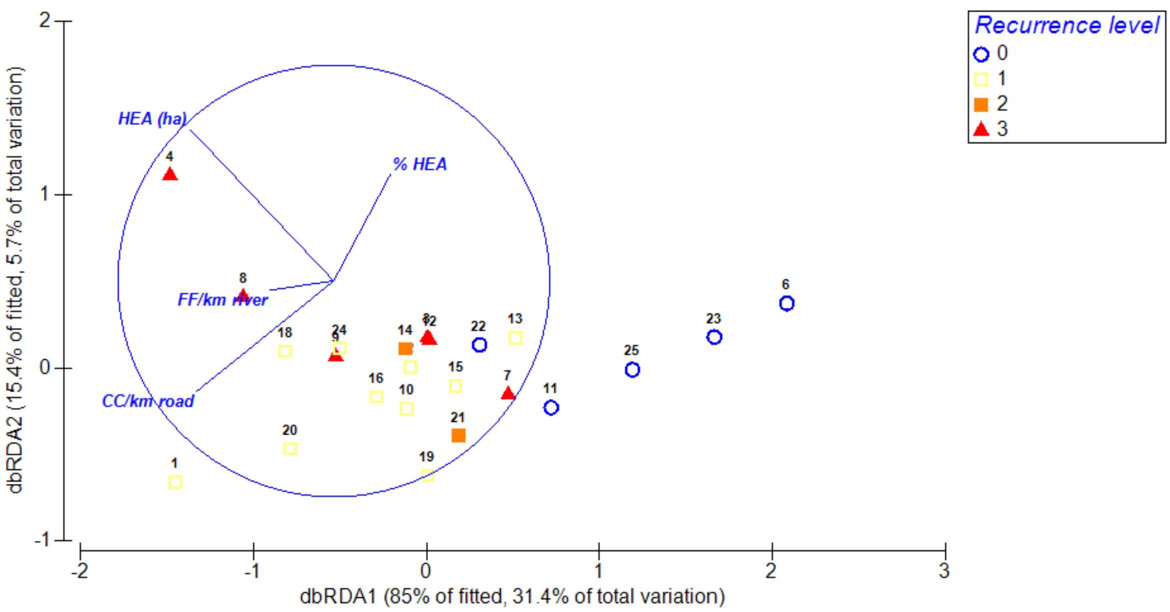


Figure 3.3 Distance-based redundancy analysis (dbRDA) ordination plots illustrating the relationship between environmental predictors that best explain the variation of typhoid (a) incidence and (b) recurrence among sub-catchments.

3.5 Discussion

Results from this study suggest that sub-catchment scale environmental factors can help explain levels of typhoid incidence and recurrence. All factors found as significant at this scale suggest increased risk of exposure where sediment yields increase following runoff.

3.51 *Hydrological function and topography*

Incidence is strongly related to total area of high erosion risk (21.4% of variation; Table 3.5), which correlates significantly with sub-catchment area (ρ =0.91) and high flood risk (ρ =0.66) (Appendix 2) and is a function of hydrology and geomorphology. Total sub-catchment area is considered a proxy for total area of high erosion risk in this context. While sub-catchment area has not previously been reported as a risk factor for typhoid fever, the hydrological consequence of increasing area is increased likelihood that habitation occurs on river flood plains and the broadened low-lying areas within catchments, thereby increasing potential for exposure. This result is supported by Dewan et al. (2013) and Corner et al. (2013) who demonstrated higher typhoid fever risk in proximity to large river floodplains and Akullian et al. (2015) and Baker et al. (2011) showing higher typhoid risk at low elevations.

Sub-catchment size and absence of vegetation largely controls the hydrologic response (Gallo et al. 2015), including faster runoff and steeper flood peaks (Griffiths et al. 2008). Larger sub-catchments have more complex drainage networks with pollutants accumulating along their length (McCarthy et al. 2012) frequently increasing nutrient concentrations and faecal coliform bacteria in receiving waters (Ekholm et al. 2000, Gallo et al. 2015). Three (6, 22, 23) of four inhabited, typhoid fever-free sub-catchments include small (<1500 people) populations located beside minor, steeply inclined, high energy, headwater systems in mountainous catchments without alluvial deposition. The remaining zero incidence sub-catchment (11) is also of low population in a steep to moderately inclined landscape formed around a small, isolated coastal river. These observations suggest that populations within small, high-energy headwater catchments and smaller streams unconnected to a larger hydrological network are at reduced risk.

3.52 *Erosion and sediment deposition*

Steep slopes, highly erodible silty clay loams and heavy rainfall predispose Central Division to high erosion risk. The total and percentage of high erosion risk area within a sub-catchment are important factors explaining both typhoid incidence (21.4% and 14.2% variation, respectively) and recurrence (12.4% and 8.7 % variation, respectively) (Table 3.5). Soil erosion is a function of slope, soil type and rainfall intensity, moderated by land cover (Shi et al. 2013) and affects the flow and water quality of streams and rivers. Poorly constructed sanitation infrastructure is frequently compromised by the combination of high rainfall and highly erodible soil (Kuylenstierna et al. 1997). Our case investigations commonly observed that soil erosion led to slumping and cracking of concrete septic tanks and undercut substrate into which latrines were built, leading to raw sewerage discharge into surrounding land and water (A. Jenkins, personal observation). As water flows across highly erodible land, associated nutrient and bacterial content is transported with eroding surface soils into receiving water bodies. Faecal contamination by *E. coli* of open water sources has been associated with proximity to soil erosion (Ngugi et al. 2014) and Rao et al. (2015) found higher *E. coli* concentrations in streams with increased turbidity and decreased dissolved oxygen.

3.53 *Road and river connectivity*

The level of connectivity between road and river networks also has implications for increased runoff exposure and was a significant factor explaining both typhoid fever incidence (12.9% variation) and recurrence (8.6% variation) (Table 3.5). The overall connectivity of the road network to the stream drainage determines the level of efficiency with which road-generated runoff and contaminants can reach receiving waters (Bracken and Croke, 2007). Subsurface flow is intercepted along road cuts and ditches and routed to surface-water systems at stream crossings as concentrated surface runoff, particularly when roads are constructed on steep slopes (Wemple and Jones, 2003). Changes in the routing of shallow groundwater and surface flow can trigger erosion, producing sediment that is delivered to downslope receiving waters (Borga et al. 2005).

In the Fijian context, roads in small catchments may be the principal source of sediment (Nelson 1987). This is particularly true in logging areas as roads are not sealed, often poorly designed and constructed on steep slopes with poor drainage (Nelson 1987), as we observed in four adjacent sub-catchments (4, 14, 18, 24) with very high-incidence (Figure 3.2 a). While road construction has been linked to outbreaks of typhoid in India and Israel due to damaged sewerage infrastructure (Bishop et al. 1998), no previous studies link road and river connectivity to typhoid fever risk, although road construction is implicated in increased transmission of numerous water–related diseases (Birley 1995). Road construction is associated with increased incidence of diahorreal disease caused by *E. coli, Giardia* and rotavirus infection (Eisenberg et al. 2006), Shigella (Tang et al. 2014), malaria (Coimbra 1988), increased mosquito biting rates (Vittor et al. 2006) and dengue vectors (Dutta et al. 1998). Mechanisms by which roads influence water related disease burden are multifarious including altering both hydrological and social processes (Eisenberg et al. 2006).

3.54 *Riparian forest fragmentation*

Riparian forest fragmentation also increases soil erosion, runoff and sediment yield in receiving waters and adjacent land. Our study highlights the importance of riparian forest fragmentation in explaining both incidence (11.9% variation) and recurrence (7.1% variation) of typhoid within a sub-catchment (Table 3.5). Shi et al. (2013) found that forest fragmentation could account for as much as 65% and 74% of the variation in soil erosion and sediment yield respectively, at a catchment scale. The buttressing effects of roots, transpiration, increased soil permeability and drainage, reduced stream velocity and dissipation of rainfall energy by canopy cover, all inhibit erosion and moderate impacts of flooding on surrounding areas (Arthington et al. 1992; Zedler 2003). Riparian fragmentation reduces the efficacy of sediment trapping and nutrient cycling (Naiman and Decamps 1997). Not only do forest buffers prevent nonpoint source pollutants from entering small streams, they also enhance the in-stream processing of both nonpoint and point source pollutants, thereby reducing their impact on downstream rivers and estuaries (Sweeny et al. 2004). Ragosta et al. (2011) demonstrated that each 1% decrease in riparian forest cover was associated with a 3.6 MPN/100 ml increase of waterborne *Enterococcus* in adjacent streams. Our results are supported by Kelly-Hope et al. (2007) who showed decreasing typhoid incidence in relation to increasing areas of forested land and Corner et al. (2013) who, in contrast, showed increased typhoid prevalence with increased urbanisation and associated vegetation loss.

3.55 *S. Typhi survival in waterlogged soil and turbid water*

Moisture content is the most important survival factor for S. Typhi in soil (Beard 1940), moderated by temperature, pH, the availability of nutrients and the antagonistic action of other competing microbes (Gerba et al. 1975). Very early research on the recovery of S. Typhi from soil has been reported up to 5.5 months (Grancher and Deschamps 1889). In soils with high water retention *S.* Typhi can survive at least 42 days and be transported over 64 m in sodden soil to receiving waters (McGinnis and DeWalle 1983), and clay loams (the dominant soil type in Central Division) will have high water retention. Lowered oxygen conditions, as seen in turbid water and water logged soils, are also known to trigger increased pathogenicity in *Salmonella*, an adaptive trait for survival in the human gut environment (Padalon-Brauch et al. 2008). Clay loams also have very high bacterial adsorption properties (Ling et al. 2002), increasing likelihood of retention and transport. Sediment deposition from erosion alters water flow, often reducing depth, flow rate, leading to pool formation, drainage congestion, water logging and increased eutrophication, particularly where there is forest clearing resulting in altered temperature regimes. Sediment particles can function as a micro-niche in which bacterial survival and replication is enhanced, not only providing shelter from grazing protozoans but where free amino acids and sugars are released from algal cells attached to sediments, providing nutrients (Winfield and Groisman 2003). In combination with nutrient loading from surface runoff, sediment-laden water and waterlogged soil likely provide enhanced growth and survival conditions for *S.* Typhi, magnifying exposure risk.

The factors related to climate were not significant in the DISTLM models. This is likely because modelled climatic conditions across the study area are largely homogenous with little variation in temperature or rainfall (Barker et al. 2006). The study was also limited to data extrapolated from a small number of rain and temperature gauges, which limited the variability seen at a smaller spatial scale.

3.6 Conclusions

While determinants such as socio-economic and behavioural factors are generally recognised as important in the transmission of typhoid (Velema et al. 1997), the configuration of land cover and infrastructure, at scales defined by hydrology and geomorphology, play important distal roles in influencing the risk of typhoid exposure at a community level. This study suggests that particular settings where sediment yields increase following runoff, can act as sites of carriage, potentially predisposing the likelihood of exposure, and therefore typhoid fever infection and disease. The development of predictive risk maps at the sub-catchment scale can be used to guide proactive interventions, including spatially targeted vaccination, improvement of water supplies and sanitation, as well as longer-term, and quite literally upstream, ecological measures such as targeted reforestation and flood prevention measures.

CHAPTER 4

Socio-ecological Determinants of Typhoid fever in the Fijian Residential Setting

4.1 Abstract

Residential setting conditions are important determinants of typhoid fever transmission, though precise factors influencing incidence and spread require local parameterisation. Case-control studies commonly focus on short-cycle transmission, without concurrently assessing spatial factors, proximal residential setting and quantifying microbiological and physicochemical characteristics of potential reservoirs within the lived environment. I used a combination of spatial characteristics, living condition observations and measured biophysical parameters to characterize risk of contracting typhoid at a residential setting level. Using a case-control design at the residential level in Central Division, Republic of Fiji, I investigated bacterial contamination and chemical composition of water and soil as vehicles of exposure, complemented with observational analysis of residential living conditions, spatial analysis of household locations and factor analysis to explore multivariate relationships. At the residential level typhoid exposure risk was significantly associated with phosphate and *E. coli* concentrations in toilet drainage soil and factors loaded with variables associated with external residential condition, drinking water contamination and sanitary condition. Socio-ecological determinants related to drainage, housing and the condition of water and sanitation provide the residential setting for poor hygiene and sanitary practice and therefore influence the risk of typhoid transmission. Environmental health practitioners can benefit from an interdisciplinary approach to categorizing environments into which *Salmonella* Typhi is shed, extending testing of causal assumptions beyond the immediate domestic domain, enhancing the scope of traditional case-control epidemiological approaches and allowing interventions to be made with greater specificity at the residential level.

4.2 Introduction

Modelling differential risk of typhoid for use in policymaking and intervention requires defining local parameters to determine the relative importance of short-cycle (household) and long cycle (environmental) transmission and the contributions of acute, convalescent and chronic carriage within that residential setting (Watson and Edmunds, 2015). While behaviours associated with faecal contamination of food and water have dominated perspectives on typhoid transmission (Valema et al. 1997), determinants related to the residential setting of the house, the condition of the lived environment, and the microbiological and physicochemical characteristics of the setting deserve more attention for their potential to influence risk of transmission. The classic case-control study remains the most widely used epidemiological approach for assessing risk of transmissible diseases such as typhoid fever, and for testing causal hypotheses in the proximal environment (Hennekens and Buring 1987), although recent geospatial studies have also shed light on risk factors at broader spatial scales (e.g., Baker et al. 2011; Dewan et al. 2013; Akullian et al. 2015; Jenkins et al. 2016)

Outside of direct faecal contamination of drinking water, high-incidence of typhoid has been associated with local climate, elevation and proximity to altered land and hydrology (Mermin et al. 1999; Kelly-Hope et al. 2007; Dewan et al. 2013; Wang et al. 2013; Akullian et al. 2015). In addition, household features have been frequently implicated in influencing risk and include: the use of untreated drinking water (Tran et al. 2005; Ram et al. 2007); poor water storage practices (Hoque et al. 1999; Sharma et al. 2009); the use of contaminated bathing water (Gasem et al. 2001); the condition of the toilet or latrine (Vollard et al. 2004; Malisa et al. 2010); and crowding and housing density (Hosoglu et al. 2005; Corner et al 2013). Inadequate drainage around the house and community has been implicated in increased risk of several enteric and diarrhoeal diseases (Cairncross et al. 1996; Moraes et al. 2003; Lall et al. 2016). Furthermore, the microbiological and biochemical properties of environmental reservoirs are also known to be associated with typhoid fever. A recent study in Kathmandu, Nepal revealed thermotolerant coliforms, nitrates, nitrites, turbidity and ammonia in drinking water were positively correlated with the presence of *Salmonella* Typhi and *Salmonella* Paratyphi A, suggesting that chemical pollution of water in this setting is likely driven by rainfall runoff and localised contamination with human faecal waste (Karkey et al. 2016). Collectively, these studies suggest that residential setting and condition of the lived environment may be important determinants of typhoid fever transmission.

To investigate this hypothesis, I used a case-control design to identify environmental risk factors operating at a residential level in Fiji that enhance typhoid fever transmission by increasing local exposure to faecally contaminated water and soil. I specifically investigated bacterial contamination and chemical composition of water and soil as vehicles of exposure and complemented these data with an observational analysis of residential living conditions and a quantitative spatial analysis of household position at each case and control location to assess risk and provide direction towards identifying intervention strategies. This combined approach not only describes the condition of the environment into which *Salmonella* Typhi is shed, but also extends the testing of causal assumptions beyond the immediate domestic domain.

4.3 Methods

4.31 *Study setting*

4.311 *Geography and demography*

The Republic of Fiji (12-22° S and 176°E-178° W) has a total land area of 18,270 km^2 spread across an archipelago of 332 islands (Neall and Trewick, 2008). This study was confined to the wettest and most populous southeastern half of the largest island of Viti Levu (10,642 km^2) in Central Division (4,293 km^2), one of Fiji's four divisions. This most populated area of Fiji (370,570 people) contains five provinces, includes the capital city of Suva (174,000 people), and is inhabited by 56.8% indigenous Fijians (*iTaukei*), 37.5% Fijians of Indian descent and 5.7% of other ethnicities (Fiji Bureau of Statistics 2007). Much of Central Division population is in Suva with the remainder in small rural villages and settlements proximal to major watercourses. The southeastern half of Viti Levu has very high mean annual rainfall (>3,200 mm), particularly during the cyclone season (November to May; Barker et al. 2006). The island of Viti Levu has steep slopes, large rivers and well-developed estuaries along coastal floodplains and complex geological origins (Neall and Trewick, 2008).

4.312 *Typhoid epidemiology*

Typhoid in Fiji is endemic with incidence increasing since the 1990s (WHO 2010), rising rapidly after 2004-05, exceeding an annual incidence of 52 cases per 100 000 in 2010 (Scobie et al. 2014). This precipitous rise in incidence may be explained by better surveillance and diagnostics, improved clinician awareness and/or an actual increase in caseload (Thompson et al. 2014). Since 2005, at least 18 typhoid outbreaks have been reported in Fiji (WHO-Division of Pacific Technical Support [WHO-DPS], unpublished data). In Fiji young adults from 15-30 years old present most frequently, in contrast to worldwide statistics where children under five are most likely to present with the illness (Thompson et al. 2014). Ninety percent of reported cases are *iTaukei* (Indigenous Fijians)

(Singh 2010). These demographics may be misleading, however, as private health care data are unavailable and blood is rarely cultured from young children. In addition, access to healthcare from the two major ethnic groups may vary (Cameron 2000). Case numbers typically peak in January to June each year, lagging the timing of the rainy season by two months (November to April; WHO/FMOH/UNDP 2011; Scobie et al. 2014), and outbreaks have been reported following cyclones and flooding (Jenkins 2010). While total number of cases is highest in urban areas, surveillance data and recent geospatial studies suggest typhoid is becoming increasingly common in rural areas (Thompson et al. 2014; Jenkins et al. 2016).

4.313 *Access to safe water and sanitation*

Little progress has been made in the past two decades to improve access to safe water and adequate sanitation in the Pacific region, where two-thirds of the population rely on unprotected sources of water and unsanitary means of excreta disposal, posing serious risks to health (WHO/UNICEF, 2016). While published statistics for Fiji show 96% access to improved drinking water and 91% access to improved sanitation (WHO/UNICEF, 2016), these data do not provide an accurate estimation of microbiological safety. An "improved" drinking water facility is generally one that "adequately protects the water from outside contamination" and includes piped household connections (Bain et al. 2014). While municipal water is largely treated, many rural and peri-urban households have piped household connections into the house or yard coming from inadequately protected and untreated surface sources (A Jenkins, personal observation), which are unaccounted for by this definition. "Improved" sanitation "hygienically separates human excreta from human contact" including septic systems, pour flush and improved pit latrines (pg. 31, WHO/UNICEF, 2016). The most recent Fiji government estimates (GOF 2006) were that 23% of the population was connected to municipal sewerage, 40% on septic systems and 37% disposing directly into land and marine environments. Pour flush and improved pit latrines are very common in rural and peri-urban areas but often shallow, subject to flooding and built into permeable soil. Septic systems are infrequently maintained and often undercut by erosion leading to cracking and leakage into the environment (Jenkins et al. 2016). For both scenarios of water and sanitation, Fiji is frequently failing to meet "improved" access.

4.32 *Residential settings*

Residential settings were measured from participants enrolled in an ongoing neighbourhood, ethnicity, and age interval (<4 years, 5-14 years, 15-24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years, 65-74 years, >75 years) matched case-control study. Patients seeking care at any of the health facilities in Central Division, who resided in Central Division, presented with a history of fever, had *Salmonella* Typhi isolated from blood culture at the Colonial War Memorial Hospital (CWMH) Clinical Microbiology Laboratory from 27 January 2014 through July 30, 2015 and whose consent/assent were obtained were defined as cases. Cases above the age of 18 years were eligible for enrollment from 27 January 2014 to May 1, 2014, thereafter all age groups were enrolled. Eighty cases and 160 controls were enrolled by July 30, 2015. Given the approximate two-week incubation period for *Salmonella* Typhi, I located and obtained accurate geospatial data for all case and control places of usual residence during the two-week window prior to onset of fever, assuming this as the most probable location of the patient coming into contact with the pathogen. All enrolled cases and controls were contacted and interviewed about their place of residence during the two-week window and geo-located by taking the position with a Garmin Map 78sc handheld Global Positioning System (GPS) placed one metre from their front door.

To recruit controls, I spun a pen at the case residence and selected the nearest house 100 steps away from the pen and in the direction of its tip (control I). Following the pen tip direction, a second control was then selected from a neighbouring village, preferably in the adjacent river basin in rural areas or the adjacent nursing zone for urban and peri-urban scenarios (control II). For control recruitment to occur, the potential control household owner had to match the case in ethnicity, must be within the same age interval and must not have experienced fever within the past one-month. The process of pen spinning was repeated until two eligible controls for each case were identified. Living conditions, microbiological contamination and physicochemical qualities of routinely contacted water and soil were assessed in a subset of 126 of the enrolled residential settings (42 cases, 84 controls). The survey methodology for each type of sampling is detailed below.

4.33 *Geographical position*

Geospatial data layers were used as inputs for deriving potential spatial risk factors for typhoid at a residential level. Table 4.1 describes the layers, their sources and the basic processing performed before potential spatial risk factors were derived. Using ArcMap 10.2, elevation and slope were precisely measured at the case and control household point locations and straight-line distance measurements were taken from this point to the nearest water body, nearest road and nearest dense forest, as described in Jenkins et al. (2016).

Table 4.1 Geospatial data layers, sources, and data processing, Fiji typhoid case-control study, 2014-15. (Adapted from Jenkins et al. 2016).

Base layer	Source	Dataset details	Processing details *
Viti Levu coastline	Fiji Department of Lands, National Government (NG)	NA	None
Central Division boundary	iTaukei Lands and Fisheries Commission, NG	NA	Removed small islands off Viti Levu
Road network	Fiji Department of Lands, NG	2015 update (sealed & unsealed)	None
River network	Fiji Department of Lands, NG	Primary network with 2nd order streams	None
Creek network	Fiji Department of Lands, NG	3rd order & higher creeks	Merged creek & river layers to create hydrology network layer
Dense forest cover	Fiji Department of Forestry (DoF), NG	Digitized from 2001 Landsat ETM+ data, verified against DoF vegetation maps of 2010	None
Digital terrain model (DTM)	Secretariat of the Pacific Community, Geoscience Division	25 metre resolution with contour shading	None
Typhoid case & control household positions	This study	Digitized from GPS Map80 position, 1m in front of house.	None

*All data transformed to UTM zone 60S with WGS 84 datum and processed in ArcMap 10.2 (ESRI).

4.34 *Living conditions*

In association with collection of water and soil samples from study households, photographs were taken of each house, the immediate external property surrounding the house, toilet and toilet drainage, bathing facilities, food gardens and nearby stream. For each household, notes were taken in relation to storm water drainage, substrate, house and yard condition, drinking water and bathing environs, solid waste disposal, condition of excreta disposal facilities, position of household garden relative to excreta disposal facility drainage and the smell near to this facility. Using photographs and notes, a post-hoc evaluation of living conditions of all households (N=126) was conducted by the author using an evaluation rubric shown in Table 4.2. Fleiss' Kappa statistic of inter-rater reliability (Landis and Koch, 1977) was used to assess the reliability of the rating measures by determining the agreement between multiple raters. A random sample of nine de-identified sets of residential setting photos and notes were given to three raters to confidently test for a greater than 0.61 kappa (substantial agreement) from four raters (the author plus his three supervisors) across five categories (alpha = 0.05, power = 0.8).

Table 4.2 Rubric for evaluation of living conditions, Fiji typhoid case-control study, 2014-15.*

Category	Blank	0	1	2	3	4
Bathing environs	Don't know	Inside, piped, treated	Inside, piped, untreated	Outside, piped, treated	Outside, piped or unpiped, untreated	Outside, stream
Drainage near house	Don't know	Excellent	Good	Moderate	Minimal	Terrible
Drinking water environs	Don't know	Inside, piped, treated	Inside, piped, untreated	Outside, piped, treated	Outside, piped or unpiped, untreated	Outside, stream
Drinking water Storage	Don't know/ Not stored	Inside, closed mouth	Inside, open mouth	Outside, closed mouth	Outside, open mouth, sheltered	Outside, open mouth, unsheltered
Faecal disposal	Don't know	Flush to sewer line	Flush to intact septic	Flush to damaged septic	Improved Pit latrine	Unimproved pit latrine
Garden position	Don't know	Distant & above toilet or septic tank	Distant & level or below toilet or septic tank	Moderate distance from toilet or septic tank	Near & above toilet or septic	Directly below toilet or septic
House condition	Don't know	Well maintained	Few repairs needed	Moderate repairs needed	Large repairs needed	Major state of disrepair
Housing density	Don't know	Very distant	Distant	Moderately close	Very close	Against another house
Smell near toilet	Don't know	None	Slight smell	Moderate smell	Clear smell of faeces or rubbish	Very strong smell of faeces or rubbish
Solid waste near house	Don't know	None	Little	Moderate	High	Very High
Substrate near house	Don't know	Paved	Fully Vegetated	Moderately vegetated	Minimally vegetated	Bare soil

*Based on a 0 – 4 rank of increased perceived likelihood of parameter facilitating or indicating disease transmission. "Blank" was regarded as equivalent to a missing value.

4.35 *Collection and analysis of water and soil samples*

Three water and three soil samples were sought from each residence wherever possible (Table 4.3). Using sterile techniques, 250 mL each of stored drinking water, the direct source of this water and water from the nearest stream or river were collected. The direct source was defined as the site from which stored water was obtained. Using sterile stainless steel trowels and measuring cylinders, 500 mL of surface soil (to 10 cm depth) was taken from 50 cm in front of the toilet, the drainage of this facility, and the food garden closest to the house. Toilet drainage samples were taken on the downhill side, one metre from the structure for external facilities and directly adjacent to where the facility drainage pipe enters the ground for municipally connected sewerage. For septic tanks, samples were taken downhill directly adjacent to the tank. To obtain measurements from these soil samples they were saturated with distilled water (500 mL at room temperature) and gently mixed for 2 minutes, then poured through a sterile stainless steel sieve (3 mL mesh) into 500 mL Pyrex sampling bottles. For all samples (water and water from soil), *in situ* measurements of pH, temperature, conductivity and dissolved oxygen concentration were taken from each sample using a Thermo Scientific Orion Star A329 (pH/ISE/Cond/DO) portable multi-meter, noting smell and colour, and placed directly into a cooler at 1 - 4°C that was transported within six hours to the Fiji Centre for Communicable Disease Control water laboratory for processing. In the laboratory, 50 mL aliquots of each sample were used to assess coliform and *Escherichia coli* contamination, 10 mL aliquots of undiluted water samples were used to measure turbidity and remaining samples were filtered to 0.45 microns (Nalgene Polysolfone PCTE filter), with filtrate retained for same day colorimetric measurement of reactive phosphorus (orthophosphate), nitrate (NO_3^-– N), and ammonia (NH_3 – N). Turbidity and colorimetric measurements were made with a Hach DR900 portable colorimeter.

To assess the microbiological quality of the water and soil specifically related to faecal contamination, I used the most probable number (MPN) method. The MPN method is a procedure to estimate the density of viable microorganisms in a test sample. It is based upon the application of the theory of probability to the numbers of observed positive growth responses to a standard dilution series of sample inocula placed in a set number of culture media tubes (McCrady, 1918). I used the 3-tube method of MPN. I inoculated 10 mL of sample into 10 mL of MacConkey broth, followed by 1 mL and then 0.1 mL of sample into 5 mL tubes of MacConkey broth. A total of 9 tubes per sample were used, 3 tubes with 10 mL MacConkey broth and 6 tubes with 5 mL MacConkey broth and, within each, an inverted Durham tube. MacConkey broth was used for the detection of coliform bacteria while the Durham tube was used for the detection of gas that is produced by the metabolic action of microorganisms. The inoculated broths were incubated at 37°C for 48 hours. After incubation, each tube was examined and those that were positive (production of acid and gas) were counted. Production of gas within the Durham tube indicated a positive reaction for gas production, while change in the colour of the MacConkey broth from the original purple to yellow indicated a positive reaction for acid production. Positives were noted as both a colour change as well as gas production. McCrady's Table was used to calculate MPN total number of coliforms in the sample (McCrady, 1918). A loop of all positive samples was placed into tubes of 3 mL of Peptone Water and then placed into a water bath at 44.5°C overnight. The following day I added 1 -2 drops of Kovak's Indole reagent to each. A brick red or bright red ring on the surface of the Peptone indicated positivity for *E. coli*. McCrady's table was used again to calculate MPN of *E.coli* in the sample.

Table 4.3 Sample sizes for microbiological/physicochemical parameters measured in residential water and soil (water from soil) samples, Fiji typhoid case-control study, 2014-15. C = cases; C*= controls; NA = Not applicable.

Microbiological/ Physicochemical Parametre	Stored Drinking Water		Drinking Water Source		Nearest Stream Water		Toilet Soil		Toilet Drainage Soil		Household Garden Soil		Total Sample Size
	C	C*	C	C*	C	C*	C	C*	C	C*	C	C*	
Coliforms (CFU/100mL)	31	52	38	77	30	41	17	25	40	77	32	55	515
***E. coli* (CFU/100mL)**	31	52	38	77	25	31	17	25	40	77	31	55	499
Turbidity (FTU)	31	52	33	67	20	22	NA	NA	NA	NA	NA	NA	225
Phosphate (mg/L)	30	50	37	74	27	27	17	23	40	74	33	53	485
Nitrate (mg/L)	30	50	36	74	25	29	17	23	39	75	32	55	485
Ammonia (mg/L)	30	50	37	76	27	34	17	24	40	76	30	56	497
Conductivity (uS/cm)	30	50	37	74	25	27	17	23	40	74	33	53	483
Temperature (°C)	30	50	37	74	25	26	17	23	40	74	33	53	482
Dissolved Oxygen (mg/L)	28	46	36	71	23	24	17	22	38	70	32	52	459
pH	30	50	37	74	24	27	17	23	40	74	33	53	482
# Measurements taken	301	502	366	738	251	288	153	211	357	671	289	485	

4.36 *Data analysis*

Initially nonparametric tests (Mann-Whitney U for continuous; Kruskal-Wallis H for categorical) were performed on the 26 residential setting scale variables (5 spatial, 11 living condition & 10 microbiological/physicochemical) to assess differences between cases and control residences. To determine the strength of association between variables, a Spearman's rank correlation coefficient (ρ) resemblance matrix was created and significance was determined at $\alpha = 0.05$ and $\alpha = 0.01$ (df = 25). To reduce data to a smaller set of summary variables and to explore underlining structure of multivariate relationships, data from 108 residences (36 cases, 72 controls) were assessed by Exploratory Factor Analysis (EFA) using Maximum Likelihood extraction. The most complete biophysical datasets (source drinking water and toilet drainage soil) were used as proxies for water and soil as they were significantly correlated ($p<0.01$) across multiple parameters. Missing values were imputed using the Expectation-Maximization algorithm (Dempster et al. 1977). I used Varimax orthogonal rotation with Kaiser normalisation to simplify the columns of the factor matrix so that factor extracts were clearly associated and separation among the variables was shown. Logistic regression was run using only significant factors to obtain odds ratios of each factor and a logistic function. The function constant is the expected value of the log-odds of typhoid risk when all of the predictor variables equal zero. Linear regressions of factor loadings against variables within each factor were used to establish relative contributions of variables within each factor and to establish a variable-based risk probability function. All statistics were performed using IBM SPSS Statistics for Windows, Version 22.0.

4.37 *Ethics*

Ethics approvals were obtained from the Fiji National Health Research Committee (FNHRC# 201370) and the Human Research Ethics Committee of Edith Cowan University (Proj # 10017). A research permit was obtained from the Fiji Ministry of Education, National Heritage Culture and Arts (Ref: RA 02/14) and permission was sought from provincial administrators and village chiefs before village visits. Verbal and written details of the study were provided in Fijian and/or English according to the participants' preferences, and written informed consent was obtained from all participants. All data were de-identified prior to analysis.

4.4 Results

4.41 *Proximal residential setting*

Spatial data revealed typhoid case residences to be significantly closer to flowing water bodies by an average of 110 m (Mann-Whitney U = 2537, n_{case} =80, $n_{control\ II}$ = 80, p =0.023 two tailed), further from the nearest road by an average of 35 m (Mann-Whitney U = 2359, n_{case} =80, $n_{control\ II}$ = 80, p =0.004 two tailed) and 24 m lower in elevation (Mann-Whitney U = 2713.5, n_{case} =80, $n_{control\ II}$ = 80, p =0.049 two tailed) on average than control II residences (Figure 4.1).

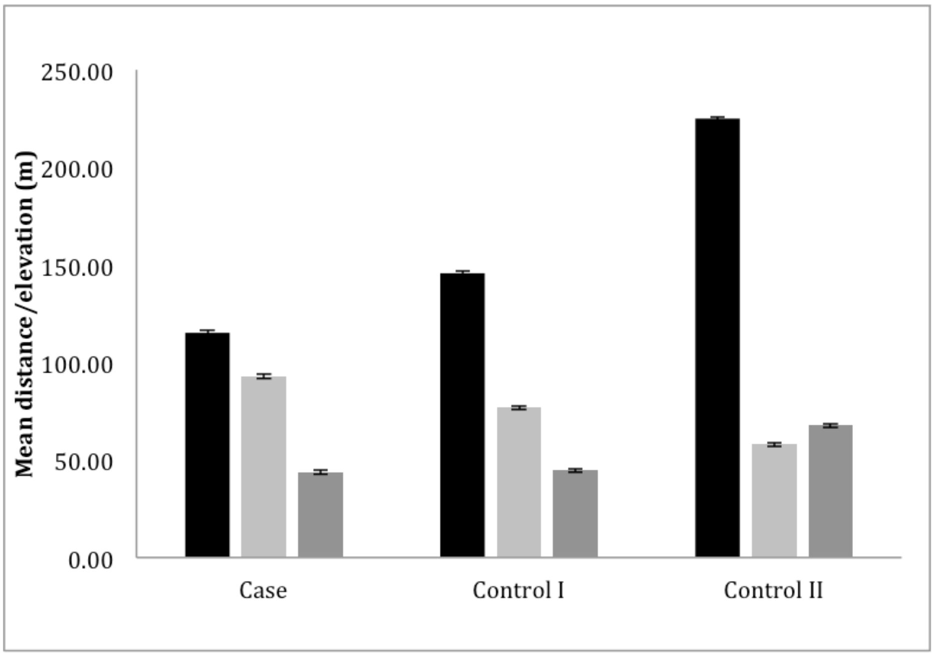


Figure 4.1 Mean proximal residential setting of typhoid cases versus control households in Central Division, Fiji (Cases; N =80, Control I; N= 80, Control 2; N=80). Black columns = nearest water; grey columns = nearest road; white columns = elevation; error bars = +/- standard error. Only significant parameters are shown.

4.42 *Household living conditions*

The Fleiss' Kappa inter-rater reliability was found to be 0.62 ($p<0.05$), indicating "substantial agreement." Several conditions in the lived environment of case households were significantly different from control households (Kruskal-Wallis H Test; $p< 0.05$) (Figure 4.2). For comparisons to both controls, case residences had significantly poorer stormwater drainage (case vs control I: X^2 = 8.758, p= 0.003; case vs control II: X^2 = 18.993, p= 0.000); more exposed bare soil (case vs control I: χ^2 = 6.967, p= 0.008; case vs control II: χ^2 = 11.763, p= 0.001), poorer household condition (case vs control I: χ^2 = 5.543, p= 0.019; case vs control II: χ^2 = 10.063, p= 0.002) and food gardens nearby to toilet or septic drainage (case vs control I: χ^2 = 16.849, p= 0.000; case vs control II: χ^2 = 17.042, p= 0.000). Compared to control II residences, cases also had significantly less contained excreta disposal (i.e. damaged septic tank or pit latrine) (case vs control II: χ^2 = 4.330, p= 0.037) and greater smell of faeces near the toilet (case vs control II: χ^2 = 10.659, p= 0.001). Within the same community, cases houses also had significantly higher amounts of unconstrained solid waste (case vs control I: χ^2 = 4.414, p= 0.036) nearby than control I houses.

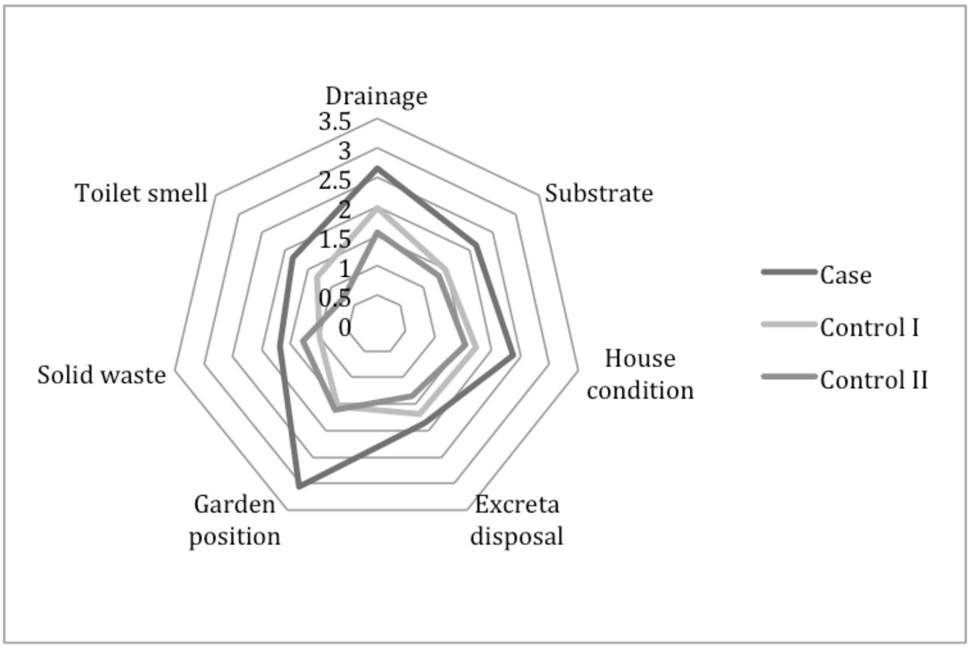


Figure 4.2 Mean rank of household living conditions for cases versus controls in Central Division, Fiji based on a 0 – 4 rank of increased perceived likelihood of condition facilitating or indicating disease transmission. Only significant conditions are shown.

4.43 *Biophysical parameters of water and soil*

4.431 *Escherichia coli in stored water*

The concentration of *E. coli* in stored drinking water in case households was significantly higher than both control I (Mann-Whitney U = 316.5, n_{case} =31, $n_{control\ I}$ = 25, p =0.032 two tailed) and control II (Mann-Whitney U = 360.5, n_{case} =31, $n_{control\ I}$ = 27, p =0.023 two tailed) households, by factors of 5 and 25 respectively, whereas controls did not differ significantly from each other (Figure 4.3).

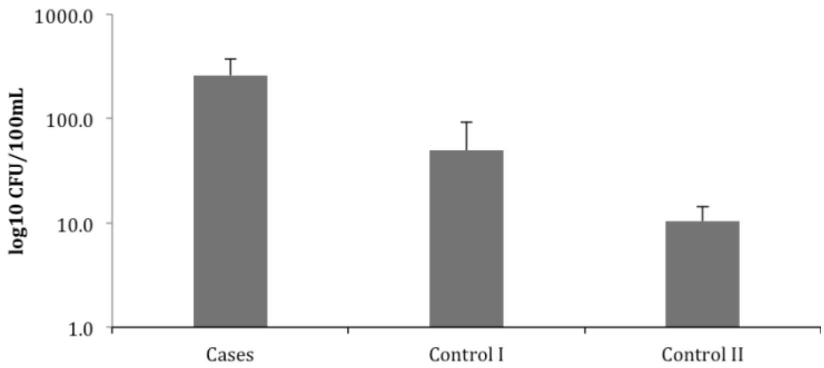


Figure 4.3 Mean most probable number (MPN) log 10 CFU of *E. coli* per 100 mL of drinking water stored by case and control households. Error bars = +/- standard error.

4.432 *Physicochemical parameters*

The mean concentration of phosphate was significantly higher in stored drinking water (Mann-Whitney U = 294.5, n_{case} =30, $n_{control\ I}$ = 24, p =0.045 two tailed) and the drinking water source (Mann-Whitney U = 446.0, n_{case} =37, $n_{control\ I}$ = 36, p =0.023 two tailed) in case households compared to both control (Mann-Whitney U = 227.0, n_{case} =30, $n_{control\ I}$ = 26, p =0.007 two tailed; Mann-Whitney U = 508.5, n_{case} =37, $n_{control\ II}$ = 39, p =0.027 two tailed) households, whereas controls did not differ significantly from each other. Cases households also had significantly higher phosphates in toilet drainage soil (Mann-Whitney U = 543.5, n_{case} =40, $n_{control\ II}$ = 38, p =0.03 two tailed) than control II households, whereas controls did not differ significantly from each other (Figure 4.4).

The mean concentration of ammonia was also significantly higher in stream water nearest to case households (Mann-Whitney U = 319.5, n_{case} =27, $n_{control\ II}$ = 17, p = 0.03 one tailed) compared to control II households. Cases and control I stream water ammonia concentration did not differ significantly from each other, though control I and control II samples were significantly different (Mann-Whitney U = 251.0, $n_{control\ I}$ =17, $n_{control\ II}$ = 17, p = 0.037 two tailed). Mean electrical conductivity was also significantly higher in toilet drainage soil of cases than control II households (Mann-Whitney U = 535.0, n_{cases} =40, $n_{control\ II}$ = 38, p = 0.024 two tailed) whereas controls did not differ significantly from each other.

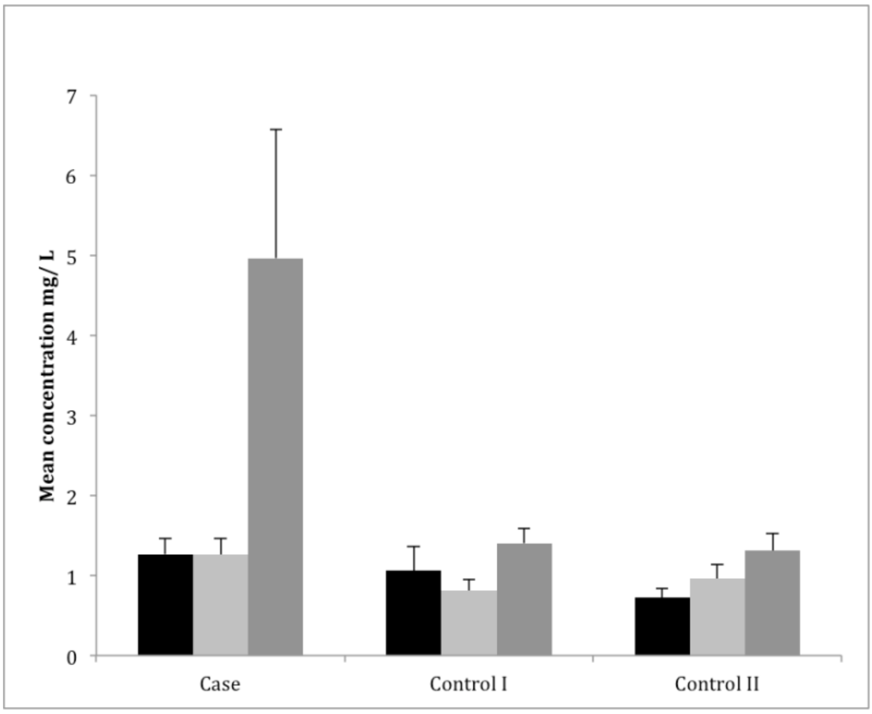


Figure 4.4 Mean concentration of phosphates in water and soil in the residential setting of cases and controls. Black columns = stored drinking water; grey columns = drinking water source; white columns = toilet drainage soil; error bars = +/-standard error. Sample sizes for cases, control I and control II: Stored drinking water: n=30, 24, 26, respectively; Drinking water source: n=37, 35, 39, respectively; toilet drainage soil: n=40, 36, 38, respectively.

4.44 *Factor analysis*

Initially the factorability of 35 variables was examined and nearest water, nearest forest and slope were excluded due to communalities below 0.3. All remaining communalities were above 0.3, confirming each variable shared some common variance with other items (Table 4.4); 30 of the 32 remaining variables were correlated at a level of 0.3 or higher with at least one other item. The Kaiser-Meyer-Olkin measure of sampling adequacy was 0.585, above a recommended value of 0.5 (Tabachnick and Fidell 2001) and Bartlett's test of sphericity was significant (χ^2 = (496) = 1197.98, p<0.05). Given these indicators, factor analysis was deemed suitable with 32 variables (Appendix 4).

Table 4.4 Summary of Exploratory Factor Analysis for residential risk of Typhoid using Maximum Likelihood estimation with Varimax rotation showing communalities, % variance explained and eigenvalues (N = 497), Fiji typhoid case-control study, 2014-15. Only significant factors and associated variables are shown. Factor loadings above 0.4 are shown in bold. SHW = source of house water; TDS = toilet drainage soil.

			FACTORS			
VARIABLES	1 (External Condition)	2 (Drinking Water Condition)	3 (Sanitary Conditions)	4 (TDS Microbial)	5 (TDS Nutrient)	Communalities
Substrate	**.827**	.000	-.008	.035	-.037	.648
Drainage	**.780**	.177	.157	-.008	.034	.706
House condition	**.724**	-.003	.006	-.041	.084	.665
Solid Waste	**.532**	-.165	.035	-.185	-.007	.515
Garden position	**.448**	.279	.236	-.101	.126	.471
***E. coli* SHW**	.078	**.665**	-.138	-.070	-.110	.487
Drinking water storage	.007	**.634**	.151	.090	.170	.506
Phosphate SHW	-.049	**.472**	-.087	-.145	.047	.408
Nearest road	.055	**.459**	.149	-.089	-.028	.427
Toilet smell	.277	-.054	**.642**	.008	.045	.510
Ammonia SHW	-.009	.094	**.420**	.165	-.080	.360
***E. coli* TDS**	-.032	-.064	.011	**.592**	.111	.405
Ammonia TDS	-.001	-.128	.356	**.590**	.085	.368
Phosphate TDS	.080	.113	-.077	.171	**.899**	.452
Eigenvalue	4.193	3.010	2.516	1.976	1.892	
Cumulative % variance	13.1	22.5	30.4	36.5	42.5	

Note: factor loadings above 0.4 appear in bold.

Exploratory factor analysis with Varimax rotation resulted in 11 factors based on eigenvalues greater than one, five of which were significant in predicting typhoid (78.7% correct) with a backwards Wald stepwise regression (Table 4.5) and explained 42.5% of the cumulative variance (Table 4.4). Variables clustered together along significant factors characterized by: [factor 1] external condition (related to substrate, drainage, house condition, amount of solid waste near house, and garden position); [factor 2] drinking water condition (related to *E. coli* concentration in source house water, drinking water storage, phosphate concentration in source house water, and distance to nearest road); [factor 3] sanitary condition (related to ammonia concentration in source house water and toilet smell); [factor 4] microbial loads (related to *E. coli* and ammonia concentration of toilet drainage soil (TDS)); and [factor 5] nutrient load (phosphate concentration) of TDS. The probable risk of typhoid exposure at a residential level in this endemic Fijian setting can be expressed as the following logistic function:

$$e^{(-0.908 + 1.312\,[\textbf{External Condition}] + 1.005[\textbf{Drinking Water Condition}] + 0.680\,[\textbf{Sanitary Condition}] + 0.810\,[\textbf{TDS - Microbial}] + 1.443\,[\textbf{TDS - Nutrient}])}$$

Table 4.5 Factors significantly predicting typhoid in the residential setting using backwards Wald logistic regression, Fiji typhoid case-control study, 2014-15. TDS = toilet drainage soil, B = regression coefficient, Exp (B) =Odds Ratio.

	B	S.E.	Wald	df	p	Exp (B)
External Condition	1.312	.349	14.119	1	.000	3.712
Drinking Water Condition	1.005	.335	8.999	1	.003	2.732
Sanitary Condition	.680	.315	4.656	1	.031	1.973
TDS - Microbial	.810	.371	4.758	1	.029	2.248
TDS - Nutrient	1.443	.710	4.134	1	.042	4.235
Constant	-.908	.284	10.246	1	.001	.404

Odds ratios of typhoid risk is highest for the factor associated with nutrient loading of toilet drainage soil (OR 4.235, p = 0.042), followed by factors loaded with variables associated with: external residential condition (OR 3.712, p = 0.000); drinking water condition (OR 2.732, p =0.003); microbial contamination of toilet drain soil (OR 2.248, p=0.029); and sanitary condition (OR 1.973, p=0.031). Linear regression of risk factors against component variables resulted in the following five functions, which indicate relative importance of the variables within each risk factor:

i) **External Condition** = - 1.830 + 0.384 (Substrate) + 0.249 (Drainage) +0.197 (House condition) + 0.146 (Solid waste)+ 0.055 (Garden position)

ii) **Drinking Water Condition** = - 0.691 + 0.509 (Drinking water storage) + 0.201 (Phosphate SHW) + 0.002 (Nearest road) + 0.001 (*E.coli* SHW)

iii) **Sanitary Condition** = - 0.611 + 2.181 (Ammonia SHW) + 0.404 (Toilet smell)

iv) **Toilet Drainage-Microbial** = - 1.617 + 0.001 (*E.coli* TDS)

v) **Toilet Drainage-Nutrient** = -3.72 +0.140 (Phosphate TDS)

4.5 Discussion

The results support the hypothesis that multiple spatial and biophysical determinants act at the residential setting scale to influence the probability of typhoid transmission, which appears to be associated with poor drainage, flooding and hygiene that increase local exposure to contaminated water and soil. These particular observations and measurements can aid prediction of typhoid exposure risk in similar endemic settings and help to prioritise remedial measures.

4.51 *External conditions*

There are several explanations for a strong relationship between typhoid exposure risk at the residential level and external conditions of the household setting. Poorly drained stormwater and household wastewater (sometimes referred to as "sullage") can create stagnant pools, providing sites for bacterial growth, exposure to pathogens and breeding sites for several disease vectors (Lall et al. 2016). Poor stormwater drainage can lead to flooding which may damage water supply or sanitation infrastructure. Further, where drainage and sanitation are inadequate, runoff can transport faeces across land and contaminate domestic water sources (Ngugi et al. 2014), and household wastewater may also contain pathogens that can pollute groundwater (Craun 1985).

In our study, patients with typhoid fever residing at lower elevations and in closer proximity to surface water bodies (i.e. streams) had poorer drainage and significantly higher *E. coli* concentrations in stored drinking water. These findings are backed by previous studies that identified the importance of elevation in predicting typhoid risk across several spatial scales. For example: Dewan et al. (2013) and Corner et al. (2013) demonstrated higher typhoid fever risk with proximity to rivers; Akullian et al. (2015) and Baker et al. (2011) showed higher typhoid risk at low elevations; and Vollard et al. (2005) demonstrated increased risk in association with flooding. The related study assessing spatial patterns of typhoid incidence in Central Division, Fiji (Chapter 3), also demonstrated increased incidence in the broadened low-lying areas within sub-catchments where potential for flooding and exposure to contaminated runoff is higher (Jenkins et al. 2016).

While the proportion of exposed soil in the residential setting has yet to be reported as a risk factor for typhoid, the mechanisms by which exposed soil can facilitate increased microbial pathogen exposure are salient. Vegetated areas produce less runoff than bare or impervious surfaces (Gaffield et al. 2003). Greater amounts of exposed soil in the residential setting contribute to higher local rates of erosion and runoff, and when combined with poor stormwater drainage, facilitate increased faecal and nutrient contamination of open water sources and a greater capacity to undermine sanitation infrastructure (Ngugi et al. 2014; Jenkins et al. 2016). I found the relationship between proportion of bare soil and level of drainage to be highly significant ($\rho = 0.563$, $p = 0.000$), as runoff from bare ground contributes directly to drainage congestion, stagnant pool formation, water logging and increased eutrophication (Gaffield et al. 2003). The high water retention and bacterial adsorption properties of clay loams, the primary soil type in the Central Division (Leslie 2012), also increase the likelihood of bacterial survival and transport into the house or nearby drainage (Ling et al. 2002). Furthermore, Jenkins et al. (2016) demonstrated that typhoid incidence and recurrence in Central Division strongly correlate with area of high erosion risk at a sub-catchment scale, indicating a mechanistic connection to exposed soil across landscapes.

This study also pinpoints that the type and maintenance of sanitation infrastructure is associated with increased typhoid risk. These results reflect both socio-economic status and occupant efforts in household maintenance and waste disposal. The mechanisms by which housing conditions and solid waste can affect likelihood of typhoid occurrence have both direct and indirect biological (e.g., poor hygiene conditions) and psychological pathways (e.g., apathy) (Smith 1990). These results are supported by the findings of Gasem et al. (2001), who found typhoid fever was associated with poor housing, and Corner et al. (2013) who found typhoid strongly associated with a quality of life factor, including mean house price and proportion of slum dwellings. Khurmi and Kumar (2011) also found that neighbourhood quality, defined by housing density, street width and roof area, provided the highest coefficient of determination in explaining the incidence of dengue, a vector-borne disease associated with the presence of stagnant water. Future research should therefore focus on direct comparisons of socio-economic status and hygiene behaviours in assessing typhoid risk.

In the Fijian context and throughout much of the Pacific, it is common practice to have a small garden of staple root crops (e.g., taro, cassava) near the house for domestic use. While propagating vegetables in nutrient rich drainage areas is a common and traditional practice throughout the region (Siwatibau 1984), our study revealed that case household gardens were positioned significantly closer to the household toilet or septic tank, and the majority of cases (76%) propagated vegetables directly on or below the toilet drainage area. Garden position on or below the drainage area correlated significantly with ammonia in the garden soil and the smell of faeces near the toilet, suggesting faecal contamination. This vegetable propagation practice can be considered a form of passive use of human waste for fertiliser. While proximity of household garden to toilet drainage has never been specifically identified as a risk factor for typhoid, active fertilization of produce with human faeces has been implicated in long-cycle typhoid fever transmission (Sears et al. 1984).

Figure 4.5 Household root crop gardens propagated directly on the toilet drainage area are common among Central Division typhoid cases.

4.52 *Drinking water conditions*

We found that typhoid risk at the residential level is associated with household drinking water conditions. The method of storing drinking water may also be important in evaluating drinking water conditions as it was significantly correlated to *E. coli* contamination at residences where wide-mouthed storage containers were kept outside the house. Mean concentrations of phosphates were also significantly higher in both the stored drinking water and the source of drinking water in case households compared to controls. Phosphate readily binds to ultrafine (e.g., clay) sediment particles, which if washed into water sources can be a primary source of contamination (Golterman 2007). This is noteworthy in light of Jenkins et al. (2016)'s (Chapter 3) finding that significant environmental determinants of typhoid at the sub-catchment level are linked to increased risk of exposure from erosion prone areas. Although sources of phosphates can be natural and anthropogenic, our finding that phosphate concentration in stored and source water is positively correlated with *E. coli* numbers and is significantly higher in the toilet drainage soil suggests faulty excreta disposal as a likely source. Among the thermotolerant coliforms, *E. coli* is the preferred microbial indicator of recent faecal contamination of drinking water and the possible presence of disease-causing pathogens (WHO 2011). While elevated phosphate in drinking water has not previously been reported as a risk factor for typhoid, a recent study by Karkey et al. (2016) revealed thermotolerant coliforms, nitrates, nitrites, turbidity and ammonia in water were positively correlated with the presence of *Salmonella* Typhi and *Salmonella* Paratyphi A, suggesting that pollution of drinking water in this endemic setting is likely driven by localised contamination with human faecal waste. The use of narrow-mouthed storage containers within the house is likely to reduce these contamination risks (Deb et al. 1986; Luby et al. 2001; Mintz et al. 2001; Sharma et. al 2009).

Typhoid case residences were significantly further from the nearest road by an average of 34.8 m compared to control II households (Figure 4.1). It is thus not surprising that the spatial measure of nearest road clustered with variables associated with drinking water condition that are correlated with poorer excreta disposal . Rural residences in Fiji and the region (where roads are fewer) are typically more remote from municipal treated drinking water and sewerage services (WHO/UNICEF, 2016). Also, roads have drains and culverts, so residences closer to roads will have greater protection from surface water flows, and water will move more quickly through an area where drains and culverts are not blocked (with the reverse being true when they are not well maintained). While this variable has not been previously reported as a risk factor for typhoid, Jenkins and Cairnscross (2010) revealed proximity to roads as a key factor for developing country communities adopting improved sanitation practices.

Our univariate analysis showed significantly higher concentration of *E. coli* in stored drinking water in case households, although the source of this drinking water did not differ significantly, suggesting contamination is occurring within the residential setting.

The literature that deals with the relationship between *E. coli* contamination and typhoid risk is conflicted, with Luby et al. (1997) showing no difference in the microbiological water quality of home drinking water between cases and controls whereas Karkey et al. (2016) found thermotolerant coliform numbers in source drinking water were positively correlated with the presence of *Salmonella* Typhi and *Salmonella* Paratyphi A. It should be highlighted that the average concentration of *E. coli* in stored water across all our study households (cases and controls) was 115.24 CFU/100 mL (N = 83, Range 3 -2400, SD 416.3), which is classified as "gross pollution" by WHO standards (WHO 2011), indicating poor residential water quality in general. In addition, the concentration of *E. coli* in water of the nearest stream was substantially greater in case than control II households (Mann-Whitney U test; p = 0.059), suggesting that variables that influence the external condition factor (e.g., poor drainage and exposed soil near the house) are likely both acting to enhance the risk of pathogen exposure during periods of heavy precipitation, either through secondary contamination of stored water or direct contamination of exposed water sources. While *E. coli* or thermotolerant coliforms in drinking water are important indicators of faecal contamination, they are imperfect and their presence does not necessarily equate with risk since water quality varies both temporally and spatially and occasional sampling may not accurately reflect actual pathogen exposure (WHO 2011). It has also been suggested that *E. coli* may be present or even multiply in tropical waters not subject to human faecal pollution (Fujioka et al. 1999), which could confound results. Cross tabulation or multivariate approaches combining results of sanitation surveys (WHO 2011) and potential for flooding will likely yield enhanced predictive power.

4.53 *Sanitation conditions*

The exposure of individuals within a residential setting to improperly disposed excreta is a clear risk factor for typhoid in an endemic context (e.g., Sharma et al. 2009; Malisa et al. 2010), as supported by the study findings that high nutrient and microbial concentration in toilet drainage soil and poor sanitary conditions are all associated with typhoid risk in Central Division, Fiji. For enteric diseases in general, it is suggested that prevention of excreta entering the domestic arena has a greater impact on health than behaviours preventing pathogens in the environment from being ingested (e.g., hand washing; Curtis et al. 2000). A residential setting that has poor drainage and frequent flooding with unimproved pit latrines and damaged septic systems, situated in permeable, highly erodible soil, is highly conducive to typhoid transmission. Pit latrines have been shown to be a risk factor for typhoid in several studies both with and without flooding being implicated (Vollard et al. 2004; Malisa et al. 2010), and damaged sanitation infrastructure has been linked to several typhoid outbreaks (Bishop et al. 1998).

4.54 *Study limitations*

First, in trying to elucidate environmental exposure, community controls (control I) were usually residing in settings relatively similar to the cases, which may mask detection of local risk factors. Controls may have also been exposed to typhoid but if afebrile in the last month were eligible for recruitment. Many significant findings related to proximal residential position, for example, only relate to second controls external to the case community, highlighting the need for multiple controls in this type of study. Second, using observational and measured data as part of a case-control study design eliminates the often criticized re-call bias (Hennekens and Buring 1987), but can also introduce observational bias as the observer is aware of which residences are cases and controls. I dealt with this for household living condition observations by measuring inter-rater reliability with de-identified observational data, however, this requires increased time and personnel investment. Third, as single observations and measurements are made after the disease has occurred, one cannot ascribe causality to the factors that are measured or establish a timeline of exposure. For example, my measurements of high phosphates in the water and soil of cases could be explained by residual detergents remaining after cases attempt to clean up in anticipation of my study team arriving. While triangulation with my other observational and measured variables suggests this is probably not the case, it cannot be ruled out as a possibility. Fourth, seasonal variation may also introduce a level of variability that is unaccounted for in this design, resulting in elevated nutrient and microbial concentration after periods of heavy rainfall (e.g., Karkey et al. 2016). Fifth, as only 42.5% of the variance in typhoid risk was explained by residential setting factors, residual variance may be explained by factors operating at a larger scales (e.g., Chapters 2, 3). Fifth, one of the commonly cited advantages of the case-control design is that it is relatively cheap and rapid (Hennekens and Buring 1987) compared to cohort or randomized controlled trials, however, introducing intensive sampling, lab analysis and GIS into the design results in time constraints, increased associated costs and limits sample sizes. As a result, sample sizes are relatively low in this study, limiting the generalizability of the results.

4.6 Conclusions

While behavioural determinants such as hygiene and sanitary practice are commonly recognised as important in the transmission of typhoid (Valema et al. 1997), environmental factors related to drainage, housing and the condition of water and sanitation provide the residential setting for these practices and therefore influence the risk of transmission. Environmental health practitioners would benefit from an interdisciplinary approach to categorizing the environment into which *Salmonella* Typhi is shed to extend the testing of causal assumptions beyond the immediate domestic domain, enhance the scope of traditional case-control epidemiological approaches and allow targeted WASH interventions to be made with greater specificity at the residential level.

CHAPTER 5

Socio-cultural, behavioural and environmental risk factors for typhoid fever in Fijian households.

5.1 Abstract

Typhoid fever is endemic in Fiji, with the highest reported annual number of cases of any country in the South Pacific, yet local risk factors for disease have not been studied. The purpose of this case-control study was to identify local risk factors to advise targeted disease control programmes. We sought patients with blood culture-confirmed typhoid fever from February 2014 through August 2016 and two age interval, gender, ethnicity, and residential area matched controls per case. Matched univariate and multivariate analysis were used to evaluate associations between exposures and risk of typhoid fever. We enrolled 160 patients with typhoid fever and 319 controls. Of cases, the median (range) age was 27 (2-78) years, 82 (51%) were female, 77 (48%) who resided in a rural area and 151(94%) were indigenous Fijian. Overall, using an unimproved pit latrine, not washing produce or hands before eating, bathing outside, where drinking water was not always accessible, having wood plank floors and attending mass gatherings were risk factors for typhoid fever. Our findings suggest transmission by consumption of unwashed produce and ingesting contaminated surface water. Additional factors related to activities in the water catchment (presence of livestock above where drinking water was sourced, dams located higher in the basin, flooding of the nearest river or stream in the last two months) likely contribute to enhanced contamination risk, confirming work done at different scale levels. Mass gatherings and poor personal hygiene practices are common and appear to increase risk. Improved sanitation facilities that protect surface water and produce from contamination by human faeces are likely to contribute to typhoid control in Fiji.

5.2 Introduction

Typhoid fever remains a substantial cause of morbidity and mortality in many regions of the developing world, with an estimated 20.6 million new infections and 223,000 deaths annually (Mogasale et al. 2014). While the majority of typhoid studies have been conducted in highly populated continental regions of Southeast Asia and Africa, few have studied the isolated, sparsely populated endemic settings of the Pacific region (Thompson et al. 2014, Jenkins et al. 2016). Several Pacific island countries have reported high-incidences and serious outbreaks, including Papua New Guinea (Talme et al. 1994, Passey 1995), Western Samoa (SDOH 1993), Nauru (Olsen et al. 2001), Tonga (Hirshman 1976) and Fiji (WHO 2010, Thompson et al. 2014, Jenkins et al. 2016). Reported annual incidence rates between 817 to 1052 per 100, 000 in rural Papua New Guinea (Passey

1995) and Fiji (Scobie et al. 2014, Jenkins et al. 2016) support a high regional estimate of approximately 100 per 100, 000 (Crump et al. 2004) for the Pacific, although accurate incidence estimates and risk assessment are often difficult in resource poor island settings with substantial underreporting and limited surveillance (Scobie et al. 2014).

The World Health Organisation (WHO) recommends use of typhoid vaccines for controlling the disease in endemic and epidemic settings, although delivery of safe water, adequate sanitation, and hygiene promotion (WASH) remain the foundation of typhoid prevention and control (WHO 2008). Specific interventions for typhoid control are primarily directed by epidemiological evidence for modifiable local risk factors that support transmission within the household (short-cycle) and in the proximal environment (long cycle), along with population specific information on acute, convalescent and chronic carriage (Watson & Edmunds, 2015). Case-control studies remain the principal epidemiological method to identify biologically convincing risk factors for typhoid in the household and proximal environment and to advise modes of interrupting transmission (e.g., Mbakaya et al. 2015; Alba et al. 2016), although geospatial analysis is increasingly used to elucidate risk factors at broader scales (e.g., Dewan et al. 2013; Akullian et al. 2015; Jenkins et al. 2016).

As *Salmonella enterica* serotype Typhi has a high infectious dose of around of around 10^4 organisms (Levine et al. 2001), direct transmission without some type of vehicle is highly unlikely and only ever documented via oral-anal sexual practices (Reller et al. 2003). Indirect (both short and long cycle) transmission involves vehicles (e.g., water or food) and is understood to be the most common route of contracting typhoid fever (González-Guzmán 1989). A wide variety of socio-cultural and behavioural risk factors and typhoid transmission vehicles are described primarily from Asian and African environments. Contaminated water and food, inadequate sanitation, poor hygiene, contact with typhoid cases, recent use of antimicrobials and socio-economic factors such as crowding and lack of education are risk factors identified from case-control studies (Appendix 5).

The most frequently described risk factor for typhoid is contaminated water for drinking and other household uses, specifically: living in a house without treated water from a municipal network (Gasem et al. 2001); using untreated water from a nearby river (Mbakaya et al. 2015); or unsafe drinking water (Tran et al. 2005; Khan et al. 2012); drinking water at a work site (Luby et al. 1998); un-boiled water (Mermin et al. 1998; Ram et al. 2006; Srikantiah et al. 2007); foul smelling water (Ram et al. 2006); or an open well

(Muti et al. 2014). Contaminated water used in preparation of ice cubes (Vollard et al. 2004), flavoured ices (Black et al. 1985) and beer (Mbakaya et al. 2015) has also been reported, though these items were accessed outside of the house. Several household water storage and dispensary practices have been reported as protective, such as using narrow mouth storage containers and tipping these to draw water (Sharma et al. 2009).

Eating contaminated food prepared outside of the household is the next most regularly reported typhoid risk factor from case-control studies (Appendix 5). Food stalls or street vendors are commonly implicated (Velema et al. 1997; Luby et al. 1998; Alba et al. 2016) but restaurants (Olsen et al. 2001) and school canteens (Black et al. 1985) have also been described. Specific food items reported as local risk factors include: raw shellfish (Strofollini et al. 1992); ice cream (Luby et al. 1998); butter and yoghurt (Sharma et al. 2009); lettuce salad, *cig kofte* (a traditional Turkish raw food; Hosoglu et al. 2005); raw fruits (e.g., papaya; Ram et al. 2006); and raw vegetables (Sharma et al. 2009).

Inadequate sanitation conditions in and around the household are often cited risk factors, including the following specific factors: close proximity to open sewers (Gasem et al. 2001); burst sewer pipes at home (Muti et al. 2014); no home latrine (Ram et al. 2006; Sharma et al 2009); and no toilet in the household (Vollard et al. 2004). Poor personal hygiene behaviour is also commonly reported including infrequently washing hands before eating or after defecation and not using soap (Vollard et al. 2004; Gasem et al. 2001; Mbakaya et al. 2015; Alba et al. 2016). Other behaviours around food have been implicated in typhoid risk such as: not routinely washing vegetables (Srikantiah et al. 2007; Sharma et al. 2009); sharing food from the same plate (Vollard et al. 2004); and attending mass gatherings where food hygiene may be compromised (Muti et al. 2014).

Elements of family or personal history have been reported as risk factors including: recent typhoid fever in household (Vollard et al. 2004); history of typhoid in a relative (Black et al. 1985); recent contact with a typhoid patient (Luxemburger et al. 2001; Tran et al. 2005); or recent use of antimicrobials (Luby et al. 1998; Srikantiah et al. 2007). Socio-economic conditions or demographic factors have also been described as typhoid risk factors, such as: crowded households (Hosoglu et al. 2005; Khan et al. 2012); poor education (Tran et al. 2005); and being unemployed (Gasem et al. 2001), a student (Srikantiah et al. 2007), elderly (Khan et al. 2012) and female (Vollard et al. 2004).

In the Pacific region over two-thirds of the population rely on unprotected sources of water and unsanitary means of excreta disposal which pose substantial risks to health

(WHO/UNICEF, 2016). Providing safe water and sanitation remains a serious regional challenge with continuous threat of natural disasters, limited water resources and poor infrastructure in a context of small urbanizing economies. While Fiji is reported to have 96% access to improved drinking water and 91% access to improved sanitation (WHO/UNICEF, 2016), these data do not provide an accurate estimation of microbiological safety. Urban water safety is questionable due to poor enforcement of water quality standards and frequent pressure loss in municipal pipelines causing ingress from the external environment (Scobie et al. 2014). Rural areas rely completely on untreated surface water sources and excreta disposal is principally via shallow pour flush or pit latrines built into pervious soil and subject to flooding (Chapter 4). Septic systems are seldom well maintained and often destabilized by erosion leading to cracking and leakage into the environment (Chapter 4). In this setting the potential for faecal contamination of soil, surface and groundwater is substantial (Scobie et al. 2014).

With the highest reported annual number of typhoid fever cases in the South Pacific, Fiji is one of the few countries in the region with a passive national reporting system and sentinel laboratory-based surveillance (Kool & Whippy 2011). While typhoid surveillance exists, insufficient attempts have been made to clarify Fiji specific risk factors for typhoid fever, possible vehicles of transmission and to advise water, sanitation and hygiene (WASH) or vaccination policies based on sound epidemiological evidence. This study aims to identify risk factors for developing typhoid in the Central Division of Fiji to assist in designing specific interventions to reduce typhoid transmission.

5.3 Methods

5.31 *Study setting*

5.311 *Geography and Demography*

The Republic of Fiji (12-22° S and 176°E-178° W) is an archipelago of 332 islands with a total land area of 18,270 km^2 (Neall and Trewick, 2008). This study was conducted in the southeastern half of the largest island of Viti Levu (10,642 km^2) in Central Division (4,293 km^2), which is the wettest (mean annual rainfall >3,200 mm) and most populous (370,570 people) of Fiji's four divisions and contains the capital city of Suva (174,000 people). 56.8% of the population of Central Division are indigenous Fijians (iTaukei), 37.5% are Fijians of Indian descent and 5.7% are of other ethnicities (Fiji Bureau of Statistics, 2007 census). While Central Division's population is concentrated in Suva, the remainder reside in small rural villages and settlements near major waterways (Chapter 3). The island of Viti Levu has complex geological origins and is characterized by steep slopes, large rivers and well-developed estuaries along coastal floodplains (Neall and Trewick, 2008).

5.312 *Typhoid in Fiji*

Fiji is a typhoid endemic setting with a recorded increase in incidence since the 1990s (WHO 2010) and an exponential rise after 2004-05 exceeding 52/100 000 in 2010 (Scobie et al. 2014). Incidence is likely underestimated because of low testing rates (< 50% of suspected typhoid cases tested), low-test sensitivity (a single blood culture will detect < 50% of typhoid infections) and limited representativeness of the surveillance system (Scobie et al. 2014). While the causes of this steep rise may represent actual increases in caseload, it may also be explained by better surveillance and diagnostics and/or improved clinician awareness (Thompson et al. 2014). Over 18 typhoid outbreaks have been reported in Fiji since 2005 (WHO-Division of Pacific Technical Support [WHO-DPS], unpublished data). In contrast to global statistics that show children under five as most likely to present with the illness, in Fiji young adults from 15-30 years present most frequently (Thompson et al. 2014). Indigenous Fijians (*iTaukei*) represent ninety percent of all reported cases (Singh 2010). As private healthcare data are unavailable and young children are rarely blood cultured, this could be a misleading demographic. Outbreaks are commonly reported following cyclones and flooding (Jenkins 2010) and January to June is the typical peak in case numbers that lags the rainy season by two months (WHO/FMOH/UNDP 2011; Scobie et al. 2014). Surveillance data and recent geospatial studies suggest typhoid incidence is becoming higher in rural areas although total numbers of cases remains highest in urban settings (Thompson et al. 2014; Chapter 3). Prevalence of antimicrobial resistance to first-line treatments remains low with ciprofloxacin as the current recommended treatment for typhoid fever in Fiji, and amoxicillin recommended for pregnant women (GOF 2010). Mass vaccination is not practiced in Fiji although area restricted vaccination campaigns have occurred in response to post-cyclone typhoid outbreaks in 2010 and 2016. A study following the 2010 campaign found annual typhoid fever incidence decreased in the post campaign year in subdivisions where a large proportion of the population was vaccinated, but increased or remained unchanged in areas where little to no vaccination occurred (Scobie et al. 2014). In August 2012, national and international typhoid fever experts convened in Suva to discuss options for control and prevention of typhoid fever (Thompson 2012). A case-control study to elucidate Fiji specific risk factors was among the primary recommendations of this expert panel.

5.32 *Case-control study*

We conducted a neighbourhood, ethnicity, and age interval matched case-control study from January 27, 2014 through August 31, 2016 in Central Division, Fiji. Patients who resided in Central Division, sought care at any Central Division health facility, presented with a history of fever, had *Salmonella* Typhi isolated from blood culture at the Colonial War Memorial Hospital (CWMH) Clinical Microbiology Laboratory and whose consent/assent were obtained were defined as cases. Only cases above the age of 18 years were eligible for enrollment until an amendment to ethics, resulting in 6 typhoid cases not being enrolled; all age groups were enrolled from May 1, 2014. Controls were recruited by spinning a pen at the case residence and selecting the nearest house 100 steps away from the pen and in the direction of its tip. A second control was then selected following the pen tip direction to a neighbouring village in rural areas or nursing zone in urban and peri-urban settings. For control recruitment to occur, the potential control house owner had to be within the same age interval (<4 years, 5-14 years, 15-24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years, 65-74 years, >75 years), match the case in ethnicity and must not have experienced fever within the past one-month. This process was repeated until two eligible controls for each case were identified. 160 cases and 319 controls were enrolled by August 31, 2015. A detailed 102-question questionnaire was administered to all enrolled participants focusing on modifiable risk factors and exposures occurring primarily during the 2-week period prior to onset of symptoms for cases and date of recruitment for controls. Questions were also asked regarding longer-term environmental factors including the occurrence of floods, droughts and tropical storms two months prior to the interview (Appendix 6).

A total of 34, 277 patients were screened by blood culture surveillance at the CWMH between February 2014 and August 2016 from which 257 (0.75 %) patients with blood culture confirmed typhoid fever were identified (Figure 5.1). Among the 257 patients identified with blood culture confirmed typhoid fever, 160 (62.3%) were enrolled in the case-control study. Of the 97 patients excluded from the study, 46 (47.4%) did not reside in the Central Division, 14 (14.4%) did not give consent, 10 (10.3%) could not be reached due to unavailability of transport, 8(8.2%) could not be located, 7(7.2%) died before an interview could be administered, 6(28.6%) were underage and not eligible for enrolment prior to the ethics amendment, 4 (4.1%) were deemed inaccessible due to remoteness of location and 2 (2.1 %) were mentally incapable of being interviewed.

5.33 *Blood culturing*

Blood cultures were collected from febrile patients at a clinicians' discretion and processed by staff of the CWMH Clinical Microbiology Laboratory. Blood was drawn for standard aerobic blood culture bottles for adults (5-10 mL) and paediatric fan bottles for children (2-5 mL). Bottles were incubated for 5-7 days at 35°C in the BacT Alert system (Organon Teknika Corp., Durham, N.C.). Positive blood culture samples were then subcultured on blood, chocolate, and MacConkey Agar. Non-lactose fermenting colonies on MacConkey agar were biochemically identified as probable *Salmonella* Typhi using Microbact identification system, Triple Sugar Iron (TSI) and Lysine Indole Motility (LIM) media. Slide agglutination was also performed for serological identification of *Salmonella* Typhi to identify Group A, Group D, and Vi positive *Salmonella.*

5.34 *Data analysis*

For the univariate analysis 1:2 matched odds ratios (OR) with exact confidence limits were calculated for categorical exposures. Normative reference categories were used for water sources, treatment and access, and flushing to municipal sewerage was used as the sanitation reference category. I conducted conditional logistic regression where candidate variables with a P value <0·05 from the univariate analysis were entered using a backwards Wald logistic regression analysis approach (Bursac et al. 2008). Variables with P >0·05 were removed from the model. History of fever in the household was removed from the multivariate model as deemed nonspecific, un-modifiable and unlikely to contribute to the causal pathway. All rural source water was coded as untreated, use of steel 44-gallon drums as septic receptacles was coded as improved pit latrines and damage to septic tanks was coded based on observations reported in Chapter 4. All statistics were performed using IBM SPSS Statistics for Windows, Version 22.0.

5.35 *Ethics*

Ethics approvals were obtained from the Fiji National Health Research Committee (FNHRC# 201370) and the Human Research Ethics Committee of Edith Cowan University (Proj # 10017). A research permit was obtained from the Fiji Ministry of Education, National Heritage Culture and Arts (Ref: RA 02/14) and permission was sought from provincial administrators and village chiefs before village visits. Verbal and written details of the study were provided in Fijian and/or English according to the participants' preferences, and written informed consent was obtained from all participants. All data were de-identified prior to analysis.

5.4 Results

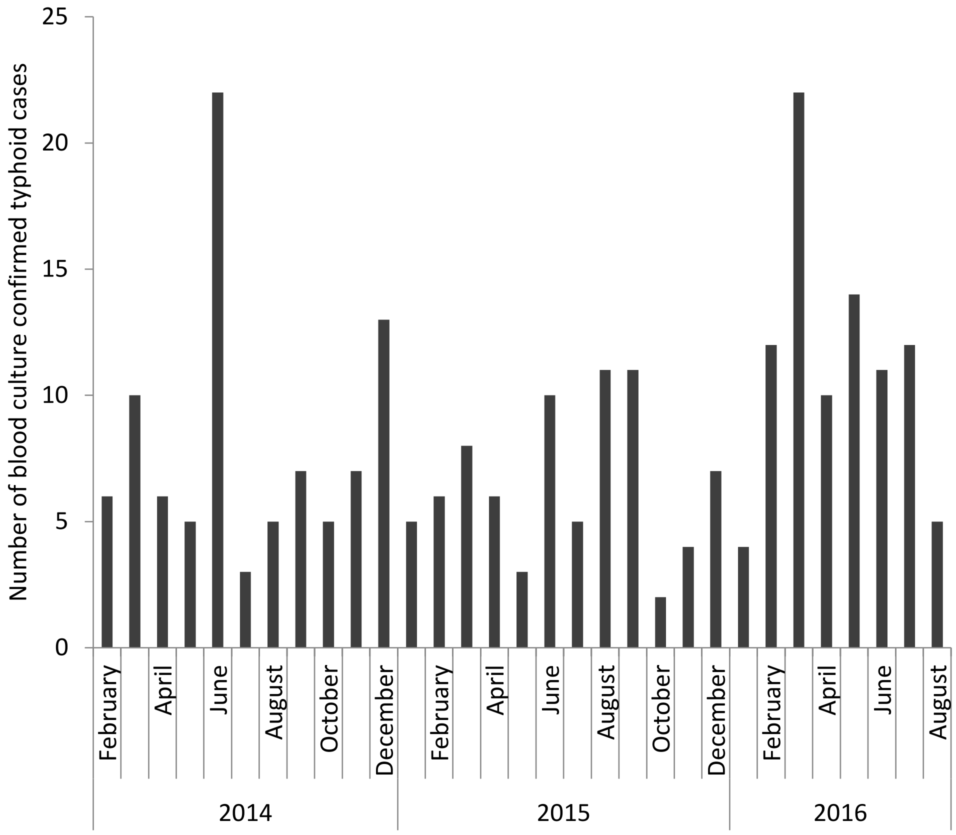


Figure 5.1 Number of blood culture confirmed typhoid cases by month in Central Division between February 2014 and August 2016. Outbreaks reported in June 2014 (unknown cause) and March 2016 (following Tropical Cyclone Winston on February 20).

During the 31-month study period 479 questionnaires were successfully administered to 160 case and 319 control subjects (Table 5.1). The median age of cases was 28.9 years (range 2– 78 years) with 16 (10%) under the age of 10 years. Cases and controls did not differ significantly by sex distribution (48.7% males *vs* 50.4%, X^2 = 0.07, *p*= 0.79). Of all study participants 94.4% were of indigenous Fijian ethnicity (iTaukei), while 15 (3.1%) were Indo-Fijian. Cases and controls were dominated by students (cases = 27.5%, controls =29.4%) and unemployed persons (cases = 26.3%, controls = 25.7%) that, together, accounted for over half of the study participants. Over half of all study participants (cases = 51.2%, controls = 52.3%) had attended secondary school and nearly half resided in rural areas (cases = 48.1%, controls = 49.2%).

Table 5.1 Demographic details of study participants, Case-control study, Central Division, Fiji (2014-2016).

	Case		Control	
Age, median (range) years	28.9 (2-78)		28.5 (1-80)	
	N	**(%)**	**N**	**(%)**
Male	78	(48.7)	161	(50.4)
Ethnicity				
Indigenous Fijian	151	(94.4)	302	(94.4)
Indo-Fijian	5	(3.1)	10	(3.1)
Other	4	(2.5)	8	(2.5)
Primary occupation				
Student	44	(27.5)	94	(29.4)
Unemployed	42	(26.3)	82	(25.7)
Housewife	16	(10.0)	53	(16.6)
Farmer	15	(9.4)	35	(10.9)
Dependent (<5)	9	(5.6)	15	(4.7)
Manual labourer	17	(10.6)	15	(4.7)
Professional	9	(5.6)	11	(3.4)
Skilled labourer	8	(5.0)	13	(4.1)
Education level				
None	11	(6.8)	22	(6.9)
Primary	46	(28.7)	81	(25.3)
Secondary	82	(51.2)	167	(52.3)
Post-secondary	9	(6.1)	17	(5.3)
University	12	(7.5)	32	(10.0)
Residential Area				
Urban	55	(34.4)	105	(32.9)
Peri-urban	28	(17.5)	57	(17.8)
Rural	77	(48.13)	157	(49.2)

In the univariate analysis 25 factors were significantly associated with typhoid (Table 5.2). Five of these factors were related directly to unimproved or damaged sanitation and include: use of an unimproved pit latrine, open defecation, use of improved pit latrine, flushing to a damaged septic tank and having built own toilet. Another five factors were related to food hygiene behaviours. Risk factors included: sharing food from the same plate, sharing food from the same plate in the last 2 weeks, and eating unwashed produce in the last 2 weeks. Significant protective behaviours included: washing produce before eating and eating produce in the last two weeks. Four factors were related to personal hygiene behaviours. Risk factors included: not washing hands before eating, not washing hands after defecation and bathing outside. Using a disinfectant for hand washing and bathing was significantly protective. Four factors were related to water access and safety. Risk factors included: drinking water accessed outside the house from a surface source, not having water always available and visiting the nearby stream on a daily or weekly basis. Sharing kava in the last 2 weeks was significantly protective. Four risk factors were related to family history and to socio-economics and included: history of fever in the household, recently attending a mass gathering, having less than four household items (e.g., electricity, vehicle) and having sand or wooden plank floors. Three risk factors were significantly related to conditions of the catchment including: presence of livestock above where drinking water was sourced, dams located higher in the basin and flooding of the nearest river or stream in the last two months.

Multivariate backward conditional logistic regression analysis for 1:2 matching showed the following factors associated with typhoid risk (Table 5.3): using an unimproved pit latrine; not washing produce or hands before eating; bathing outside; water not always accessible; having sand or wood plank floors; and attending mass gatherings.

Table 5.2 Univariate analysis of risk factors for typhoid fever among 160 cases and 319 neighbourhood, ethnicity, and age interval matched controls, Central Division, Fiji. OR = Odds ratio; U =upper 95% confidence limit; L = upper 95% confidence limit; Ca =cases; Co = controls; Obs = Observations; Ref = reference category. Significant P values are shown in bold.

Variables/Questions	OR	P	U	L	Ca	(%)	Co	(%)
Household								
>3 people per room	1.4	0.144	0.9	2.0	78	(48.8)	135	(42.3)
<4 household items (e.g., electricity, vehicle)	2.0	**0.005**	1.2	3.1	64	(40.0)	92	(28.8)
Animals in household	0.8	0.304	0.5	1.2	81	(50.6)	175	(54.9)
Wood plank or sand flooring (vs. concrete/ceramic)	2.2	**0.003**	3.6	1.3	122	(76.2)	203	(63.6)
Family history								
Fever in household	4.2	**0.000**	2.4	7.4	49	(30.6)	37	(11.6)
Water source and treatment								
Inside piped treated	Ref				75	(46.9)	153	(48.0)
Inside piped untreated	0.6	0.460	0.2	2.1	21	(13.1)	56	(17.6)
Outside piped yard treated	3.5	0.157	0.6	19.9	5	(3.1)	4	(1.3)
Outside piped yard untreated	1.1	0.912	0.2	5.3	6	(3.8)	14	(4.4)
Outside piped public untreated	2.5	0.422	0.3	24.2	3	(1.9)	3	(0.9)
Outside surface	1.5	0.567	0.3	6.9	46	(28.8)	86	(27.0)
Rain water	3.1	0.204	0.5	17.7	4	(2.5)	3	(0.9)
Main water access inside house	Ref				96	(60.0)	209	(65.5)
Main water access outside (house (piped - treated)	4.2	0.104	0.7	23.4	5	(3.1)	4	(1.3)
Main water access outside house (piped - untreated)	1.9	0.306	0.6	6.3	9	(5.6)	17	(5.3)
Main water access outside house (surface water)	2.6	**0.024**	1.1	5.8	50	(31.3)	89	(27.9)
Main water source not piped	2.1	0.110	0.8	5.1	50	(31.3)	89	(27.9)

(i.e. surface)								
Main water source not treated	0.8	0.627	0.3	2.1	80	(50.0)	162	(50.8)
Water not always available	2.4	**0.002**	1.3	4.1	114	(71.3)	261	(81.8)
Treat water at home	0.8	0.445	0.5	1.3	42	(26.3)	93	(29.2)
Drank untreated water in last 2 weeks	1.7	0.061	1.0	2.9	67	(41.9)	113	(35.4)
Store water	1.2	0.565	0.7	1.9	127	(79.4)	245	(76.8)
Store water outside house	1.7	0.333	0.6	5.1	6	(3.8)	7	(2.2)
Drank water outside house in last 2w	Ref				92	(57.5)	203	(63.6)
Drank water outside house in last 2w (other sources)	1.1	0.613	0.7	2.0	50	(31.3)	100	(31.3)
Drank water outside house in last 2w (surface water)	3.0	**0.012**	1.3	7.1	17	(10.6)	16	(5.0)
Consumed ice	1.2	0.397	0.8	1.8	65	(40.6)	118	(37.0)
Drank from street vendor	1.3	0.261	0.8	2.1	47	(29.4)	80	(25.1)
Drank kava	0.7	0.193	0.5	1.2	69	(43.1)	154	(48.3)
Shared kava in last 2 weeks	0.5	**0.004**	0.3	0.8	49	(30.6)	136	(42.6)
Food								
Grow produce	0.7	0.237	0.4	1.2	121	(75.6)	254	(79.6)
Eat produce	0.4	0.429	0.0	4.4	158	(98.8)	316	(99.1)
Ate produce last 2 weeks	0.3	**0.003**	0.1	0.6	140	(87.5)	303	(95.0)
Wash produce before eating	0.2	**0.000**	0.1	0.4	111	(69.4)	278	(87.1)
Ate unwashed produce in last 2 weeks	1.8	**0.022**	1.1	3.1	48	(30.0)	78	(24.5)
Store food	0.9	0.565	0.5	1.4	113	(70.6)	232	(72.7)
Share food in same plate	2.1	0.037	1.0	4.4	19	(11.9)	21	(6.6)
Share food in same plate last 2 weeks	2.1	**0.004**	1.3	3.6	40	(25.0)	44	(13.8)
Ate outside of house	1.5	0.055	1.0	2.3	73	(45.6)	117	(36.7)
Had dairy	0.8	0.411	0.4	1.5	141	(88.1)	288	(90.3)
Attended mass gathering	1.7	**0.016**	1.1	2.6	61	(38.1)	85	(26.6)
Sanitation Information								
Toilet in household	0.8	0.461	0.4	1.6	136	(85.0)	277	(86.8)
Flush to municipal sewerage	Ref				7	(4.4)	27	(8.5)
Flush to damaged septic	4.8	**0.037**	1.1	20.8	7	(4.4)	10	(3.1)
Flush to intact septic	2.2	0.131	0.8	6.3	73	(45.6)	175	(54.9)
Improved pit latrine	3.6	**0.024**	1.2	11.0	56	(35.0)	100	(31.3)
Open defecation	23.4	**0.010**	2.1	261.5	5	(3.1)	2	(0.6)
Unimproved pit latrine	28.9	**0.000**	4.6	181.8	12	(7.5)	5	(1.6)
Never wash hands before eating	2.4	**0.000**	1.5	3.8	124	(77.5)	188	(58.9)
Never wash hands after defecation	2.3	**0.000**	1.5	3.6	80	(50)	107	(33.5)
Built own toilet?	1.6	**0.040**	1.0	2.4	84	(52.5)	139	(43.6)
Separate water source for washing hands	0.7	0.248	0.4	1.2	34	(21.3)	78	(24.5)
Use disinfectant	0.4	**0.000**	0.2	0.7	59	(36.9)	169	(53.0)
Bathe outside	3.6	**0.000**	1.8	6.9	35	(21.9)	33	(10.3)
Prepare food out of the house	0.9	0.758	0.3	2.2	7	(4.4)	16	(5.0)
Visit stream regularly (i.e. daily /weekly)	2.5	**0.002**	1.4	4.6	44	(27.5)	55	(17.2)
Environment								
Heavy rain in last 2 weeks	1.7	0.057	1.0	2.8	47	(29.4)	73	(22.9)
Heavy rain last 2 months prior to last 2 weeks	0.6	0.136	0.4	1.1	29	(18.1)	76	(23.8)

Cyclone 2 weeks	1.3	0.773	0.2	6.9	3	(1.9)	5	(1.6)
Cyclone 2 months	0.2	0.193	0.0	2.2	3	(1.9)	10	(3.1)
Evacuated 2 weeks	0.6	0.567	0.1	3.5	2	(1.3)	6	(1.9)
Evacuated 2 months	0.5	0.624	0.0	8.0	3	(1.9)	7	(2.2)
Drought 2 weeks	2.0	0.624	0.1	32.0	1	(0.6)	1	(0.3)
Drought 2 months	0.6	0.685	0.0	7.4	1	(0.6)	3	(0.9)
Flooding adjacent 2 weeks	0.8	0.695	0.2	2.6	5	(3.1)	12	(3.8)
Flooding adjacent 2 months	0.5	0.356	0.1	2.3	2	(1.3)	8	(2.5)
Village flooded 2 weeks	1.5	0.505	0.4	5.6	5	(3.1)	7	(2.2)
Village flooded 2 months	1.3	0.671	0.4	4.5	5	(3.1)	8	(2.5)
Toilet flooded 2 weeks	2.0	0.624	0.1	32.0	1	(0.6)	1	(0.3)
Toilet flooded 2 months	2.0	0.624	0.1	32.0	1	(0.6)	1	(0.3)
River/stream flooded 2 weeks	2.2	0.083	0.9	5.6	14	(8.8)	16	(5.0)
River/stream flooded 2 months	2.6	**0.017**	1.2	5.6	18	(11.3)	17	(5.3)
Farms above water collection	2.8	0.069	0.9	8.7	11	(6.9)	12	(3.8)
Livestock above water collection	5.6	**0.034**	1.1	27.8	7	(4.4)	4	(1.3)
Logging above river basin	0.6	0.685	0.0	7.4	1	(0.6)	3	(0.9)
Road building above river basin	0.3	0.233	0.0	2.4	3	(1.9)	10	(3.1)
Dams above river basin	2.5	**0.004**	1.3	4.8	67	(41.9)	104	(32.6)
Use river/stream for fishing	0.8	0.484	0.5	1.4	38	(23.8)	82	(25.7)

Table 5.3 Multivariate analysis using backwards Wald conditional logistic regression of risk factors for typhoid fever in Central Division, Fiji. B = regression coefficient, OR =Odds Ratio.

	B	SE	Wald	df	P	OR	95.0% CI	
							Lower	Upper
Unimproved pit latrine	2.12	.95	4.86	1	.027	8.3	1.2	54.2
Unwashed produce	1.13	.33	12.03	1	.001	3.1	1.6	5.8
Bathe outside	.93	.44	4.43	1	.035	2.6	1.0	6.0
Unwashed hands before eating	.86	.26	10.62	1	.001	2.4	1.4	3.9
Water not always accessible	.80	.32	5.97	1	.014	2.2	1.1	4.2
Have sand or wooden plank floor	.80	.29	7.18	1	.007	2.2	1.2	3.9
Attended mass gathering	.65	.25	6.83	1	.009	1.9	1.1	3.1

The probable risk of typhoid exposure within a household in this endemic Fijian setting can therefore be expressed as the following logistic function:

$$e^{(2.12\,[\textbf{Unimproved Pit Latrine}] + 1.13\,[\textbf{Unwashed produce}] + 0.93\,[\textbf{Bathe Outside}] + 0.86\,[\textbf{Unwashed hands before eating}] + 0.8\,[\textbf{Water not always accessible}] + 0.8\,[\textbf{Wooden plank floor}] + 0.65\,[\textbf{Attended mass gathering}])}$$

5.5 Discussion

5.51 *Sanitation infrastructure*

This study highlights the importance of improved sanitation for preventing typhoid transmission in this setting. Univariate analysis indicated five significant risk factors directly related to unimproved or damaged sanitation (Table 5.2) and the multivariate analysis showed using unimproved pit latrines to be the highest risk factor in this setting (Table 5. 3). Several previous case-control studies highlight poor or damaged sanitation as a serious risk factor in typhoid endemic areas (e.g., Gasem et al. 2001; Muti et al. 2014) and having a toilet within the home as protective (Vollard et al. 2004; Ram et al. 2006, Sharma et al. 2009). However, my results differ from Ram et al. (2007) and Sharma et al. (2009) who found that the use of latrines for defecation decreases the risk of disease in Dhaka, Bangladesh and Darjeeling, India. This can be expected in certain Southeast Asian settings where open defecation is a common alternative to latrine use (WHO/UNICEF 2014), but contrasts to Fiji where open defecation is rare (1.4% of study participants), and flushing to a septic system is the common alternative (GOF 2006). A key concern with Fijian pit latrines is that they are often poorly constructed, shallow, built into permeable soil, and subject to flooding. 'Householders building their own toilet' was revealed as a significant risk factor in this environment (Table 5.2). Even improved pit latrines were a significant risk factor (Table 5.2) as often the primary "improvement" (48.2% of improved latrines) is simply using buried 44-gallon steel drums as the receptacle for sewerage, which rapidly corrode and leak into the surrounding environment. The high rainfall and highly erodible clay loams of the Central Division compromises sanitation infrastructure; the linked studies demonstrated susceptibility to soil erosion undercutting the substrate into which latrines were built and slumping and cracking of septic tanks, leading to raw sewerage discharge into surrounding land and water (Chapters 3, 4). Inadequate sanitation, in combination with heavy rainfall, soil erosion and poor stormwater drainage around the house, facilitates faecal contamination of household surroundings including, gardens and domestic water sources (Ngugi et al. 2014, Chapter 4), thereby increasing risk of typhoid transmission.

5.52 *Food hygiene*

A significant set of risk factors in this setting are related to food hygiene behaviours, with not washing produce revealed as one of the most hazardous behavioural factors in the multivariate model (Table 5.3). This risk factor has been reported several times in the case-control literature (e.g., Srikantiah et al. 2007; Sharma et al. 2009), which indicates that people who do not wash produce routinely before eating are at heightened risk for infection due to surface contamination of fruit and vegetables during production and harvest (Medina 1991) or in the market (Mujica et al. 1994). This finding is also illuminating in the Fijian setting given the previous finding that case household gardens in Central Division were positioned significantly closer to the household toilet or septic tank and the majority of cases (76%) propagated vegetables directly on or below the toilet drainage area (Chapter 4). Active fertilization of produce with human faeces has been previously demonstrated as a risk factor in Chile (Sears et al. 1984). In this Fijian milieu, poor produce washing practices combined with passive use of human waste for fertiliser is a discernible risk factor for typhoid fever.

A lively Fijian culture of mass gatherings and communal ceremonies, involving group food preparation and the sharing of kava (an infusion of *Piper methysticum*) has been cited as likely contributing to the spread of typhoid in this setting (Scobie et al. 2014). This study confirms this suggestion for Fiji as attending a mass gathering was found to be highly significant in the multivariate analysis (Table 5.3). Attending mass gatherings has been similarly reported as a risk factor in Zimbabwe (Muti et al. 2015). Sharing kava in the last two weeks, however, emerges as significantly protective in the univariate analysis (Table 5.2). Kava lactones, while primarily known for sedative effects, have also shown potential antimicrobial activity and kava is specifically used as a treatment for skin and urinary tract infections in traditional cultures of West Papua and Papua New Guinea (Locher et al. 1995). The antimicrobial properties of kava warrant further investigation. Although excluded from the multivariate model, the other significant risk factor in this context was sharing food from the same plate (Table 2), which has previously been cited as a risk factor in Indonesia (Vollard et. al 2004).

5.53 *Personal hygiene*

Several factors related to personal hygiene were also significant in this setting (Table 5.2). Of these, not washing hands before eating and bathing outside remained significant in the multivariate model (Table 5.3). Not washing hands before eating has specifically been reported in Indonesia (Gasem et al. 2001). The other significant univariate results of not washing hands after defecation, and the protective effect of using disinfectant for hand washing and bathing, are also well represented in the typhoid case-control literature (Vollard et al. 2004; Mbakaya et al. 2015; Alba et al. 2016). While bathing outside has not specifically been cited for typhoid, the frequent use of contaminated surface water for household uses including bathing and hand washing has commonly been described as a significant risk factor (e.g., Gasem et al. 2001; Ram et al. 2006; Mbakaya et al. 2015). In the current study, 90% of outside bathers were using the nearby river or stream as the primary bathing facility. Streams adjacent to a sample of 56 households in this study population were grossly polluted by WHO standards (WHO 2011) with an average concentration of *E. coli* of 740.4 CFU/100 mL, a microbial indicator of recent faecal contamination (Chapter 4). The high levels of faecal contamination of stream waters may contribute directly to risk via ingestion during bathing or other co-incidental uses such as washing of clothes or kitchen utensils. Study participants that visited the nearby stream frequently (daily or weekly) for any reasons were at significantly greater risk of typhoid fever (Table 5.2).

5.54 *Water access & safety*

Risk factors related to contaminated water for drinking or other household uses are the most frequently reported in the typhoid case-control literature (Appendix 5). In this Fijian study population, not having water accessible all of the time from the primary drinking water source was significant in the multivariate analysis (Table 5.3). Intermittent access to water is a well-documented public health problem in many developing countries and three primary mechanisms of enhanced risk (Ercumen et al. 2015) are evident in this study environment. First, several study participants used the nearby stream as the alternative source when the primary piped source was unavailable (A. Jenkins, personal observation). Our findings further support this mechanism (see drinking water accessed outside the house from a surface source in Table 5.2), as do the findings of many other studies (e.g., Gasem et al. 2001; Tran et al 2005; Khan et al. 2012; Mbakaya et al. 2015).

Second, pressure drops in Fijian water supply lines are frequent and the coexistence of negative pressures and leaks in the distribution system results in a high risk of contaminant ingress from surrounding groundwater (Fox et al. 2015). Scobie et al. (2014) hypothesized that this mechanism might contribute to typhoid risk in Fiji. Third, the increased usage and likelihood of contamination of stored household water in between supply cycles is also a plausible mechanism. In a subset of 83 households from this Fijian study population, significantly higher concentration of *E. coli* in stored drinking water in typhoid case households were measured, although the source of this drinking water did not differ (Chapter 4), strongly suggesting water contamination is occurring within the household and is perhaps heightened during periods of intermittent access.

5.55 *Catchment condition*

Distal conditions within the water catchment have yet to be reported as risk factors for typhoid within case-control literature though geospatial studies are beginning to elucidate factors at this level (e.g., Dewan et al 2013; Akullian et al 2015; Jenkins et al. 2016, Chapter 3). While catchment scale factors did not remain significant in our multivariate model, univariate analysis revealed three significant typhoid risk factors (Table 5.2). The presence of livestock upstream of where drinking water was sourced, was one of these significant factors. Unrestricted access of livestock to water catchments can have deleterious effects on water quality through increasing sediment from erosion of river banks (Evans et al. 2006), nutrient enrichment and elevated bacteria levels (due to defecation by livestock within or close to the stream) and reduction of riparian and in stream vegetation (Trimble and Mendel, 1995). During periods of soil saturation and high stream flow, livestock aggregation near stream channels often causes bank slumping or collapse, mobilising significant amounts of sediment (Magner et al. 2008). The trampling of riverbanks and riverbed also can re–suspend sediment, stored nutrients and bacteria (Terry et al., 2014). Reduced and fragmented riparian vegetation was shown to be significantly associated with an increased typhoid incidence and recurrence at the sub-catchment scale in Fiji (Chapter 3, Jenkins et al. 2016).

Participants reporting dams higher in the river basin was also found to be a significant (Table 5.2). While epidemiological studies have not previously identified this particular risk factor, it has been cited as contributing to increased typhoid risk in several socio-environmental impact studies (e.g., Paul et al. 2013; Babagana et al. 2015). Kinuthia et al.

(2012) reported that typhoid risk might be enhanced in rural Kenya by contamination of domestic dams with faecal materials from runoff during the rainy seasons. A study from Nigeria suggested that typhoid incidence increased as a result of dam construction, primarily due to increased intermittent flooding (Babagana et al. 2015). Massive outbreaks of typhoid have also been reported in China following burst dams and subsequent flooding (Qing, 1998). Despite repeated claims that dams can contribute to heightened typhoid risk (Tahmiscioğlu et al. 2007; Paul et al. 2013) the mechanisms by which this can occur are not well studied and warrant further investigation. It seems that direct contamination of dam surface water from which untreated drinking water is extracted, creation of stagnant conditions in which microbial growth is enhanced and where there is a heightened risk of large flood pulses are reasonable mechanisms by which typhoid risk could be enhanced (Jupiter et al. 2007).

At a sub-catchment scale, typhoid incidence in this Fijian setting is demonstrably associated with flood risk (Chapter 3, Jenkins et al. 2016) and outbreaks associated with flooding are common (Jenkins 2010). Increased incidence occurs in broadened low-lying areas within sub-catchments where potential for flooding and exposure to contaminated runoff is higher (Chapter 3, Jenkins et al. 2016). Flooding can damage water supply or sanitation infrastructure and, where drainage and sanitation are inadequate; runoff can transport faeces across land and contaminate domestic water sources (Chapter 4; Ngugi et al. 2014). It is therefore unsurprising that flooding of the nearest river or stream in the last two months is significant (Table 5.2) and is likely working in synergy with the other significant catchment condition factors elucidated above.

5.56 *Socio-economics, demographics* & *family history*

Socio-economic conditions or demographic factors such as crowded households (Hosoglu et al. 2005; Khan et al. 2012), poor education (Tran et al 2005), being unemployed (Gasem et al. 2001) or being a student (Srikantiah et al. 2007) are often cited as risk factors within the typhoid case-control literature. In the current study, crowding (>3 per room) was not significant, but two socio-economic indicators were (Table 5.2), namely having less than four household items, and having wooden plank or sand floors. Having wood plank or sand floors may be both an indicator of socio-economic status (i.e. unable to afford cement or ceramic flooring) and an independent risk factor. Gasem et al. (2001) reported having an untiled kitchen floor as a risk factor in Indonesian households although this is likely an association with living in poor housing conditions. Some very early research on *S.* Typhi recovery from different building materials reported >5 days survival in unpolished or non-vitrified building stone compared to 2 days on polished stone suggesting that roughly textured materials can extend pathogen survival (Bitter 1911 reported in Mitscherlich and Marth 2012). Melick (1917) also demonstrated *S.* Typhi has up to 58-day survival in sandy soil. While equivalent studies appear not to have been conducted for wooden substrates, roughly hewn wooden planking is more difficult to clean and it is reasonable to assume that it would provide a more suitable environmental growth surface than ceramic or concrete. Given the high infective dose needed, it seems unlikely that wooden floors act as a direct vehicle of transmission although in the context of constantly damp, poorly drained environments and failing sanitation infrastructure it seems worth further investigation as a potential transmission pathway. Students and unemployed persons represented over half (51.5%) of our study demographic, where the reduced ability to afford decent housing or building materials is likely to predispose pathogen exposure.

A recent history of fever in the household was also revealed as important (Table 5.2) and is well-represented in the case-control literature (Black et al 1985; Luxemburger et al. 2001, Vollard et al. 2004, Tran et al. 2005). However, as this finding is nonspecific to typhoid fever and largely unmodifiable, it was excluded from the final multivariate model as a potential causal factor. The median age of cases (28.9) and high percentage (94.4%) of indigenous Fijian ethnicity (*iTaukei*) is consistent with past studies in Fiji (Singh 2010; Thompson et al. 2014).

5.57 *Study limitations*

While this study is exceptional as the largest neighbourhood matched typhoid case-control study (second largest of any typhoid case-control design) and possibly the longest in duration ever conducted (Appendix 5), this introduces complications with regard to increased number of potential exposures and confounding variables. One of the most important drawbacks in case-control studies is the difficulty of acquiring dependable information about the timeline of exposure to specific risks (Schultz and Grimes 2002). During the study several outbreaks occurred which potentially bias interpretation of results towards short duration or area delimited risks rather than longer-term drivers of endemic transmission. Risk is also not measured directly and associations are made based on information gleaned from retrospective recall and thus subject to both observational and recall bias. In particular, environmental questions asking about events two months past or far afield may be difficult to accurately recollect. Investigators administering questionnaires were not blinded to the case or control status of individuals and thus may introduce observer bias (Schultz and Grimes 2002). Case-control studies are better suited to studying proximal risk and have limited ability to elucidate root causes such as ecological conditions operating distally. While we did introduce questions related to the catchment condition, distant events and conditions are better verified by direct observation or measure, which is why we sought to conduct studies at different scale levels (e.g., Chapters 3, 4). The longer duration of the study may also introduce increased exposure to factors that differ between groups thus further confounding results. Elimination of all possibility of confounding variables would require a prospective randomized control study but this was beyond cost and logistic capacities. While "over matching" of controls was reduced by obtaining a second control in an adjacent neighbourhood, the relative homogeneity of sampled environments and endemic nature of the disease may contribute to masking detection of potential risk factors. Obtaining accurate information about sexual practices that facilitate direct transmission is difficult and was not attempted. Although thought to be rare, this cannot be eliminated entirely as a potential transmission route. Case-control studies point to associations between potential risk factors and individual health outcomes but cannot ascribe causality. While matching, bias and confounding are clear limitations, this study has generated several important hypotheses that can be more rigorously tested by other methods.

5.6 Conclusions

Unimproved sanitation facilities appear to be an immediate source of *S.* Typhi in Fiji. Our findings suggest transmission by consumption of unwashed produce and ingesting contaminated surface water. Factors related to activities in the water catchment likely contribute to enhanced contamination risk. Mass gatherings and poor personal hygiene practices are common and appear to increase risk. Improved sanitation facilities that protect surface water and produce from contamination by human faeces are likely to contribute to typhoid control in Fiji. WASH interventions to promote improved hygiene behaviour such as washing hands, produce and encouraging household water treatment may also contribute to typhoid control. Interventions such as livestock, dam and erosion control will largely be a domain of activities at a different level of organisation, requiring cooperative upstream management among landowners and specific policy tools.

CHAPTER 6

A nested environmental systems approach to water-related infectious disease epidemiology and control: an example of typhoid fever in Central Division, Fiji.

6.1 Abstract

To date few epidemiological studies have examined water-related infectious disease processes through a nested system lens. I synthesized risk factors from four nested systems of organisation examined in this thesis and study how significant factors within sub-catchment, residential settings and individual/household subsystems interact using a Bayesian Network approach. I use this model to test potential intervention scenarios and elucidate the relative influences of interventions on typhoid exposure. I examine the intended and incidental outcomes of this research, suggesting a multi-level scalar intervention approach and highlight advantages and limitations of the overall research process. This synthesis suggests: 1) risk factors acting at different levels of organisation must be studied using fundamentally different approaches; 2) combined interventions within a subsystem provide greater reduction in exposure than the sum of individual interventions; 3) simultaneous interventions on select risk factors across multiple nested subsystems provides greater exposure reduction than total elimination of risk factors in any one subsystem; 4) each increasing subsystem investigation and intervention increases the purview of potential insight and strength of effect and; 5) the environment should be considered as a potential reservoir of *S.* Typhi. Through the interdisciplinary research process, the focus and purview of institutions broaden and unforeseen opportunities arise to understand and effect change in the wider spheres of both public health and environmental sustainability.

6.2 Introduction

Epidemiological processes are nested within heterogeneous and dynamic socio-ecological systems, influenced by a wide range of interacting environmental variables, human behaviour and decision-making processes acting across multiple scales of space and time (Meentemeyer et al. 2012). The Hungarian-British philosopher Koestler (1967) suggested natural systems are organized in nested subsystems (which he termed "holons") of increasing complexity that are whole in and of themselves and also part of a greater, essentially boundless, whole ("holarchy"). Unlike a hierarchical organisation that often controls from the top down, holons are bidirectional, with lower and higher subsystems influencing each other. Also unlike hierarchies, which tend to have smaller and less inclusive higher strata, higher subsystems of a holarchy include the nested subsystems below so are larger and more inclusive. The scales or boundaries in which I focus the investigation are simply imposed demarcations to help map and understand the subsystems within our visible or measurable spectrum. There is, therefore, no single natural scale or subsystem in which ecological phenomena, including the transmission of infectious disease, should be studied (Levin, 1992).

This nested system approach seeks to understand the non-linear and dynamic relationships between complex networks of subsystems which create a whole greater than the sum of the parts. Unique, whole-system characteristics 'emerge,' through processes of collective self-organisation, adaptation and co-evolution, that cannot be shown from the study of individual components (Gu et al. 2009). Varela et al. (1991) describe this pattern of emergence across multiple domains of chemical oscillations, genetic networks, population genetics, immune networks, geophysics and ecology, demonstrating that systems of interacting elements give rise to new properties. This nonlinear characteristic means scaling up or down between subsystems or scales cannot be simply additive or subtractive (Gunderson and Holling 2002). The processes operating within these systems and influencing transmission of infectious disease are also patchy and discontinuous with specific resources and opportunities concentrated within different levels of organisation (Gunderson and Holling 2002). Understanding infectious disease, from within-host disease evolution to emergence and spread at a regional scale, therefore requires a clear understanding of the socio-ecological interactions within and between nested subsystems of organisation (Johnson et al. 2015).

This requires system specific methods of investigation for each subsystem combined with integrated modelling approaches to understand causal pathways and interacting factors (Borsuk 2008), although few water-related infectious disease studies have used these methods to date (Batterman et al. 2009). To develop the predictive models needed to represent the complex interplay of ecosystem change and disease transmission, greater focus is needed on developing the tools to interface the results of interdisciplinary enquiry at disparate scales of interest (Levin 1992). The management of these interconnected processes must then be equally dynamic, adaptive and continuously innovative at the scales at which ecosystem and disease processes are operating (Gunderson & Holling 2002).

To date only a few epidemiological studies have examined water-related infectious disease processes through a nested scale, interdisciplinary lens, although the need for broadened ecological systems approaches is increasingly being recognised (Batterman et al. 2009; Parkes et al. 2010; Meentemeyer et al. 2012; Johnson et al. 2015). Both the study of, and interventions to reduce, water-related infectious disease incidence and emergence are primarily focused on proximal causes of transmission while distal determinants often receive insufficient attention (Batterman et al. 2009). The traditional individual-based approach to etiology and epidemiology emphasizes immediate and short-term risk factors while a nested systems approach requires interdisciplinary teams accounting for complexity and scale, surveillance beyond traditional public health indicators, and research and intervention agendas with extended, adaptive time horizons beyond customary disciplinary and funding practice (Myers and Patz 2009). In effect, researchers and public health interventions are often constrained by time and resource limitations, which results in limited examination of multiple systems, interventions only within the system of analysis and ultimately inadequate understanding of the richness of underlying epidemiological processes.

The few studies that have approached water-related disease through a nested system, interdisciplinary lens have been transformative in understanding the epidemiology and control of the studied diseases. Over several decades, Colwell and colleagues developed an elegant model of interdisciplinary research for cholera (Colwell 1996, Lipp et al. 2002) which resulted in predictive capacity at a global scale through remote sensing (Lobitz et al. 2000) and local scale intervention using simple filtration of untreated water through sari cloth, yielding almost 50% reduction in cholera cases (Colwell et al. 2003). Eisenberg and colleagues (2006) used an interdisciplinary and multi-level framework to explore causal links between road construction and diarrhoeal disease, incorporating processes at regional, village, individual and molecular scales using fields of political economics, anthropology, microbiology and ecology as well as traditional public health disciplines. The Eisenberg et al. (2006) study allowed interventions to be made at several temporal and spatial scales to break pathogen transmission cycles, including distal factors related to economic conditions, deforestation and road building and proximal scale factors related to sanitation. Shifting the paradigm of water-related disease epidemiology to a nested systems approach is a propitious opportunity for fostering greater understanding of both disease transmission and environmental change.

I synthesized results from the studies within this thesis, from multiple disciplines and subsystems (as presented in Figure 1.1), with a focus on the burden and transmission of typhoid in Central Division, Fiji. While proximal household factors and individual behaviours dominate opinions on typhoid transmission, here I examine the interaction between distal ecological conditions, proximal settings of the lived environment and individual behaviour on the risk of transmission. I also highlight recent molecular and human gut microbiome approaches to enhance this nested systems methodology. The molecular work reported herein was originally intended to be part of this PhD programme but, because of the preliminary nature of the results, it is only reported summarily in this chapter. I propose that understanding the determinants of typhoid and prioritising interventions in an endemic setting can be greatly enhanced by studying environmental factors acting on catchment and residential levels alongside traditional case-control investigation of the proximal household levels. I synthesize significant risk factors from four nested systems of organisation from my Fijian typhoid studies and examine how they interact using a Bayesian Network approach. I use this model to test potential intervention scenarios and elucidate the relative influences of interventions on typhoid exposure risk. I also examine the intended and incidental outcomes of this research, suggest a multi-level intervention approach and highlight advantages and limitations of the overall research process.

6.3 Methods

Following the definition of Gibson et al. (2000), in this chapter I use the word "scale" to mean the spatial, temporal, quantitative, or analytical dimensions used to measure and study any phenomena within any particular subsystem. The settings and methods from which this synthesis of results is extracted are described in detail in Chapters 2, 3, 4 and 5. A summary table of five nested subsystems in which these studies occurred, their results and incidental outcomes, potential interventions and key supporting literature are presented in Table 6.1. I summarize specific methodological approaches used in Central Division, Fiji to study typhoid, highlighting innovative elements of methodology and results, advantages and limitations at each level. I then build a Bayesian Network (BN) model to synthesize significant risk factors from three levels (sub-catchment, residential setting, within household/ individual) and examine how they individually and conjointly influence typhoid exposure risk. Finally, I discuss the emergent properties of the model, the incidental outcomes of the research process and broader implications for the management of catchments and waterborne diseases in general.

6.31 *Methodological approaches*

The following section describes the methodological approaches used within each subsystem in the studies presented in this thesis on typhoid transmission in Central Division, Fiji, and provides a summary of key results and primary advantages and limitations. These studies provide evidence from the literature for the regional subsystem, and quantitatively derived risk factors acting in each of the river basin, residential setting and individual subsystems of this model. Using a Bayesian Network approach, these data allow the testing of interactions among the quantitatively studied factors and the likely effectiveness of intervention strategies.

6.311 *Regional subsystem*

The factors acting within the Pacific Island regional subsystem on typhoid transmission (and multiple health outcomes) were explored primarily through i) literature review and ii) through the formation and activities of the Oceania Chapter of the International Association for Ecology and Health (IAEH), which I helped to establish during my candidature to champion regionally specific and integrative approaches to EcoHealth practice.

Key literature used to explore the management of socio-ecological determinants of health at the Pacific Island regional level were Jenkins and Jupiter (2015)(Chapter 2) and Jupiter et al. (2014). Jenkins and Jupiter (2015) (Chapter 2) provided a comprehensive literature review of the direct and indirect health consequences of interruptions to Pacific Island wetland ecosystem services associated with common natural disaster events and examples of how wetlands can either mitigate or contribute to health outcomes. Opportunities for improving management of wetland ecosystems for human health benefits were discussed in the context of local to regional-scale management frameworks. The improved management opportunities were drawn primarily from Jupiter et al. 2014, who evaluated 36 case studies from the Pacific against ten proposed principles of Integrated Island Management (IIM) and suggested how regional ecosystem management can be enriched by linking IIM outcomes to ecosystem services valued by people, particularly water quality and human health.

The formation of the Oceania Chapter of IAEH transpired through collaboration of multiple regional institutions recognising the need for a regional community of practice to examine the socio-ecological determinants of health at the regional level. Kingsley et al. 2015 documented the Chapter formation and provided qualitative analysis of ten semi-structured interviews with Oceania EcoHealth Chapter members, suggesting that regional policies and institutions are not sufficiently linking ecosystems with health and highlighting potential contributions to public health by regionalizing ecosystem approaches to health.

While regional determinants of typhoid were not included in the final Bayesian Network model, evidence is summarised herein for regional factors likely to influence multiple health outcomes, including typhoid transmission and control, drawing from these and other key publications (Table 6.2).

The small island developing states of the Pacific region are among the most vulnerable globally to climate change induced warming, altered rainfall patterns, increased storm severity and rising seas (IPCC, 2014). While this is a global scale phenomena, regional vulnerability is a consequence of unique geographic, demographic and socio-economic characteristics combined with heightened exposure to these changing weather patterns, the associated health risks, and a limited capacity of countries to adaptively manage these risks (McIver et al. 2015). The frequency and intensity of extreme weather events, particularly cyclones, floods and droughts, is increasing in the region, causing populations to be displaced, injuries and psychological trauma and magnified risks of malnutrition and infectious disease (WHO 2015, Jenkins and Jupiter 2015). Increasing temperatures and rainfall are magnifying the risks for both waterborne and vector-borne disease (Hunter 2003). Climate change related natural disasters are also disrupting health-care delivery and increasing disease risk, particularly among vulnerable groups (WHO, 2015).

In addition to issues of climate variability, transformation of terrestrial and aquatic ecosystems is also affecting disease exposure (Jenkins and Jupiter 2015). Of particular concern to the Pacific Islands, deforestation and other alterations to terrestrial and aquatic ecosystems are acting in concert with changing climate and affect health through interacting processes of flooding and sea level rise. Deforestation of watersheds is a major cause of flooding and landslide activity, while simultaneous impact from storm surges is amplified by sea level rise, propagating storm damage further inland (Jenkins and Jupiter 2015).

Table 6.1 Summary table of studies contributing to a nested subsystem approach to typhoid epidemiology and control in Fiji

Subsystem	Study approach	Results	Incidental outcomes (see Epilogue)	Potential Interventions	Key Reference(s)
Regional (Oceania)	Literature review, collective engagement	Water borne disease risks influenced by unique geographic, demographic and socio-economic oceanic island characteristics combined with heightened exposure to changing weather patterns and limited capacity to adaptively manage these risks.	-Formation and activities of the Oceania Chapter of the International Association for Ecology and Health (IAEH)	-Improved international, regional, national policies and networks integrating ecosystems and health - Integrated Island Management (IIM) - Strengthened models of disaster risk management at interface of wetland ecology and disaster epidemiology	Jupiter et al. 2014 Kingsley et al. 2015 Jenkins and Jupiter 2015 Chapter 2

Island/Sub-catchment	Quantitative geospatial analysis and distance-based linear models	Anthropogenic alteration of land cover and hydrology at river basin scales (via fragmentation of riparian forest and connectivity between road and river networks) increases risk of typhoid exposure where sediment increases following runoff.	- Enhanced geospatial analytical capability in Fiji MoHMS - Catchment level factors embedded in EHO typhoid case investigation - Broadened government sectoral inclusion in water borne disease discussions/meetings/interventions	- Enhanced cross-sectoral integration for both surveillance and intervention - Ecosystem management (e.g., targeted reforestation of riparian forests, minimizing impacts of road building on erosion) - Prepositioning antibiotic treatment and water, sanitation and hygiene (WASH) intervention materials	Jenkins et al. 2016 (Chapter 3)
Residential setting	Case-control design, bacterial contamination and chemical composition of water and soil, observational	Ecological determinants related to drainage, housing and the condition of water and sanitation provide a residential setting for poor hygiene and	- Enhanced drinking water quality/nutrient analytical capacity in Fiji MoHMS -Residential level factors embedded in EHO typhoid case investigations	- Enhanced drinking water source surveillance and treatment. - Improved local	Chapter 4

	analysis, spatial analysis of household position, exploratory factor analysis	sanitary practice influencing the risk of typhoid transmission.	-Improved engagement with WASH NGOs in surveillance and intervention (cross-level outcome)	storm drainage - Improved positioning of toilets and household gardens - Improved excreta and solid waste management	
Individual, Behavioural	Case-control questionnaire, multivariate conditional logistic regression	Using an unimproved pit latrine, not washing produce or hands before eating, bathing outside, water not always accessible, having sand or wood plank floors and attending mass gatherings were significant risk factors for typhoid fever	- Formalized engagement of researchers with national outbreak prone disease committee (cross-level outcome) - Broadened research partnerships formed to address questions of carriage and seroprevelance (cross-level outcome)	- Improved public health messaging around hand washing,produce washing and mass gatherings - Increased funding allocation for improving sanitation options - Improved household water quality surveillance and treatment options	Chapter 5
Molecular/Microbiome	rtPCR, metagenomics,	-Detection of S. Typhi genome in water & (possibly) soil as	- Improved local rtPCR capacity to detect *S.* typhi from environmental	- Screening of potential environmental	Karkey et al. 2016

	potential environmental reservoirs - Mobile gene pools in gut microbiome shaped by environmental selection at global and individual scales	samples - New hypotheses generated on testing characteristics of the microbiome composition for patterns of susceptibility to typhoid	reservoirs during outbreaks or in high-incidence settings -Microbiome screening for antimicrobial resistance	Brito et al. 2016

Overall, the small islands of the Pacific Ocean are among the most vulnerable to flooding because of this particular interaction between deforestation, aquatic ecosystem degradation and climate impacts such as sea level rise and increased severity of tropical storms (Knutsen et al. 2010). Fiji, for example, has experienced an increased frequency and magnitude of flooding over the last few decades, attributable to the aforementioned combination of factors and particularly affecting populations living in river deltas and on flood plains (Lata and Nunn, 2012).

Extremes in the hydrological cycle are associated with amplified diarrhoeal disease in Fiji and many other countries (Singh 2010), while peaks in typhoid cases in Fiji typically lag the rainy season (November to April; WHO/FMOH/UNDP 2011; Scobie et al. 2014) by 2 months. Typhoid outbreaks are also frequently associated with cyclones and flooding (Jenkins 2010). McIver et al. (2015) also found a correlation of typhoid incidence in Fiji with minimum temperature, which is associated with the rainy season. As conceptualized in Jenkins and Jupiter (2015) (Chapter 2), during periods of flooding and heavy rainfall, faecal matter and associated pathogens flush from the land and damaged sanitation infrastructure and contaminate drinking water sources. In addition, people crowd into dry spaces increasing likelihood of transmission. While climatic extremes are increasing in the Pacific Region, in the case of Fiji, rainfall is predicted to increase and has already shown a 10% increase over the last 100 years (UNEP 2012), likely increasing the incidence of both flooding and typhoid outbreaks, among other waterborne diseases.

In addition to climate variability, natural disasters and ecosystem transformation, increasing human population and urbanisation are likely facilitating increased incidence of typhoid among other poverty-related diseases. Population growth is highly varied among the nations of the region, although overall annual population growth is relatively high at 2.1% compared to global growth of 1.1%, while economic growth remains slow and little progress is being made in raising per capita incomes (World Bank 2016). Pacific island countries are rapidly urbanising, with the urban population set to double within the next 25 years (Jones, 2012). Particularly throughout Melanesia (including Fiji), this is leading to sprawling, largely underserviced settlements, compounding environmental, social, health and economic adversities. Access to safe water and adequate sanitation is failing to keep pace with population growth, urbanisation and ecosystem transformation, with two-thirds of the population continuing to rely on unprotected sources of water and unsanitary means of excreta disposal (WHO/UNICEF, 2016). Geographic isolation, high transport costs, small markets and a diaspora of limited specialist human resources hamper development efforts and reinforce a reliance on subsistence economies. These small economies are socio-culturally intertwined with wetland systems. In particular, with populations in both urban and rural areas concentrated around the floodplains of waterways and coastal areas, further compounding aforementioned risks. It is therefore unsurprising that the primary causes of death and disease in the Pacific Island is infectious disease, particularly respiratory diseases related to overcrowding, vector borne diseases, and enteric diseases such as typhoid that relate to water pollution, poor sanitation, and poor health and hygiene practices (WHO 2013).

The Pacific Islands region clearly faces massive sustainability challenges with regard to these interacting factors of climate change, natural disasters, population growth, slow economic growth, urbanisation and environmental change. The remoteness, small size and limited capacity that are commonly used to argue for regionalized interventions also constrain the efficacy of both national and regional service delivery (Dornan and Cain 2014). Climate change and natural disasters dominate discourse on sustainable development in the region particularly with regard to health risks (WHO 2015). These risks are inequitably distributed, in that they are concentrated in the poorest island nations, which have contributed least to the root of the problem. These clear inequities and other salient post-colonial and neoliberal economic dependencies on large regional neighbours are encouraging a regional political move towards "island- centred" regionalism with greater autonomy of decision making on regional development issues (Maclellan 2015). The increased focus on climate change and health is also providing a useful discursive point of intersection between academic disciplines that, in application, must practically involve considerations of landscape ecology, hydrology and disease epidemiology and more integrated, interdisciplinary approaches to research and management.

Jupiter et al. (2014) and Kingsley et al. (2015) point out that regional policies are not adequately linking ecosystems with health, although there are specific recommendations for how this can occur with respect to Integrated Island Management (IIM) and wetland management surrounding natural disasters (Jupiter et al. 2014, Jenkins and Jupiter 2015). Recent studies in Fiji on leptospirosis and typhoid in particular (Lau et al. 2016, Jenkins et al. 2016) are demonstrating how eco-epidemiological approaches can be used in the island region for identifying risk factors and integrating environment and health surveillance. For managing these systems (including the specific disease system of typhoid) several key principles of IIM (Jupiter et al 2014) can be utilised at this level including: 1) taking a long-term integrated approach to ecosystem management; 2) accounting for connectivity between complex social and ecological systems; 3) incorporating stakeholders through participatory governance; 4) recognising uncertainty and planning for adaptive management; and 5) organising management systems in nested layers across sectors, social systems and habitats.

Table 6.2 Summary of key socio-ecological factors and processes influencing multiple health outcomes (including typhoid transmission) at the Pacific Island regional level.

Regional factor	Influential processes	Key supporting literature
Climate change	- altered rainfall patterns - warming - increased storm severity - rising seas	- WHO 2015 - Jenkins and Jupiter 2015 (Chapter 2) - IPCC, 2014
Natural disasters	- Increased frequency and magnitude of cyclones, floods, droughts and landslides - damaged water provision and sanitation infrastructure - disrupted health-care delivery - disrupted economic recovery - poor planning at the interface of disaster-related epidemiology and wetland management	-Jenkins and Jupiter 2015 (Chapter 2)
Population growth	- crowding - inadequate provision of water and sanitation infrastructure - increased population density along low-lying floodplains and coastal margins - decreased abundance and diversity of natural resources of commercial and cultural importance	- World Bank 2016 - WHO/UNICEF 2016 - Jenkins and Jupiter 2015 (Chapter 2)
Slow economic growth	- geographic isolation - high transport costs - small markets - diaspora of limited specialist human resources	- World Bank 2016 - Jenkins and Jupiter 2015 (Chapter 2)

	- reliance on subsistence economies	
Urbanization	- urban drift - expanding settlements - inadequate urban policies, planning and services	- World Bank 2016 - Jones 2012
Environmental change	- deforestation - expanding agriculture and mining - road building - gravel extraction - dams and waterway diversions - inadequate policies and surveillance integrating ecosystems and health	- Jupiter et al. 2014 - Jenkins and Jupiter 2015 (Chapter 2) - Kingsley et al. 2015

6.312 *Island/sub-catchment subsystem*

In Jenkins et al. (2016) (Chapter 3), we sought to explore associations between distal environmental drivers and local transmission patterns at the population level. In this study, we calculated the burden and spatiotemporal nature of enteric fever attributable to S. Typhi in Central Division, Republic of Fiji, and defined the level of disease incidence and recurrence at a sub-catchment level. We used quantitative analysis to explore relationships between sub-catchment environmental characteristics and the incidence and recurrence of typhoid over 30 months (2013–2015). This study was unique in that no study of typhoid fever had yet addressed the variable risks associated with the ecological conditions of a geomorphological unit such as a sub-catchment. In summary, the study suggested that populations living on large river systems that broaden into meandering mid-reaches and floodplains with alluvial deposition are at a greater risk compared to small populations living near small, erosional, high-energy headwaters and small streams unconnected to large hydrological networks. The significant environmental determinants at this scale suggested increased risk of exposure where sediment yields increase following runoff. A crucial finding of the study is that alteration of land cover and hydrology, particularly through fragmentation of riparian forest and connections between roads and river networks, is associated with increased transmission of typhoid fever and that environmental transmission of typhoid fever is clearly important in this setting. The study at this level also points to the possibility that particular settings can act as sites of carriage, predisposing the likelihood of exposure, and therefore typhoid fever infection and disease.

This quantitative geospatial approach is important in revealing which aspects of land cover and infrastructure, within broader scales defined by hydrology and geomorphology, have distal roles in influencing risk of typhoid exposure at a community level. There were, however, several limitations to this approach encountered during the study. The Geographical Information System (GIS) data are only as good as the remote sensing methods from which they are derived and the associated model outputs reflect the accuracy of both environmental and the disease data. My disease data was a combination of retrospective and prospective tracing of cases to their residences from hospital based surveillance records (a time consuming and costly endeavor), which likely underestimated the actual infected population because only people in a severely weakened state tend to get admitted for blood culture confirmation, and currently used blood culture diagnostic methods are only around 50% sensitive (Adhikari et al. 2015). Basic environmental data layers on vegetation, land uses, topography, soil erodibility, and rainfall were difficult to acquire, often outdated, "coarse-grained" and generally from a single moment in time, not allowing the temporal dimension of environmental change to be explored or relationships made at a more "human" scale of metres. For example, the factors related to climate were not significant at this scale. Climatic conditions across our study area were largely homogenous with little variation in temperature or rainfall, but we were also limited to data extrapolated by Barker et al. (2006) from a small number of rain and temperature gauges, which did not match the sub–catchment unit of our study. Therefore, the extrapolated data was unlikely to be representative of variability at this system level.

Spatial data on community level water accessibility, sanitation and demographic data on the movement of people were also unavailable at the time of study, all of which would have been useful in interpreting the disease data. The regional and national scale drivers of land cover and hydrology alteration at this scale also remain unexplored by this study. The extent to which political will and economic resources exist among WASH and government agencies and the influence of donor agendas also shape the socio-ecological arena in which the sub-catchments are nested (Coit, 2002). Nonetheless, the study outcomes at this level can be used to develop predictive spatial risks and identify proactive intervention strategies at the sub- catchment level, such as protection from exposure to floods and erosion.

6.313 *Residential setting subsystem*

Chapter 4 investigated the contribution of the residential setting and microbiological and physicochemical characteristics of the lived environment to the risk of typhoid transmission, using a combination of spatial characteristics, living condition observations and measured biophysical parameters. Using the overarching case-control design, I investigated bacterial contamination and chemical composition of water and soil as indicators of vehicles of exposure, complemented with observational analysis of residential living conditions, spatial analysis of household locations and factor analysis to explore multivariate relationships. At this level, spatial analysis revealed typhoid case residences to be significantly closer to water bodies, further from the nearest road and lower in elevation than controls. The observational analysis revealed case residences had significantly poorer stormwater drainage, more exposed bare soil, greater state of structural disrepair and food gardens nearer to toilet or septic drainage than controls. They also had less contained excreta disposal, higher amounts of unconstrained solid waste and a greater smell of faeces near the toilet. Cases also had higher concentrations of *E. coli* in their stored drinking water, and higher concentration of phosphates at both the source, in stored drinking water and in toilet drainage soil than control households. Multivariate factor analysis revealed five factors at this level were significant in predicting typhoid and explained 42.5% of the cumulative variance. Variables clustered together along significant factors characterized by external condition (related to substrate, drainage, house condition, amount of solid waste near house, and garden position), drinking water condition (related to *E. coli* concentration in source house water, drinking water storage, phosphate concentration in source house water, and distance to nearest road), sanitary condition (related to ammonia concentration in source house water and toilet smell), microbial (related to *E. coli* and ammonia concentration), and nutrient loads (phosphate concentration) of toilet drainage soil. At this scale, residential settings with poor drainage and conditions conducive to frequent flooding, with nearby unimproved sanitation, faecally contaminated and nutrient enriched water and soil, provide an ecological arena in which the risk of typhoid transmission is enhanced by individual level risky behaviours nested within.

This study provided specific direction for several medium term interventions, at the broader Fijian residential setting level, that are rarely acknowledged in typhoid control strategies. My observations clearly support improving storm drainage in this setting to reduce localised flooding, thereby reducing spread of waterborne pathogens and creation of stagnant sites for bacterial growth and breeding sites for several disease vectors (Lall et al. 2016). Prior to my study, the proximity of household gardens to toilet drainage had not been identified as a risk factor for typhoid, and clearly improving the position of household gardens relative to toilets is a feasible medium term intervention along with health promotion messaging on the risks of passive use of human waste as fertiliser. The spatial risks of proximity to water and low elevations have only recently being acknowledged (e.g., Akullian et al. 2015; Dewan et al. 2013) and are given added support by this study, suggesting that improvements to the positioning of housing and sanitation infrastructure, where possible, will also reduce typhoid risk. Measurements at this level also demonstrated drinking water sources for typhoid cases had higher levels of faecal contamination (as indicated by faecal coliforms) and nutrient enrichment (measured as phosphates), suggesting the need to not only improve sanitation infrastructure, maintenance and runoff management but also enhance drinking water source surveillance and both source and household treatment. This result also adds evidence to support the possibility that some aspects of nutrient enrichment of water and soil support the persistence of S. Typhi external to the human host.

While there are significant merits in taking an observational and measurement approach at this residential level, as part of a case-control study, the introduction of intensive water and soil sampling, laboratory analysis and Geographical Information Systems (GIS) into the design is time consuming, increases costs and limits sample sizes, thereby reducing the often cited advantage of case-control design as cheap and rapid (Hennekens and Buring 1987). This observational and measured approach eliminates the re-call bias in the case-control design but introduces observational bias. Measuring inter-rater reliability with de-identified observational data can determine the level of observation bias but again requires some additional time and personnel investment. In the relatively homogenous environment of Central Division, Fiji, the second control is also critical to allow detection of localised risky exposures, which significantly increases the workload. The latent period between the disease exposure and observation or measurement also makes causality and timeline of exposure to the measured and observed factors difficult to ascribe.

6.314 *Individual/household subsystem*

At the individual and within-household level in Central Division, Fiji, chapter 5 examined proximal risk factors for typhoid by using the classic case-control study approach. I sought patients with blood culture-confirmed typhoid fever from February 2014 through August 2016 and two age interval, gender, ethnicity, and residential area matched controls per case and administered a detailed questionnaire to 479 participants. Matched univariate and multivariate conditional logistic regression analyses were used to evaluate associations between exposures and risk of typhoid fever. In summary, this study found that using unimproved pit latrines, not washing produce or hands before eating, bathing outside, having intermittent availability of water, having sand or wood plank floors and attending mass gatherings were significant risk factors for typhoid fever.

Commonly described from Asian and African environments, these results are among the most frequently defined risk factors revealed from case-control studies, including consuming contaminated water and food, using inadequate sanitation, poor hygiene behaviour and socio-economic factors (e.g., Sharma et al. 2009; Mbakaya et al. 2015; Alba et al. 2016). An innovative element of our study was a set of questions surrounding distal environmental conditions within the water catchment, which had yet to be reported as risk factors for typhoid in case-control literature. While catchment level factors did not remain significant in our multivariate model, univariate analysis revealed three significant catchment level typhoid risk factors unreported in the case-control literature: the presence of livestock above where drinking water was sourced, dams higher in the river basin, and flooding of the nearest river or stream in the last two months. These factors all point to distal processes influencing individual health outcomes, although distant events and conditions are better verified by direct observation or measure (Chapter 3, Chapter 4).

Case-control studies remain the primary epidemiological method to identify biologically plausible risk factors for typhoid at the individual and proximal household scale and to advise modes of interrupting transmission (e.g., Mbakaya et al. 2015; Alba et al. 2016). This study approach is relatively inexpensive and less time consuming than randomized control or cohort studies and particularly efficient for diseases such as typhoid with a relatively long latency period between exposure and disease manifestation. This long latency period, however, exposes a drawback of case-control studies that often cannot acquire reliable information about the timeline of exposure to specific risks (Schultz and

Grimes 2002). While this approach is important for questions related to behaviour and local transmission, case-control studies have limited capacity to explain root causes, such as broad social or ecological conditions, or critically examine mechanisms acting at distal scales (Eisenberg et al. 2007).

6.315 *Additional molecular & microbiome approaches*

Another innovative aspect of this project involved the attempted molecular detection of *S.* Typhi in environmental samples. To further support the notion that particular physicochemical characteristics of water and soil can support persistence of *S.* Typhi external to the human host and that particular settings can act as sites of carriage, I sought to detect *S.*Typhi in my environmental samples using real time PCR (rtPCR). *S.* Typhi are notoriously difficult to culture from environmental samples, however, recent advances in rtPCR are allowing study of possible viable environmental reservoirs (Baker et al. 2011; Karkey et al. 2016). This method uses oligonucleotides (reported in Baker et al. 2011), specific to *S.* Typhi, as primers to determine presence (and potentially, a semi-quantitative measure of the amount) of *S.* Typhi genetic material in water samples. This rtPCR method was first used to detect *S.* Typhi in well water in Nepal with success (Baker et al. 2011).

Initially, Ispiked 0.25 g of clay loam with a single colony of *S.* Typhi and, using a DNA extraction kit particularly designed for reducing inhibitors in soil (PowerSoil), and using the method described in Baker et al. (2011), was able to detect the *S.* Typhi genome (Figure 6.1). This provided proof of concept as a first successful extraction of *S.* Typhi from soil.

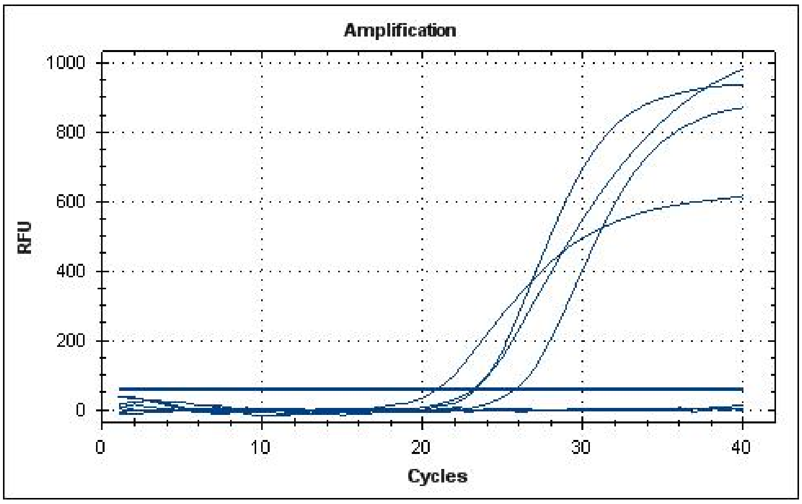


Figure 6.1 Amplification of S. Typhi genome extracted from a clay loam sample from Central Division, Fiji spiked with a laboratory culture. RFU = Relative Fluorescence Units.

During my study period, 557 environmental samples (water and soil) were collected from the residences of typhoid cases and controls, filtered and stored in the Fiji Centre for Communicable Disease Control. I have yet to fully develop the use of this assay for the environmental samples. 50 environmental samples were investigated (17 case, 33 control), five of which showed a late amplification, two of the five were from soil and all five were from case households. Bacterial colonies become diluted in environmental samples over time, soils are a highly complex media from which to extract DNA and many inhibitory factors exist that could result in this late amplification. While intriguing, my assay needs further validation to establish the quantitative nature of the signals, in soil in particular, and I need to complete processing the stored samples to see what results emerge. My future research will investigate these data, along with the meta-data surrounding each sample, to determine if any patterns in the distribution of potential environmental reservoirs around the house, within the week following infection, are present. A parallel study led by University of Melbourne, involving the genomic sequencing of corresponding blood isolates, could also enable us to identify sources and patterns of spread. There is clearly potential to examine S. Typhi ecology using molecular techniques to estimate persistence and transport characteristics external to the human host and to refine basic tools to carry out environmental investigations, such as the ability to detect the pathogen in complex environments (Remais and Eisenberg 2012).

Since the first publication of a human metagenomic study (Gill et al. 2006), the field of human microbiome research has also advanced swiftly with the development of highthroughput sequencing technologies, transforming our capacity to investigate the diversity of the microbiome and its composition in health and in disease (Waldor et al. 2015). Changes in the human microbiome, in particular that of the gut, have now been found associated with a wide variety of diseases (Bik 2016). Combining single-cell genomics with metagenomics, our recent research, comparing populations from Fiji and the United States, demonstrated that the mobile gene pools in the gut microbiome are shaped by environmental selection at global and individual scales (Brito et al. 2016). This approach generates the possibility of testing hypotheses on environmental selection, human activity and behaviour on microbiome composition and patterns of susceptibility to typhoid and other diseases. This approach also shows potential to inform stewardship of particular antibiotics at regional levels where distribution of antibiotic resistance genes among different populations' microbiomes could be described (Brito et al. 2016). These insights, if embedded within results from broader systems-level thinking and analysis, have enormous potential to improve both public health and environmental stewardship across multiple subsystems.

6.32 *The Bayesian Network Model*

Bayesian Networks (BNs) are an increasingly popular analytical platform for modeling uncertain and complex domains, understanding interrelations between components of systems, determining cause and effect and assessing risks and opportunities (Joffe et al. 2012; Fenton and Neil 2013; Lau and Smith 2016). While most widely used in ecology, engineering, economics, artificial intelligence and medical diagnosis and treatment, application of BNs in infectious disease environmental epidemiology has so far been particularly limited (Lau and Smith 2016). BNs have the advantage that they can incorporate knowledge of different uncertainties and from different scales and sources and easily handle missing data. The relatively simple graphical representation of causal pathways, hypotheses, and assumptions allows complex model building without highly technical skills and facilitates easier interpretation (Chen and Pollino 2012). The ability to represent the interrelationships between a wide variety of potential causes, consequences and exposure pathways allows a closer approximation of infectious disease transmission in the real world (Lau and Smith 2016). In addition, BNs are easily updateable as new knowledge becomes available and probability outputs are calculated quickly and efficiently even in large, complex models. Expert opinion can be used to set conditional probabilities and interactions between variables without data, and updated in the model as beliefs or hypotheses evolve. This is a particularly appealing aspect of BNs, as it is well suited to supporting the iterative process of learning and updating used in adaptive management (Uusitalo, 2007). BNs are acyclic, however, and therefore limited in their ability to represent feedback loops and dynamic relationships (Uusitalo, 2007). They are also somewhat limited in their ability to deal with continuous data, which needs to be discretized, and may only capture approximate characteristics of the original distribution (Jensen 2001).

In a BN the variables and outcomes are represented by nodes, which are linked by arrows that symbolize the dependent associations between nodes. While these arrows denote direct influence, the nature of that influence can vary and does not need be causal, although among physically distinct variables, this is the most common interpretation (Nicholson et al. 2010). The Conditional Probability Table (CPT) attached to each node defines the strength of relationship between nodes. The CPT expresses the probability that a node will be in a particular state given the states of nodes that directly affect it (parent nodes). This relationship between nodes is based on the Bayes theorem of conditional probability, which can characterize both magnitude, and direction of associations between variables (Lau and Smith 2016).

The general steps in building a BN are: 1) defining the objective of the model, 2) creating a conceptual model of how the system works, 3) transforming the conceptual model into an influence diagram, 4) describing the model variables (and assigning states), 5) parameterising the model (quantitative and qualitative), 6) evaluating the model sensitivity and accuracy, and 7) testing model scenarios (Pollino and Henderson 2010). The general objective of my model was to synthesize significant risk factors from three subsystems within this set of Fijian typhoid studies and examine how they conjointly influence typhoid exposure risk. I use the model to test potential intervention scenarios by altering the states of particular nodes to elucidate the relative influences of interventions on typhoid exposure risk.

The conceptual model of how the system works was based on my expert opinion and reasoning that outlines the likely association of significant factors with each other, described in detail in each thesis chapter. The Bayesian model structure was defined according to this conceptual model using the general methodological framework of Chen and Pollino (2012). The influence diagram and conceptual model are reflected in the final fitted BN shown in Figure 6.2. Unlike many BN models with missing or temporally disparate data and high degrees of uncertainty, I populated nodes (model variables) from measured or observed data with demonstrated significant associations with increased typhoid exposure in this setting over the same time period. The significant variables, data sources and parameterisation used to populate this model are described in Table 6.3. At the residential level, all individual component variables with factor loadings greater than 0.4 (from the Exploratory Factor Analysis in Chapter 4) were used in the BN model.

Table 6.3 Nodes used in Bayesian Network for typhoid exposure in Central Division, Fiji. RBZ = riparian buffer zone, CC = creek crossings, CFU = colony forming units. The 0-4 categorical ranking is of increased perceived likelihood of parameter facilitating or indicating disease transmission.

Node	Subsystem	Data type	States	Key source
RBZ fragments/km	Sub-catchment	GIS derived	< 1.3 > (median)	Chapter 3
CC/km x10	Sub-catchment	GIS derived	< 4.2 > (median)	Chapter 3
High erosion area (ha)	Sub-catchment	GIS derived	< 7332 > (median)	Chapter 3
Garden position	Residential	Observational ranking	0-4 categorical ranking	Chapter 4
Solid waste	Residential	Observational ranking	0-4 categorical ranking	Chapter 4
House condition	Residential	Observational ranking	0-4 categorical ranking	Chapter 4
Substrate	Residential	Observational ranking	0-4 categorical ranking	Chapter 4
Drainage	Residential	Observational ranking	0-4 categorical ranking	Chapter 4
Water storage	Residential	Observational ranking	0-4 categorical ranking	Chapter 4
Toilet smell	Residential	Observational ranking	0-4 categorical ranking	Chapter 4
Nearest road (m)	Residential	GIS derived	<50> (median)	Chapter 4
***E. coli* source water (CFU/ml)**	Residential	Measured	0-10, >10-100, >100 (WHO standard)	Chapter 4
***E. coli* toilet drainage (CFU/ml)**	Residential	Measured	<500> (expert opinion)	Chapter 4
Ammonia toilet drainage (mg/L)	Residential	Measured	<0.04> (median)	Chapter 4
Phosphate toilet drainage (mg/L)	Residential	Measured	0-1, >1-10, >10 (expert opinion)	Chapter 4
Phosphate source water (mg/L)	Residential	Measured	<1> (expert opinion)	Chapter 4
Bathe outside	Individual	Questionnaire	Yes or No	Chapter 5
Unimproved pit latrine	Individual	Questionnaire	Yes or No	Chapter 5
Unwashed produce	Individual	Questionnaire	Yes or No	Chapter 5
Unwashed hands	Individual	Questionnaire	Yes or No	Chapter 5
Water not always available	Individual	Questionnaire	Yes or No	Chapter 5
Wood plank or sand floor	Individual	Questionnaire	Yes or No	Chapter 5
Attended mass gathering	Individual	Questionnaire	Yes or No	Chapter 5

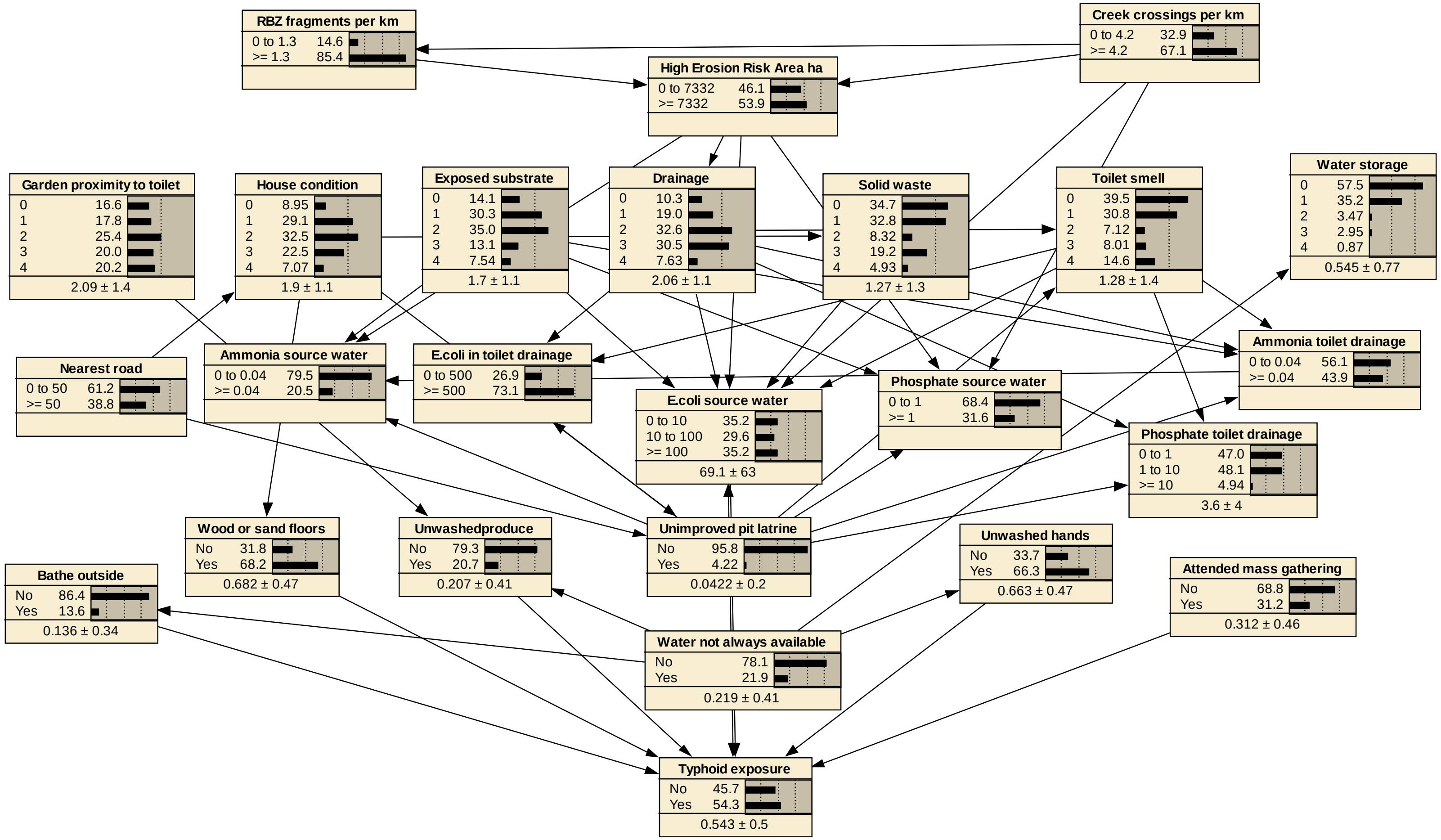


Figure 6.2 Bayesian network model of factors determining exposure to *S.* Typhi in Central Division, Fiji.

The model was evaluated by sensitivity analysis to verify whether the model's response correctly conformed to expectation, to identify which variables have the most influence on typhoid exposure, and subsequently which interventions are more likely to be influential (Chen and Pollino 2012). Sensitivity analyses apply variance reduction calculations to continuous variables and entropy reduction calculations to discrete or categorical variables (Uusitalo, 2007). The BN model was built using the Netica software (Norsys Software Corp.) and the sensitivity analyses were conducted using the 'sensitivity to findings' function in Netica. The function works by systematically varying the evidence entered into each of the nodes to simulate 'typhoid exposure' and records the probability distribution for the states of this output node (Norsys Software Corp., 2006). The resulting variance reduction or mutual information statistic (also referred to as entropy reduction) indicates the variance in the 'typhoid exposure' node that is explained by changes in the respective input nodes (Norsys Software Corp., 2006). The conditional probabilities of the model were estimated from the input data using an Expectation-Maximization (EM) algorithm in Netica, which iteratively calculates maximum likelihood estimates for the parameters given the data and the model structure (Spiegelhalter et al. 1993). Simulated interventions were then undertaken by systematically modifying the states of specific nodes to reduce particular risk factors by 100% in the model and assessing the contribution of these particular interventions on the overall risk of typhoid exposure. These included within subsystem interventions, subsystem -by- subsystem interventions, and a final example of a multiple subsystem intervention.

6.4 Results

Using the measured and observational data Chapters 3, 4 and 5 and the BN structure, the conditional probability tables and final network output are shown in Figure 6.2, indicating a 54.3% probability of typhoid exposure given this dataset. The sensitivity analysis results for the 'typhoid exposure' node (Table 6.4) indicated that *E. coli* concentration in source water has the strongest influence by far in this system. Distal sub-catchment nodes of creek crossings per kilometre, riparian buffer zone fragments per kilometre and area of high erosion risk were second, third and fifth most influential nodes, despite being the furthest removed from typhoid exposure within the network structure. Other primary influential nodes were the proximal behavioural and sanitation factors of not washing produce and using unimproved pit latrines. The results of the sensitivity analysis conformed to my expectations based on the nature of the input data.

Table 6.4 Sensitivity of 'Typhoid exposure' due to a finding at another node. The nodes are ranked according to their degree of influence on the 'Typhoid exposure' node.

Node	Variance Reduction	Percent	Mutual Info	Percent
***E.coli* in source water**	0.0631	25.4	0.20251	20.4
Creek crossings per km	0.0298	12	0.09124	9.17
RBZ fragments per km	0.01092	4.4	0.03403	3.42
Unwashed produce	0.007101	2.86	0.02129	2.14
High Erosion Risk Area	0.004501	1.81	0.01311	1.32
Unimproved pit latrine	0.004482	1.81	0.01474	1.51
Solid waste	0.002613	1.05	0.0077	0.775
Attended mass gathering	0.001062	0.428	0.0031	0.312
Toilet smell	0.0008788	0.354	0.00257	0.259
Bathe outside	0.0007923	0.319	0.00233	0.234
Unwashed hands	0.000792	0.319	0.0023	0.231
Garden proximity to toilet	0.0007537	0.304	0.0022	0.221
Phosphate source water	0.0005764	0.232	0.00168	0.169
House condition	0.0005448	0.22	0.00158	0.159
Drainage	0.0004707	0.19	0.00137	0.138
Ammonia source water	0.0002723	0.11	0.00079	0.0799
Exposed substrate	0.0001816	0.0732	0.00053	0.0531
Water not always available	7.94E-05	0.032	0.00023	0.0232
Nearest road	5.06E-05	0.0204	0.00015	0.0148
Phosphate toilet drainage	4.02E-05	0.0162	0.00012	0.0117
Wood or sand floors	2.41E-05	0.00971	0.00007	0.00704
Ammonia toilet drainage	2.13E-05	0.00857	0.00006	0.00622
***E. coli* in toilet drainage**	7.94E-06	0.0032	0.00002	0.00232
Water storage	3.51E-06	0.00142	0.00001	0.00103

6.41 *Sub-catchment subsystem intervention*

This model indicates if an intervention reduced all nodes to the lowest state at the sub-catchment level, without changing nodes in residential or individual levels, then exposure would increase by 2.7%. This result is counterintuitive, however, if the creek crossings per km node are increased to a higher state, while erosion area and riparian fragmentation are reduced, then typhoid exposure is reduced by 10.1%, despite being mediated by nodes in residential and individual subsystems. This might suggest that proximity to road infrastructure acts as a proxy for access to services (e.g., municipal treated water) and that only if this variable increased while forest fragmentation and erosion were reduced could overall typhoid exposure also be reduced.

6.42 *Residential setting subsystem intervention*

As stated above, from the sensitivity analysis, the most influential node in this subsystem (and overall) is *E. coli* in source water. If an intervention were to reduce *E. coli* in source water to between 0 and 10 CFU/mL (considered low risk by WHO), then typhoid exposure would be reduced by 17.3%. By also intervening on the nodes that comprise additional variables within the 'water condition risk factor' (Chapter 4) (i.e. by reducing phosphate in source water to below 1 mg /L, storing water in narrow mouthed, capped containers and having roads 50 m or less from the house), then an additional 1.9% reduction in exposure occurs (19.2 % reduction overall). If all measured parameters in this subsystem, including the *E. coli* and nutrient concentrations in water and toilet drainage and road proximity, are reduced to the lowest category of risk, no additional reduction in typhoid exposure occurs. Sensitivity analysis of each of the observed nodes confirms a high degree of influence on measured nodes, therefore the additional removal of observed risk factors does not change overall typhoid exposure. These results suggest intervening by addressing the residential conditions that increase probability of faecal coliform contamination of source water, in combination with direct treatment of source water, are most likely to be effective at reducing typhoid exposure in this subsystem.

6.43 *Individual/household subsystem interventions*

Simulated interventions to improve individual food and hygiene behaviour (i.e. always wash hands and produce, only bathe inside) resulted in a 12.7% reduction in typhoid exposure. If water and sanitation access interventions were made so that water was always available (not changing the quality of water) and people were not using unimproved latrines, only 1.9% reduction in exposure occurred. Similarly, modifying only structural and social behavioural factors (wood and sand floors, attending mass gatherings) resulted in only 4.1 % reduction of exposure. If states for all proximal individual/behavioural level factors were reduced to no risk, typhoid exposure was reduced by 22.9%. Importantly, the results of each individual intervention were not simply additive and an additional 4.2% reduction in exposure was gained when factors were addressed simultaneously.

6.44 *Multiple nested subsystem intervention*

Aside from the elimination of all risk factors in all investigated subsystems, which resulted in a complete elimination of typhoid exposure in the model, targeted interventions on the most influential nodes in each subsystem were an improved approach to acting only within individual subsystems. By systematically varying the states of influential nodes across all subsystems to find the combination of practically achievable interventions that resulted in the greatest possible exposure reduction, a hypothetical multiple nested system intervention strategy is herein proposed (Figure 6.3).

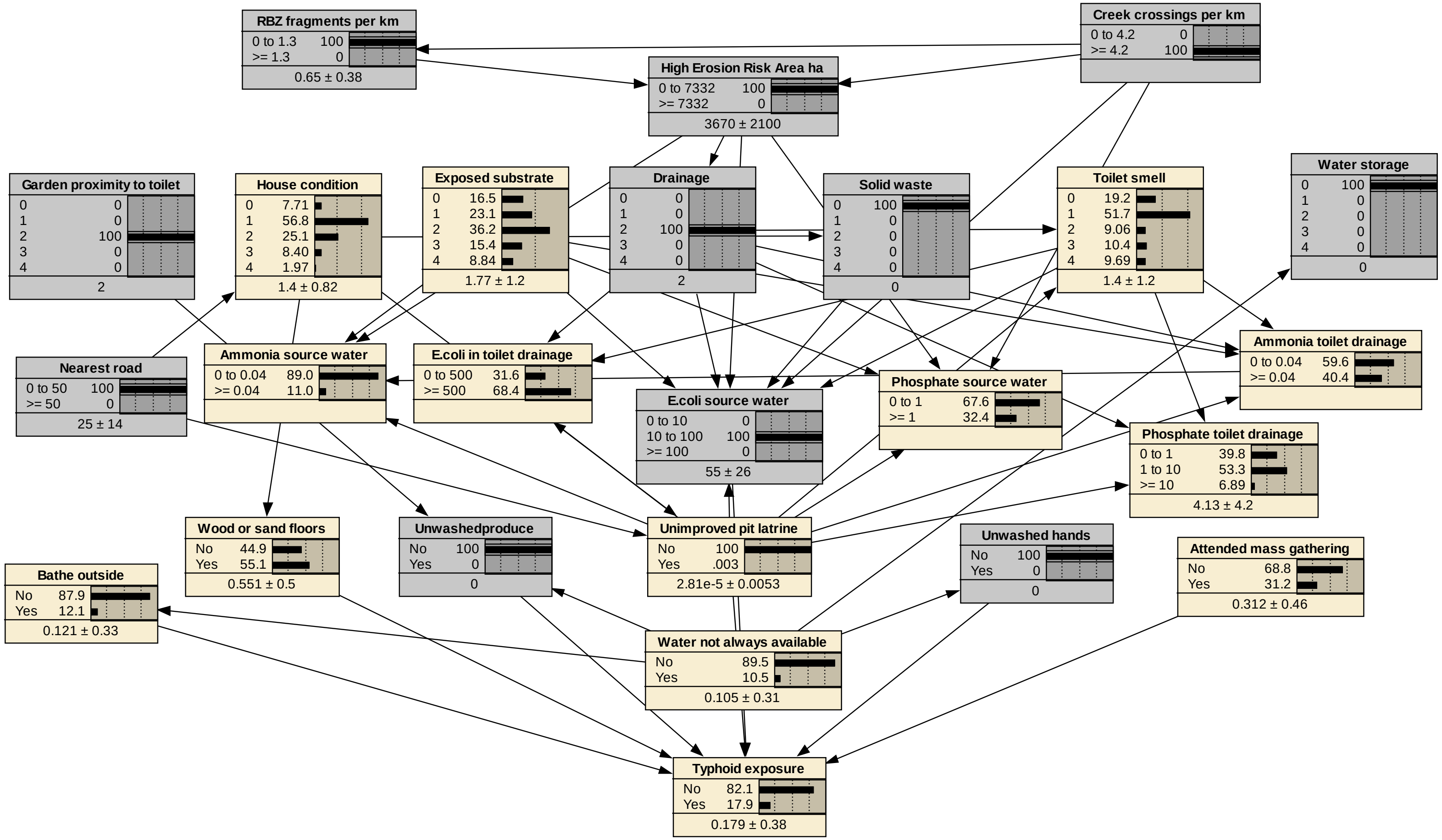


Figure 6.3 A hypothetical multiple nested system intervention strategy. Grey nodes indicate points of intervention, and are explained in the text.

In the short-term, food and personal hygiene are critical, with both produce and hands always needing to be washed before eating. In the medium term, in the broader residential setting, I propose a moderate improvement (node state 2) in drainage and the positioning of gardens relative to toilets, removal of solid waste and storing of water in capped, narrow mouthed containers, alongside measures that would result in a mean reduction of *E. coli* in source water to below 100 CFU/mL. In the long term, in the sub-catchment, road infrastructure development will likely continue and numbers of creek crossings will increase to a higher state, with nearby communities potentially gaining improved access to associated services as a result. If, through long-term catchment level restoration and sound development practice, this was achieved while reducing both the area of high erosion risk and level of riparian fragmentation, this would contribute to reduced typhoid exposure. This particular combination of selected targeted interventions within three nested subsystems resulted in a 36.4 % reduction in typhoid exposure, 19% greater than the mean total reduction of all risk factors within any individual subsystem.

6.5 Discussion

6.51 *BN model and intervention strategies*

The BN model presented here is just that, a model. While it is based on sound data and improved knowledge of risk factors and interactions, it should be viewed as the first iteration in an ongoing process of understanding system function and advising adaptive management. It is presented here to give an example of an analytical framework in which to incorporate data from multiple sources and levels and hence gain insight into the critically-needed nested system approach to eco-epidemiology, but it is by no means definitive. The ability to iteratively update data and knowledge on interacting processes within the BN framework is possibly the key advantage of BN models, also reflecting a central tenet of systems thinking that "management has to be flexible, adaptive and experimental at scales comparable to critical ecosystem functions" (Gunderson and Holling 2002). The reasoning machinery of BNs also can be efficient even if the relationships are non-linear and complex (Uusitalo 2007). However, clearly a major disadvantage of this BN approach is the inability to support feedback loops and the need to discretise continuous variables (Uusitalo 2007). The model output would change considerably by varying the thresholds at which continuous variables were discretised. In light of these advantages and limitations, the outputs of this model under different intervention scenarios should not be taken as absolute but rather as relative to one another within the constraints of this particular model structure.

While exploring approaches to system level analysis is important, I also purposefully built this model to explore the potential relative impact of specific interventions for typhoid control within this particular setting. Within the individual/household subsystem, the interventions to improve food and personal hygiene (i.e. washing produce and hands) yielded the greatest effect on typhoid exposure reduction. These were also clearly important factors in the case-control study, although use of unimproved pit latrines was a significantly higher risk (Chapter 5). Across various study designs and pathogens, there is clear and consistent evidence that hand washing with soap is strikingly effective at improving multiple health outcomes, although it depends on access to water (e.g., Cairnscross et al. 2010). The simulated water and sanitation intervention to only improve access to water (not necessarily quality) and remove unimproved pit latrines as a risk factor only yielded a small (1.9%) reduction in exposure. This is noteworthy, given the paucity of conclusive evidence for the health benefits of sanitation interventions in low-income communities, as generally weak study designs restrict scientific inference (Cairnscross et. al 2010; Luby 2014). The most rigorous study so far, using a carefully conducted cluster- randomized controlled trial, demonstrated that improved mean village–level latrine cover from 9 - 63% in Odisha, India, did not reduce the prevalence of diarrhoea, soil-transmitted helminth infection, or stunting in children younger than 5 years (Clasen et. al 2014).

The intervention in this chapter, simulating risk reduction for solely socio-economic, social and behaviour factors of the individual also only yielded a small reduction in exposure. However, when I reduced all risk factors in this subsystem the total reduction in exposure was greater than the sum of the individual water, sanitation and hygiene interventions. The improvement of health outcomes from combined interventions is somewhat conflicted in the literature. Some studies show protective effects of better sanitation at the community level is increased by better drinking water at the community level (e.g., Komarulzaman et al. 2016), while others show multiple interventions (consisting of combined water, sanitation, and hygiene measures) were not more effective than interventions with a single focus (e.g., Fewtrell et al. 2005). This suggests the relationship between risk factors (and subsequent interventions) is not a linear, additive process and other influences might be important in each study, such as river basin or regional context.

The sensitivity analysis revealed the most influential node on typhoid exposure within the model was the indicator of *E. coli* within the source water in the residential subsystem (Table 6.4). This reflects several of my findings in this setting which indicate faecal contamination of drinking water contributes to typhoid risk (Chapters 4, 5), although the broader literature that deals with the relationship between *E. coli* contamination in drinking water and typhoid risk is conflicted (e.g., Luby et al. 1997; Karkey et al. 2016). My simulated intervention of only treating water at the source (i.e. reduction of *E. coli* to below 10 CFUs/mL at the dam or reservoir) had the single greatest effect on reducing typhoid exposure within the model. From an intervention point of view, this is similar to results of systematic reviews on WASH interventions to reduce diarrhoea in less developed countries, which show that point-of-use water treatment has a consistently high impact and is more effective than previously thought (Fewtrell et al. 2005; Cairnscross et al. 2010). Only an additional 1.9% reduction in exposure was gained by reducing all risk factors in this subsystem as opposed to simply improving the quality of the source water. This result suggests that this model is likely over parameterised and only factors that most affect water quality should be included in further iterations.

The sensitivity analysis also revealed that distal sub-catchment nodes were among the most influential on typhoid exposure despite being mediated by multiple proximal nodes within the network structure (Table 6.4). Individual sensitivity analysis of each of these sub-catchment level nodes revealed that their primary influence was through strong effects on the most influential node in the network (*E. coli* in source water). The simulated intervention in this distal subsystem was somewhat surprising, in that altering all nodes to the lowest risk state actually increased typhoid exposure by 2.7%. If a tradeoff were made of increasing creek crossings to the higher state, then typhoid exposure dropped by 10.1%. This could suggest that an intervention at this scale needs to balance the increase in access to infrastructure and medical services provided by more roads while also reducing riparian fragmentation and erosion. While our previous study demonstrates an association between sub-catchment factors and the incidence and recurrence of typhoid in this setting (Chapter 3), other equivalent studies demonstrating these effects on typhoid transmission are virtually absent from the literature. Intervention studies at the river basin scale to demonstrate improved infectious disease outcomes are also scant, although several studies demonstrate the ability of intact wetlands and well-forested watersheds to filter pollutants and pathogens from surface water supplies (Pattanayak and Wendland 2007; Braumen et al. 2007). Pattanayak and Wendland (2007) provide a rare and particularly relevant example, demonstrating that improved base flow (water quantity) from a less deforested and managed watershed in Flores, Indonesia, correlated with both reduced diarrhoea and typhoid in downstream populations. Distal measures such as targeted reforestation and flood prevention measures could have impacts on reducing typhoid exposure (Chapter 3), although the longer time horizon and associated high costs invariably revert focus to shorter term and smaller scale interventions including basic public health messaging and immunization.

Although the delivery of safe water, adequate sanitation, and hygiene promotion remain the foundation of typhoid prevention and control, typhoid vaccination is considered an important intervention in endemic and epidemic settings (WHO 2008). The large economic costs and long timelines required to implement infrastructure and behaviour change, in combination with rapid urbanisation and emerging multidrug resistance, are focusing attention on this shorter term solution (Steele et al. 2016). Two typhoid vaccines are currently licensed for use in persons above 2 years of age, an injectable Vi polysaccharide (ViPS) and an oral, live-attenuated Ty21a strain of Typhi. The ViPS vaccine is ~70% effective and is administered as one dose with immunity lasting 3 years, and the Ty21a vaccine is 53–78% effective and is administered as 3–4 doses with immunity lasting 5 years (WHO 2008). Recent investment in new typhoid conjugate vaccines holds promise of longer-term immunity but have yet to be licensed (Steele et al. 2016). A typhoid vaccination campaign was conducted in Fiji after a category 4 cyclone in 2010 in cyclone-affected areas which reduced incidence in the post-vaccination year in those areas with high to medium vaccination coverage (Scobie et al 2014). Typhoid still remains endemic within these areas and incidence levels have risen again since this time (Fiji CDC, personal communication). The best current typhoid vaccination models suggest that to eliminate the disease, a combination of vaccination and WASH interventions (instead of vaccination alone) is needed (Pitzer et al. 2014, Date et al. 2015).

Our suggested multiple nested subsystem intervention model does not include vaccination, but yields insights into potential study approaches and combined WASH and environmental management strategies. The multi-subsystem model suggests that strategic interventions on the most influential risk factors in multiple nested subsystems has a greater effect than the total reduction of all risk factors within any individual subsystem. This system level effect also occurs within components of a single subsystem, where the exposure reduction effect of a combined intervention within an individual subsystem is greater than the sum of the individual interventions. This system level effect where the 'whole is greater than the sum of the parts' is exactly the type of emergent property unlikely to be predicted by traditional reductionist methods that study individual components at single levels.

The set of studies presented here also demonstrate that key risk factors acting at different levels of organisation must be studied using fundamentally different approaches. For example, the contribution of forest fragmentation to increased typhoid incidence in a sub-catchment cannot be accurately determined using a household case-control questionnaire, just as the individual behavioural risk of developing typhoid from not washing produce cannot be accurately ascertained by using geospatial methods. Using appropriate methodology, however, each subsystem can be examined simultaneously through use of BN methods and focus on the same problem within the same nested boundary, with the network of results from several disciplines yielding greater insight than the side-by-side results of each individual study. Management interventions resulting from such multi-level, interdisciplinary studies can simultaneously address the multiple nested subsystems within the scope of study. In this example of typhoid prevention and control, a combination of individual (e.g., personal and food hygiene, vaccination), residential (improved water treatment, storage and sanitation) and river basin (catchment restoration, flood prevention) nested subsystems can be acted upon simultaneously, supported by an evidence base from each and across all studied systems. To address the temporal dimension, medium and long-term strategies can be sub-divided again into sequential sets of achievable short-term actions to suit political or funding constraints but the interventions can be targeted at each of the studied subsystems simultaneously.

Perhaps the clearest benefit of this nested systems approach is that with each increasing level of investigation and intervention the purview of potential insight and effect also grows. Vaccination for typhoid at the individual scale will only address this disease. Addressing water and sanitation in the broader residential setting will help address a wide range of water and food-borne diseases (e.g., leptospirosis, shigellosis) and have positive local effects on socio-economic and mental well-being. Addressing issues at the river basin scale will have profound effects on wide ranging concerns of water, food security and public health. In a local example, the clearing and modification of catchments associated with high-incidence and recurrence of typhoid in Fiji (Chapter 3) also causes the loss of abundance and diversity of fishes that people rely on for livelihoods and cultural practice (Jenkins et al. 2010). Addressing the same determinants (alterations to catchment land cover resulting in increased occurrence and duration of flooding, sedimentation and associated pollution to waterways) will strengthen cross-sectoral engagement, improve public health and environmental provisioning services while optimizing costs. Addressing issues at a regional scale by adopting long-term integrated approaches to ecosystem and disaster risk management and organising management systems in nested layers across sectors, social systems and habitats, will strengthen regional resilience to vicissitudes of market forces, globalization and climate change (Jupiter et al. 2014). This study provides further evidence that research and intervention approaches that consciously address scale and dynamic system linkages are more successful at assessing problems and finding politically and ecologically sustainable solutions (Cash et al. 2006).

6.52 *On the notion of environmental reservoirs of typhoid*

There is a certain anthropocentric assumption that humans are the only reservoir of typhoid that, from an ecological systems perspective, is worthy of closer consideration. In the infectious disease literature, the variety of different and contradictory definitions of what constitutes a disease reservoir leads to confusion and conflicted understanding (e.g., Ashford 1997; Haydon et al. 2002). Ashford (1997), recognising the system level problems and multiplicity in the use of the term disease reservoir, proposed an "ecological system in which the infectious agent survives indefinitely." Haydon et al. (2002) later proposed a definition where the reservoir of infection included any host that is epidemiologically connected to (i.e. contribute to transmission to) the target host. The Oxford English Dictionary definition of reservoir as a medical term is: "A continuing source of pathogens for a particular disease, *esp.* an animal or plant that is not itself susceptible to the disease." (OED online, 2016). Without arguing the semantics of these definitions, it is clear that our contemporary models of typhoid transmission lack crucial understanding of the parameters dealing with persistence and fate of viable *S.* Typhi in the environment (Watson and Edmunds 2015).

S. Typhi needs to survive and remain viable in the environment prior to transmission to another human host. Aside from oral-anal sexual practice, the environment always has a role in transmission. The environment into which *S.* Typhi is shed and the physicochemical characteristics of the setting determines how persistent the bacteria are outside of the human host. As stated in Chapter 1, in certain nutrient rich media (e.g., cheese), and in particular saprophytes, *S.*Typhi can be viable for almost a year (Mitscherlich and Marth, 2012). Early research on the recovery of *S.*Typhi from clay loam soil has been reported up to 5.5 months (Grancher and Deschamps 1889) and experimental work suggests *S.* Typhi may multiply in oysters (Mitscherlich and Marth, 2012). In another example of systems nesting within systems, many intracellular bacterial pathogens use protozoa as environmental reservoirs to assist in increased survival and persistence in the environment and increase virulence (Barker 1994). The free-living amoeba *Acanthamoeba castellani*, a common protozoan in soil and water and host of several bacterial pathogens, increased the survival of *S.* Typhi threefold when grown in co-culture (Douesnard-Malo and Daigle 2011). Potentially, the *S.* Typhi serotype can survive and multiply intracellularly in *A.castellani*, like many other bacterial pathogens.

Progress on understanding environmental persistence has been hampered by the difficulty of culturing *S.* Typhi from environmental samples, but recent advances in molecular microbiology now allow the study of viable environmental reservoirs (Baker et al. 2011). This current set of studies from Fiji suggests that environmental transmission of typhoid fever is important in Fiji, and provides evidence that settings with high erosion, sediment yields and associated elevated nutrients could be considered as potential sites of carriage. How long must *S.* Typhi persist in such settings for the environment to be considered a reservoir of the disease? From a systems perspective, particularly in such high-incidence, endemic settings, the environment should be considered as a potential reservoir of *S.* Typhi.

6.6 Conclusions

It is useful to conclude with a healthy dose of reality. Behaviour and institutional change are, by necessity, slow processes. Advances in reduction of cigarette smoking, for example, have mainly come about through intergenerational embedding of key messages in educational systems and popular media. While there have been numerous hand washing and food hygiene media campaigns and village-based information sessions in Fiji, they have achieved little in changing behaviour (Greenwell et al. 2013). Cyclone intensity is increasing in Fiji (ABM and CSIRO, 2011). In this context, there is scant opportunity for decision makers to focus on long or even medium-term strategies. Mass vaccination with a, yet to be sufficiently trialed, conjugate vaccine is currently being discussed. While this may reduce typhoid transmission, the scope of such an approach is narrow and inefficient in effecting the system level change needed to address the host of other diseases and sustainability challenges. Taking a nested ecosystems approach to both research and intervention offers a sorely needed opportunity to expand the jurisdiction and efficiency of institutions tackling these challenges. Tackling persistent issues of WASH and poor environmental governance will take considerable time and effort, but will have incremental effects on reducing vulnerability of island ecosystems and their inhabitants to issues of water and food security. Even broader-scale and longer-term systemic action on the regional and global stage is needed to effect the change in climate patterns that add yet another level of vulnerability. As I have demonstrated, it is clearly possible, within a reasonable amount of time, to take a nested ecosystem approach to a problem and propose appropriate interventions across and within several nested subsystems. Through this process, the focus and ambit of institutions will broaden and unforeseen opportunities will arise to understand and effect change in the wider spheres of public health and sustainability.

6.7 *Epilogue*

A key aspect of interdisciplinary systems research is recognising the unforeseen consequences that resulted from the broadened extent of the research and engagement process. From this process perspective, I found it useful to document (Table 6.1) the incidental outcomes of formal and informal institutional change and how diverse sectors, involved in the Typhoid research in Fiji during my candidature, sought to connect their range of interests to find practical collaborative actions.

Undertaking this research process in the context of Fijian government and NGO institutions stimulated both capacity building and a broadened scope within several ministries and NGOs. Within the Ministry of Health and Medical Services (MoHMS) water laboratory, in which much of my laboratory work occurred, infrastructure and capacity to undertake nutrient analytics and process non-water environmental samples (i.e. soil) were limited prior to my project. Through a process of technique and equipment introduction (Edith Cowan University), as well as training of laboratory personnel (Edith Cowan University, Melbourne University), the remit of this government laboratory expanded to include a new suite of environmental sample processing procedures within their laboratory implementation plan. Capacity building of staff and new technique introduction also occurred (ECU, MU) within the fledgling MoHMS PCR laboratory, where I initiated new protocols to run assays on environmental samples in comparison to the standard laboratory practice of using human tissue.

Geographical Information System expertise and infrastructural capacity with MoHMS remains poor, although communication and interaction with the environmental NGO sector (Wildlife Conservation Society), which have greater capacity in this regard, has improved. Realizing the value of GIS in communicating, predicting and managing health outcomes, the MoHMS has begun actively engaging in developing their in-house capacity for GIS through collaboration with University of the South Pacific and WHO, partially as a result of my project. Engagement of the environmental NGO sector in this research also broadened the scope of their ordinary focus on habitat and species conservation to include infectious disease prevention. WASH NGOs (UNICEF, CARE) ordinarily focussed on delivery of water, sanitation and hygiene public health messaging and products, have become more actively engaged in the process of supporting and using the typhoid research results to guide their interventions.

Although reticent at first, senior MoHMS officials became more convinced of the potential of environmental determinants for typhoid transmission, and the sectoral inclusion in key meetings broadened. At first, environmental health officers (EHOs) were summoned more frequently and included in discussions usually reserved for senior epidemiologists. Over time, Department of Environment (DoE) and environmental NGO sector personnel became more routinely invited to discussions on waterborne disease prevention and control. As the primary investigator of the project, I became formally engaged and invited to usually "closed door" meetings of the National Taskforce on Communicable and Outbreak Prone Diseases (NTCOPD), a first for an ecologist. This also led to my inclusion in WHO and MoHMS discussions on exotic fish introduction for control of dengue, which benefitted from an ecological system perspective. Although this is a positive incidental outcome of the research process, the reciprocal engagement of MoHMS staff by DoE and environmental NGOs in key discourse on environmental management has been less forthcoming.

Following key presentations at Pacific WASH cluster meetings, several WASH NGOs, primarily engaged in public outreach and social marketing, gave financial and technical support to my project to assist in surveillance and building the evidentiary base for WASH interventions. Within the specific field of typhoid research within Fiji, the range of research projects broadened as a result of institutional connections and collaborative interaction generated from this project. The in-country typhoid research has expanded to include genomic sequencing of blood isolates, estimation of carriage from gall stone tissue, seroprevalence studies and testing of novel diagnostic methods. Our collaboration on gut microbiome research (Brito et al. 2016) also led to important new hypotheses on the role of microbiome composition on patterns of susceptibility to typhoid and other diseases.

The process of conducting this research, while being situated within the Fiji Center of Communicable Disease Control, also led to greater interaction and ecologically focused discourse with senior MoHMS officials, resulting in input to key policy and surveillance tools. Of particular note was our input to the Fiji National Typhoid Strategic Plan in which environmental and geospatial approaches to surveillance and control have now been included. Also, as a direct result of the research outcomes of this project, catchment level and residential level factors are now embedded within typhoid case investigation forms of environmental health officers. As a result of being accessible and working on integrative research, I was engaged during the aftermath of Tropical Cyclone Winston in February 2016 to assist the MoHMS, Fiji National Drinking Water Quality Committee and WASH cluster members to integrate nationally collected data on drinking water quality, sanitation, syndromic and confirmed water-borne diseases and provide integrated assessment of community health risk. This novel integrated approach to simultaneous surveillance of environmental and health outcomes stemmed, at least in part, from the broadened discourse surrounding our typhoid research.

The many positive incidental outcomes of this interdisciplinary research approach were not achieved without persisting through numerous epistemological and institutional challenges. Disciplinary silos of public health and ecology are tenacious and institutionally entrenched with regard to the types of knowledge that are acceptable, methodological approaches and how problems are defined. Senior disciplinary experts tend to regard fields other than their own sceptically and interdisciplinary approaches as being too speculative (Baigent et al. 1982). However, despite these challenges, my in-country research team has made some progress in advancing synthetic and integrative approaches by "straddling" the fields over a period of several years and building mutual trust and respect. This was cultivated by long-term commitment to capacity building within and across Fijian institutions and sectors. Remaining confident in one's own discipline without being defensive and having the open mindedness to learn new disciplinary skill sets was central to this commitment. Finding the space and time for sharing knowledge, different framing of problems and construction of methods allowed the transparency for relationships and trust to build. Issues of hierarchy and politics often affected the co-ordination of genuine participation and exchanging knowledge during the research process. However, having a shared focus on solving the specific, complex and real problem of typhoid in Fiji allowed for enough directed interdisciplinary discourse to occur to affect certain facets of institutional change.

7.0 References

Asian Development Bank and International Food Policy Research Institute. 2009. Building climate resilience in the agricultural sector of Asia and the Pacific. Asian Development Bank, Manila

Adger WN. 2006. Vulnerability. Global Environ Chang 16:268-281

Adhikari A, Rauniyar R, Raut PP, Manandhar KD, Gupta BP. 2015. Evaluation of sensitivity and specificity of ELISA against Widal test for typhoid diagnosis in endemic population of Kathmandu. BMC Infect Dis 15(1):523

Ahern M, Kovats RS, Wilkinson P, Few R, Matthies F. 2005. Global health impacts of floods: epidemiologic evidence. Epidemiol Rev 27(1):36-46

Akullian A, Ng'eno E, Matheson AI, Cosmas L, Macharia D, Fields B, Bigogo G, Mugoh M, John-Stewart G, Walson JL, Wakefield J. 2015. Environmental Transmission of Typhoid Fever in an Urban Slum. PLoS Negl Trop Dis. 9(12):e0004212

Alba S, Bakker MI, Hatta M, Scheelbeek PF, Dwiyanti R, Usman R, Sultan AR, Sabir M, Tandirogang N, Amir M, Yasir Y. Risk Factors of Typhoid Infection in the Indonesian Archipelago. PloS one. 11(6):e0155286

Albrecht G. 2005. Solastalgia: A new concept in human health and identity. Philos Activ Nat 3: 41-55

Alhamlan F, Al-Qahtani A, Al-Ahdal M. 2015. Recommended advanced techniques for waterborne pathogen detection in developing countries. The Journal of Infection in Developing Countries. Available at:http://www.jidc.org/index.php/journal/article/view/6101. Date accessed: 15 Jul. 2016

Anderson M, Gorley RN, Clarke RK. 2008. Permanova+ for Primer: Guide to Software and Statistical Methods. PRIMER-E Ltd, Plymouth

Arthington A, Bunn S, Catterall C. 1992. The Ecological Roles of Riparian Vegetation. In Woodfull J, Finlayson B, McMahon, T. Workshop proceedings: The Role of Buffer Strips In the Management of Waterway Pollution from Diffuse Urban & Rural Sources. University of Melbourne Occasional Paper Series Land and Water Resources Research and Development Corporation

Ashford RW What it takes to be a reservoir host. 1997. Belg J Zool. 127:85–90

Atherton J, Olson D, Farley L, Qauqau I. 2005. Fiji Watersheds at Risk: Watershed Assessment for Healthy Reefs and Fisheries. Wildlife Conservation Society, Suva, Fiji

Australian Bureau of Meteorology and CSIRO. 2011. Climate change in the Pacific: scientific assessment and new research. Volume 1: Regional Overview. Pacific Climate Change Science Program, Aspendale

Babagana A, Dungus B, Bello SA, Kolo BS. 2015, Problems and prospects of Alau Dam Construction in Alau community, Konduga Local Government Area, Borno State, Nigeria. Eur Sci J. 11(20): 194-207

Baigent M, Leigh R, Lincoln H. 1982. The Holy Blood and the Holy Grail. Bantam Doubleday Dell Publishing Group, New York

Bain R, Cronk R, Hossain R, Bonjour S, Onda K, Wright J, Yang H, Slaymaker T, Hunter P, Prüss-Ustün A, Bartram J. 2014. Global assessment of exposure to faecal contamination through drinking water based on a systematic review. Trop Med Int Health 19(8):917-27

Baird AH, Bhalla RS, Kerr AM, Pelkey NW, Srinivas V. 2009. Do mangroves provide an effective barrier to storm surges? Proc Natl Acad Sci USA 106 (40): E111-E111.

Bakach I, Just MR, Gambhir M, Fung IC. 2015. Typhoid Transmission: A Historical Perspective on Mathematical Model Development. T Roy Soc Trop Med H 109 (11): 679-689

Baird A, Kerr A. 2008. Landscape analysis and tsunami damage in Aceh: Comment on Iverson and Prasad (2007). Landsc Ecol 23:3–5

Baker S, Holt KE, Clements ACA, Karkey A, Arjyal A, Boni MF, Dongol S, Hammond N, Koirala S, Duy PT, Nga TVT, Campbell JI, Dolecek C, Basnyat B, Dougan G, Farrar JJ. 2011. Combined high-resolution genotyping and geospatial analysis reveals modes of endemic urban typhoid fever trans- mission. Open Biol 1: 110008

Barbier EB, Koch EW, Silliman BR, Hacker SD, Wolanski E, Primavera J, Granek EF, Polasky S, Aswani S, Cramer LA, Stoms DM, Kennedy CJ, Bael D, Kappel CV, Perillo GME, Reed DJ. 2008. Coastal ecosystem-based management with nonlinear ecological functions and values. Science 319:321-323

Barnett J, Campbell J. 2010. Climate change and small island states: power, knowledge and the South Pacific. Earthscan Ltd., London

Barnett J. 2007. Food security and climate change in the South Pacific. Pac Ecol 2007: 32-36

Barker GM, Price RJ, McGree S .2006. Climate surfaces for Fiji. LandCare Research, Hamilton, New Zealand

Barr KJ. 2007. Squatters in Fiji: The need for an attitudinal change. Citizen Constitutional Forum Housing and Social Exclusion Paper. Suva, Fiji.

Barrett B, Charles JW, Temte JL. 2015. Climate change, human health, and epidemiological transition. Prev Med *70,* 69–75

Batterman S, Eisenberg J, Hardin R, Kruk M E, Lemos MC, Michalak AM, Wilson ML. 2009. Sustainable control of water-related infectious diseases: a review and proposal for interdisciplinary health-based systems research. Environ Health Persp 117(7), 1023-1032

Bayas JC, Marohn C, Dercon G, Dewi S, Piepho PH, Laxman J, van Noordwijk M, Cadisch G. 2011. Influence of coastal vegetation on the 2004 tsunami wave impact in West Aceh. Proc Natl Acad Sci USA 108 (46): 18612–18617

Beard PJ. 1940. Longevity of Eberthella Typhosus in Various Soils. Amer J Publ Health Nat Health 30(9):1077-82

Bell JD, Kronen M, Vunisea A, Nash WJ, Keeble G, Demmke A, Pontifex S, Andrefouet S. 2009. Planning the use of fish for food security in the Pacific. Mar Policy 33 (1) 64 -76

Below R, Wirtz A, Debarati G. 2009. Disaster category classification and peril terminology for operational purposes. WHO Centre for research on the epidemiology of disasters (CRED) and Munich Reinsurance Company (Munich RE) Working paper 264. Université catholique de Louvain, Brussels

Bertuzzo EL, Mari L, Righetto M, Gatto R, Casagrandi I, Rodriguez-Iturbe, Rinaldo H. 2012. Hydroclimatology of dual peak cholera epidemics: inferences from a spatially explicit model. Geophys Res Lett 39(5):5403

Bik EM. 2016. Focus: Microbiome: The Hoops, Hopes, and Hypes of Human Microbiome Research. Yale J Biol Med. 89(3):363

Birley MH. 1995. *The Health Impact Assessment of Development Projects* (HMSO, London)
Bishop PK, Misstear BD, White M, Harding NJ. 1998. Impacts of sewers on groundwater quality. Wat Env J. 12 (3):216-23

Black RE, Cisneros L, Levine MM, Banfi A, Lobos H. 1985. Case - control study to identify risk factors for paediatric endemic typhoid fever in Santiago, Chile. Bull WHO 63: 899

Borga M, Tonelli F, Fontana GD, Cazorzi F. 2005. Evaluating the influence of forest roads on shallow landsliding. Ecol Model 187: 85–98

Borsuk ME. 2008. Ecological Informatics: Bayesian Networks. In: S. E. Jorgensen and B. Fath, (Eds.) Encyclopedia of Ecology. Elsevier, Oxford, UK pgs 307-317

Bracken LJ, Croke J. 2007. The concept of hydrological connectivity and its contribution to understanding runoff-dominated geomorphic systems. Hydrol Process 21: 1749–1763

Bradshaw CJA, Sodhiw NS, Pehwz KSH, Brook BW. 2007. Global evidence that deforestation amplifies flood risk and severity in the developing world. Glob Change Biol 13(11): 2379–239

5

Cabral JPS. 2010. Water microbiology, bacterial pathogens and water. Int J Environ Res Public Health 7: 3657-3703

Brauman KA, Daily GC, Duarte TKE, Mooney HA. 2007. The nature and value of ecosystem services: An overview highlighting hydrologic services. Annu Rev Environ Resour 32(1):67–98.

Brito IL, Yilmaz S, Huang K, Xu L, Jupiter SD, Jenkins AP, Naisilisili W, Tamminen M, Smillie CS, Wortman JR, Birren BW. 2016. Mobile genes in the human microbiome are structured from global to individual scales. Nature. 21; 535(7612):435-9

Bunch M, McCarthy D, Waltner-Toews D. 2008. A family of origin for an ecosystem approach to managing for sustainability. In: The Ecosystem Approach: Complexity, Uncertainty, and Managing for Sustainability, Waltner-Toews D, Kay J, Lister N-M (editors), Columbia University Press, New York, pp 125–138

Bunch MJ, Parkes M, Zubrycki K, Venema H, Hallstrom L, Neudorffer C, Morrison, K. 2014. Watershed management and public health: An exploration of the intersection of two fields as reported in the literature from 2000 to 2010. Environ Manage 54(2): 240-254

Bursac Z, Gauss CH, Williams DK, Hosmer DW. 2008. Purposeful selection of variables in logistic regression. Source Code Biol Med 16; 3(1):1

Cairncross S, Blumenthal U, Kolsky P, Moraes L, Tayeh A. 1996. The public and domestic domains in the transmission of disease. Trop Med Int Health 1:27–34

Cairncross S, Hunt C, Boisson S, Bostoen K, Curtis V, Fung ICH, Schmidt WP. 2010. Water, Sanitation and Hygiene for the Prevention of Diarrhoea. Int J Epidemiol 39 (S1): I193-I205

Cabral JPS. 2010. Water microbiology, bacterial pathogens and water. Int J Env Res Pub Health 7: 3657-3703

Cameron J. 2000. Confronting social policy challenges in Fiji. Chapter 6 in: Confronting Fiji Futures, ANU Press, Canberra p.133

Carter S, Williams M, Paterson J, Iusitini L. 2009. Do perceptions of neighbourhood problems contribute to mental health. Findings from the Pacific Islands Families study. Health Place 15 (2): 622-630

Cash D, Adger WN, Berkes F, Garden P, Lebel L, Olsson P, Pritchard L, Young O. 2006. Scale and cross-scale dynamics: governance and information in a multilevel world. Ecol Soc 11(2):8

Chapman R, Howden-Chapman P, Capon A. 2016. Understanding the systemic nature of cities to improve health and climate change mitigation. Environ Int 94:380-387

Charron DF. 2012. Ecohealth Research in Practice: Innovative Applications of an Ecosystem Approach to Health, Insight and Innovation in Development, International Development Research Centre, New York: Springer and Ottawa, Canada

Chen SH, Pollino CA. 2012. Good practice in Bayesian network modelling. Environ Model Soft 37:134-45.

Cherry, JA. 2012. Ecology of Wetland Ecosystems: Water, Substrate, and Life. Nat Educ Know 3(10):16

Cho JC, Kim SJ. 1999. Viable, but non-culturable, state of a green fluorescence protein-tagged environmental isolate of Salmonella typhi in groundwater and pond water. FEMS Microbio Let 170: 257-64

Chughtai S, Blanchet K. 2017. Systems thinking in public health: a bibliographic contribution to a meta-narrative review. Health Pol Plan 6:czw159

Church JA, White NJ, Hunter JR. 2006. Sea-level rise at tropical Pacific and Indian Ocean islands. Glob Planet Change 53(3):155–168

Clasen T, Boisson S, Routray P. 2014. Effectiveness of a rural sanitation programme on diarrhoea, soil-transmitted helminth infection, and child malnutrition in Odisha, India: a cluster-randomised trial. Lancet Glob Health; published online Oct 10. http://dx.doi.org/10.1016/S2214- 109 X (14)70307-9

Cleaveland S, Taylor LH, Laurenson MK. 2002. Identifying reservoirs of infection: a conceptual and practical challenge. Emerg Infect Dis 8(12):1468-73

Cochard R. 2011. On the strengths and drawbacks of tsunami-buffer forests. Proc Nat Acad Sci 108(46): 18571-18572

Cockburn A, St Clair J, Silverstein K. 1999. The Politics of "Natural" Disaster: Who Made Mitch So Bad? Int J Health Serv 29(2): 459-462

Coimbra CEA Jr. 1988. Human factors in the epidemiology of malaria in the Brazilian Amazon. Hum Organ 47: 254–260

Coit K. 2002. The mismatch between politics, aid and environmental health with particular reference to cholera in Madagascar. Environ Urban 14(1):247–259

Colwell RR. 1996. Global climate and infectious disease: the cholera paradigm. Science 274(5295): 2025–2031

Colwell RR, Huq A, Islam MS, Aziz KM, Yunus M, Khan NH, Mahmud A, Sack RB, Nair GB, Chakraborty J, Sack DA. 2003. Reduction of cholera in Bangladeshi villages by simple filtration. P Natl Acad Sci 100(3):1051-5.

Cook A, Watson J, van Buynder P, Robertson A, Weinstein P. 2008. 10th Anniversary Review: Natural disasters and their long term impacts on the health of communities. J Environ Monitor 10(2): 167-175

Corner RJ, Dewan AM, Hashizume M. 2013. Modelling typhoid risk in Dhaka Metropolitan Area of Bangladesh: the role of socio-economic and environmental factors. Int J Health Geog 12:13-15

Corvalan CF, Hales S, McMichael AJ. 2005. Ecosystems and Human Well-Being: Health Synthesis. World Health Organization, Geneva

Costa MH, Botta A, Cardille JA. 2003. Effects of large-scale changes in land cover on the discharge of the Tocantins River, Southeastern Amazonia. J Hydrol 283 (1-4):206-217

Costanza R, D'Arge R, De Groot R, Farber S, Grasso M, Hannon B, Limburg K, Naeem S, O'Neill RV, Paruelo J, Raskin RG, Sutton, P, van den Belt M. 1997. The value of the world's ecosystem services and natural capital. Nature 387:253–260

Craun GF. 1985. A summary of waterborne illness transmitted through contaminated groundwater. J Environ Health 48:122–7

Cressie N. 2015. Statistics for spatial data. John Wiley & Sons, New York, 887 pgs

Crump JA, Luby SP, Mintz ED. 2004. The global burden of typhoid fever. Bull WHO 82: 346–353

Cumming JG. 1917. An epidemic resulting from the contamination of ice cream by a typhoid carrier. J Amer Med Assoc 68(16): 1163-1165

Curtis V, Cairncross S, Yonli R. 2000. Domestic hygiene and diarrhoea–pinpointing the problem. Trop Med Int Health 5(1):22-32

Daily GC, Ehrlich PR. 1996. Global change and human susceptibility to disease. Ann Rev Energy Env 21:125–144

Dakers A, Evans J. 2007. Wastewater management in Rarotonga: It is not just a matter of a technological fix? In: Proceedings of the Workshop on Innovation and Technology for On-site Systems, Patterson RA (ed), Armidale, NSW

Danielsen F, Sorensen MK, Olwig MF, Selvam V, Parish F, Burgess ND, Hiraishi T, Karunagaran VM, Rasmussen MS, Hansen LB, Quarto A, Suryadiputra N. 2005. The Asian tsunami: A protective role for coastal vegetation. Science 310 (5748):643

Das S, Vincent JR. 2009. Mangroves protected villages and reduced death toll during Indian super cyclone. Proc Natl Acad Sci USA 106(18) 7357-7360

Date KA, Bentsi-Enchill A, Marks F. 2015. Typhoid fever vaccination strategies. Vaccine 33:C55–61

Davidson NC. 2014. How much wetland has the world lost? Long-term and recent trends in global wetland area. Mar Freshw Res 65, 934-941.
Deb BC, Sircar BK, Sengupta PG. 1986. Studies on interventions to prevent el tor cholera transmission in urban slums in Kolkata. Bull WHO 64, 127–131

Dempster AP, Laird NM, Rubin DB. 1977. Maximum likelihood from incomplete data via the EM algorithm. J Roy Stat Soc Series B (methodological) 1:1-38

Dengler L, Preuss J. 2003. Mitigation lessons from the July 17 1998 Papua New Guinea Tsunami. Pure Appl Geophys 160 (10): 2001 -2031

Dennison L, Kiem M. 2009. The health consequences of flooding. Stu Br Med J 17:110–111

Dewan AM, Corner R, Hashizume M, Ongee ET. 2013. Typhoid fever and its association with environmental factors in the Dhaka metropolitan area of Bangladesh: a spatial and time-series approach. PLoS Neg Trop Dis 7(1) e1998

Dewan AM, Corner RJ, Hashizume M. 2014. Modelling spatiotemporal patterns of typhoid cases between 2005 and 2009 using spatial statistics. In Dhaka Megacity (pp. 345-365). Springer, Netherlands

Dillaha TA, Reneau, RB, Mostaghimi S, Lee D. 1989. Vegetative filter strips for agricultural nonpoint source pollution control. T Am Soc Agri Eng 32: 513-519

Doocy S, Dick A, Daniels A, Kirsch TD. 2013. The Human Impact of Tropical Cyclones: a Historical Review of Events 1980-2009 and Systematic Literature Review. PLOS Curr Disaster. doi: 10.1371/s2664354a5571512063ed29d25ffbce74.

Dornan M, Newton CT. 2014. Regional service delivery among Pacific Island countries: an assessment. Asia Pac Pol Stud 1(3):541-60.

Douesnard-Malo F, Daigle F. Increased persistence of Salmonella enterica serovar Typhi in the presence of Acanthamoeba castellanii. 2011. Appl Env Micro 77(21):7640-6

Drummond W, Va'ai-Wells O. 2004. Health and human development models across cultures. Nagare Press, Palmerston North

Dupon, JF. 1986. Atolls and the Cyclone Hazard: A Case Study of the Tuamotu Islands. South Pacific Regional Environment Programme (SPREP)/South Pacific Commission (SPC), Apia and Noumea

Dutta P, Khan SA, Sharma CK, Doloi P, Hazarika NC, Mahanta J. 1998. Distribution of potential dengue vectors in major townships along the national highways and trunk roads of northeast India. South Asian J Trop Med Pub Health (29): 173-176

Eisenberg NS, Cevallos W, Ponce K, Levy K, Bates SJ, Scott JC, Hubbard A, Vierira N, Endara P, Espinel M, Trueba G, Riley LW, Trostle J. 2006. Environmental change and infectious disease: How new roads affect the transmission of diarrheal pathogens in rural Ecuador. **Proc Natl Acad Sci** U S 103(51): 19460-19465

Eisenberg, JNS, Desai MA, Levey K, Bates SJ, Liang S, Naumoff K, Scott JC. 2007. Environmental determinants of infectious disease: a framework for tracking causal links and guiding public health research. Environ Health Persp 1216-1223

Eisenberg JNS, Trostle J, Sorensen RJ, Shields, KF. 2012. Toward a systems approach to enteric pathogen transmission: from individual independence to community interdependence. Ann Rev Pub Health 33: 239-242

Ekholm P, Kallio K, Salo S, Pietiläinen OP, Rekolainen S, Laine Y, Joukola M. 2000. Relationship between catchment characteristics and nutrient concentrations in an agricultural river system. Wat Res 34(15):3709-16

El Azar GE, Habib RR, Mahfoud Z, El-Fadel M, Zurayk R. 2009. Effect of women's perceptions and household practices on children's waterborne illness in a low income community. EcoHealth 6:169–179

Ellison JC. 2009. Wetlands of the Pacific Islands region. Wet Ecol Manage 17(3): 169-206

Elsarnagawy D. 1978. Viability of some Salmonella strains in Algerian eggs. Arch Inst Pasteur Alger 53: 282-90

Ercumen A, Arnold BF, Kumpel E, Burt Z, Ray I, Nelson K, Colford JM. 2015. Upgrading a Piped Water Supply from Intermittent to Continuous Delivery and Association with Waterborne Illness: A Matched Cohort Study in Urban India. PLOS Med, DOI:10.1371/journal.pmed.1001892

Evans D, Gibson C, Rossell R. 2006. Sediment loads and sources in heavily modified Irish catchments: A move towards informed management strategies. Geomorph 79, 93-113

Eustace KL, MacDonald C, Long NR. 1999. Cyclone Bola: a study of the psychological after-effects. Anx Stress Copin 12(3):285–98

Ewalt PL, Mokuau N. 1995. Self-determination from a Pacific perspective. Soc Work 40(2):168–175

Fabricius KE. 2005. Effects of terrestrial runoff on the ecology of corals and coral reefs: review and synthesis. Mar Pollut Bull 50(2): 125-146

Falkland T. 1999. Water Resources Issues of Small Island Developing States. Nat Resour Forum 23(3): 245–60

Feingold BJ, Vegosen L, Davis M, Leibler J, Peterson A, Silbergeld E. 2010. A niche for infectious disease in environmental health: rethinking the toxicological paradigm. Environ Health Persp 1165-1172

Fenton N, Neil M. 2013. Risk assessment and decision analysis with bayesian networks. CRC Press, Taylor & Francis Group, Boca Raton

Fewtrell L, Kaufmann RB, Kay D, Enanoria W, Haller L, Colford JM. 2005. Water, Sanitation, and Hygiene Interventions to Reduce Diarrhoea in Less Developed Countries: A Systematic Review and Meta-Analysis. Lancet Infect Dis 5 (1): 42-52

Fiji Bureau of Statistics. 2007. Census of Population and Housing. Fiji Bureau of Statistics. Online resource: http://www.statsfiji.gov.fj/statistics/2007-census-of-population-and-housing. Accessed 12 October 2016

Fiji Department of Information. 2014. Kalokalevu villagers welcome access to clean drinking water. http://www.fiji.gov.fj/Media-Center. Accessed 2 July 2015

Fiji Government. 2004. Preliminary Estimates of Flood Affected Areas. Press release 17 April, Suva

Finlayson CM, Horwitz P, Weinstein P (eds). 2015. Wetlands and Human Health, Wetlands: Ecology, Conservation and Management 5, Springer, New York. Pgs 169 -191

Forget G, Lebel J. 2001. An ecosystem approach to human health. Int J Occup Environ Health 7(Suppl. 2):S3–S38

Fox S, Shepherd W, Collins R, Boxall J. 2015. Experimental quantification of contaminant ingress into a buried leaking pipe during transient events. J Hydraul Eng 142(1):04015036.

Fujioka R, Sian-Denton C, Borja M, Castro J, Morphew K. 1999. Soil: the environmental source of *Escherichia coli* and enterococci in Guam's streams. J Appl Micro Symp Supp 85, 83S-89S

Fuller JA, Eisenberg JNS. 2016. Herd Protection from Drinking Water, Sanitation, and Hygiene Interventions. Amer J Trop Med Hyg 6:15-0677

Galea S, Nandi A, Vlahov D. 2005. The epidemiology of post- traumatic stress disorder after disasters. Epidemiol Rev 27(1): 78–91

Galea S. 2007. The long-term health consequences of disasters and mass traumas. Can Med Assoc J 176(9): 1293–1294

Gaffield SJ, Goo RL, Richards LA, Jackson RJ. 2003. Public health effects of inadequately managed stormwater runoff. Amer J Pub Health 93(9):1527-33

Gallo EL, Meixner T, Aoubid H, Lohse KA, Brooks P. 2015. Combined impact of catchment size, land cover, and precipitation on streamflow and total dissolved nitrogen: A global comparative analysis, Glob Bio Cycle 29: 1109–1121, doi: 10.1002/2015GB005154

Gasem MH, Dolmans WM, Keuter MM, Djokomoeljanto RR. 2001. Poor food hygiene and housing as risk factors for typhoid fever in Semarang, Indonesia. Trop Med Int Health 6:484–90

Gatto M, Mari L, Bertuzzo E, Casagrandi R, Righetto L, Rodriguez-Iturbe I, Rinaldo A. 2013. Spatially explicit conditions for waterborne pathogen invasion. Amer Natur 182(3):328-46

Garschagen M, Hagenlocher M, Kloos J, Pardoe J, Lanzendörfer M, Mucke P, Radtke K, Rhyner J, Walter B, Welle T, Birkmann J. 2015. *World Risk Report 2015*. Bündnis Entwicklung Hilft and UNU-EHS

Gaudet JJ. 1978. Effects of a tropical swamp on water quality. Verhan Internat Vereinigung Limnol 20:2202-2206

Gaynor K, Katz A, Park S, Nakata M, Clark T, Effler P. 2007. Leptospirosis on Oahu: an outbreak associated with flooding of a university campus. Am J Trop Med Hyg 76:882–885

Geist EL, Titov VV, Synolakis CE. 2006. Tsunami: Wave of change. Sci Am 294:56–63

Gillett R. 2009. The contribution of fisheries to the economies of Pacific island countries and territories. Asian Development Bank, Suva

Gerba CP, Wallis C, Melnick JL. 1975. Fate of wastewater bacteria and viruses in soil. J Irrig Drain Eng 3 (101): 157-174

Gibson CC, Ostrom E, Ahn TK. 2000. The concept of scale and the human dimensions of global change: a survey. Eco Econ 32(2):217-39

Gill SR, Pop M, Deboy RT, Eckburg PB, Turnbaugh PJ. 2006. Metagenomic analysis of the human distal gut microbiome. Science 312: 1355–1359. doi: 10.1126/science.1124234

Golterman HL. 2007. The chemistry of phosphate and nitrogen compounds in sediments. Springer Science & Business Media, New York

González-Guzmán J. 1989. An epidemiological model for direct and indirect transmission of typhoid fever. Math Bio 96:33–46

Government of Fiji. 2006. Fiji National Liquid Waste Management Strategy and Action Plan. International Waters of the Pacific Islands. Suva, Fiji. 72 pgs

Government of Fiji. 2010. Guidelines for the diagnosis, management, and prevention of typhoid fever. Ministry of Health, Fiji Islands. 10 pgs

Grancher J, Deschamps E. 1889. Archives de medecine experimentale et d'anatomie pathologique (Paris) 1:33

Griffiths GA, McKerchar AI. 2008. Dependence of flood peak magnitude on catchment area. J Hydro (New Zealand) 47(2):123

Greenwell J, McCool J, Kool J, Salusalu M. 2013. Typhoid fever: hurdles to adequate hand washing for disease prevention among the population of a peri-urban informal settlement in Fiji. Western Pacific Surveillance and Response Journal : WPSAR, 4(1), 41–45

Gu M, Weedbrook C, Perales A, Nielsen MA. 2009. More really is different. Physica D: Nonlin Phenom 238: 835–9

Gubler DJ, Reiter P, Ebi KL, Yap W, Nasci R and Patz JA. 2001. Climate variability and change in the United States: potential impacts on vector- and rodent-borne diseases. Environ Health Persp 109(2): 223–233

Gunderson LH, Holling CS. 2002. Panarchy: understanding transformations in systems of humans and nature. Island, Washington

Gupta A. 1988. Large floods as geomorphic events in the humid tropics. In: Baker VR, Kochel RC, Patton PC (eds) Flood Geomorphology, John Wiley & Sons, New York, p 301–315

Hamiton R, Ramohia P, Hughes A, Siota C, Kere, N, Giningele M, Kereseka J, Taniveke F, Tanito N, Atu W, Tanavalu L. 2007. Post-Tsunami Assessment of Zinoa Marine Conservation Area, South Choiseul, Solomon Islands. The Nature Conservancy Pacific Island Countries Report No. 4/07

Hansen MC, Stehman SV Potapov PV. 2010. Quantification of global gross forest cover loss. Proc Natl Acad Sci USA 107 (19) 8650-8655

Harbin M, Faris R, Gad AM, Hafez ON, Ramzy R, Buck AA. 1993. The resurgence of lymphatic filariasis in the Nile delta. Bull WHO 71(1):49-54

Harper SL, Friedrich B, Hacker J, Hasnain SE, Mettenleiter TC, Schell B. 2012. Climate change and infectious diseases. Epidemiol Infect 140(4): 765

Harvell CD, Mitchell CE, Ward JR, Altizer S, Dobson A, Ostfeld RS, Samuel MD. 2002. Climate warming and disease risks for terrestrial and marine biota. Science 296 (5576):2158–2162

Haydon DT, Cleaveland S, Taylor LH, Laurenson MK. 2002. Identifying reservoirs of infection: a conceptual and practical challenge. Emerg Infect Dis 8(12):1468-73

Hendrickson LA, Vogt RL, Goebert D, Pon E. 1997. Morbidity on Kauai before and after Hurricane Iniki. Prev Med 26(5): 711–716

Hennekens CH, Buring JE. 1987. Case-control Studies. In: Mayrent SL, editor. Epidemiology in Medicine. Lippincott Williams & Wilkins, Philadelphia, pp. 132–152

Hirshman JH. 1976. Communicable disease in the South Pacific islands. Med J Aust. 2: 794–8.

Hoque BA, Chakraborty J, Chowdhury JT, Chowdhury UK, Ali M, El Arifeen S, Sack RB. 1999. Effects of environmental factors on child survival in Bangladesh: a case control study. Pub Health 113(2):57-64

Horwitz P, Finlayson M. 2011. Wetlands as Settings for Human Health: Incorporating Ecosystem Services and Health Impact Assessment into Water Resource Management. BioScience 61: 678–

688

Horwitz P, Finlayson M, Weinstein P. 2012. Healthy Wetlands, healthy people: a review of wetlands and human health interactions. Ramsar Technical Report No 6. Secretariat of the Ramsar Convention on Wetlands, Gland & World Health Organization, Geneva

Hosoglu S, Celen MK, Geyik MF, Akalin S, Ayaz C, Acemoglu H, Loeb M. 2006. Risk factors for typhoid fever among adult patients in Diyarbakir, Turkey. Epid Infect 134(03):612-6

Hunter PR. 2003. Climate change and waterborne and vector-borne disease. J Appl Microbiol.94 Suppl: 37S–46S (http://www.ncbi.nlm.nih.gov/pubmed/12675935, accessed 13 August 2014)

IFRC. 2013. Emergency appeal: Republic of the Marshall Islands/Pacific drought. Emergency appeal n° MDRMH001, GLIDE n° DR-2013-000053-MHL 20 December 2013

IPCC. 2007. Climate change 2007: the physical science basis. Interngovernmental Panel on Climate Change, Geneva, Switzerland

IPCC. 2014. Climate Change 2014: Synthesis Report. Contribution of Working Groups I. II and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Geneva, Switzerland

Isaacson M. 1998. Aspects of Typhoid Fever. J Trav Med 5(4):230

Iverson LR, Prasad AM. 2007. Modeling tsunami damage in Aceh: A reply. Landscape Ecol 23:7–10

Jenkins K. 2010. Post Cyclone Tomas Support to Typhoid fever control in Fiji March 2010. Fiji Health Sector Improvement Program, Suva, Fiji

Jenkins MW, Cairncross S. 2010. Modelling latrine diffusion in Benin: towards a community typology of demand for improved sanitation in developing countries. J Wat Health 8(1):166-83

Jenkins AP, Mailautoka, K. 2011. Fishes of Nadi basin and bay: conservation ecology and habitat mobility. In: Askew N, Prasad, SR (eds) Proceedings of the Second Fiji Conservation Science Forum 2011. Wildlife Conservation Society Fiji Program, Suva

Jenkins AP, Jupiter SD. 2011. Spatial and seasonal patterns in freshwater ichthyofaunal communities of a tropical high island in Fiji. Environ Biol Fish 91(3):261-274

Jenkins AP, Jupiter SD, Qauqau I, Atherton J. 2010. The importance of ecosystem-based management for conserving migratory pathways on tropical high islands: A case study from Fiji. Aquat Conserv 20(2):224-238

Jenkins AP, Jupiter SD. 2015. Natural disasters, health and wetlands: A Pacific small island developing state perspective. In: *Wetlands and Human Health*, Wetlands: Ecology, Conservation and Management 5, Finlayson CM, Horwitz P, Weinstein P (eds). Springer, New York. Pgs. 169 -191

Jenkins AP, Jupiter SD, Mueller U, Jenney A, Vosaki G, Rosa V, Naucukidi A, Mulholland K, Strugnell R, Kama M and Horwitz, P. 2016. Health at the sub-catchment scale: typhoid & its environmental determinants in Central Division, Fiji. Ecohealth DOI 10.1007/s10393-016-1152-6

Jenkins C, Dimitrakalds M, Cook I, Sanders R, Stallman N. 1989. Culture change and epidemiological patterns among the Hagahai, Papua New Guinea. Human Ecol 17:27–57

Jha AK, Stanton-Geddes Z. 2013. Strong, Safe, and Resilient: A Strategic Policy Guide for Disaster Risk Management in East Asia and the Pacific. Directions in Development. World Bank, Washington, DC doi:10.1596/978-0-8213-9805-0

Jobin W. 1999. Dams and Disease: Ecological Design and Health Impacts of Large Dams, Canals, and Irrigation Systems. E&FN Spon, London

Joffe M, Gambhir M, Chadeau-Hyam M, Vineis P. 2012. Causal diagrams in systems epidemiology. Emerg Themes Epidemiol 2012; 9:1

Johnson PT, De Roode JC, Fenton A. 2015. Why infectious disease research needs community ecology. Science. 349(6252):1259504

Jones, P. 2012. Managing Urbanisation in Papua New Guinea: Planning for Planning's Sake? Working Papers Series Two, No. 33. Alfred Deakin Research Institute, Geelong

Jupiter SD, Jenkins AP, Long WJ, Maxwell SL, Carruthers TJ, Hodge KB, Govan H, Tamelander J, Watson JE. 2014. Principles for integrated island management in the tropical Pacific. Pacific Conserv Biol 20(2):193-205

Jupiter SD, Jenkins AP, Lee Long WJ, Maxwell SL, Watson JEM, Hodge KB, Govan H, Carruthers TJB. 2013. Pacific Integrated Island Management - Principles, Case Studies and Lessons Learned. Secretariat of the Pacific Regional Environment Programme (SPREP), Apia

Jupiter SD, Marion GS, McCulloch MT, Hoegh-Guldberg O. 2007. Long-term changes to Mackay Whitsunday water quality and connectivity between terrestrial, mangrove, and coral reef ecosystems: Clues from coral proxies and remote sensing records. ARC Centre of Excellence for Coral Reef Studies, Brisbane, Australia

Kaplan M, Renaud FG, Lüchters G. 2009. Vulnerability assessment and protective effects of coastal vegetation during the 2004 tsunami in Sri Lanka. Nat Hazard Earth Syst 9:1479–1494

Kathiresan K, Rajendran N. 2005. Coastal mangrove forests mitigated tsunami. Estuar Coast Shelf Sci 65(3):601–606

Karkey A, Arjyal A, Anders KL, Boni MF, Dongol S, Koirala S, Baker, S. 2010. The burden and characteristics of enteric fever at a healthcare facility in a densely populated area of Kathmandu. PloS one 5(11) e13988

Karkey A, Thompson CN, Tran Vu Thieu N, Dongol S, Le Thi Phuong T. 2013. Differential Epidemiology of Salmonella Typhi and Paratyphi A in Kathmandu, Nepal: A Matched Case Control Investigation in a Highly Endemic Enteric Fever Setting. PLoS Negl Trop Dis 7(8): e2391

Karkey A, Jombart T, Walker AW, Thompson CN, Torres A, Dongol S, Thieu NT, Thanh DP, Ngoc DT, Vinh PV, Singer AC. 2016. The ecological dynamics of fecal contamination and Salmonella

Typhi and Salmonella Paratyphi A in municipal Kathmandu drinking water. PLoS Negl Trop Dis 6; 10(1):e0004346

Kawata K. 1978. Water and other environmental interventions—the minimum investment concept. Amer J Clinical Nutr 31:2114–2123

Kelly-Hope, LA, Alonso WJ, Thiem VD, Anh DD, DO GIA, CANH, Lee H, Smith DL, Miller MA (2007) Geographical distribution and risk factors associated with enteric diseases in Vietnam. Amer J Trop Med Hyg 76(4): 706-712

Kerr AM, Baird AH. 2007. Natural barriers to natural disasters. Bioscience 57(2):102–103

Kibret S, Wilson GG, Ryder D, Tekie H, Petros B. 2015. The influence of dams on malaria transmission in sub-Saharan Africa. EcoHealth 18:1-2

Khan MI, Ochiai RL, Soofi SB, Von-Seidlein L, Khan MJ, Sahito SM, Habib MA, Puri MK, Park JK, You YA, Ali M. 2012. Risk factors associated with typhoid fever in children aged 2–16 years in Karachi, Pakistan. Epidem Infection 140(04):665-72

Khurmi HM, Kumar L. 2011. Modeling dengue fever risk based on socioeconomic parameters, nationality and age groups: GIS and remote sensing based case study. Sci Tot Environ 409(22):4713-9

Kingsley J, Patrick R, Horwitz P, Parkes M, Jenkins A, Massy C, Henderson-Wilson C, Arabena K. 2015. Exploring ecosystems and health by shifting to a regional focus: perspectives from the oceania ecoHealth chapter. Int J Env Res Pub Health. 12(10):12706-22.

Kinuthia GK, Gicheru MM, Ngure PK, Kabiru EW. 2012. Lifestyles and practices that enhance malaria and typhoid fever in Njoro District, Kenya. J Comm Health 37(1):224-33.

Knutson TR, McBride JL, Chan J, Emanuel K, Holland G, Landsea C, Held I, Kossin JP, Srivastava AK, Sugi M. 2010. Tropical cyclones and climate change. Nat Geosci 3(779):157–163

Koestler A. 1967. The ghost in the machine. Hutchinson, London

Komarulzaman A, Smits A, de Jong E. 2016. Clean water, sanitation and diarrhoea in Indonesia: Effects of household and community factors. Glob Pub Health 1-15

Kool J, Whippy D. 2011. Typhoid vaccination for outbreak control in Fiji. World Health Organization, Fijian Ministry of Health, Suva, Fiji

Kouadio IK, Aljunid MS, Kamigaki T, Hammad K, Oshitani H. 2012. Infectious diseases following natural disasters: prevention and control measures. Expert Rev Anti-infect Therap 10 (1) 95-104

Kovacs SD, Mullholland K, Bosch J, Campbell H, Forouzanfar MH, Khalil I, Lim S, Liu L, Maley SN, Mathers CD, Matheson A. 2015. Deconstructing the differences: a comparison of GBD 2010 and CHERG’s approach to estimating the mortality burden of diarrhea, pneumonia, and their etiologies. BMC Infect Dis 15(1):1

Krishnamoorthy K, Jambulingam P, Natarajan R, Shriram AN, Das PK, Sehgal SC. 2005. Altered environment and risk of malaria outbreak in South Andaman, Andaman & Nicobar Islands, India affected by tsunami disaster. Malaria J 4:32

Kuylenstierna JL, Bjorklund G, Najlis P. 1997. Future sustainable water use: challenges and constraints. J Soil Wat Conserv 52(3): 151

Lal PN, Singh R, Holland P. 2009. Relationship between natural disasters and poverty: a Fiji case study. SOPAC miscellaneous report No. 678. International Strategy for Disaster Reduction, Suva

Lall C, Kumar KV, Raj RV, Vedhagiri K, Vijayachari P. 2016. Prevalence and Diversity of Leptospires in Different Ecological Niches of Urban and Rural Areas of South Andaman Island. Microbe Environ 31(1):79

Landis, JR, Koch, GG. 1977. The measurement of observer agreement for categorical data. Biometrics 33:159-174.

Lata S, Nunn P. 2012. Misperceptions of climate-change risk as barriers to climate-change adaptation: a case study from the Rewa Delta, Fiji. Climatic Change 110:169–186

Lau CL, Clements ACA, Skelly C, Dobson AJ, Smythe LD. 2012. Leptospirosis in American Samoa – Estimating and Mapping Risk Using Environmental Data. PLoS Negl Trop Dis 6(5): e1669. doi:10.1371/journal.pntd.0001669

Lau CL, Smith CS. 2016. Bayesian networks in infectious disease eco-epidemiology. Rev Environ Health 31(1):173-7

Lau CL, Smythe LD, Craig SB, Weinstein P. 2010. Climate change, flooding, urbanisation and leptospirosis: fuelling the fire? Trans Roy Soc Trop Med Hyg 104:631-638

Lau CL, Watson CH, Lowry JH, David MC, Craig SB, Wynwood SJ, Kama M, Nilles EJ. 2016. Human Leptospirosis Infection in Fiji: An Eco-epidemiological Approach to Identifying Risk Factors and Environmental Drivers for Transmission. PLoS Negl Trop Dis 10(1):e0004405

Lechat MF. 1976. Disaster epidemiology. Ann Soc Belge Med Trop 56(4-5):193-197

Leslie D. 2012. A reference manual for utilizing and managing the soil resources of Fiji. Secretariat of the Pacific Community. Land Resources Publication Unit, Nabua, Fiji

Leslie DM, Seru VG. 1998. Fiji Soil Taxonomic Unit Description Handbook (supplement to the national soil map). Manaaki Whenua Press, Landcare Research NZ Limited. 2 volumes, 928 pp

Letourneur Y, Kulbicki, Labrosse P. 1998. Spatial structure of commercial reef fishes along a terrestrial runoff gradient in the northern lagoon of New Caledonia. Environ Biol Fish 51: 141-159

Levin SA. 1992. The problem of pattern and scale in ecology: the Robert H. MacArthur award lecture. Ecology 73(6):1943-67.

Levine MM, Black RE, Lanata C. 1982. Precise estimation of the numbers of chronic carriers of Salmonella typhi in Santiago, Chile, an endemic area. J Infect Dis 146:724–6

Levine MM, Tacket CO, Sztein MB. 2001. Host-Salmonella interaction: human trials. Microbes Infect 3(14-15):1271-9

Likens GE, Bormann FH, Johnson NM, Fisher DW, Pierce RS. 1970. Effects of forest cutting and herbicide treatment on nutrient budgets in the Hubbard Brook watershed-ecosystem. Ecol Monogr 40(1):23-47

Ling T, Achberger E, Drapcho C, Bengtson R. 2002. Quantifying adsorption of an indicator bacteria in a soil-water system. Trans Amer Soc Agric Eng 45: 669–674

Lipp EK, Huq A, Colwell RR. 2002. Effects of Global Climate on Infectious Disease: the Cholera Model. Clin Microbiol Rev 15 (4): 757-770

Lobitz B, Beck L, Huq A, Wood B, Fuchs G, Faruque ASG, Colwell RR .2000. Climate and infectious disease: use of remote sensing for detection of *Vibrio cholerae* by indirect measurement. Proc. Natl. Acad. Sci. USA 97:1438–1443

Locher CP, Burch MT, Mower HF. 1995. Anti-microbial activity and anti-complement activity of extracts obtained from selected Hawaiian medicinal plants. J Ethnopharmacol 49:23-32

Lowrance RR, Altier LS, Newbold JD, Schnabel RR, Groffman PM, Denver JM. 1997. Water quality functions of riparian forest buffer systems in the Chesapeake Bay Watershed. Environ Manage 21: 687-712

Luby S. Is targeting access to sanitation enough? 2014. Lancet Glob Health 2(11):e619-20

Luby SP, Agboatwalla M, Razza A & Sobel J. 2001. A low cost intervention for cleaner drinking water in Karachi, Pakistan. Int J Infect Dis 5: 144–150

Luby SP, Faizan MK, Fisher-Hoch SP, Syed A, Mintz ED, Bhutta ZA, McCormick JB. 1998. Risk factors for typhoid fever in an endemic setting, Karachi, Pakistan. Epid Infect 120(02):129-38

Luhmann N. 1995. Social systems. Stanford University Press, Stanford, CA

Luxemburger C, Duc CM, Lanh MN, Wain J, Hien TT, Simpson JA, Thuy NT, White NJ, Farrar JJ. 2001. Risk factors for typhoid fever in the Mekong delta, southern Viet Nam: a case-control study. Trans Roy Soc Trop Med Hyg 95(1):19-23

Mackenzie E, Prasad B, Kaloumaira A. 2005. Economic impact of natural disasters on development in the Pacific. University of the South Pacific, Suva

Mackenzie JS, Gubler DJ, Petersen LR. 2004. Emerging flaviviruses: the spread and resurgence of Japanese encephalitis, West Nile and dengue viruses. Nat Med 10(12):98-109

Maclellan N. 2015. Transforming the regional architecture: New players and challenges for the Pacific Islands. Asia Pac 118:1–8

Magner, JA, Vondracek B, Brooks KN. 2008. Grazed riparian management and stream channel response in southeastern Minnesota (USA) streams. Environ Manage 42, 377-390

Malek EA. 1975. Effect of Aswan High Dam on prevalence of schistosomiasis in Egypt. Trop Geogr Med 27(4): 359-364

Malisa A, Nyaki H. 2010. Prevalence and constraints of typhoid fever and its control in an endemic area of Singida region in Tanzania: Lessons for effective control of the disease. J Pub Health Epid 2(5):93-9

Maltby E, Acreman MC. 2011. Ecosystem Services of Wetlands: pathfinder for a new paradigm. Hydrolog Sci J 56(8):1– 19

Max-Neef MA. 2005. Foundations of transdisciplinarity. Ecol Econ 53(1):5-16

Mbakaya BC, Mukora-Mutseyekwa F, Chideme-Munodawafa A, Mwale CM, Letcher MM. 2015. Factors associated with development of typhoid fever at Kaziwiziwi Coal Mining Area in Rumphi District, Malawi: A Retrospective Case Control Study. Euro Scien J 1; 11(33)

McBride AJ, Athanazio DA, Reis MG, Ko AI. 2005. "Leptospirosis". *Curr Opin Infect Dis* **18** (5): 376–86.

McCarthy DT, Hathaway JM, Hunt WF, Deletic A. 2012. Intra-event variability of Escherichia coli and total suspended solids in urban stormwater runoff. Water Res 46(20):6661-70

McGinnis JA, DeWalle F. 1983. The movement of typhoid organisms in saturated, permeable soil. J (Amer Wat Works Assoc) 1:266-71

McGregor DP, Morelli PT, Matsuoka JK, Rodenhurst R, Kong N, Spencer MS. 2003. An ecological model of native Hawaiian well-being. Pac Health Dialog 10(2)106-128

McIver L, Kim R, Woodward A, Hales S, Spickett J, Katscherian D, Hashizume M, Honda Y, Kim H, Iddings S, Naicker J. 2015. Health impacts of climate change in Pacific island countries: a regional assessment of vulnerabilities and adaptation priorities. Environ Health Perspect. 2015 Dec 8

McIvor AL, Möller I, Spencer T, Spalding M. 2012. Reduction of wind and swell waves by mangroves. Natural Coastal Protection Series: Report 1. Cambridge Coastal Research Unit Working Paper 40. The Nature Conservancy and Wetlands International

McIvor AL, Spencer T, Möller I, Spalding M. 2013. The response of mangrove soil surface elevation to sea level rise. Natural Coastal Protection Series: Report 3. Cambridge Coastal Research Unit Working Paper 42.The Nature Conservancy and Wetlands International

McKergow LA, Weaver DM, Prosser IP, Grayson RB, Reed AEG. 2003. Before and after riparian management: sediment and nutrient exports from a small agricultural catchment, Western Australia. J Hydrol 270 (1):253-272

McCrady MH. 1918. Tables for rapid interpretation of fermentation-tube results. Pub Health J 9(5):201-20

McMichael AJ. 1997. Integrated assessment of potential health impact of global environmental change: prospects and limitations. Environ Model Assess 2:129–137

McMullin J. 2005. The call to life: revitalizing a healthy Hawaiian identity. Soc Sci Med 61(4), 809–820

Medina E. 1991. Epidemic of cholera in Chile. 1991. Rev Med Chile 119, 943–956

Meentemeyer RK, Haas SE, Václavík T. 2012. Landscape epidemiology of emerging infectious diseases in natural and human-altered ecosystems. Annu Rev Phytopathol 50:379-402

Mehta L. 2016. Community-Led Total Sanitation and the Politics of Scaling Up. Negotiating Water Governance: Why the Politics of Scale Matter 9:231

Melick CO. 1917. The possibility of typhoid infection through vegetables. J Infect Dis 21(1):28-38

Mermin JH, Villar R, Carpenter J, Roberts L, Gasanova L, Lomakina S., Bopp C, Hutwagner L, Mead P, Ross B, Mintz, ED. 1999. A massive epidemic of multidrug-resistant typhoid fever in Tajikistan associated with consumption of municipal water. J Infect Dis *179*(6): 1416-1422

Millenium Ecosystem Assessment. 2005. Ecosystems and Human Well-being: Synthesis. Island Press, Washington, DC

Mills P. 2000. Strategic Plan for Far North Queensland Peninsula and Torres Strait Island Community Health Services. FNQPTSI Community Health Services, Thursday Island

Mintz E, Bartram J, Lochery P & Wegelin M. 2001. Not just a drop in the bucket: Expanding access to point-of-use water treatment systems. Amer J Pub Health 91:1565–1570

Mitscherlich E, Marth EH. 2012. Microbial survival in the environment: bacteria and rickettsiae important in human and animal health. Springer Science & Business Media, London

Mogasale V, Maskery B, Ochiai RL, Lee JS, Mogasale VV, Ramani E, Kim YE, Park JK, Wierzba TF .2014. Burden of typhoid fever in low-income and middle-income countries: a systematic, literature-based update with risk-factor adjustment. Lancet Glob Health 31;2 (10):e570-80

Mohanty M. 2006. Urban squatters, the informal sector and livelihood strategies of the poor in the Fiji Islands. Develop Bull *70*:65-68

Monack DM. 2012. Salmonella persistence and transmission strategies. Curr Opin Microbio 15(1):

p. 100–7

Moore M, Townsend M, Oldroyd J. 2006. Linking human and ecosystem health: The benefits of community involvement in conservation groups. Ecohealth 3(4) 255-261

Moraes LR, Cancio JA, Cairncross S, Huttly S. 2003. Impact of drainage and sewerage on diarrhoea in poor urban areas in Salvador, Brazil. Trans Roy Soc Trop Med Hyg 97(2):153-8

Mosley LM, Sharp DS, Singh S. 2004. Effects of a tropical cyclone on the water quality of a remote Pacific island. Disasters 28(4): 393-405

Muti M, Gombe N, Tshimanga M, Takundwa L, Bangure D, Mungofa S, Chonzi P. Typhoid outbreak investigation in Dzivaresekwa, suburb of Harare City, Zimbabwe, 2011. 2014. Pan Afr Med J 18; 18(1)

Mujica OJ, Quick RE, Palacios AM. 1994. Epidemic cholera in the Amazon: the role of produce in disease risk and prevention. J Infect Dis 169, 1381–1384

Myers SS, Patz J. 2009. Emerging threats to human health from global environmental change. Annu Rev Env Res 34:223-252

Myers SS, Gaffikin L, Golden CD, Ostfeld RS, Redford KH, Ricketts TH, Turner WR, Osofsky SA. 2013. Human health impacts of ecosystem alteration. P Natl Acad Sci www.pnas.org/cgi/doi/10.1073/pnas.1218656110

Naiman RJ, Decamps H. 1997. The ecology of interfaces: riparian zones. Annu Rev Ecol System 28:621-658

Neall VE, Trewick SA. 2008. The age and origin of the Pacific islands: a geological overview. Philos Trans Roy Soc B 363: 3293–3308

Nelson D. 1987. Watershed Management Study: Land conservation in the Rewa and Ba watersheds. FIJ/86/001. Field Document 1. United Nations Environment Program and Food and Agriculture Organisation

Neudoerffer RC, Waltner-Toews D, Kay JJ, Joshi DD, Tamang MS. 2005. A Diagrammatic approach to understanding complex eco-social interactions in Kathmandu, Nepal. Ecol Soc 10(2): Article 12. http://www.ecologyandsociety.org/vol10/iss2/ art12/. Accessed Jun 2015

Ngugi HN, Home PG, Mutwiwa UN. 2014. Impacts of Water and Sanitation Activities on the Environment in the Upper Mara Basin. Civil Environ Res 6.1: 9-16

Nicholls RJ, Hoozemans MJF, Marchand M. 1999. Increasing flood risk and wetland losses due to global sea-level rise: regional and global analyses. Glob Env Chang 9(1): 69-87

Nicholls RJ, Wong PP, Burkett VR, Codignotto J, Hay JE, McLean RF, Ragoonaden S, Woodroffe CD. 2007. Coastal Systems and Low-lying Areas In: Parry ML, Canziani OF,Palutikof JP, van der Linden PJ, Hanson CE (eds) Climate Change 2007: Impacts, Adaptation and Vulnerability. Cambridge University Press, Cambridge

Nicholson A, Woodberry O, Twardy C. The "Native Fish" Bayesian networks. Technical Report. 2010/3, Bayesian Intelligence. http://www. bayesian-intelligence. com/publications. php; 2010 Nov 18

Nishio T, Nakamori J, Miyazaki K. 1981. Survival of Salmonella typhi in oysters. Zentralbl Bakteriol Mikrobiol Hyg 172: 415-426

NIWA. 2012. Island Climate Update 140. http://www.niwa.co.nz/climate/icu/island-climate-update-140-may-2012. Accessed 12 Jan 2014

Norris V. 1993. The use of buffer zones to protect water quality: a review. Water Resour Manag 7: 257-272

Norsys Software Corp, 2006. Sensitivity to Findings. Netica Software Documentation. www.norsys.com

OED online. Oxford: Oxford University Press 2016. Available from: URL: http://dictionary.oed.com

Olsen SJ. 2001. Restaurant-associated outbreak of Salmonella Typhi in Nauru: an epidemiological and cost analysis. Epidemiol Infect 127(3): 405-412

Ostfeld RS. 2009. Climate change and the distribution and intensity of infectious diseases. Ecology 90(4): 903–905

Padalon-Brauch G, Hershberg R, Elgrably-Weiss M, Baruch K, Rosenshine I, Margalit H, Altuvia S . 2008. Small RNAs encoded within genetic islands of Salmonella typhimurium show host-induced expression and role in virulence. Nucl Acid Res 36 (6):1913-27

Parkes MW, Horwitz P. 2009. Water, ecology and health: eco- systems as settings for promoting health and sustainability. Health Promo Inter 24(1): 94–102

Parkes M, Panelli R, Weinstein P. 2003. Converging paradigms for environmental health theory and practice. Environ Health Persp 111:669–675

Parkes MW, Bienen L, Breilh J, Hsu L-N, McDonald M, Patz JA. 2005. All hands on deck: transdisciplinary approaches to emerging infectious disease. EcoHealth 2(4):258–272

Parkes MW, Morrison KE, Bunch MJ, Venema HD. 2008. Ecohealth and Watersheds: Ecosystem Approaches to Re-integrate Water Resources Management with Health and Well-being. Network for Ecosystem Sustainability and Health (Publication Series No. 2) and the International Institute for Sustainable Development, Winnipeg, MB

Parkes MW, Morrison KE, Bunch MJ, Hallströ̈m LK, Neudoerffer RC, Venema HD, Waltner-Toews D. 2010. Towards integrated governance for water, health and social-ecological systems: the watershed governance prism. Glob Environ Change 20(4): 693–704

Parry C. 2005. Typhoid fever and cholera. Medicine 33(7):34–36

Passey M. 1995. The new problem of typhoid fever in Papua New Guinea: how do we deal with it? PNG Med J. 38: 300–4

Pattanayak SK, Wendland KJ. 2007. Nature's care: Diarrhea, watershed protection, and biodiversity conservation in Flores, Indonesia. Biodivers Conserv 16(10):2801–2819

Patz JA. 2000. Climate change and health: new research challenges. Ecosyst Health 6(1): 52-58

Patz JA, Epstein PR, Burke TA, Balbus JM. 1996. Global climate change and emerging infectious diseases. J Am Med Ass 275(3):217-23

Patz JA, Daszak P, Tabor GM, Aguirre AA, Pearl M, Epstein J. 2004. Unhealthy landscapes: Policy recommendations on land use change and infectious disease emergence. Environ Health Perspect 112(10):1092-1098

Paul S, Singh HB, Hazarika R. 2013. Environmental Impacts In: The Construction of Dams. Int J Innovat Res Develop 30; 2(11)

Prüss-Üstün A, Bos R, Gore F, Bartram J. 2008. Safer water, better health: costs, benefits and sustainability of interventions to protect and promote health. World Health Organization, Geneva

Pitzer VE, Bowles CC, Baker S, Kang G, Balaji V, Farrar JJ. 2014. Predicting the impact of vaccination on the transmission dynamics of typhoid in South Asia: a mathematical modeling study. PLoS Neglect Trop Dis 8:e2642

Pimentel D, Allen J, Beers A, Guinand L, Hawkins A, Linder R, McLaughlin P, Meer B, Musonda D, Perdue D, Poisson S, Salazar R, Siebert S, Stoner K. 1993. Soil erosion and agricultural productivity. In: Pimentel D (ed) World Soil Erosion and Conservation. Cambridge University Press, Cambridge

Pollino CA, Henderson C. 2010. Bayesian networks: A guide for their application in natural resource management and policy. Landscape Logic, Technical Report 14

Qing DQ. 1998. **The World's Most Catastrophic Dam Failures: The August 1975 Collapse of the Banqiao and Shimantan Dams. ME Sharpe, New York**

Ragosta G, Evensen C, Atwill ER, Walker M, Ticktin T, Asquith A, Tate KW. 2010. Causal connections between water quality and land use in a rural tropical island watershed. Ecohealth 7(1):105-113

Ram PK, Naheed A, Brooks WA, Hossain MA, Mintz ED, Breiman RF, Luby SP. 2007. Risk factors for typhoid fever in a slum in Dhaka, Bangladesh. Epidemiol Infect 135(03):458-65

Rao G, Eisenberg JNS, Kleinbaum DG, Cevallos W, Trueba G, Levy K. 2015. Spatial Variability of *Escherichia coli* in Rivers of Northern Coastal Ecuador. Water 7(2), pp.818-832

Reller ME, Olsen SJ, Kressel AB, Moon TD, Kubota KA, Adcock MP, Nowicki SF, Mintz ED. 2003. Sexual transmission of typhoid fever: a multistate outbreak among men who have sex with men. Clinical Infect Dis 37(1)141-144

Remais JV, Eisenberg JNS. 2012. Balancing Clinical and Environmental Responses to Infectious Diseases. Lancet 379(9824): 1457–1459

Rich, ED. 1923. A typhoid fever epidemic traced to cheese. Amer J Pub Health 13(3) 210-215

Rosgen DL. 1994. A classification of natural rivers. Catena 30; 22(3):169-99

Roth CH. 2004. A framework relating soil surface condition to infiltration and sediment and nutrient mobilization in grazed rangelands of northeastern Queensland, Australia. Earth Surf Proc Land 29:1093-1104

Salinger MJ, Lefale P. 2005. The Occurrence and Predictability of Extreme Events over the Southwest Pacific with Particular Reference to ENSO. In: Natural Disasters and Extreme Events in Agriculture. Sivakumar MVK, Motha RP, Das HP (eds). Springer, Berlin p 39-49

Saul A, Smith T, Maire N. 2013. Stochastic simulation of endemic Salmonella enterica serovar Typhi: the importance of long lasting immunity and the carrier state. PLOS ONE 8:e74097

Schulz KF, Grimes DA. 2002. Case-control studies: research in reverse. Lancet. 359(9304):431-4

Scobie H. 2011. Preliminary Report: Impact Assessment of the 2010 Mass Typhoid Vaccination Campaign, Republic of Fiji. Centers for Disease Control and Prevention, World Health

Organization, Fiji Ministry of Health, Australian Agency for International Development, Suva, Fiji

Scobie HM, Nilles E, Kama M, Kool JL, Mintz E, Wannemuehler I, Date K. 2014. Impact of a targeted typhoid vaccination campaign following cyclone Tomas, republic of Fiji, 2010. Amer J Trop Med Hyg 90(6), 1031-1038

SDOH. 1993. Reported Cases of Typhoid Fever Data in Western Samoa 1989–1993. Samoa Department of Health, Samoa.

Sears SD, Ferreccio C, Levine MM, Cordano AM, Monreal J, Black RE, D'Ottone K, Rowe B. 1984. The use of Moore swabs for isolation of Salmonella typhi from irrigation water in Santiago, Chile. J Infect Dis 149(4): 640-642

Seru VB, Leslie DM. 1986. Soil Map of Fiji. Scale 1:50,000. Land Use Section, Land Resource Planning and Development Division, Ministry of Primary Industries, Fiji

Sharma PK, Ramakrishnan R, Hutin Y, Manickam P, Gupte MD. 2009. Risk factors for typhoid in Darjeeling, West Bengal, India: evidence for practical action. Trop Med Int Health 14:696–702

Sherif MM, Singh VP. 1996. Saltwater intrusion. In: Singh VP Hydrology of Disasters, vol 18, Klewer Academic Publishers, Dordrecht p 269-319

Shi ZH, Ai L, Li X, Huang XD, Wu GL, Liao W. 2013. Partial least-squares regression for linking land-cover patterns to soil erosion and sediment yield in watersheds. J Hydrology 19(498):165-76

Shultz JM, Russell J, Espinel Z. 2005. Epidemiology of tropical cyclones: the dynamics of disaster, disease, and development. Epidemiol Rev 27(1) 21–35

Singh RBK, Hales S, de Wet N, Raj R, Hearnden M, Weinstein P.2001. The influence of climate variation and change on diarrheal disease in the Pacific Islands. Environ Health Persp 109:155-159

Siwatibau S. 1984. Traditional Environmental Practices in the South Pacific: a case study of Fiji. Ambio. 1:365-8

Singh S. 2010. Epidemiology of Laboratory Confirmed Typhoid Fever Cases from Year 2000 to July 2010 in the Central Eastern Division in Fiji, in Department of Microbiology. College of Medicine, Nursing and Health Sciences, Fiji National University: Suva, Fiji

Smith SJ. 1990. Health status and the housing system. Soc Sci Med. 31(7):753-62

SOPAC. 2013. Regional progress report on the implementation of the Hyogo Framework for Action (2011-2013). Secretariat of the Pacific Community, Suva

Spiegelhalter DJ, Dawid AP, Lauritzen SL, Cowell RG. 1993. Bayesian analysis in expert systems. Stat Sci 1:219-47

Srikantiah P, Vafokulov S, Luby SP, Ishmail T, Earhart K, Khodjaev NM, Jennings G, Crump JA, Mahoney FJ. 2007. Epidemiology and risk factors for endemic typhoid fever in Uzbekistan. Trop Med Int Health 12(7):838-47

Staab JP, Grieger TA, Fullerton CS. 1996. Acute stress disorder, subsequent posttraumatic stress disorder and depression after a series of typhoons. Anxiety 2(5):219–225

Stanton BF, Clemens J. 1987. Socioeconomic variables and rates of diarrhoeal disease in urban Bangladesh. Trans Roy Soc Trop Med Hyg 81:278–282

Steele, A. Duncan, Deborah C. Hay Burgess, Zoey Diaz, Megan E. Carey, and Anita K. M. Zaidi. 2016. "Challenges and Opportunities for Typhoid Fever Control: A Call for Coordinated Action." Clinical Infect Dis 62 (Suppl 1): S4-S8. doi:10.1093/cid/civ976

Strathern A, Stewart PJ, Carucci LM, Poyer L, Feinberg R,Macpherson, C. 2002. Oceania: An Introduction to the Cultures and Identities of Pacific Islanders. Carolina Academic Press, Durham, N.C

Stroffolini T, Manzillo G, De Sena R, Manzillo E, Pagliano P, Zaccarelli M, Russo M, Soscia M, Giusti G.1992. Typhoid fever in the Neapolitan area: a case-control study. Eur J Epidemiol 8(4):539-42

Sweeney BW, Bott TL, Jackson JK, Kaplan LA, Newbold JD, Standley LJ, Hession WC, Horwitz RJ . 2004. Riparian deforestation, stream narrowing and loss of stream ecosystem services. Proc Nat Acad Sci USA 101(39): pp.14132-14137

Szreter S. 1988. The importance of social intervention in Britain's mortality decline c.1885–1914: a reinterpretation of the role of public health. Social His Med 1:1–37

Tabachnick BG, Fidell LS. 2001. Principal components and factor analysis. In Using multivariate statistics (4th ed., pp. 582–633). Needham Heights, MA: Allyn & Bacon

Tahmiscioğlu MS, Anul N, Ekmekçi F, Durmuş N. 2007. Positive and negative impacts of dams on the environment. In: International Congress on River Basin Management 2007, 22-24 March, Antalya, pgs 305-309

Talme J, Passey M, Suve N.1994. Very high incidence of typhoid fever in the highlands. Thirtieth Annual Symposium of the Medical Society of Papua New Guinea, Mt Hagen

Tang F, Cheng Y, Bao C, Hu J, Liu W, Liang Q, Chen F .2014. Spatio-Temporal Trends and Risk Factors for *Shigella* from 2001 to 2011 in Jiangsu Province, People's Republic of China. PLoS ONE 9(1), e83487. http://doi.org/10.1371/journal.pone.0083487

Terry JA, Benskin CMH, Eastoe EF, Haygarth PM. 2014. Temporal dynamics between cattle in-stream presence and suspended solids in a headwater catchment. Environmental Science: Process Impact 16: 1570-1577

Terry JP, Falkland AC. 2009. Responses of atoll freshwater lenses to storm-surge overwash in the Northern Cook Islands. Hydrogeol J 18(3): 749–759

Terry JP, Garimella S, Kostachuck RA .2002. Rates of floodplain accretion in a tropical island river system impacted by cyclones and large floods. Geomorphology 42: 171–182

Thompson CN. 2012. Typhoid Fever in Fiji: a report prepared for an expert meeting on control of typhoid fever in Fiji, 28-30 August 2012 Suva. Fiji Ministry of Health, Australian Agency for International Development: Suva, Fiji.

Thompson CN, Kama M, Acharya S, Bera U, Clemens J, Crump JA, Mulholland K. 2014. Typhoid fever in Fiji: a reversible plague? Trop Med Int Health 19(10), 1284-1292

Tran HH, Bjune G, Nguyen BM, Rottingen JA, Grais RF, Guerin PJ. 2005. Risk factors associated with typhoid fever in Son La province, northern Vietnam. Trans Roy Soc Trop Med Hyg 99(11):819-26

Trimble SW, Mendel AC. 1995. The cow as a geomorphic agent - a critical review. Geomorphology 13 (1): 233-253

Trochim WM, Cabrera DA, Milstein B, Gallagher RS, Leischow SJ. 2006. Practical challenges of systems thinking and modelling in public health. Am J Public Health 96(3): 538- 546

Twyford IT, Wright ACS. 1965. The Soil Resources of the Fiji Islands, 2 volumes. Government Press, Suva. 570 pp

UNDP South Pacific Office. 2002. Natural disaster risk reduction in Pacific Island countries, final report for international decade for natural disaster reduction 1990–2000. United Nations Development Programme, Fiji

United Nations International Strategy for Disaster Reduction (UNISDR). 2005. Hyogo Framework for Action 2005-2015: Building the Resilience of Nations and Communities to Disasters. http://www.unisdr.org/wcdr. Accessed 10 Jan 2014

United Nations, World Health Organization. 2014. Drinking Water, Sanitation and Hygiene. Geneva

Usfar AA, Iswarawanti DN, Davelyna D, Dillon D. 2010. Food and personal hygiene perceptions and practices among caregivers whose children have diarrhea: a qualitative study of urban mothers in Tangerang, Indonesia. J Nut Educat Behav 42:33–40

Uusitalo L. 2007. Advantages and challenges of Bayesian networks in environmental modelling. Ecol Model 203(3):312-8

Uyanik MH, Yazgi H, Ayyildiz A. 2008. Survival of *Salmonella typhi* and *Shigella flexneri* in Different Water Samples and at Different Temperatures. Turkish J Med Sci 38 (4): 307-310

Varela FJ, Thompson E, Rosch E 1991. The embodied mind: Cognitive science and human experience. MIT Press, Cambridge, MA

Velema JP, Wijne G, Bult B, Naerssen T. 1997. Typhoid fever in Ujung Pandang, Indonesia – high-risk groups and high-risk behaviours. Trop Med Int Health 2(11): 1088–1094

Vener HI, Stevens, GM. 1940. Typhoid Fever Outbreak in the City of Los Angeles. Epidemiological Investigation and Report. Los Angeles City Board of Health Commissioners Bulletin (65) 1-28

Vittor AY, Gilman RH, Tielsch J, Glass G, Shields TIM, Lozano WS, Pinedo-Cancino V, Patz JA. 2006. The effect of deforestation on the human-biting rate of *Anopheles darlingi*, the primary vector of falciparum malaria in the Peruvian Amazon. Am J Trop Med Hyg 74(1):3-11

Vollaard AM, Ali S, van Asten HAGH, Widjaja S, Visser LG. 2004. Risk factors for typhoid and paratyphoid fever in Jakarta, Indonesia. J Amer Med Assoc 291: 2607–2615

Wain J, Hendriksen RS, Mikoleit ML, Keddy KH, Ochiai RL. 2015. Typhoid fever. Lancet 385: 1136–45

Waldor MK, Tyson G, Borenstein E, Ochman H, Moeller A, Finlay BB, Kong HH, Gordon JI, Nelson KE, Dabbagh K, Smith H. 2015. Where next for microbiome research? PLoS Biol 13(1):e1002050.

Waltner-Toews D, Neudoerffer C, Joshi DD, Tamang MS. 2005. Agro-urban ecosystem health assessment in Kathmandu, Nepal: epidemiology, systems, narratives. EcoHealth 2(2): 155–164

Walzer PD, Judson FN, Murphy KB, Healy GR, English DK, Schultz MG. 1973. Balantidiasis outbreak in Truk. Am J Trop Med Hyg 22(1), 33–41

Wang LX, Li XJ, Fang LQ, Wang DC, Cao WC, Kan B. 2012. Association between the incidence of typhoid and paratyphoid fever and meteorological variables in Guizhou, China. Chinese Med J

125(3):455–460

Wang JF, Wang Y, Zhang J, Christakos G, Sun JL. 2013. Spatiotemporal Transmission and Determinants of Typhoid and Paratyphoid Fever in Hongta District, Yunnan Province, China. PLoS Neglect Trop Dis 7(3): e2112

Watson CH, Edmunds WJ. 2015. A review of typhoid fever transmission dynamic models and economic evaluations of vaccination. Vaccine 33: C42–C54

Watson JT, Gayer M, Connolly MA. 2007. Epidemics after natural disasters. Emerg Infect Dis 13(1):1-5

Weiss RA, McMichael AJ. 2004. Social and environmental risk factors in the emergence of infectious diseases. Nature Med 10(12): S70–S76

Wemple BC, Jones JA. 2003. Runoff production on forest roads in a steep, mountain catchment. Water Resource Res 39: 1220

Westerhoff HV, Palsson BO. 2004. The evolution of molecular biology into systems biology. Nature Biotech 22: 1249–52

Wilcox B, Colwell R. 2005. Emerging and reemerging infectious diseases: biocomplexity as an interdisciplinary paradigm. EcoHealth 2(4): 244–257

Wilcox B, Kueffer C. 2008. Transdisciplinarity in EcoHealth: status and future prospects. EcoHealth 5:1–3

Wilson SK, Fisher R, Pratchett MS, Graham NAJ, Dulvey NK, Turner RA, Cakacaka A, Polunin NVC, Rushton SP. 2008. Exploitation and habitat degradation as agents of change within coral reef fish communities. Glob Chang Bio 14(12): 2796-2809

Winfield MD, Groisman EA. 2003. Role of nonhost environments in the lifestyles of Salmonella and Escherichia coli. Appl Environ Micro 69(7): 3687-3694

World Bank. 2016. Effects of Population Growth and Urbanization in the Pacific Islands. Accessed at http://siteresources. worldbank.org/INTPACIFICISLANDS/Resources/Chapter+1.pdf

World Health Organization. 2011. Guidelines for drinking-water quality. World Health Organization, Geneva 216:303-4

World Health Organization and UNICEF Joint Monitoring Programme (JMP). 2015. Progress on Drinking Water and Sanitation, 2015 Update and MDG Assessment, WHO, Geneva

World Health Organization. 2008. Typhoid vaccines: WHO position paper. Weekly Epidemiol Rec 83: 49–59

World Health Organization. 2010. Meeting Report: Expert Consultation on Typhoid Fever Vaccination in Fiji. Fiji Ministry of Health: Suva, Fiji

WHO/FMOH/UNDP. 2011. Protecting Human Health from Climate Change: Working Paper – Climate-Sensitive Infectious Diseases in Fiji. World Health Organization, Fiji Ministry of Health, United Nations Development Programme, Suva, Fiji

World Health Organization. 2012. Global report for research on infectious diseases of poverty 2012, Geneva, Switzerland: http://whqlibdoc.who.int/publications/2012/9789241564489_eng. pdf. Accessed June 12, 2015

World Health Organization. 2015. Human health and climate change in Pacific Island states. http://www.iris.wpro.who.int/bitstream/handle/10665.1/12399/ 9789290617303_eng.pdf. Accessed 15 Jan 2016

World Health Organization. 2013. Outbreak surveillance and response priorities for mitigating the health impact of disaster. Tenth Pacific health ministers meeting. Agenda Item 9. http://www.wpro.who.int/southpacific/pic_meeting/2013/documents/PHMM_PIC10_9_Outbreak. Accessed 10 Jan 2014

World Health Organization/United Nations Childrens Fund. 2014. Progress on drinking water and sanitatation: 2014 update. Geneva, Switzerland. 110 pg

World Health Organization/United Nations Childrens Fund. 2016. Sanitation, Drinking-Water and Health in Pacific Island Countries: 2015 update and future outlook. Geneva, Switzerland. 108 pg

Yeager BA, Lanata CF, Lazo F, Verastegui H, Black RE. 1991. Transmission factors and socioeconomic status as determinants of diarrhoeal incidence in Lima, Peru. J Diarrhoeal Disentary Res 9:186–193

Young S, Balluz L, Malilay J. 2004. Natural and technologic hazardous material releases during and after natural disasters: a review. Sci Total Environ 322(1–3):3–20

Zedler JB. 2003. Wetlands at your service: reducing impacts of agriculture at the watershed scale. Front Ecol 1 (2): 65-72

8.0 Appendicies

8.1 Appendix 1. Initial sub-catchment scale variables identified as potential environmental risk factors for typhoid fever infection.

Environmental variables*	Variable details
1. Area (ha)	Geodesic area of sub-catchment
2. Incidence/area	Incidence of typhoid within a sub-catchment divided by area of sub-catchment
3. Dense forest (%)	Percentage cover of dense forest
4. 100m river buffer (ha)	Area within 100 m linear buffer on both sides of river network
5. 100m RBZ dense forest (ha)	Area of 100 m RBZ containing dense forest
6.100 m RBZ forested (%)	Percentage of 100 m RBZ containing dense forest
7. 50 m river buffer (ha)	Area within 50 m linear buffer on both sides of river network
8. 50 m RBZ dense forest (ha)	Area of 50 m RBZ containing dense forest
9. 50 m RBZ forested (%)	Percentage of 50 m RBZ containing dense forest
10. Length water (km)	Length of rivers and streams within sub-catchment
11. Forest fragments in 50 m RBZ	Number of forest fragments within 50 m linear buffer on both sides of river network
12. Forest fragments in 50 m RBZ per km	Number of forest fragments per km of river in 50 m linear buffer on both sides of river network
13. Forest fragments in 100 m RBZ	Number of forest fragments within 100 m linear buffer on both sides of river network
14. Forest fragments in 100 m RBZ per km	Number of forest fragments per km of river in 100 m linear buffer on both sides of river network
15. Road length (km)	Length of road within sub-catchment
16. Road density (km/ha)	Density of roads
17. Unsealed road length (km)	Length of unsealed road within sub-catchment
18. Unsealed road density (km/ha)	Density of unsealed roads
19. Sealed road length (km)	Length of sealed road within sub-catchment
20. Sealed road density (km/ha)	Density of sealed roads
21. Creek crossings	Number of intersections between creeks or rivers and roads within the sub-catchment
22. Creek crossings/km	Creek crossings per kilometre of road
23. High Erosion Area (ha)	Area of surface soil of high risk of erosion
24. High Erosion Area (%)	Percentage of surface soil of high risk of erosion
25. Very High Erosion Area (ha)	Area of surface soil of very high risk of erosion
26. Very High Erosion Area (%)	Percentage of surface soil of very high risk of erosion
27. Total High Erosion Area (ha)	Area of surface soil of high and very high risk of erosion
28. Total High Erosion Area (%)	Percentage of surface soil of high and very high risk of erosion
29. High Flood Risk Area (ha)	Surface area high risk of flooding
30. High Flood Risk Area (%)	Percentage of surface area of high risk of flooding
31. Very High Flood Risk Area (ha)	Surface area very high risk of flooding
32. Very High Flood Risk Area (%)	Percentage of surface area of very high risk of flooding
33. Total High Flood Risk Area (ha)	Surface area high and very high risk of flooding
34. Total High Flood Risk Area (%)	Percentage of surface area of high and very high risk of flooding
35. Rainfall – monthly min (mm)	Average minimum monthly rainfall
36. Rainfall – monthly max (mm)	Average maximum monthly rainfall
37. Rainfall – annual (mm)	Average annual rainfall
38. Temperature – monthly min (C°)	Average minimum monthly temperature
39. Temperature – monthly max (C°)	Average maximum monthly temperature
40. Temperature – Aug monthly max (C°)	Average maximum monthly temperature in August (coolest month)
41. Temperature – Aug monthly min (C°)	Average minimum monthly temperature in August (coolest month)
42. Temperature – Feb monthly max (C°)	Average maximum monthly temperature in February (hottest month)
43. Temperature – Feb monthly min (C°)	Average minimum monthly temperature in February (hottest month)

***** These variables were chosen initially following my previous work on catchment alteration in Fiji and its associated effects on aquatic communities (see Jenkins et al. 2010, Jenkins & Jupiter 2011). I hypothesized that typhoid occurrence, and the decline in diversity of aquatic communities in Fiji, are affected by the same determinants, namely alterations to catchment land cover that result in increased flooding, sedimentation and associated pollution to waterways. In addition, given the demonstrated seasonality of the disease (Scobie et al. 2014), climate data including rainfall and temperature were obtained for inclusion in the analysis.

8.2 Appendix 2. Spearman's rank correlation resemblance matrix for environmental predictor variables. Correlation coefficient (ρ) significant * when $\rho \leq 0.381$ (α= 0.05, df =25) or highly significant ** when $\rho \leq 0.487$ (α= 0.01, df =25). Key: DF = dense forest; RBZ = forested riparian buffer zone; FF=forest fragments; RL=road length; RD = road density; CC = creek crossings; HEA = High & very high erosion risk areas; HFRA = high and very high flood risk areas; RM = minimum monthly rainfall; RA = annual average rainfall; TM = minimum monthly temperature).

	Area (ha)	DF (%)	RBZ (%)	FF/km	RD (km/ha)	CC	CC/km	HEA	HEA (%)	HFRA (ha)	% HFRA	RM(mm)	RA(mm)	TM(Co)
Area (ha)	1.000													
DF (%)	.060	1.000												
RBZF (%)	-.036	.686**	1.000											
FF/km	-.303	-.627**	-.377	1.000										
RD (km/ha)	.062	-.698**	-.520**	.708**	1.000									
CC	.490*	-.539**	-.429*	.415*	.711**	1.000								
CC/km	.039	.184	.182	.168	-.132	.204	1.000							
HVEA	.910**	.236	.132	-.357	-.204	.337	.216	1.000						
HEA (%)	-.193	.454*	.361	-.104	-.543**	-.277	.544**	.160	1.000					
HFRA (ha)	.659**	-.510**	-.275	.254	.548**	.665**	-.274	.482*	-.484*	1.000				
% HFRA	.202	-.651**	-.270	.532**	.694**	.596**	-.263	.035	-.450*	.839**	1.000			
RM (mm)	.282	-.344	-.366	-.115	.178	.257	-.165	.249	-.262	.310	.262	1.000		
RA (mm)	.023	.097	-.188	-.324	-.399*	-.182	.100	.187	.189	-.251	-.326	.684**	1.000	
TM (C°)	.102	-.668**	-.323	.556**	.724**	.570**	-.167	-.159	-.492*	.616**	.749**	-.061	-.601**	1.000

8.3 Appendix 3. Demographics of enrolled Typhoid cases (N=236) from Central Division, Fiji (2013 -2015)

Age (median (range))	28 (2-78)
	N (%)
Male	121 (51.3)
Ethnicity	
Indigenous Fijian	231 (97.9)
Fijian of Indian descent	4 (1.7)
Other	1 (0.4)
Residential Area	
Urban	127 (53.7)
Peri-urban	32 (13.8)
Rural	77 (32.5)
Primary Occupation*	
Unemployed	21 (26.3)
Student	20 (25.0)
Labourer	13 (16.3)
Housewife	11 (13.7)
Farmer	8 (10.0)
Professional	4 (5.0)
Dependent (<5 yrs)	3 (3.7)

*Only collected from prospective cases (N=80)

8.4 Appendix 4. Variables used in Exploratory Factor Analysis. SHW = source of drinking water; TDS = toilet drainage soil; DO = dissolved oxygen; CFU = colony forming units.

Variable
1. **Nearest road (m)**
2. **Elevation (m)**
3. **Drainage (0-4)**
4. **Substrate (0-4)**
5. **House condition (0-4)**
6. **Excreta disposal (0-4)**
7. **Garden position (0-4)**
8. **Bathing environs (0-4)**
9. **Drinking water environs (0-4)**
10. **Drinking water storage (0-4)**
11. **Housing density (0-4)**
12. **Solid Waste (0-4)**
13. **Toilet smell (0-4)**
14. **Coliforms SHW (CFU/100mL)**
15. ***E. coli* SHW (CFU/100mL)**
16. **Phosphate SHW (mg/L)**
17. **Nitrate SHW (mg/L)**
18. **Ammonia SHW (mg/L)**
19. **Turbidity SHW (FTU)**
20. **Temperature SHW (°C)**
21. **Conductivity SHW (µS /cm)**
22. **DO SHW (mg/L)**
23. **pH SHW**
24. **Coliforms TDS (CFU/100mL)**
25. **E. coli TDS (CFU/100mL)**
26. **Phosphate TDS (mg/L)**
27. **Nitrate TDS (mg/L)**
28. **Ammonia TDS (mg/L)**
29. **Temperature TDS (oC)**
30. **Conductivity TDS (µS/cm)**
31. **DO TDS (mg/L)**
32. **pH TDS**

8.5 Appendix 5. Typhoid case-control studies, risk factors and interventions/conclusions (1985 – 2016). C = case; C*=control; CI = confidence interval.

Reference	Design	Sample	Location	Risk factors	Odds Ratio	CI (95%)	Intervention/Conclusion
Alba et al. 2016	Health facility- based matched case-control	C = 449, C*=484	Sulawesi, Kalimantan and Papua	Hand washing (sometimes/never)	3.16	2.09 - 4.79	Ensuring adherence to adequate hand-washing practices
				Eating food out in food stalls or restaurant	6.9	4.41 - 10.8	
Black et al. 1985	Neighbourhood matched case control, (3-14 yrs. only)	C=81, C*=81	Santiago, Chile	History of typhoid in a relative	3.2	NA	Consuming food- stuffs prepared outside individual's home and shared with or sold to children
				Bought lunch at school	4.0	NA	
Gasem et al. 2001	Neighbourhood matched case control, structured observation of living environment	C=75, C*=75	Semarang, Indonesia	Living in a house without water supply from the municipal network	29.18	2.12 - 400.8	Associated with poor housing and inadequate food and personal hygiene.
				Open sewers	7.19	1.33 - 38.82	
				Never or rarely washing hands before eating	3.97	1.22 - 12.93	
				Being unemployed or having a part-time job	31.3	3.08 - 317.4	
Khan et al. 2012	Vaccine trial (2-16 yr.), control group clusters	C = 65, C* = 60	Karachi, Pakistan	Increasing age	0·89	0·83 - 0·95	High population density and lack of access to safe water in Pakistan. A combination of environmental and biological interventions
				Increase in population density	1·13	1·05 -1·21	

				Using a safe drinking-water source	0·63	0·41 - 0·99	
Luby et al. 1998	Neighbourhood matched case control, microbial investigation	C = 100, C* = 200	Karachi, Pakistan	Eating ice cream	2.3	1.2 - 4.2	Improving commercial food hygiene and decreasing unnecessary antimicrobial use
				Eating food from a roadside cabin during the summer months,	4.6	1.6 - 13.0	
				Taking antimicrobials in the 2 weeks preceding the onset of symptoms	5.7	2.3 -13.9	
				Drinking water at the work-site	44.0	2.8 - 680	
Luxemburger et al. 2001	Hospital & community based matched case control	C = 144, C* = 288	Mekong delta, Viet Nam	Contact with a patient with typhoid fever hospital controls, Community controls	5.2 11.9	1.7-15.9 2~3-60-7	Strategies directed towards the persons in contact with a patient
Mbakaya et al. 2015	Symptom based neighbourhood unmatched case control	C = 50, C* = 50	Kaziwizi coal mine, Malawi	Use of untreated water from a nearby river	2.7	1.2 - 6.3	Water from the river needs to be treated before use and health education campaigns with targeted health promotion messaging
				Drinking locally prepared thobwa (sweet mild beer) and	1.8	0.8 - 3.96	
				Not having a facility for hand washing after toilet use	2.6	0.8 - 3.96	
Mermin et al. 1998	Facility based matched case-control (outbreak investigation)	C = 45, C* = 123	Dushanbe, Tajikistan	Drinking un-boiled water	7	3 - 24	Chlorination and coagulation were begun at the treatment plants and a water conservation campaign was initiated to improve water

							pressure
Muti et al. 2014	Facility based unmatched case control (outbreak investigation)	C = 115, C* = 115	Dzivaresekwa, suburb of Harare City, Zimbabwe	Drinking water from a well	6.2	2.01-18.7	Contaminated water from unprotected water sources was the probable source of the outbreak. Invest in repairing water and sewage reticulation systems in the city.
				Attending a gathering	11.3	4.3 - 29.9	
				Boiling drinking water	0.21	0.06 - 0.76	
				Burst sewer pipe at home	1.19	0.67 -2.14	
Olsen et al 2001	Neighbourhood matched case-control (outbreak investigation)	C = 50, C* = 50	Nauru	Restaurant M	11	1.3 - 96	Routine or emergency immunization campaigns targeting school-aged children
				Restaurant I	5.8	1.2 - 29	
Hosoglu et al. 2005	Facility based matched case control (Adults only)	C = 64, C* = 128	Diyarbakir, Turkey	Living in a crowded household	3·31	1·58 - 6·92	Living in a crowded household and consumption of raw vegetables outside the home
				Eating cig kofte (a traditional raw food)	5·29	2·20 - 12·69	
				Lettuce salad	3·55	1·52 - 8·28	
Ram et al. 2006	Facility based matched case-control	C = 41, C* = 82		Drinking un-boiled water at home	12.1	2·2–65·6	Improved chlorination of the municipal water supply or disinfecting drinking water at the household level
				Water from primary source foul-smelling	7·4	2·1–25·4	
				Eating papaya	5·2	1·2–22·2	
				Using a latrine for defecation (protective)	0.1	0·02–0·9	

Sharma et al. 2009	Facility based matched case control	C = 123, C* = 123	Darjeeling, West Bengal, India	Less likely to store drinking water in narrow-mouthed containers	0.4	0.2 - 0.7	Chlorinate drinking water at the point of use, wash/cook raw fruits and vegetables and ensure safer preparation/storage of local milk products.
				Tip containers to draw water	0.4	0.2–0.7	
				Have home latrines	0.5	0.3–0.8	
				More likely to consume butter, yoghurt, raw fruits and vegetables,	2.3 2.3 2.1	1.3–4.1 1.4–3.7 1.2–3.9	
Srikantiah et al. 2007	Facility based matched case control	C = 97, C* = 192	Samarkand region of Uzbekistan	Consumption of un-boiled surface water outside the home	3.0	1.1–8.2	Targeted efforts at improving drinking water quality, especially for students and young adults, Measures to decrease the unnecessary use of antimicrobials
				Use of antimicrobials in the 2 weeks preceding onset of symptoms	12.2	4.0–37.0	
				Being a student	4.0	1.4–11.3	
				Routinely washing vegetables	0.06	0.02–0.2	
				Dining at a tea-house	0.4	0.2–1.0	
Stroffolini et al. 1992	Facility based matched case control	C = 51, C* = 102	Neapolitan area, Italy	Consumption of raw shellfish	13.3	5.5 - 32.8	Hazardous dietary habits and inadequate sewage treatment facilities, combined with lack of sanitation in the harvesting and marketing of shellfish, play a major role in the endemicity of typhoid fever in the Neapolitan area.

Tran et al. 2005	Hospital-based matched case—control study	C = 90, C* = 180	Son La province, northern Vietnam	Recent contact with a typhoid patient	3.3	1.7—6.2,	Improving quality of drinking water must be a priority and health education strategies targeted at individuals with no schooling, contacts of patients,
				No education	2.0	1.0—3.7	
				Drinking untreated water	3.9	2.0—7.5	
Velema et al 1997	Hospital-based unmatched case-control	C = 50, C* = 42	Ujung Pandang, Sulawesi, Indonesia	Consumption of food from *warungs* (Food stalls in the street)	45	3.9 -279	Emphasize the importance of thorough hand washing and the need to take care in the selection of street-foods.
				Cases used soap significantly less often	30	4.0 -255	
Vollard 2004	Community-based case-control study	C = 69, C* = 667	Jatinegara district, Jakarta, Indonesia	Recent typhoid fever in the household	2.38	1.03-5.48	
				No use of soap for handwashing	1.91	1.06-3.46	
				Sharing food from the same plate	1.93	1.10-3.37	
				Use of ice cubes	2.27	1.31-3.93	
				No toilet in the household	2.20	1.06-4.55	
				Female sex	1.79	1.04-3.06	

8.6 Appendix 6. Enrolment questionnaire for case and control study

Epidemiology of Typhoid fever in Fiji

CRF: Enrolment questionnaire for case and control

[Note: You need not to administer the questionnaire, the way it is written in English. Use local terminologies so that it is easily understandable by the interviewee. Always start with an open question and then lead the respondents with closed questions as appropriate. Never prompt an answer; provide interviewee with sufficient time for an appropriate response. There are instructions after certain questions; follow them]

1. Is it a case or control: ☐ [Case=1; Control=2]
2. Please insert the corresponding case or control ID: ☐☐☐☐☐☐☐☐

Demographic information:

3. Subject ID: ☐☐☐☐☐☐☐☐
4. Date of enrolment: ☐☐ ☐☐ ☐☐☐☐
   DD MM YYYY
5. Age: ☐☐ Day/Month/Year
   (Use an event calendar to calculate age if exact date of birth is unknown)
6. Date of birth: ☐☐ ☐☐ ☐☐☐☐
   DD MM YYYY
   (Use event calendar to approximate the date of birth)
7. Sex: ☐ [Male=1;Female=2]
8. Residential area: ☐ [Urban=1; Rural=2; Peri-urban=3]
9. Insert the GPS coordinate of the resident: S ☐☐ ☐☐ ☐☐☐
   E ☐☐☐ ☐☐ ☐☐☐
10. What is your (your child's) primary occupation: ☐
    [Dependant (if the subject is less than five years) =1; student=2; manual labourer=3 skilled labourer (obtained through certified course) =4; farmer= 5; business=6; small traders=7;

professional (after completing a recognized degree e.g. teacher, doctor, engineer, any office work etc.)=8; housewife=9; Unemployed=10; sedentary=11]

Note: Circle the given answer and also put the code in the box

11. How many people live in your (your child's) household?
(Confirm by asking who they are)

12. Can you please tell the age and sex of the people live in your (your child's) household
(Can construct a table to list all the people)

No.	Relation (mother, father, brother, sister etc.)	Age	Sex[Male=1;Female=2]
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			

13. How many sleeping rooms are there in your (your child's) household?

14. How far have you (your child) studied in an educational institute?
[Attended primary=1; completed primary=2; secondary=3; completed secondary=4; Post-secondary=5; University=6; No formal education=7; religious education only=8]

Note: Circle the given answer and also put the code in the box

Family history

15. Has anybody in your (your child's) household had a fever in the last two weeks?
[Yes=1;No=2] If "NO" go to Q 16 otherwise continue.
15a. if yes do you know whether any one of them was diagnosed as typhoid fever?
[Y=1; No=2]

15b. was anyone of them treated with antimicrobials/any medicine in the last two weeks? [Yes=1; No=2]

15c.If yes can you please name the medicine? ____

16. Do you know anybody in your (your child's) household has been diagnosed with gall bladder disease? ☐ [Yes=1;No=2]
17. Has anyone in your household been told that they are a typhoid carrier? ☐=1;No=2]

    If "No" go to Q 18 otherwise continue

    17a. If yes who? ____

    17b. If yes when he/she was told ☐☐days/months/years ago

    17c. if yes have they been treated? ☐ [Yes=1; No=2]

18. Have you ever been vaccinated for typhoid fever? ☐ [Yes=1;No=2]

    18a.If yes when? ☐☐ys/months/years ago

19. Has anybody in your (your child's) household been vaccinated for typhoid fever? ☐=1;No=2]

    If yes,

    19a. When ☐☐ days/moths/years ago

    19b. How many of the household members were vaccinated ☐☐

Household asset:

Note: for question no 19-21 circle the given answer and also put the code in the box

20. What is the predominant structure of your (your child's) house floor [only one can be ticked]
    a. Earth/sand ☐ [Yes=1; No=2]
    b. Dung ☐ [Yes=1; No=2]
    c. Wood plunks ☐ [Yes=1; No=2]
    d. Palm/bamboo ☐ [Yes=1; No=2]
    e. Parquet or polished wood ☐ [Yes=1; No=2]
    f. Cement ☐ [Yes=1; No=2]
    g. Ceramic tiles ☐ [Yes=1; No=2]
    h. Carpet ☐ [Yes=1; No=2]

21. Do you have any of the following in your household: [Tick all that apply]
    a. Electricity ☐ [Yes=1; No=2]
    b. Television ☐ [Yes=1; No=2]

☐

c. Radio [Yes=1; No=2]

d. Refrigerator [Yes=1; No=2]

e. Bi cycle [Yes=1; No=2]

f. Motorized vehicle (car, bike etc.) [Yes=1; No=2]

g. Telephone (land/mobile) Yes=1; No=2]

h. Non-motorized vehicle [Yes=1; No=2]

i. Agricultural land Yes=1; No=2]

j. None of the above [if the person interviewed has none of the above put 0]

22. Do any of the following animals live in your household [tick all that apply]

a. Cow [Yes=1; No=2]

b. Goat [Yes=1; No=2]

c. Sheep [Yes=1; No=2]

d. Horse/donkey/mule [Yes=1; No=2]

e. Fowl [Yes=1; No=2]

f. Dog [Yes=1; No=2]

g. Cat [Yes=1; No=2]

h. Other [Yes=1; No=2]

i. No animal [if there're is no animal in the interviewees house put 0]

Water Source and treatment

23. What is the main water source for drinking water in your household [only one can be ticked]

a. Piped into the house (from a public supply system) Yes=1; No=2]

b. Piped into the yard (from a public supply system) Yes=1; No=2]

c. Shared public tap [Yes=1; No=2]

d. Shallow tube well [Yes=1; No=2]

e. Deep tube well [Yes=1; No=2]

f. Covered well [Yes=1; No=2]

g. Open well [Yes=1; No=2]

h. River water [Yes=1; No=2]

i. Lake water [Yes=1; No=2]

j. Dam [Yes=1; No=2]

k. Pond [Yes=1; No=2]

l. Rain water [Yes=1; No=2]

m. Spring water (protected) [Yes=1; No=2]

n. Spring water (unprotected) [Yes=1; No=2]

o. Bottle water (bought) [Yes=1; No=2]

p. Other____________ [Yes=1; No=2]

Note: Circle the given answer and also put the code in the box

23a. Is water available all the time from the main source mentioned above?

[Yes-1; No=2] If "YES" go to Q 24 otherwise continue

23b. If 'no' how often has the water been available from this main source in the last two weeks?

a. Several hours a day=1

b. Few times in a week=2

c. Never=3

Note: Circle the given answer and also put the code in the box

24. Is water from the main source treated? [Yes=1;No=2;Don't Know=3]

24a. If yes, is it treated all the time? [Yes=1; No=2; Don't Know=3]

25. Do you usually treat drinking water at home? [Yes=1;No=2]
If "no" go to question no 26 otherwise continue

25a. If yes what method do you usually use to treat water? [Only one can be ticked]

a. Boil=1
b. Filter through a cloth=2
c. Filter through ceramic=3
d. Add chlorine, alum or any tablets=4
e. Solar disinfection=5

Note: Circle the given answer and also put the code in the box

26. In the last two weeks did you (your child) drink water that was not treated?
[Yes=1; No=2]
27. If yes how many times you (your child) drank untreated water in the last two weeks?

28. In the last two weeks preceding your (your child) present illness did you (your child) drink water at home from any of the following? (Confirm that main source of water and potable water is same).

And can you please remember approximately how many times you drank water from the sources you have mentioned? (prompt sources) [Yes=1; No=2]

Source	Y/N	How many times
a. Piped into the house (from a public supply system)		
b. Piped into the yard (from a public supply system)		
c. Shared public tap		
d. Shallow tube well		
e. Deep tube well		
f. Covered well		
g. River water		
h. Lake water		
i. Dam		
j. Pond		
k. Rain water		
l. Spring water (protected)		
m. Spring water (unprotected)		
n. Bottle water (bought)		
o. Other_____________		

29. Do you store water? ☐ [Yes=1; No=2]
If "NO" go to Q30 otherwise continue

29a. If yes where do you store water? ☐

a. In the house=1
b. In the courtyard=2
c. Overhead tank=3

Note: Circle the given answer and also put the code in the box

29b. Is your storage container (most commonly used) ☐

d. Narrow mouthed and capped=1
e. Narrow mouthed and uncapped=2
f. Wide mouthed and capped=3
g. Wide mouthed and uncapped=4

Note: Circle the given answer and also put the code in the box

29c. how do you dispense water from the container? ☐

h. Pour=1

i. Scoop with a cup=2

j. Scoop with a ladle=3

k. Through a faucet=4

Note: Circle the given answer and also put the code in the box

30. In the last two weeks preceding your (your child) present illness did you (your child) drink water outside of home from any of the following? And can you please remember how many times you drank water from the sources? (prompt sources) [Yes=1; No=2]

Source	Y/N	How many times
a. Piped into house (from a public supply system)		
b. Piped into the yard (from a public supply system)		
c. Shared public tap		
d. Shallow tube well		
e. Deep tube well		
f. Covered well		
h. River water		
i. Lake water		
j. Dam		
k. Pond		
l. Rain water		
m. Spring water (protected)		
n. Spring water (unprotected)		
o. Bottle water (bought)		
p. Other_____________		

[Continue if answer to this question is YES otherwise go to Q 34]

31. If yes where did you (your child) drink water from the source outside the house?

a. Work place (mention the place e.g. office/farm/agricultural land etc.)=1

b. School=2

c. Restaurant=3

d. Community gathering (funeral/religious/wedding)=4

e. Other__________________=5

Note: Circle the given answer and also put the code in the box

32. If yes do you know whether the water you (your child) drank outside was treated? [Ye No=2; Do not know=3]

33. Was the water you (your child) drank outside of home was stored?

[Yes=1; No=2; Do not know=3]

33a. if yes do you know where it was stored?

[Yes=1; No=2; Do not know=3]

33b. if yes can you tell me how it was dispensed

a. Pour=1
b. Scoop with a cup=2
c. Scoop with a ladle=3
d. Through a faucet=4
e. Do not know=5

Note: Circle the given answer and also put the code in the box

34. Did you (your child) use ice in the drinking water or beverages in the last two weeks?
    [Yes=1; No=2; Do not know=3]
35. Did you (your child) drink water/beverages in any restaurant in the last two weeks?
    [Yes=1; No=2; Do not know=3]
36. Did you (your child) drink any beverages/water from the street vendor?
    [Yes=1; No=2; Do not know=3]
37. Do you (your child) drink KAVA? [Yes=1;No=2]
    If "NO" go to Q 40 otherwise continue
38. Did you share KAVA with anybody in the last two weeks? [Yes=1; No=2]
39. Do you know the source of water used to prepare Kava?
    a. Piped into the house (from a public supply system)=1
    b. Piped into the yard (from a public supply system)=2
    c. Shared public tap=3
    d. Shallow tube well=4
    e. Deep tube well=5
    f. Covered well=6
    g. Open well=7
    h. River water=8
    i. Lake water=9
    j. Dam=10
    k. Pond=11
    l. Rain water=12
    m. Spring water (protected)=13
    n. Spring water (unprotected)=14
    o. Bottle water (bought)=15
    p. Other____________=16

Note: Circle the given answer and also put the code in the box

Food:

40. Do you (your child) grow your own produce? [Yes=1;No=2]

    If "NO" go to Q 44 otherwise continue

41. If yes what type of manure/fertilizer do you use to grow those vegetables?
    a. Chemical fertilizer=1
    b. Livestock or poultry manure=2
    c. Other natural fertilizer=3
    d. Human excreta=4
    e. Do not use any manure or fertilizer=5

    Note: Circle the given answer and also put the code in the box

42. How much fertilizers do you use per month [skip Q 42&43 if you have circled "e" in Q 41]
    a. 10-100 kg=1
    b. 101-500 kg=2
    c. 501-1000 kg=3
    d. Over 1000 kg=4

    Note: Circle the given answer and also put the code in the box

43. How often do you use fertilizers?
    a. Daily=1
    b. Weekly=2
    c. Monthly=3
    d. Other__________________=4

    Note: Circle the given answer and also put the code in the box

44. Do you (your child) eat produce? [Yes=1;No=2]

45. Did you (your child) eat produce in the last two weeks? [Yes=1;No=2]
46. Do you (your child) wash produce before eating? [Yes=1;No=2]
47. Did you (your child) eat unwashed produce in the last two weeks? [Yes=1;No=2; Do not know=3]
48. Who usually prepares food in your household?
    a. Self=1
    b. Spouse=2
    c. Parent=3
    d. Grandparent=4
    e. Sibling=5
    f. Other relative=6
    g. Domestic help=7

Note: Circle the given answer and also put the code in the box

49. Can you please state the following of the person who prepares food in your household
    a. Age ☐☐ Years
    b. Gender ☐ [Male=1; Female=2]
    c. Any recent history of typhoid fever ☐ [Yes=1; No=2; Do not know=3]
    d. Any history of gall bladder disease ☐ [Yes=1; No=2; Do not know=3]

50. Do you usually store cooked food for subsequent meals? ☐ [Yes=1;No=2]

50a. if yes, do you refrigerate stored food? ☐ [Yes=1; No=2]

50b. if yes, do you usually heat pre-cooked food before consumption ☐ [Yes=1; No=2}

51. Do you (your child) usually eat or share from the same plate with others? [Yes=1;No=2] ☐
52. Did you (your child) eat or share food with others in the last two weeks?
    [Yes=1; No=2; Do not know=3] ☐
53. Did you (your child) eat any food from outside of home in the last two weeks (other than places mentioned above)? ☐ [Yes=1; No=2; Do not know=3]

55a. If yes where? ☐

a. Restaurant=1
b. Street vendor=2
c. Friend /relatives house=3
d. Other______________=4

Note: Circle the given answer and also put the code in the box

54. Did you (your child) have any of the dairy products in the last two weeks? ☐
    [Yes=1; No=2; Do not know=3]
55. If yes can you name them? ☐
    a. Milk=1
    b. Yoghurt=2
    c. Butter=3
    d. Cheese=4
    e. Cream=5
    f. Ice cream=6

g. Other=7

Note: Circle the given answer and also put the code in the box

56. Did you (your child) eat kai (mussells) in the last few weeks? ☐

    [Yes=1; No=2; Do not know=3]

57. Did you (your child) eat lolo (squeezed coconut milk) in the last two weeks? ☐

    [Yes=1; No=2; Do not know=3]

58. Did you (your child) attend any mass gathering in the last two weeks? ☐ [Yes=1;No=2]

59. If yes name them and date please

    a. Wedding: ☐☐ ☐☐ ☐☐☐☐

       DD MM YYYY

    b. Funeral: ☐☐ ☐☐ ☐☐☐☐

       DD MM YYYY

    c. Religious festival: ☐☐ ☐☐ ☐☐☐☐

       DD MM YYYY

    d. Other: ☐☐ ☐☐ ☐☐☐☐

       DD MM YYYY

Sanitation information

60. Do you (your child) have a toilet in the household? ☐ [Yes=1; No=2]

61. What kind of toilet facility do you (your child) have in the household ☐

    a. Flush toilet=1
    b. Pour flush toilet=2
    c. Ventilated improved pit (VIP) latrine=3
    d. Traditional pit latrine=4
    e. Improved water seal toilet=5
    f. No facility: Bush/field/ground/stream/open sewer=6
    g. Other=7

    Note: Circle the given answer and also put the code in the box

62. Have you or someone from your family has built the toilet for your use? ☐

    [Yes=1; No=2]

    If "NO" go to Q65 otherwise continue

63. If yes, what kind of substrate is used to build the toilet? ☐

    a. Clay=1

b. Loam=2

c. Sand=3

d. Gravel=4

e. Coral rubble=5

f. Soap stone=6

g. Other=7

h. Do not know=8

Note: Circle the given answer and also put the code in the box

64. Do you know how deep the toilet is?

a. Arm's length=1

b. Outstretched arm's length=2

c. More than two arm's length=3

d. Do not know=4

65. If you have a flush toilet please can you tell us the type of septic tank that the toilet has?

[Please check the response in Q61 to answer this question]

a. Concrete=1

b. 44 gallon drum=2

c. Plastic=3

d. Fibre glass=4

e. Other=5

f. Do not know=6

g. Do not have a flush toilet=7

Note: Circle the given answer and also put the code in the box

Ask Q 66 (to the primary caregiver) if the case or control is very young and do not use a toilet by him/her self

66. Where do you usually dispose of your child's faeces?

a. Toilet=1

b. Bury=2

c. Scatter in the yard=3

d. Bush/ground/stream/open sewer=4

e. Do nothing=5

f. Other=6

Note: Circle the given answer and also put the code in the box

67. When do you (your child) usually wash your hand? [always=1; sometimes=2; never=3; not applicable=4] Check all that apply

67a. Before eating:

67b. Before cooking:

67c. Before preparing child's food:

67d. After cleaning a child who defecated:

67e. After you defecate:

67f. Other:

68. Do you have separate source of water for hand washing? [Yes=1; No=2]
69. Do you use any disinfectant while washing hand? [Yes=1; No=2]
70. If yes what do you usually use
    a. Soap=1
    b. Ashes=2
    c. Mud=3
    d. Other____________________________=4

Note: Circle the given answer and also put the code in the box

71. Where do you usually bathe?
    a. In house, piped water=1
    b. In house, stored water=2
    c. In river/stream=3
    d. Other__________________=4

    Note: Circle the given answer and also put the code in the box
72. Where do you usually wash clothes?
    a. In house, piped water=1
    b. In house, stored water=2
    c. In river/stream=3
    d. Other__________________=4

    Note: Circle the given answer and also put the code in the box
73. Where do you usually prepare food?
    a. In the house=1
    b. In a communal outdoor setting=2
    c. At the farm=3

    Note: Circle the given answer and also put the code in the box
74. How often do you visit the local river/stream?
    a. Daily=1
    b. Weekly=2
    c. Monthly=3

d. Rarely=4

e. Never=5

Environment

75. How has the rainfall been in the last two weeks?
    a. Heavy rain=1
    b. Moderate rain=2
    c. Little rain=3
    d. No rain=4
76. How has the rainfall been in the last two months but prior to last two weeks?
    e. Heavy rain=1
    f. Moderate rain=2
    g. Little rain=3
    h. No rain=4
77. Have you been affected by a cyclone/tropical storm in the last 2 weeks?
    [Yes=1; No=2]
78. Have you been affected by a cyclone/tropical storm in the last 2 months?
    [Yes=1; No=2]
79. Have you been evacuated from your home in the last two weeks?
    [Yes=1; No=2]
80. Have you been evacuated from your home in the last two months?
    [Yes=1; No=2]
81. Have you been afffected by drought in the last two weeks?
    [Yes=1; No=2]
82. Have you been affected by drought in the last 2 months?
    [Yes=1; No=2]
83. Did your house flood in the last two weeks?
    [Yes=1; No=2]
84. Did your house flood in the last two months?
    [Yes=1; No=2]
85. Has there been flooding adjacent to your house in the last two weeks?
    [Yes=1; No=2]
86. Has there been flooding adjacent to your house in the last two months?
    [Yes=1; No=2]
87. Has the village flooded in the last two weeks?
    [Yes=1; No=2]
88. Has the village flooded in the last two months?
    [Yes=1; No=2]
89. Has the toilet/latrine that you use been flooded in the last 2 weeks?

[Yes=1; No=2]

90. Has the toilet/latrine that you use been flooded in the last 2 months?

[Yes=1; No=2]

91. Has the nearest stream/river flooded in the last two weeks?

[Yes=1; No=2]

92. Has the nearest stream/river flooded in the last two months?

[Yes=1; No=2]

93. Are there farms above where water is collected for household use?

[Yes=1; No=2]

94. Are there livestock above where water is collected for household use?

[Yes=1; No=2]

95. Are there latrines/toilets above where water is collected for household use?

[Yes=1; No=2]

96. Is there logging activities higher in the river basin?

[Yes=1; No=2]

97. Are there road building activities higher in the river basin?

[Yes=1; No=2]

98. Are there mining activities (including sand dredging) higher in the river basin?

[Yes=1; No=2]

99. Are there dams higher in the river basin?

[Yes=1; No=2]

100. Do you use the nearby river/stream for fishing or collecting food

[Yes=1; No=2]

If yes to Q 100 then continue otherwise stop interview here

101. If so, what are you fishing/collecting?

a. Fish (Ika) [Yes=1; No=2]

b. Clam (Kai) [Yes=1; No=2]

c. Prawns (Ura) [Yes=1; No=2]

d. Other_______ [Yes=1; No=2]

Note: Circle the given answer and also put the code in the box

102. If you go for fishing how much time do you spend per trip in the river?

a. 0-1 hr [Yes=1; No=2]

b. 1-3 hrs [Yes=1; No=2]

c. Half a day [Yes=1; No=2]

d. One full day [Yes=1; No=2]

e.Other____________ ☐ [Yes=1; No=2]

Note: Circle the given answer and also put the code in the box

Initials of the interviewer:

Signature of the interviewer:____________________________________

Date: