PH.D. THESIS

Geographical Patterns and Environmental Risks of Inflammatory Bowel Disease and Diarrhoea: A Comparative Study Using Spatial and Statistical Modelling

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Declaration

I confirm that the work presented in this thesis is based on the original research which has been carried out by me under the supervision of my supervisors Professor Peter M. Atkinson, Professor Roger W. Pickup and Doctor Manoj Roy. This thesis has not been previously submitted elsewhere for the award of any other degree. The information derived from other sources has been acknowledged in the text, and a list of references is provided.

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Geographical Patterns and Environmental Risks of Inflammatory Bowel Disease and Diarrhoea: A Comparative Study Using Spatial and Statistical Modelling

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Abstract

The aim of this PhD study is to investigate multiple aspects of environmental and epidemiological factors influencing inflammatory bowel disease (IBD) in the UK and diarrhoeal disease in children under five in two informal settlements of Accra, Ghana: Gbegbeyise (GB) and Madina Zongo (MZ). While IBD is a chronic non-communicable condition with rising incidence in industrialised countries, diarrhoeal diseases remain an acute public health threat in low-income urban environments. This thesis comprises four studies that apply spatial analysis and regression-based modelling to examine these distinct disease contexts.

The first study investigated IBD in the UK using a novel dataset of 5,452 survey respondents. Grid-based mapping and age-sex standardised morbidity rates (ASMRs) were employed to identify spatial patterns. Findings indicated relatively uniform spatial distributions of Crohn's disease (CD) and ulcerative colitis (UC) cases but a notable cluster of high CD:UC ratios in North-West England. The second study builds on this by Poisson modelling the relationship between CD risk and the proportion of pasture land, used as a proxy for exposure to *Mycobacterium avium* subspecies *paratuberculosis* (MAP). A Poisson regression model at the hydrological catchment level indicated a significant association between CD incidence and pasture proportion, but not for UC, supporting the hypothesis that MAP exposure may contribute to CD risk.

The third and fourth studies were conducted in two informal settlements in Accra, Ghana, and focused on childhood diarrhoea. The third study analysed household survey data collected biweekly over a period of more than two years and identified a statistically significant association between diarrhoea incidence and antecedent rainfall and proximity to flood-prone areas. The fourth study evaluated the effect of a WASH intervention in one of the settlements, where a 39.8% reduction in diarrhoea cases was observed. This PhD thesis presents novel findings that enhance the understanding of the spatial distribution of diseases such as IBD and diarrhoea and their relationship with environmental risk factors, providing evidence to the existing literature.

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List of Abbreviations

ASMR	Age- and sex-standardized morbidity rate
CCUK	Crohn's and Colitis UK
CD	Crohn’s disease
CSIR	Council for Scientific and Industrial Research
DAERA	The Department of Agriculture Environment and Rural Affairs
DDS	Diarrhoeal disease surveillance
DEFRA	The Department for Environment Food and Rural Affairs
GB	Gbegbeyise
GIS	Geographic information systems
GLM	Generalised linear model
GP	General practitioner
HH	Household
IBD	Inflammatory bowel disease
IC	Indeterminate colitis
JD	Johne’s disease
LMICs	Low- and middle-income countries
MAP	*Mycobacterium avium spp. paratuberculosis*
MC	Microscopic colitis
MZ	Madina Zongo
NCDs	Non-communicable diseases
RR	Relative risks
SDG	Sustainable Development Goal
SEPA	Scottish Environment Protection Agency
UC	Ulcerative colitis
VIF	Variance inflation factor
WASH	Water, sanitation and hygiene

Chapter 1

1. Introduction

Diseases cause significant problems that can both threaten human health at the individual level and negatively impact societies at the population level.

Diseases can be of various types, including communicable and non-communicable. Communicable diseases are infectious diseases that can be transmitted between people, between animals, and from animal to humans and *vice versa*. (e.g. influenza, HIV/AIDS and malaria). Non-communicable diseases (NCDs) are health conditions that usually develop because of a combination of genetic predisposition, environmental and/or lifestyle factors, such as dietary habits, lack of physical activity, and alcohol and tobacco use. The most common NCDs include cardiovascular disease, cancer, diabetes, and chronic respiratory diseases.

Communicable diseases are illnesses caused by infectious agents that can be transmitted from one host to another through various mechanisms such as inhalation, direct contact or via vectors. A major category of communicable diseases includes those transmitted directly between humans. For example, respiratory infections like influenza and COVID-19 typically spread from an infected individual to a non-infected individual. Another important group is zoonotic diseases, which are infections that originate in animals and can be transmitted to humans [1]. These diseases can spread through direct contact with an infected animal (as in the case of rabies) or indirectly via a vector such as mosquitoes or ticks [2]. Vector-borne zoonotic diseases, thus, involve a third party—usually an insect or arthropod—that acquires the pathogen from an infected animal and subsequently transmits it to a human, commonly through a bite. Malaria is a classic example of a vector-borne zoonotic disease, where mosquitoes act as carriers of the *Plasmodium* parasite from one host to another. In contrast, rabies is transmitted directly through the bite of an infected animal, with no vector involved.

The environment can play an important role in the spread of infectious diseases. Pathogens can survive, multiply and be transported under the influence of environmental factors [3–6]. Water pollution can accelerate the spread of bacterial and viral diseases in particular, and environmental factors can facilitate the transmission of these pathogens to humans [7]. The environment is an important factor in the spread of diseases not only as a means of transport, but also as a habitat for pathogens. In this context, understanding environmental factors plays a critical role in developing strategies to prevent the spread of diseases.

This thesis focuses on two different diseases: Crohn's disease (CD), which is chronic, and diarrhoea, which is normally acute. CD can affect any part of the gastrointestinal tract (GI) [8] and its aetiology is not fully known [9]. In the literature, it is suggested that the bacterium *Mycobacterium avium subsp. paratuberculosis* (MAP) is strongly associated with CD [10], and this bacterium is considered a pathogen that can potentially be transmitted to humans through contaminated food, water, milk and meat products [11, 12]. Therefore, it is considered to be a potential zoonotic agent [13]. MAP can infect ruminants including cattle causing Johne's Disease (JD) [14] and this can be spread between animals through faecal shedding [15]. The hypothesis that environmental factors may affect the transmission of MAP from animals to humans reveals the importance of environmental factors in understanding the spread dynamics of the disease [16, 17].

Contrasting with CD, diarrhoea is an acute disorder that can be clinically classified by the duration of the symptom [18]. It is an infectious disease that can spread through human-to-human transmission or directly from the environment facilitated by environmental factors [19]. Microbial agents (comprising viruses, bacteria, protozoa, fungi and helminths) responsible for diarrhoeal infections can persist in the environment, especially in water sources, making contaminated water a major route of disease transmission. Access to clean water, improved sanitation practices and hygiene habits are vital in preventing diarrhoea, particularly in low- and middle-income countries (LMICs) where infrastructure is often inadequate [20]. In such settings, heavy rainfall is known to trigger the spread of waterborne diseases [21] and increase the amount of bacteria and viruses in surface waters [22].

Many environmental variables can affect the spread of a disease, such as diarrhoea [23–26]. Each of these factors can interact in different ways, and it can be difficult to predict the impact of these interactions. For example, factors like water pollution, climate change, agricultural practices, and urbanization can all affect the spread of diarrhoea, but it can be difficult to separate the effects of each factor. Some environmental factors interact with each other in the spread of diseases, making it even more complicated to determine the causes of the disease [27, 28]. These factors can include a variety of variables including time, space and social dynamics. In addition, environmental conditions often shape disease spread through indirect effects, and these effects are difficult to measure quantitatively. Therefore, detailed analyses based on accurate environmental data and reliable data collection methods are required to clearly demonstrate the role of environmental variables in disease spread.

The spread of disease over a wide geographic area can make it even more difficult to determine environmental effects. In such cases, integration of different data sources may be required, and it is important to take regional differences into account [29]. Similarly, examining the dynamics of disease spread over time poses a significant methodological challenge. Disease spread rates can vary depending on changes in environmental conditions. Therefore, time-series data and continuous observations are needed to characterize long-term trends [30].

Measuring environmental factors has become easier thanks to remote sensing technologies and other spatial datasets. Remote sensing provides high-quality measurements of environmental variables over large geographic areas, making it possible to examine the effects of environmental factors on disease distribution and spread more comprehensively. For example, remote sensing-derived land surface temperature (LST) data have been used to assess heat exposure and its link to vector-borne diseases [31]. Satellite remote sensing, aerial photography and geographic information systems (GIS) are among the basic tools for collecting and analysing environmental data. GIS has been used widely to map disease incidence in relation to environmental hazards, such as proximity to contaminated water sources [32]. In addition, geographic information on disease cases can be collected and linked to environmental factors through internet-supported surveys. For example, participatory mapping platforms and online health surveys have been used to track the spread of respiratory infections during the COVID-19 pandemic [33]. These tools make it possible to communicate quickly and effectively with large numbers of people and to examine disease patterns at a local level. In this way, the relationship between environmental factors and disease cases can be determined more accurately.

Time-series data are critical to understanding the spread of diseases. GIS-based approaches allow for accurate mapping of repeated household (HH) surveys. This is particularly useful in long-term, sequential data collection processes. Associating each survey with a specific location allows tracking of changes over time and spatial analysis of disease transmission. Such data are also useful for understanding how environmental factors affect HH health and how these interactions change over time.

In the analysis of data obtained from different sources, it is necessary to ensure data compatibility and to apply appropriate analysis techniques for each type of data. This process is important to achieve accurate and reliable results. Advanced statistical and spatial analysis methods should be used to ensure the integration of data. These methods allow for better characterization of relationships by accurately modelling the intersection of environmental factors and disease cases. In this context, statistical models (e.g., generalised linear regression models) provide an important analytical framework for assessing the impact of environmental variables on disease dynamics [34, 35].

Poisson regression, a type of GLM, is an effective method for modelling numerical data of rare events [36]. Poisson regression models how the number of disease cases is influenced by independent variables including environmental factors. Poisson regression also allows for flexible modelling of nonlinear relationships. It can handle both continuous and categorical variables. It also minimizes the effects of zero values and over-dispersion, allowing for more reliable results. Therefore, it is used widely in studies examining the relationship between disease cases and environmental factors.

This thesis combines high-quality surveys, GIS and statistical Poisson regression to investigate the relationship between the incidence of CD and diarrhoea and environmental control factors. High-quality surveys play an important role in understanding the effects of environmental factors on disease by providing detailed data collected at the local level. GIS is used for spatial analysis of environmental factors and allows us to track how these factors change at local and regional levels. These technologies are important for understanding how diseases interact with environmental conditions. The integration of these methods can allow a more accurate assessment of the effects of environmental factors on the spread of diseases.

There still exists uncertainty about how specific environmental factors, such as pasture exposure or flooding, contribute to the occurrence of diseases like Crohn's disease in the UK or diarrhoea in sub-Saharan Africa, respectively. The innovations and tools mentioned above have made studying the impact of environmental factors on diseases more accessible and increased the accuracy of results. The use of GIS, high-quality surveys, and Poisson regression can help resolve such uncertainty, particularly in understanding the infection patterns of diseases, for example, CD cases in the UK and diarrhoea cases in Africa, as in this thesis. Intersecting disease cases with environmental data can enable more precise measurement of the strength of association between disease occurrence and environmental factors.

Specifically, this thesis will examine the relationship between environmental factors and (i) the patterns of CD across the UK and (ii) diarrhoea in children under five in two informal settlements in Accra, Ghana — Gbegbeyise (GB) and Madina Zongo (MZ).

The aetiology of CD is complex and its relationship with MAP remains controversial [37]. Although many studies suggest that MAP is significantly associated with CD [10], there is no definitive evidence that MAP is causal. In this thesis, the relationship between CD and environmental factors will be examined and, in particular, the risk of CD will be evaluated as a function of environmental proxies for MAP, and new data will be presented to investigate this relationship.

The reasons for the high frequency of diarrhoeal cases in Africa vary from region to region [38, 39]. There is no uncertainty as to whether deficiencies in water, sanitation and hygiene (WASH) practices increase diarrhoeal rates in the region. Poor sanitation conditions, drinking water pollution and inadequate hygiene practices are known to be effective in promoting the spread of diarrhoeal cases, and comprehensive data and analysis can confirm this relationship. In this thesis, the effect of WASH interventions on diarrhoea will be analysed in relation to environmental factors, and how they affect the incidence of this disease will be explored.

Based on the above, the tools of spatial data, location-specific survey, GIS, and statistical regression are used to test the following hypotheses:

i. The relative risk for CD is positively associated with the proportion of pasture land in hydrological basins, with CD occurrence higher in areas with greater proportions of pasture land. This hypothesis is based on the possible association between CD in humans and MAP, which is prevalent in grazing animals with JD and in the environment where such animals graze and considering the pathogen's possible transport in surface water via rainfall and rivers which may increase human exposure.
ii. In African informal settlements (GB and MZ), the prevalence of diarrhoea in children under five years of age is significantly influenced by environmental factors such as antecedent rainfall and temperature, and particularly that diarrhoea cases are more common in areas prone to flooding. This hypothesis is based on initial exploration of the data for GB and MZ, where rainfall and temperature were found to be associated with diarrhoeal disease transmission.
iii. A WASH intervention, amounting to an improvement in sanitation infrastructure, in an informal settlement is hypothesised to significantly reduce diarrhoea in children under five years of age. The experimental design of the WASH intervention in Accra, Ghana was undertaken specifically to test this hypothesis.

1.1. Thesis contributions

In this thesis, we investigated multiple aspects of environmental and epidemiological factors influencing inflammatory bowel disease (IBD) in the UK and diarrhoeal disease in children under five in Accra, Ghana. The research spans two distinct contexts: large-scale, UK-wide study on IBD (Chapters 3 and 4) and an analysis of diarrhoeal disease dynamics in two low-income informal settlements in Accra, Ghana (Chapters 5 and 6). By integrating spatial epidemiology with statistical modelling techniques, this thesis seeks to fill critical gaps in knowledge, providing new insights into the complex interactions between disease and environmental conditions.

The thesis contributes to knowledge by (i) providing a novel UK-wide spatial analysis of CD and UC cases, utilizing a large-scale survey dataset to assess geographical patterns, (ii) developing a comprehensive framework that incorporates environmental variables like land use, climate and hydrology, to better understand their influence on IBD risk, (iii) comparing the geographical distribution and relative risk of CD and UC across various regions in the UK, offering a broader perspective on the spatial epidemiology of IBD to advice on health policy for IBD, (iv) applying Poisson regression modelling to quantify the relationship between IBD risk and environmental and demographic factors, (v) calculating age- and sex-standardized morbidity rates (ASMRs) to identify and highlight demographic disparities in the prevalence of IBD, (vi) exploring the role of environmental parameters, particularly meteorological factors, in the transmission of diarrhoeal diseases in two informal settlements in Accra, Ghana, (vii) evaluating the impact of a WASH intervention in reducing the incidence of diarrhoeal disease in these communities, and (viii) demonstrating the value of combining spatial, statistical and epidemiological methods to create a robust framework for public health risk assessments.

This IBD study contributes to our understanding of IBD prevalence in the UK and provides new evidence on the relationship between CD incidence and biogeography. Likewise, the research conducted in the GB and MZ settlements underscores the significant role that meteorological factors, particularly rainfall, and proximity to flood-prone areas play in increasing diarrhoeal disease incidence among children. This research not only enhances our understanding of disease-environment interactions but also provides valuable evidence to inform targeted public health interventions in vulnerable communities.

1.2. Thesis structure

This thesis consists of eight chapters:

Firstly, this Chapter (1) provides a general introduction followed by a literature review in Chapter 2 to support the two studies undertaken in this thesis: the UK-wide IBD study and diarrhoeal disease in children under five in Africa.

In Chapter 3, the geographical distribution and relative risk of CD and UC across the UK were analysed using primary data from a large-scale national survey. The survey was used to collect comprehensive information from several thousand participants, allowing us to investigate how these diseases are spread geographically and how different demographic factors, such as age and sex, influence the prevalence of CD and UC. The chapter provides an in-depth analysis of the spatial patterns of IBD, highlighting areas of high relative risk and the potential for future research.

Chapter 4 focuses on the impact of environmental factors on the risk of CD in the UK. Variables including pasture area, urban areas, rainfall, temperature, river width, and population (used as an offset) which were examined for their association with CD prevalence. Using data from our UK-wide survey, we used a Poisson regression model to investigate possible associations between CD risk and environmental factors, particularly pasture area. This chapter provides a comprehensive and novel approach to understanding how environmental variables contribute to IBD risk in the UK and provides the basis for further research on the role of environmental exposures in the development of IBD.

In Chapter 5, the environmental determinants of diarrhoeal disease in children under five in two low-income informal settlements in Accra, Ghana were examined. The focus of this chapter is on how the effects of lagged rainfall and temperature, and the proximity of HHs to flood-prone areas, contribute to the incidence of childhood diarrhoeal diseases. We analysed the environmental covariates mentioned above using data from children with diarrhoea collected over two years in two separate Poisson regression models. By analysing the relationship between environmental variables and disease occurrence, we aimed to shed light on how climate and environment affect public health outcomes in WASH-limited settings.

Chapter 6 assesses the impact of the WASH intervention on the incidence of diarrhoeal diseases in the GB settlement in Accra, Ghana. This chapter investigates the effectiveness of public health interventions aimed at reducing diarrhoeal morbidity through improved sanitation practices and water management systems using statistical analysis techniques. Additionally, ASMR analysis was used to demonstrate the reduction in the number of children with diarrhoea after the intervention. This chapter examines the role of WASH interventions in reducing diarrhoeal cases, making an important contribution to understanding the impact of such public health strategies in low-resource settlements.

A general discussion will be presented in Chapter 7, and an overall conclusion will be presented in Chapter 8.

1.3. Status of publications

Chapter 3 was published in *PLOS ONE* on 28 August 2025 with the title “A spatially explicit survey of inflammatory bowel disease in the UK”. The article is open access and accessible online at doi.org/10.1371/journal.pone.0329317.

Chapter 4 was submitted to *BMC Public Health* for publication on 4 February 2025 with the title "Influence of Landscape on the Distribution of Inflammatory Bowel Disease in England and Wales". Submission ID is **27f04d22-5e59-42ee-88fe-964703ba1856**.

Chapter 5 was submitted to *Environmental Research* for publication on 30 June 2025 with the title "Diarrhoea in Children Under 5 Years in Two Informal Settlements in Accra, Ghana: The Impact of Antecedent Rainfall and Flooding" and accepted for publication on 11 November 2025 . Article reference number is **YENRS_123455.**

Chapter 6 was submitted to *BMC Public Health* for publication on 1 July 2025 with the title "The Impact of a WASH intervention on Diarrhoea in Children Under 5 Years in Accra, Ghana". Submission ID is **6b71daf3-95e1-41f6-bb8b-c602a21a84d9**.

Chapter 2

2. Literature review

2.1. Relationship of diseases with environmental factors

The relationship between human health and environmental factors has long been acknowledged as a critical focus of public health research. Health is not solely determined by genetic or biological factors but is also significantly influenced by the environment. The environment can shape the patterns of disease occurrence and distribution across populations [40]. In particular, it is increasingly accepted that environmental factors play a profound role in the aetiology and burden of both communicable and non-communicable diseases [41, 42]. In this context, environmental changes can directly or indirectly alter human exposure to health risks and affect health outcomes. Environmental factors can be considered as one of the main determinants of health and, thus, contribute to the morbidity and mortality rate [43–46]. Understanding the effects of environmental factors on public health and the nature of these interactions is critical both to implementing effective interventions and to reducing the adverse health consequences of environmental changes.

Environmental factors can play a pivotal role in shaping human health outcomes. Air quality, water availability and quality, soil conditions, temperature, and the built environment can collectively or individually influence the occurrence and progression of numerous health problems. Exposure to poor air quality, for example, negatively impacts lung-related illnesses like asthma [47], chronic obstructive pulmonary disease (COPD) [48, 49] and lung cancer [50]. Contaminated water sources are major contributors to GI infections, including typhoid fever [51, 52] and diarrhoeal diseases [53] such as cholera [54]. Inadequate sanitation and poor waste management further exacerbate infection risks, especially in low- and middle-income countries [55–57]. Additionally, soil contamination is linked to malnutrition [58], foodborne illnesses [59] and chemical exposures [60]. The intricate link between environmental exposures and health outcomes highlights the need for integrated and preventive approaches to public health.

International organizations such as the World Health Organization (WHO) and the Intergovernmental Panel on Climate Change (IPCC) have documented extensively the health impacts of environmental factors. According to the World Health Organization, environmental risks — including unsafe water, poor sanitation and inadequate hygiene — contribute significantly to the global burden of disease. For example, an estimated 1.5 million deaths per year are attributed to diarrhoeal diseases, many of which are preventable [61]. However, the organization emphasizes that effective environmental interventions can prevent such diseases and alleviate the burden on healthcare systems. These solutions can also significantly reduce treatment costs, which are becoming an increasingly important problem in many countries [62].

The IPCC, in its sixth assessment reports on climate change, emphasizes that rising global temperatures, extreme weather events and shifting precipitation patterns pose serious threats to human health. It also warns that climate change will exacerbate existing health disparities by increasing the frequency of heat-related illnesses and vector-borne diseases. Furthermore, the report identifies climate change as a multiplier of health risks, disproportionately affecting populations in low-income regions where adaptive capacity is limited [63].

2.2. Relationship of chronic and acute diseases with environmental factors

Chronic and acute diseases can respond differently to environmental stressors, depending on the nature, duration and intensity of exposure. Chronic diseases often result from long-term exposure to environmental risks. It has been reported that chronic diseases like CD [64, 65], cardiovascular diseases [66] and some types of cancer [67, 68] may develop due to long-term, cumulative environmental exposures. Air pollution [69], long-term contact with chemical pollutants [66, 70] and dietary patterns affected by environmental degradation [71] may play an important role in the progression of these conditions. For example, research suggests that urbanization and industrialization have led to an increase in autoimmune disorders [72, 73]. Furthermore, chronic exposure to environmental toxins, namely heavy metals in water sources [74, 75] or pesticides in agriculture [76, 77], has been associated with inflammatory responses that contribute to the onset of chronic illnesses.

Conversely, acute diseases emerge as an immediate response to short-term environmental changes. Extreme weather events, sudden temperature shifts and contamination of food or water supplies are major drivers of acute conditions like diarrhoeal diseases, heatstroke and respiratory infections. For example, studies have shown that increased diarrhoeal disease cases occur following heavy rainfall and flooding events [78]. In particular, heavy rainfall events following dry antecedent conditions have been associated with increased diarrhoeal disease incidence in urban areas [79]. Similarly, spikes in air pollution levels can trigger acute asthma attacks and other respiratory complications [80]. These short-term environmental hazards may also increase the risk of long-term complications, especially in vulnerable groups like children and the elderly.

2.3. CD and its relationship with environmental factors

2.3.1. Aetiology of CD and the role of environmental factors

IBD in humans encompasses a group of chronic inflammatory disorders of the gastrointestinal (GI) tract, primarily including Crohn's disease (CD), ulcerative colitis (UC), microscopic colitis (MC) and indeterminate colitis (IC) [81–84]. CD and UC represent the most prevalent subtypes of IBD. CD can affect any part of the GI tract, with the terminal ileum and colon being the most common [82]. UC, by contrast, is characterised by continuous mucosal inflammation limited to the colon [85, 86]. CD patients experience symptoms like diarrhoea, abdominal pain and weight loss. While its exact aetiology remains unclear, CD is widely accepted to result from a complex interplay between genetic susceptibility, immune system dysregulation, the gut microbiome and environmental exposures.

UC is another major subtype of IBD, distinguished by continuous inflammation confined to the mucosal layer of the colon. The disease typically begins in the rectum and may extend proximally in a continuous manner [87]. Common clinical manifestations include bloody diarrhoea [88, 89], rectal urgency [89, 90] and abdominal pain [87, 89]. Unlike CD, UC is not characterised by transmural inflammation or granuloma formation [91]. Although its aetiology also involves genetic and environmental factors, which will be discussed later, studies have not demonstrated a strong association between UC and MAP. This absence of association supports the notion that MAP-related mechanisms may be specific to CD, reinforcing the value of UC as a comparative condition in exploring disease-specific environmental triggers.

Several studies have highlighted a potential association between CD and MAP, suggesting that MAP may play a role in its pathogenesis. Bull *et al*. (2003) [92] reported that MAP DNA was detected in 92% of patients with CD compared to only 26% of non-IBD controls, indicating a statistically significant association. In a review of 60 studies, Naser *et al*. (2004) [93] investigated the presence of MAP in the blood and faeces of CD patients and found MAP in 50% of the peripheral blood samples. However, they reported that it was only detected in the faeces of UC patients. These findings support the notion that MAP may be a potential cause of CD. Moreover, Feller *et al*. (2007) [10] conducted a meta-analysis and found a significantly higher prevalence of MAP in CD patients than in individuals with UC or non-IBD controls, with PCR-based studies showing a pooled odds ratio of 7.01 against healthy individuals and 4.13 against UC patients. These findings suggest that MAP is more specifically associated with CD than with UC, reinforcing the hypothesis that MAP may contribute to CD pathogenesis in genetically susceptible individuals.

A range of environmental factors have been implicated in the onset and progression of CD. These include diet, antibiotic exposure, smoking, hygiene and air quality. Poor dietary habits (e.g., Western-style diet) are considered important risk factors for the development of CD [94]. Similarly, CD has been reported to increase in incidence in previously low-risk countries such as Japan and India with the adoption of a western lifestyle [95]. Specific dietary patterns characterized by meats, fatty foods and desserts, are positively associated with CD [96]. Lo *et al*. (2020) [97] reported that individuals consuming diets with high inflammatory potential have an increased risk of developing CD, but not UC. They also highlighted that the inflammatory load of the diet contributes to CD pathogenesis with both a dynamic and cumulative effect. Another study showed that high consumption of red and processed meat, processed foods and refined sugars, and inadequate intake of vegetables, fruits and fiber-rich foods are associated with the incidence and/or progression of CD [98].

Antibiotic exposure is linked to an increased risk of CD development [99, 100]. Antibiotic use during the first year of life is associated with a moderately increased risk of CD, but the absolute risk is very low [101]. Furthermore, 71% of CD cases had antibiotic use within 2–5 years before diagnosis, compared with 58% of controls [102]. Faye *et al*. (2023) [103] reported that exposure was associated with an increased risk for CD, particularly in individuals aged 40 years and older. Exposure to antibiotics has been associated with an increased risk of newly diagnosed CD, particularly in children [104]. Moreover, repeated antibiotic exposure has been identified as a potential risk factor for the development of paediatric CD, with a more pronounced effect observed in boys [105]. Similarly, several meta-analyses and large cohort studies have demonstrated a connection between antibiotic use and an increased risk of developing UC [65, 106, 107]. This risk seems to be dose-dependent, with a higher cumulative use of antibiotics being linked to an elevated likelihood of developing UC [106]. Some studies have indicated that this association is stronger for certain classes of antibiotics, particularly those that have a broad impact on the gut microbiome, such as fluoroquinolones [106, 107]

Smoking has been identified as an environmental factor that not only increases the risk of developing the disease but may also worsen its progression. Estimates show that smoking is prevalent among roughly 50% of CD patients in Europe [108]. It has been reported that those with CD had a higher rate of having a smoking habit before the disease than the control group, and this association was stronger than in those who continued to smoke [109]. Mahid *et al*. (2006) [110] reported that smoking doubles the risk of CD compared to controls. Furthermore, it is known that there is a possibility of disease recurrence after surgical intervention and a poor response to medical treatment [111]. Smokers with CD experience more frequent flares, increased need for steroids and immunosuppressants, and a lower quality of life. The risk of developing CD is higher in smokers compared to non-smokers, and smoking cessation can improve the disease course [112–114]. In addition to the effects of smoking shown in studies, it has also been stated that it does not increase the risk of CD in ethnic groups other than non-Jewish whites [115]. On the other side, studies in the literature have shown that smoking does not cause UC and, in fact, current smoking is consistently associated with a decreased risk of developing UC [116–

118]. However, former smokers are at higher risk than those who have never smoked [118]. The relationship between smoking and UC is complex and distinct from its effect on CD.

There is a complex relationship between CD and hygiene. Various factors associated with poor environmental hygiene have been found to be inversely related to the risk of developing CD [119]. For example, frequent tooth brushing may have a protective effect against the development of CD [120, 121]. Conversely, behaviours like thumb sucking and/or nail biting during early childhood, particularly at school enrolment or during coming-of-age ceremonies, are linked to an increased risk of CD [122]. However, certain hygiene-related factors do not show a significant association with the risk of CD [123] and in some cases, they may even contribute to an increased likelihood of developing IBD, particularly CD [64]. According to Lashner and Loftus (2006), multiple early childhood exposures to enteric pathogens may protect against the later development of CD, whereas individuals raised in more sanitary environments are at a higher risk of developing CD in adulthood [124]. Additionally, studies suggest that better living conditions during childhood are correlated with an elevated risk of CD later in life [125].

The relationship between UC and hygiene remains inconclusive, with studies presenting mixed findings. Some evidence suggests that early-life respiratory and GI infections may protect against UC, supporting the hypothesis that reduced microbial exposure increases susceptibility [125, 126]. Similarly, limited access to toilets and hot water has been associated with higher UC risk in certain populations [119, 126]. However, other studies found no strong link between hygiene indicators and UC, emphasizing instead the role of established risk factors such as family history, smoking, and appendectomy [123, 127]. Interestingly, certain markers of better hygiene—such as having a private bed or improved toilet facilities—have also been linked to lower UC risk, suggesting context-specific effects [127, 128]. In terms of oral hygiene, findings are also mixed: while poor oral health has been associated with reduced IBD risk, conditions like periodontitis may elevate UC risk, pointing to a complex interplay [121, 129]

Air pollution has been implicated as an environmental risk factor for CD, although the relationship remains complex and inconsistent across studies. Ding *et al*. (2022) [69] reported that exposure to airborne pollutants such as PM2.5, ozone (O_3) and carbon monoxide (CO) significantly increases the risk of CD, particularly during warmer seasons.

Similarly, exposure to nitrogen dioxide (NO_2) has been associated with a higher risk of developing CD among middle-aged individuals [130]. However, findings from Opstelten *et al*. (2016) [131] did not support a consistent link between air pollution and CD. Water pollution may also be a potential environmental factor that increases the risk of CD [132]. Several studies have reported a positive association between air pollution and UC. Long-term exposure to nitrogen oxides (NOx, NO_2) and fine particulate matter (PM2.5) has been linked to a 19–26% increased risk of developing UC compared to lower exposure levels, with no similar association observed for CD [133]. Additionally, short-term increases in PM2.5 levels have been associated with a rise in outpatient visits for UC, particularly among younger individuals [134]. In regions with high pollution, exposure to PM2.5 has also been linked to more severe cases of UC and irritable bowel syndrome, suggesting that air pollution may influence both disease onset and severity [135].

Several studies have explored the link between CD and water-related exposures, but findings remain inconclusive. In Belgium, patients with CD were found to consume more well water and less tap water than controls, suggesting a potential risk associated with untreated water sources [136]. Clusters of CD have also been observed in areas where untreated water—possibly contaminated by agricultural runoff or animal waste—is used, with MAP suspected as a contributing factor, although direct evidence remains inconsistent [137]. Contrary to this, a case-control study found no association between CD and MAP-contaminated water or dairy products [138]. Additionally, high iron levels in drinking water have been linked to an increased risk of CD, UC and other IBD types, possibly due to the role of iron in promoting oxidative stress and bacterial growth [139]. However, other studies, including one from Eastern Croatia, found no significant relationship between water quality and CD activity [140], while research from Northern France suggested a possible link between CD incidence and heavy metal exposure in agricultural soils [141].

Numerous studies have explored the potential association between milk consumption and the onset of CD and UC. Evidence suggests that milk consumption may reduce the risk of CD, with certain serum metabolites, such as isoleucine and valine, potentially influencing disease onset [142]. However, while some studies have reported a protective effect, a definitive dose-response relationship between CD risk and milk intake has not been established [143]. On the other hand, it has been reported that milk could serve as a factor in the aetiology of CD and potentially worsen the condition by penetrating the small intestine, which is more susceptible in CD patients [144]. Sigala-Robles *et al*. (2022) [145] reported that fermented milk containing specific lactic acid bacteria alleviated IBD symptoms. In relation to UC, early sensitivity to cow's milk may be associated with a higher risk of disease development [146]. Although frequent dairy consumption could offer protective benefits against both CD and UC [147], there remains insufficient evidence to firmly establish a link between the incidence of CD and MAP in milk [148]. Nonetheless, contamination of raw milk with MAP has been documented in certain regions, raising concerns about its potential role in the transmission of the pathogen to humans [149, 150]. While no clear evidence currently links milk and dairy products to the incidence or progression of inflammatory bowel diseases, they are commonly excluded from the diets of IBD patients, which may influence clinical outcomes [151]. Additionally, Ayele *et al*. (2005) [152] investigated MAP contamination in pasteurized milk in the Czech Republic. 1.6% of commercially pasteurized milk and 2% of locally pasteurized milk tested positive for MAP. Higher contamination rates were found in raw milk from infected herds. The findings suggest that pasteurized milk may be a route of human exposure to this pathogen.

2.3.2. Comparison of the known and hypothesised mechanisms of the effects of environmental factors on CD

Understanding how environmental factors contribute to the development of CD requires careful examination of both well-established and emerging hypotheses regarding their underlying biological mechanisms. Among the most well-documented mechanisms is the impact of smoking, which has been shown to exacerbate CD through impairment of the intestinal barrier [153], altered immune response [154] and changes in the gut microbiome [155]. Similarly, early-life antibiotic use is associated with increased CD risk due to its long-lasting effects on microbial diversity [156] and immune system development [157]. Dietary factors - for example, high intake of ultra-processed foods and low fiber consumption - are also associated with CD [98] and alter microbial composition [158], contributing to CD onset in individuals [159].

Several hypothesised mechanisms have gained attention in recent years but remain under investigation. One notable example is the potential role of environmental mycobacteria, *Mycobacterium avium* subspecies *paratuberculosis* (MAP). MAP is the causative agent of Johne's disease (JD) in animals [160, 161] and it is a chronic and progressive intestinal disease [162] that can affect a wide range of animal species, including primates [163–165]. Clinically and sub-clinically infected animals can shed significant amounts of MAP in their faeces onto pastures. Therefore, MAP is likely to be present in pastures and livestock environments [166]. There is significant evidence linking MAP presence in human tissues to CD [10, 92], but not with UC although more research is needed to establish this connection conclusively.

Other hypothesised pathways include the effects of urbanization and climatic variability, which may influence exposure to environmental microbes or modify local ecological conditions relevant to disease risk. A study by Blanchard *et al*. (2001) [167] on IBD aimed to determine the differences in IBD incidence and the sociodemographic factors associated with these differences. The incidence of CD was found to be higher in urban areas compared to rural areas. To evaluate this relationship, the Poisson regression model was used in multivariate analyses and adjusted incidence rate ratios were calculated. It was emphasized in the study that some environmental exposures may cause the development of IBD, but an additional factor may be required for the emergence of CD.

2.3.3. Association of CD with factors such as urbanization, climate and geography

In a retrospective study conducted by Carpio *et al*. (2015) [168], the effect of residence (urban/rural vs. coastal/inland) on the prevalence, phenotype and clinical course of CD was investigated. Data were analysed using logistic regression with statistical tests. According to the findings, living in urban areas was determined as a significant risk factor for CD. It was stated that the ecological design used in the study was limited in terms of making inferences at the individual level, but that it could be useful for investigating environmental factors.

Zeng and Anderson (1996) [169] observed that CD symptoms reached their highest levels in the fall and winter months, while symptoms decreased significantly in the summer months. This finding suggests that the disease is affected by seasonal changes. On the other hand, Aratari *et al*. (2006) [170] reported that the onset of CD symptoms occurred more frequently during the spring and summer months. The authors suggested that environmental factors—such as seasonal infections or immune changes—may potentially trigger the clinical onset of CD. Although this does not establish causality, it highlights the possibility that symptom onset may be influenced by seasonal patterns.

Rivers are another potential environmental factor that may be effective in the spread of CD. Rainfall on pastures contaminated with MAP is likely to wash this pathogen into surface waters and rivers [21]. This makes it possible for humans to be exposed to MAP via aerosols [171]. Pickup *et al*. (2005) [16] demonstrated in their study conducted in South Wales that runoff from MAP-contaminated hill pastures can carry the pathogen into the River Taff. Of the water samples collected over one year, 32.3% tested positive for IS900 by PCR. Similarly, the epidemiological analysis conducted in this study revealed an increased incidence of CD in areas adjacent to the river and a spatial pattern influenced by the prevailing wind direction. In addition to the molecular findings, a linear regression analysis was conducted to assess the relationships between MAP presence and environmental variables, revealing a large correlation between river flow and elevation, both of which were significantly associated with MAP detection [16].

In a comparative study on the River Tywi in South Wales, Pickup *et al*. (2006) [17] found that 68.8% of water samples tested positive for MAP. The pathogen, originating from contaminated pastures, was associated with suspended solids in the river water, which were partially removed during treatment. MAP was also found in domestic cold-water tanks, indicating potential human exposure. Rainfall was significantly linked to the presence of MAP, especially rainfall 5–7 days before sampling. Higher river flow and height were also associated with positive MAP tests, suggesting runoff plays a role in pathogen transport. Analysis of variance (ANOVA) was used to assess the relationship between MAP presence and river flow, height and rainfall, and linear discriminant analysis was employed to predict the likelihood of MAP detection based on environmental variables [17].

2.3.4. Summary of previous studies and findings

In summary, a comprehensive review of the literature highlights the significant role of environmental factors in the onset and progression of CD. Environmental factors such as diet, antibiotic use, smoking and hygiene are well-established risk factors for CD. Western-style diets, early-life antibiotic exposure and smoking are strongly associated with an increased risk of developing CD. Hygiene practices during childhood also play a role, with behaviours like thumb sucking or nail biting potentially increasing the risk. Air pollution and water contamination, particularly high iron levels in drinking water, have also been implicated in CD development. Several hypotheses suggest other environmental factors may contribute to CD. These include microbial exposure, particularly changes in gut microbiota diversity and composition, which has been linked to CD [172–175]. Additionally, urbanization, climatic changes, and seasonal environmental factors may influence disease onset and progression [167–170]. While these mechanisms are still under investigation, they highlight the complex role of environmental factors in CD development.

2.4. Diarrhoea and its relationship with environmental factors

2.4.1. Aetiology of diarrhoea and the role of environmental factors

Considering the impact of environmental factors on health, diarrhoea stands out as an acute disease with significant public health implications. It is one of the leading causes of morbidity and mortality among children under five years old [176, 177], particularly in low-income countries [177, 178]. The aetiology of diarrhoea is multifactorial, with infectious agents like *E. coli, Vibrio cholerae, Shigella spp.,* rotavirus, norovirus and adenovirus being the most common pathogens [176–178]. Diarrhoea contributes to dehydration [179], electrolyte imbalance [180], dysbiosis [181], malnutrition [182, 183] and impaired physical development [182, 183]. Environmental factors play a central role in both the onset and persistence of diarrhoeal diseases. Poor sanitation, contaminated water sources and inadequate hygiene practices are key drivers of transmission [184, 185]. Additionally, climatic conditions such as heavy rainfall [186] and temperature [19] can lead to an increase in diarrhoeal cases.

2.4.2. Comparison of the known and hypothesised mechanisms of the effects of environmental factors on diarrhoea

The relationship between diarrhoeal diseases and environmental factors is supported by both known mechanisms and some hypotheses. Known mechanisms include the faecal-oral transmission of pathogens [187, 188] and inadequate sanitation, unsafe drinking water and poor hygiene practices, often summarized as WASH deficiencies [184, 185, 189–191]. These factors also provide direct contact with microorganisms responsible for diarrhoea, especially in areas where open defecation or unsafe waste disposal is common. In addition, contaminated floodwater [192, 193] and stagnant surface water [194, 195] facilitate the spread of pathogens.

Several hypothesised mechanisms have been proposed to explain how environmental factors may influence diarrhoeal disease transmission. For example, the impact of temperature change on diarrhoeal diseases has been demonstrated in previous studies [196–198]. On the other hand, some studies have reported that lower temperatures or dry conditions can enhance the activity of pathogens, subsequently leading to an increase in the number of cases [199, 200]. Similarly, previous studies have indicated that heavy rainfall contributes to the occurrence of waterborne illnesses by elevating microbial loads in surface water sources and by creating environmental conditions that support the survival and transmission of pathogenic microorganisms [21, 22, 201]. However, some studies have highlighted the association of reduced rainfall with increased diarrhoeal cases [14]. In particular, inadequate rainfall during the dry season, together with higher maximum temperatures, has been reported to contribute to increased diarrhoeal cases in children under three in Sub-Saharan Africa [38]. Another study found that low rainfall was associated with a 4% increase in diarrhoeal cases in children under five, suggesting that water scarcity and poor hygiene practices may be the main factors driving disease outcomes [202]. These mechanisms are not yet fully understood and often show contradictory patterns across different settlements. Therefore, further research is needed to clarify these pathways, particularly in vulnerable urban areas where infrastructure is weak and environmental exposures are highly variable.

2.4.3. Association of diarrhoea with environmental factors (rainfall, temperature and flooding)

An analysis of 33,927 reported diarrhoeal cases in Esmeraldas Province, Ecuador (2013–2014) examined the potential impact of climate change on disease patterns. Using mixed-effects Poisson regression models, the study explored the relationship between heavy rainfall events, antecedent rainfall conditions and diarrhoeal incidence. No significant associations were found in rural areas. However, in urban settings, dry antecedent conditions followed by heavy rainfall events were linked to a notable rise in cases. This pattern was attributed to a flushing effect, where accumulated faecal contamination during dry spells is mobilized by sudden heavy rains [203].

Six serial case-control studies conducted in Ecuador explored how rainfall conditions affect the relationship between diarrhoeal disease risk and unimproved water and sanitation access. Using HH-level logistic regression models with robust standard errors, the analysis found that both unimproved water sources and unimproved sanitation were significantly associated with increased odds of diarrhoea. The risk associated with unimproved water was highest following periods of heavy rainfall, while the risk related to unimproved sanitation peaked after minimal rainfall. These findings suggest that rainfall can modify the impact of environmental exposures, emphasizing the need for integrated interventions that account for local climate variability [204].

Bandyopadhyay *et al*. (2012) [38] showed that rainfall shortages during the dry season increased diarrhoea prevalence among children under the age of three in 14 Sub-Saharan African countries. In contrast, high rainfall reduced diarrhoea prevalence by approximately 3%. A rise in maximum temperature raised the risk of diarrhoea, while a decrease in minimum temperature lowered it. The study employed fixed effects, random effects and ordinary least squares (OLS) regression models, incorporating climate zones as well as socio-economic and environmental variables. The findings highlight that water scarcity strongly limits child health through its impact on hygiene practices and emphasizes the importance of infrastructure and early warning systems in the face of climate variability [14].

The association between precipitation and diarrhoeal mortality was found to vary across different climate zones. An analysis of data from 29 locations in eight middle-income countries revealed that in tropical climates, extreme rainfall increased diarrhoeal mortality by 17.8%. In temperate and arid climates, both extremely dry and wet conditions were linked to higher mortality. For example, in extremely dry conditions, the risk rose by 3.8% in temperate regions and by 5.5% in arid zones. The study employed a two-stage statistical approach, starting with conditional Poisson regression models for each location, followed by meta-analysis to pool coefficients by climate zone. These results emphasize the importance of considering regional climatic differences when projecting global diarrhoeal mortality related to precipitation [205].

Horn *et al*. [206] analysed weekly data from Mozambique (1997–2014) to examine the association between precipitation and diarrhoeal disease. Using an over-dispersed Poisson regression with a four-week unconstrained distributed lag model, they found that one additional wet day per week increased diarrhoeal cases, particularly in the southern region (up to 2.09%). The models were adjusted for time, temperature and spatial variation. Secondary analysis showed a positive link with temperature as well. The study highlights the need for climate-informed early warning systems to reduce disease burden.

The impact of heavy rainfall events on hospital admissions due to intestinal infectious diseases was investigated in Ho Chi Minh City, Vietnam. Using a Poisson regression model, the short-term effects of each heavy rainfall event on intestinal infectious disease, including changes in level and trend, were assessed over a 30-day period. Meteorological variables such as temperature and humidity were controlled using natural cubic splines with three degrees of freedom, and day-of-week effects were modelled with dummy variables. The study found significant increases in intestinal infectious diseases approximately 4–6 days after heavy rainfall events, with a rise of around 13%. However, the effects varied across different events. These findings have important public health implications, suggesting that climate change-induced increases in heavy rainfall may elevate the risk of intestinal infectious diseases [207].

It has been reported in the literature that the frequency of diarrhoeal diseases changes with changes in temperature. Philipsborn *et al*. (2016) [198] conducted a systematic literature review to investigate the relationship between the incidence of diarrhoeagenic virulent *Escherichia coli* and temperature. They reviewed studies with at least one year of data on the monthly incidence of this pathogen and analysed seasonal disease patterns from 28 studies. Using monthly weather data from 18 studies, they applied univariate Poisson models to individual studies and performed a meta-analysis using a generalized estimating equation on the combined dataset. The analysis revealed an 8% increase in the incidence of diarrhoeagenic *E. coli* for each 1°C rise in mean monthly temperature.

A systematic review and meta-analysis was conducted to assess the relationship between ambient temperature and the incidence of infectious diarrhoea. The aim was to quantify the effect of temperature on the risk of infectious diarrhoea through a meta-analysis of 27 studies using a random-effects model. The results revealed a significant increase in the risk of infectious diarrhoea as temperatures rose. The study suggests a close link between temperature and the incidence of infectious diarrhoea, emphasizing the need for preventive measures in response to climate change [208].

The relationship between weather and enteric pathogens was examined, focusing on young children in rural Bangladesh. Higher temperatures were found to be linked to an increased prevalence of diarrhoea and several pathogens, including Shiga toxin-producing *E. coli* (STEC) and *Cryptosporidium*. Additionally, above-median weekly precipitation (>13 mm) was associated with a 29% higher rate of diarrhoea and a greater prevalence of multiple enteric pathogens [209].

There is well established evidence that floods significantly contribute to the spread of waterborne infectious diseases such as diarrhoea. The study by Birhan *et al*. (2023) [210] assessed the prevalence of diarrhoeal disease and its predictors among children under five in flood-prone areas of the South Gondar zone in Northwest Ethiopia. Descriptive statistics were used to describe the study population, followed by bivariate binary logistic regression analysis to identify associations between variables. They found a 29% prevalence rate of diarrhoea among children under five.

The main factors contributing to the spread of diarrhoea among children aged 1–6 years in flood-prone areas were investigated. Logistic regression analysis was used to explore the determinants of diarrhoea. Key factors identified included inadequate water and sanitation conditions and the consumption of contaminated water. These findings emphasize the need to improve water, sanitation, and hygiene conditions in regions frequently affected by floods to protect children's health and reduce the spread of diarrhoea [211].

Yazdi *et al*. (2024) [79] aimed to evaluate the association between floods and infectious diarrhoea through a systematic review and meta-analysis. They used the inverse variance method to pool adjusted relative risks (RR) and prioritised adjusted estimates to reduce bias. Heterogeneity across studies was assessed using the I^2 statistic, which guided the selection between fixed and random effects models. Meta-regression was performed in cases of moderate to high heterogeneity. Their findings highlighted a significant increase in the risk of diarrhoea following floods, particularly for bacterial and parasitic infections, and the need for targeted public health interventions in flood-prone areas.

The impact of flooding risks on diarrhoea prevalence among children under 5 in flood-prone areas of Bangladesh was assessed using a multilevel random intercept model and a linear probability model. The analysis focused on how environmental vulnerability interacts with sanitation conditions to influence child health outcomes. Results indicated that unimproved sanitation in flood-prone areas was significantly associated with a higher prevalence of diarrhoea. This suggests that flooding not only disrupts living conditions, but also exacerbates existing sanitation challenges, increasing exposure to faecal contamination. The findings underscore the importance of improving sanitation infrastructure in vulnerable regions to mitigate the health risks associated with recurrent flooding [212].

2.4.4. Impact of WASH interventions on diarrhoea cases

WASH practices are crucial in reducing diarrhoea incidence and lack of clean water, improper waste management and poor hygiene can increase the risk of diarrhoea, especially in children. Anne-Testard *et al*. (2023) [213] conducted a secondary analysis of a cluster-randomized trial to evaluate how WASH interventions influence child diarrhoea in rural Bangladesh. Using GLMs (modified Poisson regression with robust variance), and generalized additive models (GAM), they assessed the effects of WASH across socioeconomic strata and seasons. The intervention led to significant reductions in diarrhoea, especially among the poorest children and during the monsoon season. The study revealed that WASH minimized existing inequalities in diarrhoea prevalence.

A systematic review and meta-analysis was conducted to evaluate the impact of WASH interventions on childhood diarrhoea in low- and middle-income countries. Using random-effects meta-analyses and meta-regression models, the analysis included 124 studies involving over 200,000 children. Water treatment at the point of use was associated with significant reductions in diarrhoea risk. Sanitation interventions led to a 24% overall risk reduction, with sewer connections producing a greater effect. Additionally, handwashing with soap was found to reduce diarrhoea by 30% [185].

Pickering *et al*. (2019) [214] evaluated the impact of HH-level WASH interventions on child growth and diarrhoea in three randomized controlled trials conducted in Bangladesh, Kenya and Zimbabwe. While improved infant and young child feeding interventions had a significant effect on linear growth, WASH interventions did not lead to improvements in children's length-for-age *z*-scores (LAZ). Notably, a reduction in diarrhoea prevalence (31–40%) was observed only in Bangladesh, where intervention delivery was more intensive. The authors emphasized that frequent contact with behaviour change promoters might be necessary for WASH interventions to be effective in reducing diarrhoea.

A systematic review and meta-analysis was conducted to assess the seasonal variation in the effectiveness of WASH interventions on childhood diarrhoea in low- and middle-income countries. The analysis included both randomized and non-randomized controlled trials, with data stratified by season and examined using meta-regression and random effects models. Results indicated that WASH interventions were more effective during the dry season, reducing diarrhoea risk by 33%, compared to an 18% reduction in the rainy season. This seasonal difference was evident for water and handwashing interventions, but not for sanitation. The findings underscore the importance of considering seasonal dynamics when evaluating WASH strategies, particularly in the context of climate change [215].

Determining the precise relationship between flooding and disease occurrence remains challenging because of the multifaceted pathways through which infections spread. Nevertheless, research findings highlight that inadequate drainage systems and recurrent flooding events are associated with higher levels of illness within affected populations [216]. In addition, when flooding occurs on a large scale, the resulting damage to water distribution and drainage systems can create conditions that amplify the risk of widespread epidemics [217, 218].

Govender et al. (2011) [219] investigated the impact of inadequate sanitation, poor housing, and faecal contamination of runoff water on diarrhoeal disease in low-income settlements of Cape Town, South Africa. They conducted a cross-sectional survey in 336 dwellings (1,080 residents) across four communities and analysed runoff water samples for *Escherichia coli*. The study found that nearly 15% of households disposed of soiled products into storm water drains, contributing to environmental contamination, while 14% of respondents reported diarrhoeal episodes in the preceding two weeks. These findings suggest that poorly managed storm drains, together with substandard sanitation and housing, significantly increase the risk of diarrhoeal disease, highlighting the need for integrated interventions targeting drainage, sanitation, and housing improvements.

In another study, the relationship between open drain flooding and paediatric enteric infections was investigated in a low-income urban neighbourhood in Vellore, India. A cohort of 230 children was followed over two years, with stool samples analysed for enteric pathogens, household flooding and drain exposure recorded, and rainfall data incorporated into multivariable spatial and logistic regression models. Results indicated that infection risk increased with monthly rainfall in areas prone to drain flooding, suggesting that poor drain management may contribute to enteric disease transmission and highlighting that improvements in drain maintenance and cleaning could potentially reduce infection risk [220].

In another systematic review and meta-analysis, studies investigating the association between diarrhoeal disease and sanitation at both household and neighbourhood levels were evaluated. Neighbourhood sanitation was defined to include interventions such as improvements in sewerage and drainage infrastructure, elimination of open defecation, and the absence of exposed wastewater or open drains. The analysis included 21 observational studies and one randomized controlled trial, and pooled effect estimates were calculated using an inverse variance random-effects model. Findings indicated that enhanced neighbourhood sanitation, alongside household sanitation, was associated with reduced diarrhoeal morbidity. These results underscore the potential importance of well-managed local drainage systems and appropriate sanitation infrastructure as components of effective WASH interventions [221].

Opryszko et al. (2010) [222] conducted a randomized controlled trial in rural Afghanistan to evaluate the effectiveness of interventions aimed at reducing diarrhoeal diseases. Thirty-two villages were randomized into five groups: liquid sodium hypochlorite with improved water vessels, hygiene education, improved tubewells, a combination of all three interventions, and a control group. Approximately 400 households were enrolled in each group, and diarrhoea was defined as three or more loose stools in the past 24 hours. Interventions were delivered through household visits, education sessions, and regular follow-up. Results showed that the combined intervention group experienced a significant reduction in diarrhoeal incidence compared with the control group. However, technical and security challenges during well construction highlighted the practical limitations of implementing RCT designs in complex field settings.

Acknowledging the gap between efficacy in randomized controlled trials (RCTs) and effectiveness in real-world settings is central to recent advances in implementation science. Large-scale RCTs in Bangladesh, Kenya, and Zimbabwe tested improved WASH interventions with and without infant feeding support. While intensive household visits in Bangladesh led to measurable reductions in diarrhoea, less frequent visits in Kenya and Zimbabwe showed little impact, despite strong observational associations between child growth and WASH. These findings suggest that the success of interventions under controlled trial conditions may not easily translate into everyday practice, underlining the importance of considering the efficacy–effectiveness gap when evaluating public health strategies [223].

2.4.5. Summary of previous studies and findings

The literature cited above highlights that environmental factors play an important role in the spread of diarrhoea. Climate change, especially changes in temperature and precipitation patterns, can significantly affect the prevalence of diarrhoea. Excessive rainfall increases bacterial and viral loads in water sources, leading to the spread of waterborne diseases. Studies have shown that heavy rainfall following dry periods mobilizes accumulated faecal contamination, leading to an increase in diarrhoeal cases. Conversely, low rainfall levels and inadequate water supply have been associated with higher rates of diarrhoea, particularly in children. Many studies have reported that WASH interventions are highly effective in reducing the spread of diarrhoea, with greater effects observed during the dry season. Furthermore, local climatic conditions shape the risk of diarrhoea, and the combination of infrastructure deficiencies and environmental factors exacerbates public health risks, especially in low-income areas. These studies highlight the role of climate change and environmental factors in diarrhoeal transmission, emphasizing the importance of tailored intervention strategies based on local conditions. Additionally, evidence from randomized trials highlights that while WASH interventions are effective under controlled conditions, their impact in real-world settings depends on contextual factors such as adherence, frequency of engagement, and logistical constraints, illustrating the gap between efficacy and effectiveness.

2.5 Summary

This study attempts to fill a critical gap by examining the chronic disease, Crohn's Disease, and the acute condition, diarrhoea, together through the lens of environmental exposures. The study provides a spatially detailed analysis of Crohn's disease risk across the UK and offers new insights by investigating its potential link to grazing density. In parallel, it investigates how climatic factors such as rainfall and flood exposure affect diarrhoeal disease risk in informal urban settlements in Africa. By incorporating both environmental diversity and WASH-related infrastructure, it highlights how acute disease patterns are shaped by dynamic environmental conditions. With its multi-scale and multi-disease approach, this research, thus, aims to make original contributions to the understanding of environment-health interactions in both chronic and acute contexts.

Chapter 3

3. Geographic Distribution of Inflammatory Bowel Disease in the UK: A spatially explicit survey

Abstract

Inflammatory bowel disease (IBD) is characterized by chronic inflammation in the gastrointestinal (GI) tract, with two main forms: Crohn's disease (CD) and ulcerative colitis (UC). While CD can affect any part of the digestive system, UC predominately affects the colon and rectum. The incidence and prevalence rates of IBD cases are increasing worldwide, including in Europe where the UK has one of the highest incidence and prevalence rates. This study reports on a new survey of IBD cases in the UK, involving 5,452 respondents. The survey was promoted periodically by multiple IBD organizations across the UK over 307 days (01 Dec 2021 to 03 Oct 2022) and collected data on participants' IBD diagnoses and histories. The distributions of CD and UC cases were examined on a grid scale and based on these distributions, relative risk was calculated and mapped in regions where CD and UC cases were recorded. In addition, age- and sex-standardized morbidity rates (ASMRs) for CD and UC were calculated. The results of this UK-wide IBD study reveal an even geographical distribution of reported IBD cases and relative risk across the UK. The ASMR analysis revealed that the reported morbidity

rate for women (in the 20-59 age range) was much higher than the morbidity rate for men in both CD and UC cases. In addition, the CD:UC ratio, which has the advantage of normalizing for possible sampling biases, revealed a cluster of large values (i.e. relative risk of CD) in the North-West England which may require further investigation.

In this chapter, Mehmet Akif Veral was responsible for curating the dataset, performing the statistical analyses, creating maps, methodology, interpreting the results and writing – original draft.

3.1. Introduction

In humans, inflammatory bowel disease (IBD) is a collective term for the conditions of Crohn's Disease (CD), Ulcerative Colitis (UC), Microscopic Colitis (MC) and Indeterminate Colitis (IC) characterized by chronic inflammation of the gastrointestinal (GI) tract [81–84, 224]. CD and UC are the most common types of IBD. CD can affect any part of the GI tract, but typically affects the terminal ileum, colon and perianal area. It can occur in different phenotypic forms such as inflammatory, penetrating and stricturing, or different combinations of these forms [8, 225, 226]. UC, on the other hand, is marked by persistent and widespread inflammation of the colon, starting from the rectum and extending in a variable manner towards the caecum [85, 86, 227].

The incidence and prevalence of IBD are increasing worldwide [228–231]. Current estimates indicate that approximately 3.9 million females and 3 million males are affected by IBD globally [228]. Although the largest numbers of cases worldwide occur in the USA and China [231], the highest incidence rates have been reported in Canada [232, 233], Northern Europe [225, 234] and Australia [235]. Currently, approximately 0.2% of the European population is reported to have IBD [236]. Among European countries, the UK has one of the highest incidence and prevalence rates of IBD [225, 236, 237], including when age-standardized [228]. Studies have shown that the incidence and prevalence of IBD in the UK have risen steadily over the past few decades [238, 239]. Currently, an estimated 540,000 people in the UK live with Crohn’s and Colitis (CCUK, 2024). It was reported that the prevalence of IBD is higher in countries with a high socio-demographic index (SDI) [228, 231], such as the UK, and that the burden of IBD has consistently increased over time [228, 229].

Some epidemiological studies have revealed that environmental factors may play an important role in the pathogenesis of IBD [139, 240–249]. Smoking is an especially important risk factor for CD and increases the risk of disease recurrence and the need for surgical intervention. In addition, it was observed that the disease regresses positively when smoking is stopped [247]. Dietary practices have been related to the course of IBD, while the risk of IBD increases in diets high in saturated fatty acids and processed meats [249], it was observed that the risk of CD decreases in diets rich in fiber [244]. Further, it was found that the use of antibiotics increases the risk of IBD [243] and that the potential for developing CD may be higher when used at an early age [248]. Although environmental factors such as urbanization [240, 245], air [139, 241, 246] and water pollution [242] have been studied as possible infection routes for IBD, little information is available about the aetiology of the disease more generally.

The aim of this study was to provide a comprehensive and geographically explicit analysis of the spatial distribution of IBD cases, specifically CD and UC, across the UK, thereby filling a gap in the current literature by offering spatial insights that can aid in understanding the patterns of IBD prevalence and the possible role of environmental and geographical factors influencing these patterns. To achieve this aim, a new UK-wide IBD survey was conducted. Spatially referenced IBD data were collected through a UK-wide online survey (wp.lancs.ac.uk/ibdsurvey; ethically approved by Lancaster University), which included current postcode, postcode at first diagnosis and previous postcodes (up to 15 years). Further data on the UK's population for use in interpreting the survey data, including age and gender distribution, were obtained from the WorldPop database (hub.worldpop.org). Using the acquired survey data, the spatial distribution of CD and UC cases in the UK at 10 km2 grid resolution was examined, including when normalized to the UK population in those grid squares, and when normalized between diseases (i.e., CD:UC ratio) to mitigate against any possible reporting bias. The age- and sex-standardized morbidity ratios (ASMRs) of CD and UC cases were also analysed

3.2. Materials and Methods

3.2.1. Study site, online survey and data

This study was focused on the whole UK. The study data, including an online survey of people with IBD (see appendix-1), UK population data including age and gender, and the spatial grid boundary definitions are described in following sections. The survey data were collected through an online portal prepared using Qualtrics (Qualtrics, Provo, UT) on a dedicated website (wp.lancs.ac.uk/ibdsurvey).

In national surveys of diseases, such as reported here, it is important to maximize the response rate, while at the same time ensuring an even spatial coverage in terms of the likelihood of response, to avoid unintended reporting bias. Therefore, participants from the UK were recruited through advertisements placed with a wide range of IBD organizations in the UK (CCUK, IBDUK, CICRA, Cure Crohn's Colitis, Crohn's MAP Vaccine, Guts UK and IBD Coach). The survey was promoted on both the official websites and social media accounts of these organizations for 307 days (01 December 2021- 3 October 2022). Repeat requests for participation were sent via CCUK which represents the largest membership group with 47 local user networks covering the UK spatially. Additionally, to reach larger audiences and increase the number of survey participants, a promotional page was created on Facebook to advertise the study.

The specific data collected on each individual participant in the online survey comprised demographics (age, gender, ethnicity and occupation), type of diagnosis (CD, UC, Microscopic Colitis and Indeterminate Colitis), family IBD history, and postcodes from the current address, address at first diagnosis and previous addresses (up to 15 years) to allow spatial localization of the results. Ethnicity and occupation were not included in the present analysis. First diagnosis postcodes of people diagnosed with CD and UC were mapped in ArcGIS. Only the first diagnosis postcodes were included in the statistical analysis reported here, as these are most likely to reflect the geographical context in which the disease first emerged.

Ethical approval for the survey was granted by Lancaster University Faculty of Health and Medicine Ethics Committee (FHMREC20164). All participants under the age of 16 were requested to answer the questions with permission from their guardians. All participants from outside the UK and those submitting missing/incorrect/unlocalized information were excluded from the final dataset

3.2.2. UK population data

Population data were required both to estimate general CD and UC risk at the grid level and to analyse relative disease risks across age and gender groups. For this purpose, we used constrained WorldPop 2020 datasets for the UK, which provide population counts [250] and age–sex structures (0–1 year and 5-year bands up to 80+) at a spatial resolution of 100 m [251], in Geotiff format with WGS84 projection; areas without settlements were marked as 'NoData', based on the Built-Settlement Growth Model (BSGM) outputs [252].

3.2.3. Spatial grid boundaries

Since the focus of this research was to examine the spatial distributions of CD and UC cases and CD and UC risks using the survey data, it was decided to conduct the analysis on units of pixels. Considering the UK-wide distribution of cases, pixel units can be useful for revealing regional differences and have the advantage of consistency in the sampling support (e.g. the size, geometry and orientation of the space on which the observations are defined). In this way, small but important focal areas can be identified, and a more detailed picture of the case density can be obtained. In this context, the UK geography was divided into 10 km2 grid squares in ArcGIS Pro 3.0. To determine the relative risk of CD and UC in each grid square, the ratio of the total number of reported CD and UC cases relative to the general population in the relevant grid squares was calculated.

3.2.4. Age- and sex-standardized morbidity ratio (ASMR)

ASMR is a statistical measure that is used to compare the observed number of cases in a particular population to the expected number of cases in a standard population for a particular age and/or sex category. The ASMR allows comparison of disease incidence while accounting for age and sex distributions [253] and is described as:

$$SMR = \frac{Observed\ num.\ of\ cases}{Expected\ num.\ of\ cases} \tag{1}$$

$$Expected\ num.of\ case = \frac{Observed\ num.of\ cases}{UK\ population} x\ pop.of\ each\ age\ \&\ gender\ group \quad (2)$$

The observed number of cases is the total number of CD or UC positive cases reported in the UK-wide IBD study, while the expected number of cases represents the total number of observed cases divided by the total population, multiplied by the total population of each age and gender group. The age groups for both sex types were defined as 0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69 and 70+.

An ASMR of < 1.0 means that there are fewer cases than expected in the local population. Conversely, an ASMR of > 1.0 indicates that the observed number of cases in the local population is higher than expected. In the case of equality, the number of observed cases equals the number of expected cases in the study population.

3.3. Results

3.3.1. Exploratory data analysis

The UK-wide IBD survey produced a total of 5,452 participants who reported four different IBD conditions: Crohn's Disease (CD), Ulcerative Colitis (UC), Microscopic Colitis (MC) and Indeterminate Colitis (IC). The numbers of individuals identified for each IBD condition were as follows: CD (2,672; 49%), UC (1,946; 35.7%), MC (24; 0.44%) and IC (292; 5.35%). Participants from outside the UK, participants submitting missing/incorrect/unlocalized postcodes and those who did not answer the IBD and postcode questions were excluded from the study (518; 9.5%). Among the remaining participants, 1,047 cases (21.2%) could not be geocoded. Therefore, the final numbers of reported cases of CD, UC, MC and IC were 2,085 (53.64%), 1,559 (40.10%), 19 (0.48%) and 224 (5.76%), respectively.

3.3.2. Spatial distribution of IBD cases across the UK

The location where a patient was first diagnosed was selected as defining 'location' for this study (postcodes post-first diagnosis were disregarded as they cannot influence onset). Maps of CD, UC and all IBD cases normalized by the population and spatially referenced to the postcode at first diagnosis are given in Figure 3.1.

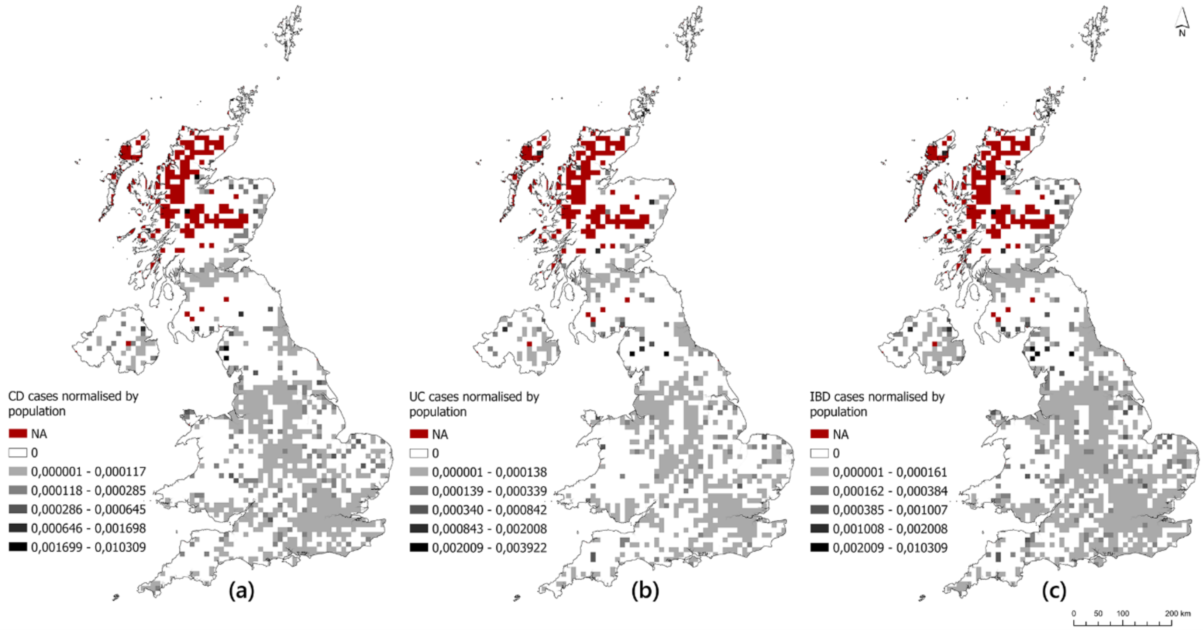


Figure 3.1. Distribution of IBD cases normalised by population across the UK according to the postcode at first diagnosis: (a) CD, (b) UC and (c) all IBD cases.

Examining the distribution of reported IBD cases (participated in survey) normalised by population across the UK, that is, relative risk, it was observed that grid squares with no population (marked in red) are concentrated in Scotland. Grid squares with a positive population, but no survey participation (marked in white), are common for CD and UC in rural areas such as Wales, parts of Scotland, and the North, South-West and East of England. CD relative risk is higher in some grid squares in Wales, Northern England and Southern Scotland (Figure 3.1.a), while UC relative risk is higher in a few grid squares in Northern England and Southern Scotland (Figure 3.1.b). It was observed that risk is high for both CD and UC cases in some grid squares in Scotland, due to low sample size.

3.3.3. Age and gender distribution across the UK

The age and gender of all IBD cases participating in the study were examined and grouped accordingly. For reported CD cases, the age range was 1-81 years. The age ranges of 1,529 female (73.3%) and 539 male (25.85%) CD cases were found to be 8-81 years and 1-79 years, respectively. In terms of gender, 5 participants (7-59 years) preferred not to answer, 6 participants (18-42 years) answered non-binary, 1 participant (37 years) answered trans-feminine, 1 participant (35 years) answered agender. Although three participants

(33-64 years) chose the preference to self-identify, they did not provide any input in the relevant field.

The age range of the UC cases was found to be 6-95 years, while four UC participants answered the age question inconsistently. The age ranges of 1,196 female (76.71%) and 357 male (22.89%) UC cases were also found to be 7-95 years and 6-80 years, respectively. One participant (34 years) did not respond even though they preferred to choose to self-identify and one participant (40 years) answered non-binary.

The age range of IC cases was found to be 6-83 years, while one participant answered the age question inconsistently. The age ranges of 169 female (75.44%) and 53 male (23.66%) IC cases were 13-83 years and 6-79 years, respectively. One participant (26 years) answered non-binary. Of the cases included in the study, MC cases were the least reported of the IBD types. In total, all 19 MC cases were women, and the age range was 32-75 years.

The spatial distribution of CD and UC cases by gender, normalized by the population, is given in Figure 3.2. The reported relative risk appears to be clustered in densely populated urban areas, and it is seen that the female population, which constitutes nearly ¾ of the survey participants for both IBD types, has a more extensive distribution compared to the male population for both CD and UC (Figure 3.2).

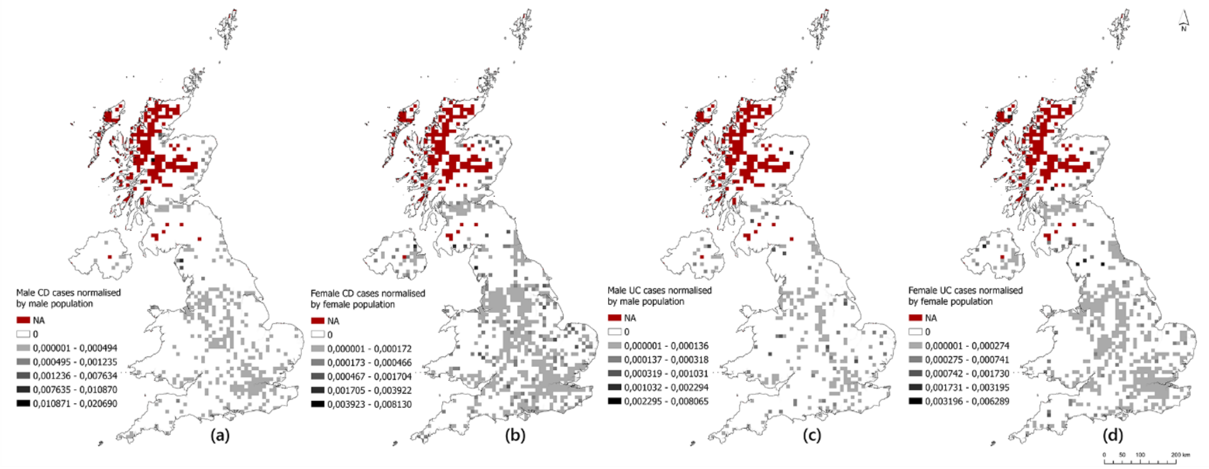


Figure 3.2. Distribution of (a) male and (b) female CD cases, and (c) male and (d) female UC cases, normalised by population across the UK.

3.3.4. Age- and sex-standardized morbidity ratio

ASMR analysis results for both the CD and UC cases, calculated according to both age and sex, are given in Figure 3.3. Among male CD cases, an ASMR >1 was detected only for the 30-39 age group, while an ASMR<1 was observed for all other male age groups. For the female CD cases, an ASMR>1 covered a wide range between the ages of 20-69 and an ASMR<1 was found only in cases 0-19 and 70+.

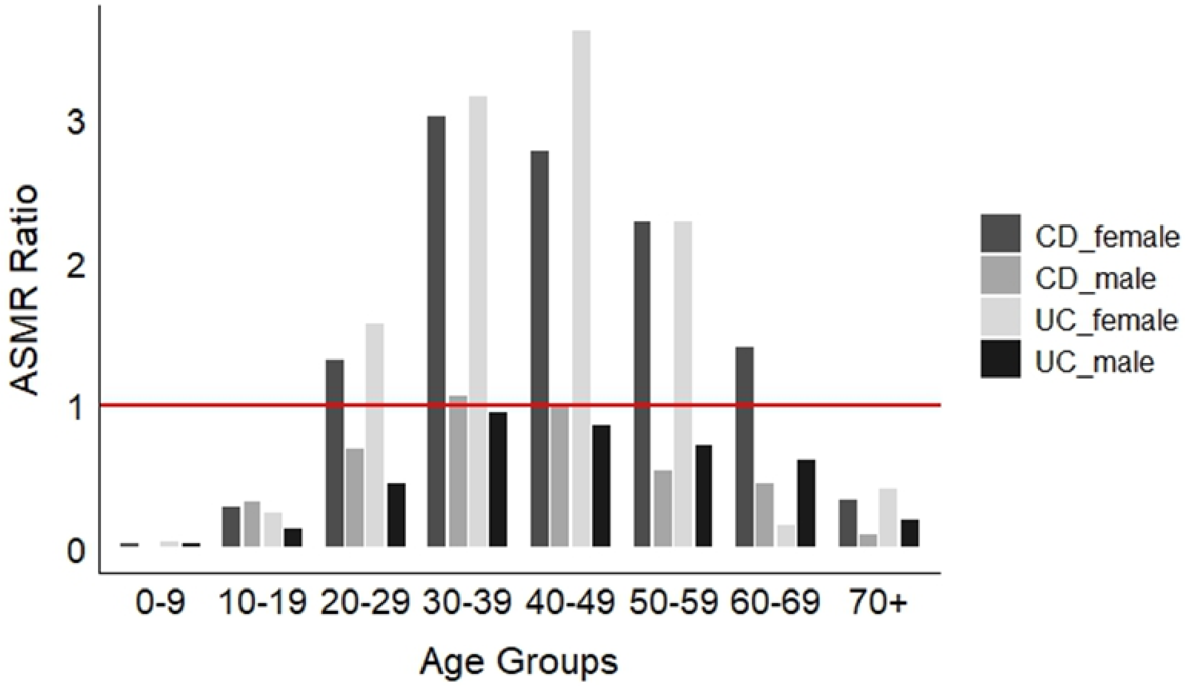


Figure 3.3. ASMR for CD and UC by gender plotted against age, represented in eight age categories. The horizontal red line represents equity of risk such that risks above the red line represent greater than expected risk and risks below the red line represent less than expected risk.

For the UC cases, no ASMR>1 value was detected in any of the age groups of male UC cases. For female UC cases, an ASMR>1 value was detected in the 20-59 age range, while an ASMR<1 was found only for the 0-19 and 60-70+ age categories.

Figure 3.3 shows that females between the age categories of 20-29 and 60-69 (CD) or 50-59 (UC) have significantly higher reported morbidity rates for both CD and UC than men, and this rate is particularly pronounced in the 30-39 to 50-59 age range. For the age categories 30-39 and 40-49, the ASMR for females is about three times higher than expected. This analysis, thus, shows that middle-aged women exhibit the highest reported morbidity rates for both CD and UC

3.3.5. Inter-disease risk analysis

The number of reported CD and UC cases in each grid was used to calculate the CD:UC ratio and its distribution was mapped across the UK (Figure 3.4). In some grid squares, the number of UC cases was zero, while in some grid squares, both CD and UC cases were zero. These grid squares where the UC count was zero and calculation of a proportion was not possible were recorded as NA and marked in white in Figure 3.4. Cells where the CD count was zero, but the UC count was positive are marked in red.

It can be seen from Figure 3.4 that the CD:UC ratio was relatively high in some grid squares in North-West England around Manchester. Similarly high ratios can be seen in some isolated grid squares in Scotland (Edinburgh and Glasgow) and London. Lower CD:UC ratios can be seen in many grid squares across the UK and are more common in London and Birmingham. It is worth noting that there exists greater spatial variation in the CD:UC ratio across the UK than in the CD:population and UC:population ratios presented in Figure 3.1 and 3.2, which exhibited mostly small values with some isolated peaks.

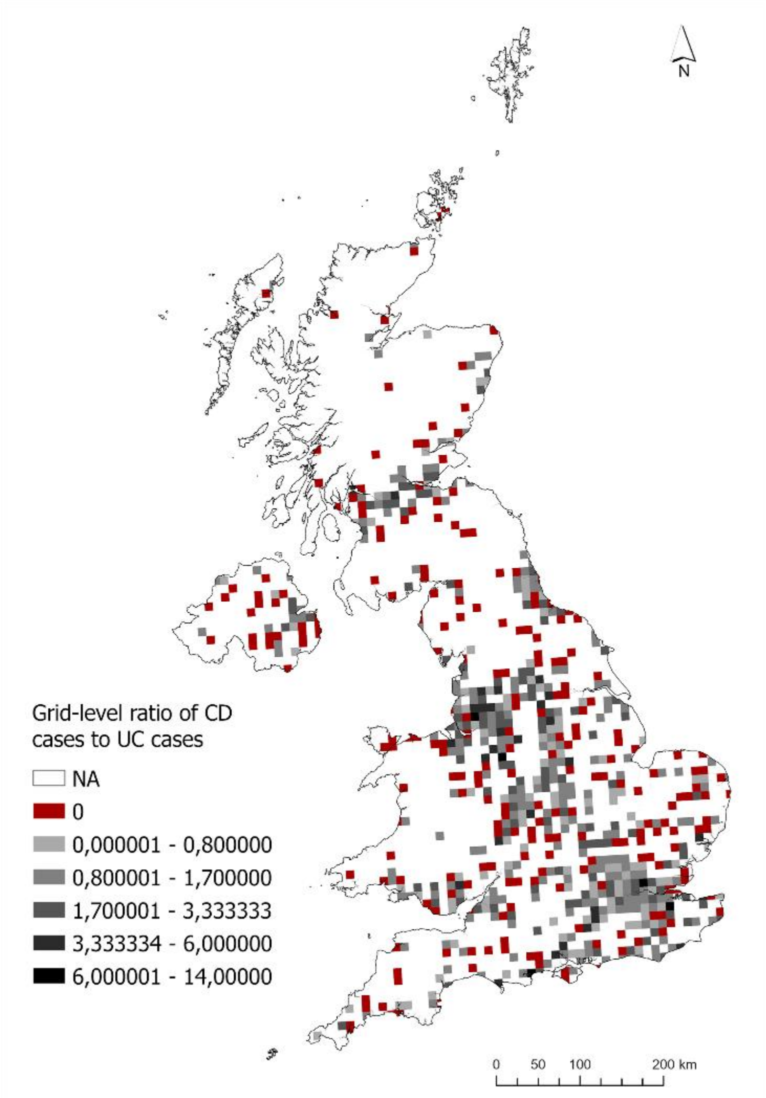


Figure 3.4. Distribution of CD:UC ratio for each grid square across the UK. White squares represent grid cells where calculation of a ratio is not possible (i.e., UC is zero), and red squares represent grid cells where the ratio is zero (i.e., CD is zero and UC is positive).

3.4. Discussion

3.4.1. Discussion of results

The main aim of this study was to report the design, execution and results of a novel UK-wide survey on four diseases within the general IBD class. We used the resulting survey data to provide a preliminary investigation of the geographical distribution of CD and UC cases in the UK, calculated the ASMR of the CD and UC cases, and calculated relative IBD risk based on both the underlying population and by comparing the diseases to each other, with the latter having the benefit of mitigating against possible reporting bias. The data used consisted of the georeferenced cases for the four diseases obtained from the UK-wide IBD survey (wp.lancs.ac.uk/ibdsurvey), and population data including age and sex obtained from WorldPop (www.worldpop.org). Therefore, this study, carried out at a spatial resolution of 10 km2 grid squares, is novel in this context.

The data on the 5,452 cases who participated in the online survey, were classified according to IBD type, age, gender and address (current, first diagnosis and previous postcodes (up to 15 years). Due to an insufficient number of participants, the MC and IC cases were not considered in the analysis. For both the CD and UC reported cases, approximately ¾ of the participants for both types of IBD were female. The female:male ratios were found to be 2.8 and 3.3 for CD and UC cases, respectively. Brant and co-workers reported in their analysis of data from several large-scale studies that female CD cases outnumbered male CD cases, with a female: male ratio ranging from 1.2 to 2.2, but no significant difference was observed when UC cases were considered [254]. A study conducted in Western countries on the risk of developing IBD according to age found that women are more likely to be affected by CD after the age of 10 and that this risk peaks in their 70s; while men are less likely to develop UC before the age of 45, this risk increases after the age of 45 [255].

The UK has one of the highest incidence and prevalence rates of IBD in Europe [225, 228, 236, 237]. In places where the incidence is high, CD cases are mostly seen in young women (20-40 years old), while they are seen in men at older ages [256]. The age-specific incidence of ulcerative colitis (UC) in women decreases with age [234] and many women have been reported to become infected with IBD during their reproductive years [257]. The risk of CD is lower in those under 20 years (up to 10-14 years) and this risk may increase in later years [255]. It was determined that the lowest age range in which women's CD and UC morbidity >1 is 20-29 and the highest age range is 50-59, revealing strong demographic differences in IBD amongst women. It is unknown whether this reflects higher survey participation rates for women although the literature suggests that this might be the case [258–260].

Considering the distribution of CD and UC cases in the UK according to first diagnosis postcodes, the largest clusters were observed in core urban areas such as London, Birmingham, Manchester, Leeds and Scotland, as expected because participation is related to population density. However, considering the inter-disease risk analysis (CD:UC ratio), surveyed CD cases were higher than UC cases in the North-West England in the Manchester area. In contrast, large values were observed in London and Scotland in only isolated grid cells. Further analysis of possible environmental factors and exploration using different spatial resolutions (e.g., different grid cell sizes) may be useful in identifying risk factors around Manchester and may help to understand why the ratio of CD to UC cases is elevated there. While the CD:UC ratio provides a means of comparing disease types within the same sample and helps reduce the influence of population-related reporting bias, no additional statistical correction (e.g., smoothing or Bayesian adjustments) was applied to account for small counts. Therefore, the observed spatial patterns, particularly in grid cells with few cases, should be interpreted with caution. In our survey sample, CD cases (n=2,085; 53.6%) outnumbered UC cases (n=1,559; 40.1%), yielding a CD:UC ratio of approximately 1.34. This differs from clinical datasets, such as King et al. (2020) [261], which consistently report higher prevalence of UC compared to CD in the UK population.

Analysis of the ASMR for CD and UC revealed that the age range in which the ASMR value was greater than 1 in both men and women for both types of IBD was observed in the 30-39 age group. Especially in women, the ASMR value for both CD and UC was greater than 1 in the 20-59 age range, which reveals that young, middle-aged and older adult women may have a higher risk of contracting, developing and ultimately reporting both CD and UC. In addition to the finding that women, in particular, may face the risk of CD at an early age [255], we found a wide age range at which women may have an elevated risk compared to men, and this finding is supported by other studies [262].

3.4.2. Limitations

We acknowledge several limitations of this study. These include reaching a small proportion of the likely population of IBD cases in the UK and possible misdiagnosis of IBD types. Since the number of reported cases constitutes the backbone of the study, we collected data through an online questionnaire with wide availability. Many voluntary charities and organizations were contacted and the UK-wide IBD survey was promoted periodically on social media and across several online platforms. We aimed to maximize our reach to as many IBD sufferers across the UK as possible and ensure an even geographical coverage, for example, by contacting potential respondents through CCUK, which has 47 local user networks covering the UK evenly. We also assume that there is no systematic difference in the likelihood of survey participation (selection bias) between CD cases and those with other forms of IBD, which is important when interpreting relative risk comparisons. However, we acknowledge that it may not have been possible to reach cases who did not follow IBD organizations, did not use social media, or faced barriers to survey participation, such as digital exclusion among the elderly and complexities of obtaining consent for children. Furthermore, it is difficult to compare this survey with others as the data collected by others were for biomedical analysis (Nottingham/Astra ZenecA prospective IBD cohort study, 2022-2024) or more numerical, analysing for location (CCUK/Nottingham University Crohn’s and Colitis Survey, 2024).

A total of 3,085 grid cells were specified in the study, and the number of grid cells with no survey participation was found to be 2,276 (73.7%) for CD and 2,375 (76.9%) for UC. It was also determined that there was no population in 296 (9.5%) of the grid cells. Across the UK, an estimated 540,000 people live with Crohn's Disease or Ulcerative Colitis. The total number of IBD cases included in the study is 5,452. Although this community participation survey represents one of the largest of its kind in the UK, the number of respondents, therefore, likely represents only 0.7% of all IBD patients, a small proportion of the overall case number in the UK [263]. To access more IBD case data in future studies, government health agencies could be contacted, or access to the online electronic general practitioner (GP) health records database could be requested [264]. A greater sample size would be useful in providing a clearer picture of local spatial distributions and clustering of IBD cases and supporting analyses at the postcode level. This limitation should be considered when interpreting the spatial patterns observed in this study.

This study focused on regional variation in IBD prevalence, without exploring environmental determinants. We recognize that ecological factors, such as food environments, could play a significant role in the observed geographical distribution of IBD [265]. While our current study emphasizes the spatial patterns of CD and UC cases, we agree that a broader discussion of environmental factors, including diet, urbanization, and other ecological contributions, would strengthen the interpretation of our findings. In future work, we plan to incorporate a discussion on these environmental influences and refer to relevant studies that explore their potential impact on IBD prevalence.

The ASMR results may reflect, to some extent, a reporting bias in females related to males. The finding that the ASMR is highly consistent between CD and UC suggests that this may be the case, although further analysis is required to establish this more firmly. Thus, some caution must be exercised when interpreting these results. When diagnosing IBD subtypes, there is a possibility of misdiagnosis [266, 267]. It is not always easy to distinguish CD from UC accurately, especially since they have similar symptoms, which leads to various difficulties in the diagnostic process. Data analysis was based on direct input from IBD survey participants and, therefore, input from clinically undiagnosed or misdiagnosed participants may be included. This may also relate to the consistency in some of the results for CD and UC, including in the ASMR analysis

3.5. Conclusions

This study presents a new survey and analysis of IBD cases in the UK and illustrates the spatial distribution and characteristics of the data acquired. Unlike previous studies that relied on survey-based case data analysis, our approach was novel in analyzing case numbers and population counts for each 10 km^2 cell across the UK. The maps of CD and UC relative risk (Figure 3.1) showed little spatial variation across the UK; some isolated peaks were observed in Scotland and a few other areas which may be related to small sample size. Interestingly, considering the CD:UC ratio, higher relative risk of CD was observed in core urban areas in the North-West England, especially Manchester and Bolton, with lower risk in the periphery and rural areas. This finding will be explored in subsequent analysis. The ASMR analysis revealed that age-standardized risk of CD in the UK appears to be much greater in women than men and spread across a wide age range (ASMR=1 to 3; ages 20-29 to 60-69). The results of this study may provide insights for understanding regional and demographic patterns of IBD incidence, particularly for Crohn's Disease and Ulcerative Colitis. These findings could also serve as the basis for future research on factors influencing IBD risk. This analysis platform supports the spatial analysis of IBD cases by providing a scalable approach for grid-scale studies, particularly across multiple countries where larger datasets are available.

Chapter 4

4. Influence of Landscape on the Distribution of Inflammatory Bowel Disease in England and Wales

Abstract

Mycobacterium avium subspecies *paratuberculosis* (MAP) is the bacterial pathogen which causes Johne's disease (JD) in animals and is significantly associated with Crohn's disease (CD) in humans. Johne's disease-infected animals shed large numbers of MAP onto pastures. Previous studies have detected MAP in pasture areas deposited by sub-clinically and clinically infected animals with Johne's Disease and in areas outside pastures spread by non-farmed animals. Rainfall washes the pathogen from pastures via surface water and drains into rivers, thus, providing a route for human exposure from infected cattle via potable water supplies and riverine aerosols. Based on a large UK-wide IBD survey, in which a total of 5,452 IBD participants were surveyed, we tested the hypothesis that the relative risk of CD in humans is related to ruminant grazing and hydrological transport of the pathogen by associating CD risk with the proportion of pasture land using the hydrological catchment as the spatial support. Specifically, we investigated the association between the number of CD cases relative to the population (used as an offset) and

biogeographical features measured at the hydrological catchment level by fitting a Poisson regression model. Covariates comprised pasture proportion (selected as a proxy for ruminant grazing), urban proportion, monthly average temperature, monthly average precipitation and river width. The same model was fitted for ulcerative colitis (UC) to provide comparative control. A statistically significant relationship was found between the number of CD cases and pasture proportion, while the association between number of UC cases and pasture proportion was statistically insignificant. This research is the first to demonstrate an association between CD risk and the proportion of pasture at the national scale, thus, providing evidence to support the hypothesis that living within catchments with a greater proportion of pasture upon which MAP-infected animals graze may increase the likelihood of CD amongst the at-risk population.

In this chapter, Mehmet Akif Veral was responsible for curating the dataset, performing the statistical analyses, creating maps, methodology, interpreting the results and writing – original draft.

4.1. Introduction

Inflammatory bowel disease (IBD) encompasses conditions such as Crohn's Disease (CD), Ulcerative Colitis (UC), Microscopic Colitis (MC) and Indeterminate Colitis (IC), all of which are characterized by chronic inflammation of the gastrointestinal (GI) tract [81, 82, 84]. It is estimated that approximately 7 million people worldwide are affected by IBD [228]. The disease is considered specific to industrially developed western countries, with the highest incidence and prevalence rates detected in North America and Europe [229]. However, a significant increase has been observed in the incidence rates of industrializing countries in the Middle East, Asia and South America [253]. IBD incidence and prevalence rates are relatively high in Europe [225, 236, 237], and in this context, the UK has one of the highest rates worldwide [236, 263].

The two major types of IBD are CD, which can affect any part of the GI tract and cause chronic inflammation of the intestine [8, 226, 268] and UC, which is limited to the colon [85, 86, 269]. CD and UC can present common symptoms, such as diarrhoea, abdominal pain and weight loss. Moreover, it is hard to determine the type of IBD in cases where symptoms are limited to the colon and no endoscopic findings are observed [270].

Although it has been emphasized that environmental, genetic and immune system regulating factors are effective in the development of IBD, it is still unclear what causes CD or UC [9]. The pathogen Mycobacterium avium subspecies paratuberculosis (MAP) is the etiologic agent of Johne's disease (JD) in animals [160, 162], a chronic and progressive intestinal disease [162]. JD is contagious, and it can infect ruminant and non-ruminant species, including primates [163–165, 271, 272]. MAP is a slow-growing member of the Mycobacterium avium complex [163, 164, 273]. The presence of MAP in human tissues has also been found to have a significant association with CD [10, 92, 274, 275] but there is a need for more evidence. Although the potential role of MAP in contributing to the onset of CD remains a topic of discussion [37, 276–280], this has been extended to possible environmental routes through which humans might be exposed to MAP [16, 17, 281]. A temporal lag has been reported in some countries between the importation of Johne's diseased cattle and an increased incidence of Crohn's Disease (e.g. Iceland , Czech Republic and Japan [282–284].

MAP can persist for long periods in the digestive tract of an infected animal without causing clinical disease [285]. Subclinical infections have been found to occur frequently in domestic ruminants [165] and pathogenic activity has been documented globally, with notable occurrences in Europe [165, 286] and North America [287, 288]. Clinically and sub-clinically infected ruminants can shed significant numbers of MAP in their faeces onto pastures. Regardless of the intracellular persistence of MAP which causes JD, it is still shed by sub-clinically and clinically infected cattle in dung and, hence, the environment. Animals may become infectious (stage 2) after a period of time (months to years) and the shedding of MAP will increase as the disease progresses. As an animal may not exhibit (stage 3) clinical signs for many more years, undetected shedding from an infectious animal can continue for a long time [289]. MAP then persists in the environment, raising the risk of infection among a wide range of animals [290–292]. Importantly, MAP can persist outside its host for extended periods and can be carried by surface waters into rivers and transported downstream in hydrological catchments, causing potential exposure to humans via aerosols [16, 17, 281]. We hypothesised that clusters of CD sufferers were associated with exposure to wind-driven MAP containing aerosols [16, 293]. The presence of MAP in rivers has been revealed in previous studies where MAP was detected in a significant portion of samples taken from rivers [16, 17] at concentrations of 1–103 CE L−1 [293]. It follows, from a hydrological perspective, that it is possible that precipitation regime and river flow have an impact on determining the distribution of MAP in the environment [16, 17].

A conceptual model representing the transmission of MAP from infected animals to humans, developed initially by Pickup et al (2006) [17] and adapted here, is shown in Figure 4.1. It is suggested that MAP enters the environment not only by infected animals, but also by farming practices such as animal slurrying practices, subsequent soil redistribution after water purification and [17, 278]. Slurrying practices are a result of shedding cattle (both dairy and beef) during winter months with their waste subsequently being spread onto the land, particularly pasture. Waste is often stored in tanks prior to spreading, but MAP survives for a prolonged period before application to the land [294]. Sheep graze on pasture all year round whilst graze cattle through spring to autumn. Further studies have detected MAP in drinking water [281, 295, 296], meat [297, 298], milk [152, 299–302] and dairy products [303–305].

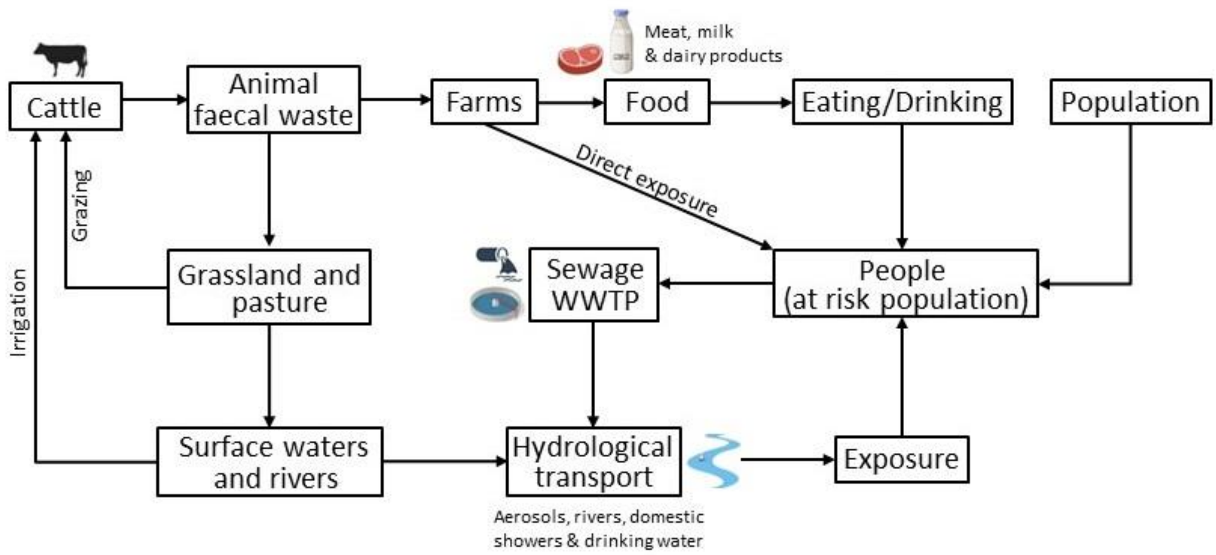


Figure 4.1. Conceptual model of transmission of MAP from infected animals to humans (adapted from Pickup et al. 2006).

Based on the conceptual model described in Figure 4.1, we hypothesise that biogeographical features, particularly the spatial distribution of pasture supporting ruminants in the UK, may increase the risk of human exposure to MAP and, consequently, influence the national distribution of the CD population. To test this hypothesis, we use the proportion of pasture as a proxy for ruminant grazing, examining its link to CD relative risk in humans and the potential role of MAP in (and shed by) ruminants. We are confident about this proxy because pasture generally supports ruminant grazing across the UK.

Additionally, IBD participant data were collected through a UK-wide online survey which included current postcode, postcode at first diagnosis and previous postcodes (up to 15 years) allowing spatial analysis of relative risk. Population data were obtained from the WorldPop database [250] to represent the at-risk population. The hydrological catchment area was considered as the spatial support that would enable the association to integrate the possible hydrological transport of the pathogen. A Poisson regression model was fitted to the relation between the total number of CD cases and wide range of biogeographic covariates (proportion of pasture and urban area, monthly average temperature and precipitation data, and maximum river width) to see if pasture proportion was significant and the others were not. A second Poisson regression model was fitted to the relation between the number of UC cases participating in the survey and the same covariates to provide a comparative control.

4.2. Methods

4.2.1. Study site and data

The study site was defined as England and Wales. A variety of data sources were used for the research including a comprehensive online survey of individuals with IBD, population and five covariates (including proportions of pasture and urban area, monthly average temperature and precipitation, and maximum river width) as well as spatial catchment boundary definitions, as detailed in this section.

4.2.2. UK-wide IBD survey

A novel survey targeting individuals diagnosed with IBD across the UK was conducted, with data collected using an online platform on a purpose-built website via Qualtrics (Qualtrics, Provo, UT).

The survey focused only on IBD cases living in the UK. We engaged several IBD organisations (CCUK, IBDUK, CICRA, Cure Crohn's Colitis, Crohn's MAP Vaccine, Guts UK and IBD Coach) to increase the survey's profile, and ultimately response rate. During a 307-day data collection period (01 December 2021 – 03 October 2022), the study was featured periodically in posts from these organisations. As CCUK is the largest and most widespread IBD organisation in the UK with 47 local networks, promoting the study on its official website and social media accounts increased the likelihood of equal participation rates and even geographical coverage.

Within the scope of the survey, participants were asked to share their demographic information (age, gender, ethnicity and occupation), diagnosis type (CD, UC, MC or IC), whether there was a previous IBD case in their family, and their postcodes (current, first diagnosis and previous postcodes (up to 15 years). The analysis used the postcode at first diagnosis to represent the likely area of long-term exposure, under the assumption that individuals typically reside in the same area for some time before diagnosis. Participants under the age of 16 were required to complete the survey with the consent of their guardians. Data from individuals located outside the UK and those submitting incomplete, inaccurate or unlocalized information were excluded from the final dataset used in the research. Ethical approval for the survey was obtained from Lancaster University (FHMREC20164).

4.2.3. Covariates

Any measurable variable that is believed to be statistically associated with a dependent variable can be considered a potential covariate. Within the scope of this research the following covariates were selected for analysis.

a) Population data and the spatial distribution of population across England and Wales were obtained from constrained WorldPop 2020 datasets at 100 m resolution [250], including age–sex structures [251] and settlement-based 'NoData' areas derived from the Built-Settlement Growth Model (BSGM) [252].
b) Data on pasture and urban areas across England and Wales with a spatial resolution of 100m were obtained from the CORINE Land Cover (CLC) 2018 [306].
c) Monthly average temperature (June, July and August) and precipitation (November, December and January) data between 1991 - 2020 with a spatial

resolution of 2 km were obtained from the Met Office Climate Data Portal [307, 308].

d) River data for England and Wales were obtained from data.gov.uk [309] and the length (m) of the widest river was used as a covariate in the regression model for each hydrological catchment area.

4.2.4. Catchment boundaries in England and Wales

Figure 4.1 shows the conceptual environmental pathway that could link the ruminant source of MAP to potential human exposure to MAP, including MAP from infected animals being deposited onto pasture areas and subsequently washing from pastures into rivers and surface waters downstream. To test the hypothesis that biogeographic features connected to the at-risk population may pose an increased risk of MAP, it was decided that the analysis should be undertaken using hydrological catchment basin units as the spatial support (i.e. the map units). Consequently, humans living in each catchment are automatically and correctly associated to any upstream sources of MAP (such as ruminants or the pasture that they graze on) because both the at-risk population and the source fall within the same catchment. Alternatives such as raster grids would lack this automatic association.

Data regarding the boundaries of catchment areas were obtained from The Department for Environment Food and Rural Affairs (DEFRA) for England and Wales, The Department of Agriculture Environment and Rural Affairs (DAERA) for Northern Ireland, and the Scottish Environment Protection Agency (SEPA) for Scotland. The collected catchment boundaries data were integrated into a single catchment boundaries dataset using ArcGIS Pro 3.0.

Of 495 hydrological catchment areas identified within the UK, 365 (73.73%) were in Scotland. Of the catchments in Scotland, 289 (79.17%) were found to have no survey participation. Due to the absence of survey data or very small sample sizes in Scotland, the study was conducted on hydrological catchment areas in England and Wales only.

4.2.5. Poisson regression model

Poisson regression is used to model numerical data of rare events. It usually estimates the frequency of events occurring in a specific time-period or spatial area. It is particularly suitable for analysing the distribution of low-frequency events (i.e. small numbers of cases) [36] and for performing analyses based on count data, expressed as:

$$\log(\lambda_i) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n + \log(N_i)$$

where λ is the number of observed cases (i.e. number of CD or UC cases) and β_0 is the intercept. $\beta_1, \beta_2 \ldots, \beta_n$ are the coefficients of covariates and $X_1, X_2, \ldots, X_n$ are the covariates.

The model was fitted within the Generalized Linear Model (GLM) framework using the glm function in R. Since the dependent variable (number of CD, or UC, cases participating in the IBD survey) was a count variable, the error structure was set to Poisson distribution, and the log link function was used. A log link function, which is standard for Poisson regression, was employed to model the relationship between the covariates and the expected log count of cases. The covariates used in the model (proportion of pasture and urban area, monthly average precipitation and temperature, and maximum river width) were chosen based on their theoretical relevance to environmental factors influencing disease distribution. Population (N_i), which varies across the hydrological catchment areas in England and Wales, was used as an offset term in the regression model to adjust for population differences across regions. This allows the response variable to represent proportions rather than raw counts.

Covariate selection for the final model followed an iterative approach based on the results of the initial model. Initially, all theoretically relevant covariates such as pasture and urban ratio, monthly average rainfall and temperature, and maximum river width were included in the model. After fitting the initial model, variables with large p-values (i.e. not statistically significant at $p<0.05$) were identified and removed one-by-one. At each step, the model was refitted, and the impact of removing each variable on the model's overall fit and performance was assessed. This process was repeated iteratively until only statistically significant covariates remained. The selection process ensured that the final model was both consistent and statistically valid while retaining variables with meaningful contributions to explaining the variation in the response variable.

4.3. Results

4.3.1. Exploratory data analysis

A total of 5,452 people participated in the survey. The breakdown of participants into one of four specific types of IBD was as follows: 2,672 individuals with CD (49%), 1,946 individuals with UC (35.7%), 24 individuals with MC (0.44%) and 292 individuals with IC (5.35%). 518 (9.5%) participants who provided missing, incorrect or unlocalised postcode information, resided outside the UK, did not identify their IBD type or did not provide postcode information were excluded from the final dataset. The remaining 4,934 participants were subjected to geocoding based on their postcodes. Of these, 1,047 cases (21.2%) could not be geocoded, leaving a final adjusted dataset of 2,085 CD cases (53.64%), 1,559 UC cases (40.1%), 19 MC cases (0.48%), and 224 IC cases (5.76%).

CD:587, UC:387, MC:5, IC: 68

The numbers of CD and UC cases who have never changed address were found to be 182 (8.72%) and 152 (9.74%), respectively. However, the numbers of CD and UC cases who moved once or several times before diagnosis but did not move out of the catchment area were found to be 703 (33.71%) and 468 (30.01%), respectively. These findings are presented only within the scope of this exploratory analysis and were not considered in the regression model.

4.3.1.1. Distribution of IBD cases across England and Wales

First-diagnosis postcodes are crucial because the location of a patient after being diagnosed does not affect the course of the disease. CD, UC and all IBD cases in catchment areas in England and Wales were first normalized to population and then mapped (Figure 4.2). Considering first the relative survey participation rate of CD cases across England and Wales, it was found that the rate of CD cases was higher in some hydrological catchment areas compared to others, although the pattern is not clear. The highest rate of UC cases relative to the population was in a catchment area near Middlesbrough, followed by some catchment areas in North-West England.

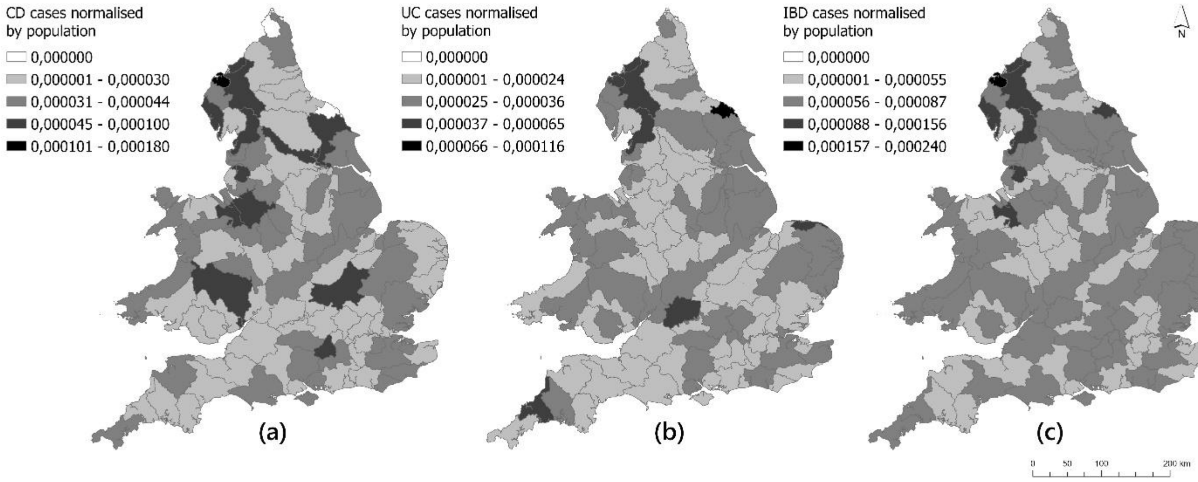


Figure 4.2. Spatial distribution of (a) CD, (b) UC and (c) all IBD cases in England and Wales, normalized by population. The distribution of the relative rate of participation for each disease in the survey is divided into five classes: ranging from no cases (marked in white) to the highest relative rate (marked in black). Note that since the survey response is lower than the total number of cases in the population the rate must be considered in relative terms only.

4.3.1.2. Distribution of covariates across England and Wales

Covariates considered to be related to the dependent variable (λ) were calculated for each hydrological catchment area and mapped. The distribution of these covariates across England and Wales is given in Figure 4.3.

With respect to the distribution of pasture areas (Figure 4.3.b), it can be observed that, as expected, the proportion increases from the eastern catchments to the western catchments. The catchments with the largest pasture proportion are located generally in the western part of the UK.

The catchments with the highest monthly average precipitation were found to be in Wales, followed by some catchment areas in the north and south-west of England (Figure 4.3.d). Conversely, although some catchment areas in south-east England received moderate precipitation, the lowest precipitation was found in some catchment areas in the south-east (i.e. around London) and north-west (i.e. around Liverpool) of England.

Areas with the largest maximum river widths (m) were identified in regions around London and the Midlands (Figure 4.3.f). Catchments with moderate to slightly above moderate maximum river widths are located in the northwest of England and in some catchments across Wales.

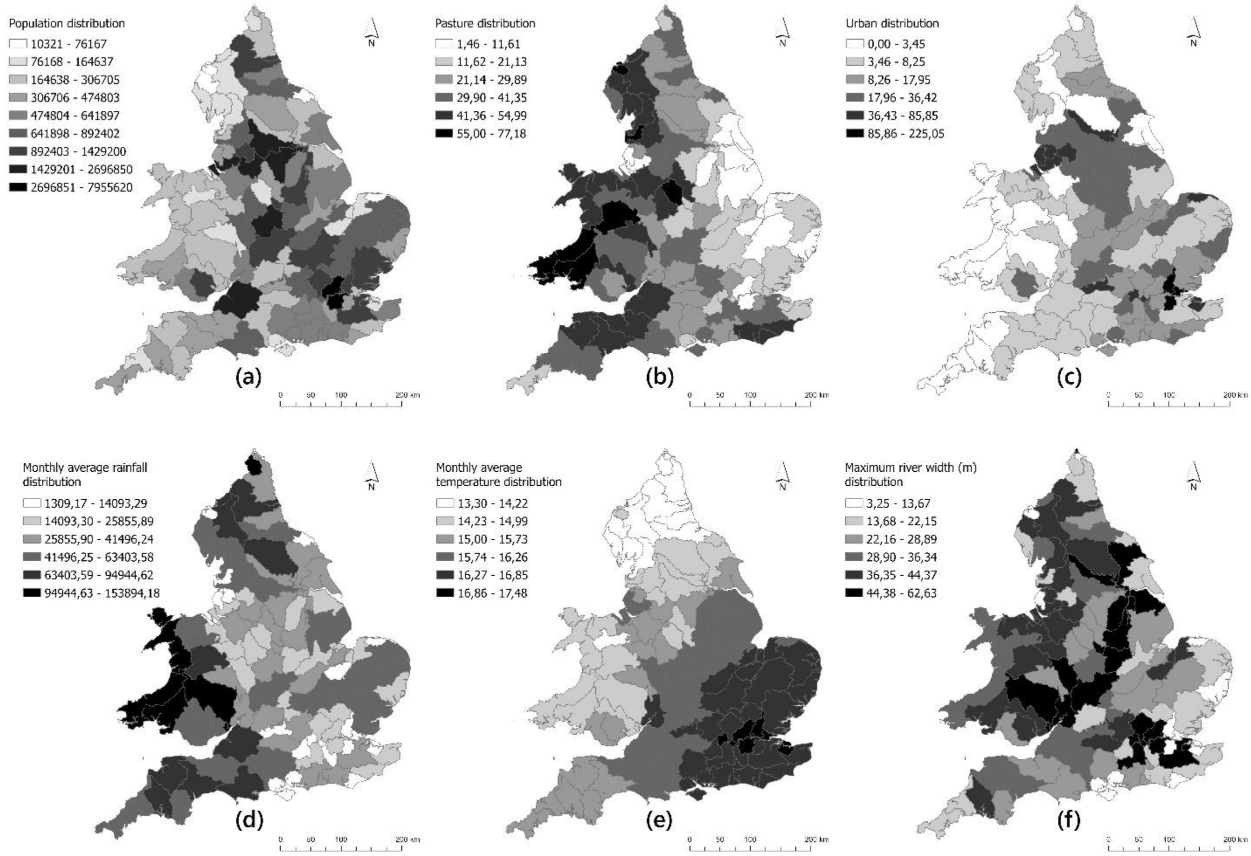


Figure 4.3. Distribution of covariates used in the Poisson regression model across England and Wales. (a) population, (b) pasture proportion, (c) urban proportion, (d) monthly average precipitation, (e) monthly average temperature and (f) maximum river width.

4.3.2. Poisson regression model

The initial fitted Poisson regression model results produced a statistically significant relationship between CD cases and pasture proportion (p = 0.00724). Importantly, this relationship was not significant for UC (p = 0.6169; Table 4.1). Similarly, a statistically significant relationship was found between CD cases and monthly average precipitation (p = 0.03046) and temperature (p = 0.02646), but no statistically significant relationship with urban areas and river width. Moreover, UC showed no statistical relation with any of the covariates.

Table 4.1. Results of the initial Poisson regression model established for CD and UC cases.

Covariates	**CD**				**UC**			
	Estimate	Std. Error	*z* value	Pr (>|*z*|)	Estimate	Std. Error	*z* value	Pr (>|*z*|)
River width	-1.984e-03	1.815e-03	-1.093	0.27437	9.318e-04	2.115e-03	0.441	0.6596
Urban proportion	-1.737e-03	9.487e-04	-1.831	0.06715	-1.889e-03	1.174e-03	-1.608	0.1078
Pasture proportion	5.271e-03	1.963e-03	2.685	0.00724	1.160e-03	2.319e-03	0.500	0.6169
Monthly avg temp.	-6.719e-02	3.027e-02	-2.219	0.02646	-6.224e-02	3.500e-02	-1.778	0.0753
Monthly avg precip.	-2.867e-06	1.325e-06	-2.164	0.03046	1.127e-06	1.497e-06	0.753	0.4512

Considering the distribution of fitted values across England and Wales, the initial Poisson regression model predicted similarly large values in some catchment areas with large numbers of CD cases who participated in the survey (i.e. some Midlands catchments and some south-eastern catchment areas of England (Figure 4.4.b). Some catchment areas across England and Wales showed negative (i.e. the model over-predicted) and positive (i.e. the model under-predicted) residual values. The residual values were between -2.53 and 3.53 and generally found to be free of large deviations with little evidence of spatial autocorrelation (Figure 4.4.c).

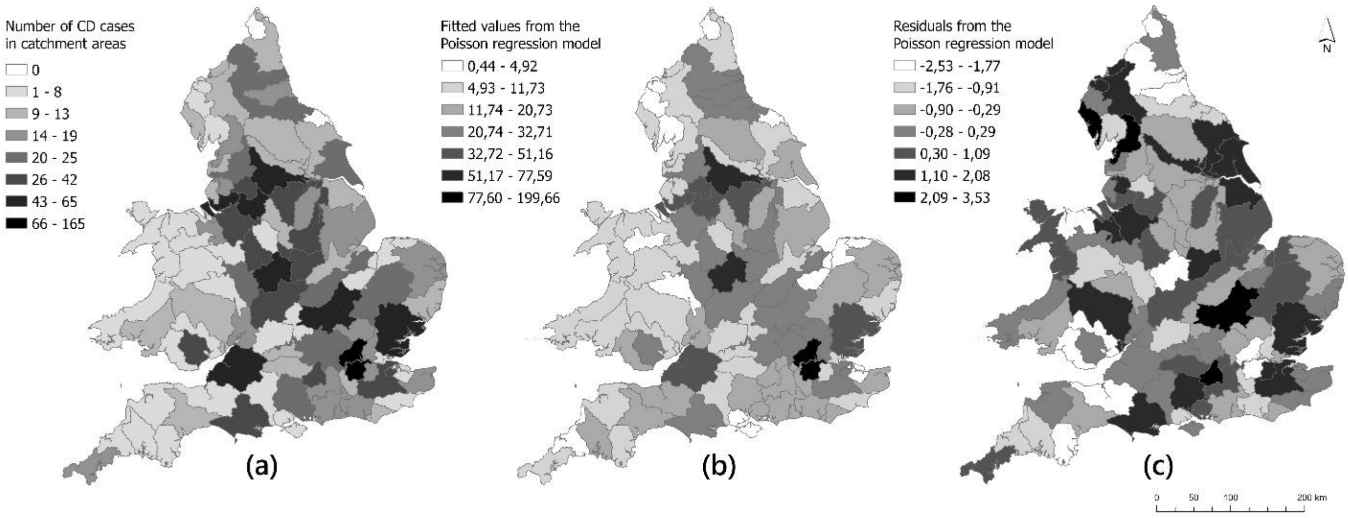


Figure 4.4. Distribution of (a) CD cases participating in the survey, (b) fitted values, and (c) residuals predicted by the initial Poisson regression model for hydrological catchment areas in England and Wales.

After the initial model was fitted, the final regression model was obtained by removing the statistically non-significant parameters ($p < 0.05$) one-by-one for both the CD and UC models until all remaining parameters were significant, ensuring that the final set of auxiliary variables contributed significantly to explaining the variation in the response variable. In the final Poisson regression model, it was found that there was a statistically significant relationship between CD cases and pasture proportion (p = 6.74e-05). Differently, a statistically significant relationship was found between UC cases and monthly average temperature (p = 0.00126) with no association to pasture proportion.

Table 4.2. Results of the final Poisson regression model established for CD and UC cases.

Covariates	**CD**				**UC|**			
	Estimate	Std. Error	z value	Pr (>|z|)	Estimate	Std. Error	z value	Pr (>|z|)
Pasture proportion	0.006505	0.001632	3.985	6.74e-05	NA	NA	NA	NA
Monthly avg temperature	NA	NA	NA	NA	-0.08787	0.02724	-3.225	0.00126

The final Poisson regression model fitted values resulted in a distribution very similar to the distribution of CD cases who participated in the survey (Figure 4.5.b). Residual values ranged from -3.39 to 3.65 and showed negative and positive results as in the initial model across England and Wales (Figure 4.5.c). The largest residual values were found in the north of England and some Midlands catchment areas, while the lowest residual values were found in catchment areas around London, in south-west England and in Wales.

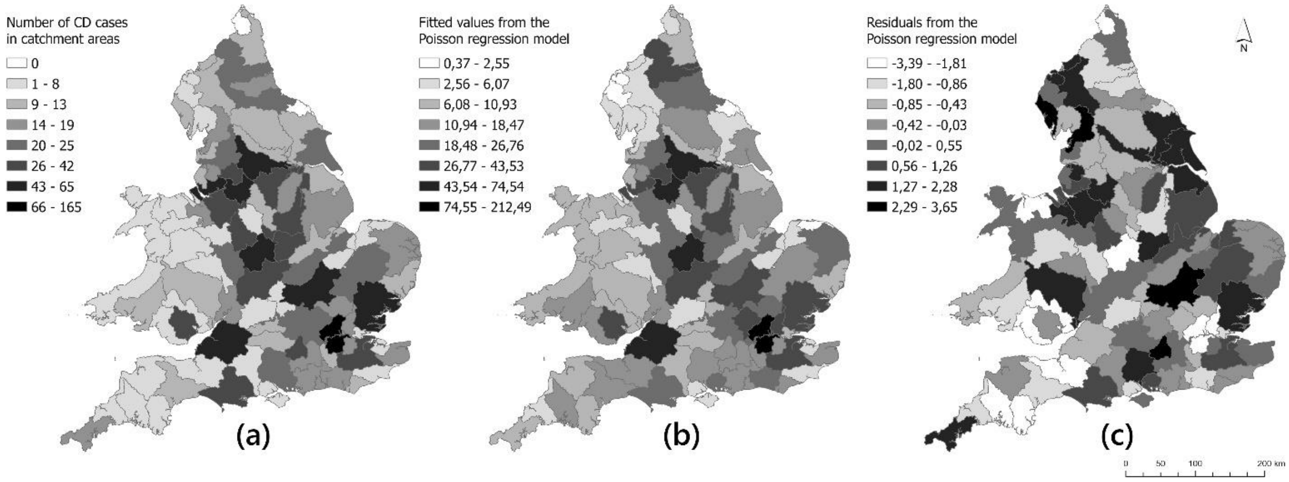


Figure 4.5. Distribution of (a) CD cases participating in the survey, (b) fitted values, and (c) residuals predicted by the final Poisson regression model for hydrological catchment areas in England and Wales

4.4. Discussion

The main question addressed in this research was whether MAP constitutes a risk factor in CD through the hypothesized environmental pathways [16, 17, 281]. To examine this, two Poisson regression models were fitted for the number of CD cases and the number of UC cases. According to the initial Poisson regression model results (Table 4.1), pasture proportion was found to have a statistically significant relationship with CD cases (p = 0.00724), but not with UC cases (p = 0.6169). Similarly, in the initial model (shown here to aid interpretation of the model fitting process), CD was associated significantly to monthly average temperature (p = 0.02646) and monthly average precipitation (p = 0.03046), but pasture proportion was more significant than them. A backward stepwise approach was employed to remove any statistically insignificant variables one-by-one from the initial model. This process aimed to ensure that only significant covariates remained in the model after covariate de-selection and, thereby, minimize model complexity. The final model presented in Table 4.2, which included only the pasture proportion variable, produced a more statistically significant coefficient for pasture proportion (p = 6.74e-05) compared to the initial model. By focusing on only significant variables, the final model is valid, and simultaneously more parsimonious and interpretable.

Regarding the relationship between UC and temperature, although the final model for UC (Table 4.2) identified a statistically significant association with monthly average temperature (p = 0.00126), this does not suggest that temperature alone explains the variation in UC. Temperature variation in the UK generally follows a north-south gradient, meaning that there is a greater risk of UC in the north than in the south (since the parameter is negative), and while temperature is shown here to be associated with UC risk, other factors that vary along this gradient may also play a role. A similar argument can be made, albeit to a lesser extent (p = 6.74e-05), for the relationship between CD cases and pasture proportion. However, it is the *difference* between the CD and UC model results that is key.

The hypothesis tested in this research was whether the rate of CD cases relative to the population was related to the distribution of biogeographic features (with a specific interest in pasture areas). MAP is the etiologic agent of Johne's disease and can affect many species (primarily sheep, cattle and goats) including primates [163, 165, 271]. Animals infected with MAP, either clinically or sub-clinically, can shed substantial amounts of the pathogen in their faeces, contaminating pastures [310]. Subsequently, MAP disseminates into the environment, where it can persist for extended periods outside a host [16, 17, 311]. Within hydrological catchments, MAP is carried to adjacent rivers through surface water flow [16, 17]. Thus, our interest was in whether a statistically significant relation could be found between the number of CD cases (while accounting for the underlying population) and biogeographic features, including pasture proportion, when analysed at the catchment level. Importantly, the relationship between the number of UC cases and biogeographic features was used as a control. By comparing the estimated parameters and their statistical significance for the CD and UC models, we were able to control effectively for other possible explanations for the significance of pasture proportion such as survey response bias related to geographical location.

The contribution of this UK-wide IBD study was, thus, to add to the limited body of knowledge on the etiology of CD in the context of geographical factors, in addition to previous extensive studies on the relationship of IBD with environmental factors [139, 240, 241, 243].

4.4.1. Relationship to previous research

The endemic nature of Johne's Disease worldwide is reflected in the UK [312] with an estimated JD herd prevalence of 68 %, based on bulk milk samples from 225 herds [313, 314]. Following exposure to MAP, infected cattle enter a prolonged incubation period followed by the subclinical and clinical stages of infection [315]. The subclinical stage is characterized by the onset of bacterial shedding within faeces [314, 316], significantly depositing MAP onto pastures [139]. In the UK, previous studies showed that the spatial distribution of MAP increased from north to south and was significantly correlated with increasing cattle numbers over the same longitudinal axis [311], including its presence in pasture areas [310]. In this research, we found a statistically significant relationship between CD (but not UC) and pasture proportion (Figure 4.1).

At a more local level, Pickup and co-workers showed that proximity to rivers that received water from high intensity grazing areas influenced the distribution of CD sufferers [16, 17, 281], and that aerosols, as an exposure route, may play a role in CD epidemiology [281]. Specifically, it was found that people living along stretches of the River Taff in Cardiff, Wales, UK have a greater probability of being diagnosed with CD [16]. Moreover, MAP deposition in soil from infected animals was found to be significantly associated with cattle distribution, and consequently, pasture distribution [139]. This research supports this research from a national perspective. Moreover, this research, for the first time, provides evidence to support the hypothesis that living within catchments that have a greater proportion of pastureland upon which MAP-infected animals graze may also increase the likelihood of CD amongst the at-risk population, in line with the conceptual model of the relationship between humans, animals, MAP and the environment (Figure 4.1). To assess the robustness of this relationship across different spatial scales, we also conducted a grid-based analysis using cells ranging from 5 km^2 to 50 km^2 (i.e. 5, 10, …, 45, 50), which consistently revealed a significant positive association between pasture proportion and CD incidence. The risk of CD onset may also increase, of course, with long-term exposure to other pathways such as food (beef [297], milk and dairy products [302], as well as drinking water [281, 295], but this risk is assumed to be fairly homogeneous across England and Wales at the level of the catchment units used in the analysis, and is not considered here.

4.4.2. Limitations

A We acknowledge the limitation that the study survey reached only a small proportion of IBD cases in the UK. According to CCUK, 540,000 people across the UK are living with Crohn's or Colitis (CCUK, 2024). Although it was one of the largest surveys of its kind in the UK, the number of participants (3,887) accounts for approximately 1% of all IBD cases. While the sample represents only 1% of all IBD cases, it includes a wide geographic spread across England and Wales, allowing for spatial analysis. The main risk of bias lies in potential underrepresentation of certain regions, which could influence spatial patterns. However, the use of UC as a control—drawn from the same sample—mitigates against this. The differing results for CD and UC cannot be explained by possible sampling bias. This analysis, as well as that in Chapter 3, assumes that there is no systematic difference in survey response rates between individuals with CD and those with other forms of IBD.

The research was conducted at the catchment level across England and Wales. This was done to capture the hypothesized conceptual links between biogeographical features such as the distribution of grazing ruminants and potential human exposure to the MAP agent. The ability to integrate the location of the potential source with the location of exposure is helpful. However, it is acknowledged that the spatial resolution of the analysis is consequently relatively coarse and, thus, while the use of UC as a control makes the evidence more compelling the results need to be treated with some caution. The results are, thus, presented as additional supporting evidence for the *possible* association between Johne's disease/MAP [10] in ruminants and CD in humans via the MAP agent and hydrological transport pathways [16, 17]. Future research will investigate the local associations between cases and biogeographical features at a finer spatial resolution, for example, via (marked) point pattern analysis.

The case data used in this research were collected via an online survey prepared via Qualtrics and promoted at regular intervals by several voluntary IBD organisations across the UK to reach the maximum number of participants. Promotion was carried out on both the official websites and social media accounts of the organisations. Although we aimed to maximize the participation rate and create geographically equal coverage by promoting the survey widely across the UK, it was not possible to reach the entire IBD community as many sufferers may have been unaware of the survey or chose not to participate. We recognize that certain groups, including the elderly who may be digitally excluded and children for whom consent is more complex, might have been underrepresented in the survey. An analysis with more participants could be helpful in revealing the spatial distribution of IBD cases across the UK with greater granularity and support the analysis proposed above. In future research, government health authorities may also be contacted to request access to the online electronic general practitioner (GP) health records database [264].

4.5. Conclusion

In this research, the distribution of IBD cases participating in a UK-wide IBD survey, was analysed for England and Wales using a Poisson regression model to assess whether there were associations with potential biogeographic covariates. Poisson regression models were fitted for CD and UC. In the initial Poisson model, a statistically significant relationship was found between CD cases and pasture proportion (p = 0.00724), while no relationship was found between UC cases and pasture proportion (p = 0.6169; Table 4.1). In the final fitted model, a significant fit (p = 6.74e-05) was obtained between CD cases and pasture proportion (Table 4.2), while no such relationship was found for UC. This is the first national-scale study to report an association between CD cases and pasture proportion, suggesting that pasture areas and, thereby the distribution of ruminants, may play a role in CD risk.

Chapter 5

5. Diarrhoea in Children Under 5 Years in Two Informal Settlements in Accra, Ghana: The Impact of Antecedent Rainfall and Flooding

Abstract

Diarrhoea is a common and critical public health problem among children under five years of age in Africa's urban informal communities, resulting in high mortality. Heavily influenced by poor sanitation and high bacterial and viral concentrations in surface waters, environmental parameters such as rainfall, particularly during floods, and temperature can increase the incidence of diarrhoeal diseases. However, information on the dynamic effects of these covariates is limited. This research was conducted in two informal settlements, Gbegbeyise (GB) and Madina Zongo (MZ), in Accra, Ghana, to examine the relationship between diarrhoea cases among children under five years and environmental factors. Data on diarrhoea cases were collected from selected households every two weeks for over two years, consisting of a pre-intervention and an intervention period. This paper analyses the pre-intervention 40 visits, which were known to be relatively temporally stationary, using two Poisson regression models. The first model, which was fitted to time-series data, identified a

statistically significant relationship between the number of children with diarrhoea and antecedent (up to 1 week) rainfall and temperature values, with lagged rainfall being a significant covariate in both settlements, while temperature was significant only in GB. The second model examined the association between the total count of diarrhoea cases and the spatial proximity of households to flood-prone areas, and elevation, revealing that diarrhoea cases are expected to increase with proximity to flood areas. Thus, not only does the analysis establish the importance of antecedent rainfall in driving up disease risk, but it also establishes a strong potential pathway (flood water), thereby, linking disease risk more concretely to the antecedent rainfall that caused the flooding. This is not least because standing water and ponding arise after the rainfall has occurred. These findings highlight the clear role of rainfall in diarrhoeal disease transmission and underscore the importance of integrating climate-sensitive health interventions in informal settlements. Understanding these associations can help inform targeted public health strategies and community awareness through education as an early warning system to mitigate the impact of diarrhoea outbreaks in vulnerable communities exposed to flooding and poor sanitation.

In this chapter, Mehmet Akif Veral was responsible for curating the dataset, performing the statistical analyses, creating maps, methodology, interpreting the results and writing – original draft.

5.1. Introduction

Childhood diarrhoea is defined as three or more watery stools per day or an increase in stool frequency with an increase in stool fluidity [317]. One in 10 deaths in children under five worldwide is caused by diarrhoea, with most of these deaths occurring in regions such as Sub-Saharan Africa and Southeast Asia [318]. According to the World Health Organization (WHO, 2024), diarrhoeal diseases are the third leading cause of death in children under 5 years worldwide, causing approximately 450,000 deaths each year and affecting approximately 1.7 billion children globally [319]. The main complications of diarrhoea in children are dehydration due to excessive water loss from the body [320] and negative nutritional balance due to nutrients passing through the digestive system, but these remain neglected in informal settlements [20]. During diarrhoea, the digestive system works faster than normal, preventing adequate absorption [321] and stunting growth [322]. Environments that do not provide clean and safe conditions, such as informal settlements (also known as 'slums'), can pose a serious risk of death for children (WHO, 2002). Access to clean water, improved water and sanitation hygiene (WASH) practices are critical to preventing diarrhoea This is particularly relevant to UN Sustainable Development Goal (SDG) 6 and links to SDG 3. However, inadequate WASH practices account for 88% of diarrhoea-related deaths [184], and this is also true in sub-Saharan Africa due to limited access to clean water, inadequate sanitation practices and lack of good hygiene [323]. Urban poverty analysts report a dramatic decrease in health outcomes in informal settlements compared to other settlements, by as much as 50 times higher for under-five mortality rates, 50% greater for children under five who are underweight or underheight for their age, and 13% higher for the prevalence of diarrhoea containing blood among children [324].

Environmental factors play an important role in the incidence of diarrhoea [186, 208, 325] and its occurrence is often associated with increased rainfall [19, 206, 326]. Climate variability and extreme weather events can create a favourable environment for pathogens resulting in increased risk, particularly in areas in Africa with poor water and sanitation infrastructure [327, 328]. In particular, heavy rainfall following a dry period can cause an increase in diarrhoea, while rainfall following a wet period can dilute pathogen concentrations, potentially reducing diarrhoea [329]. Flooding following heavy rainfall can spread disease-causing pathogens, with a consequential increase in diarrhoeal diseases [78]. It has also been reported that high temperatures can lead to an increase in diarrhoeal cases [19, 38, 330]. This is explained by the fact that hot weather conditions facilitate the longer survival and spread of microbial pathogens. However, the relationship between temperature and diarrhoea in children exposed to high temperatures has been reported to show regional differences, being positive in some regions and negative in others [39].

Accra, on the southern coast of Ghana (latitude: 5.614818 and longitude: -0.205874) has two main periods of rainfall throughout the year. The first period covers March to July, while the second period covers September to November, with the first period accounting for 66% of the annual rainfall [331]. A significant relationship has been found between the number of diarrhoeal cases and flooding in this region [78]. Gbegbeyise (GB) and Madina Zongo (MZ), two low-income informal settlements in Accra, the capital of Ghana, were selected as the study areas for this research. Inadequate WASH practices and infrastructural deficiencies in these settlements can facilitate the spread of waterborne diseases, especially when environmental conditions increase the risk. In particular, household flood preparedness was reported to be low in the GB settlement [332]. Floods not only increase the mobility of microbial pathogens but also increase the likelihood of new diarrhoeal cases arising due to environmental conditions. This suggests that households affected by flooding will be at higher risk of contracting diarrhoea over time and that cases may reoccur [333].

We hypothesize that environmental factors such as rainfall, temperature and floods may be important drivers of diarrhoeal disease in children in the GB and MZ settlements in Accra, Ghana. To test this hypothesis, households in both settlements were profiled, and children's health data were collected through a total of 65 household visits conducted every two weeks over a 2-year period. Household information was collected from the household head regarding children's age, gender, diarrhoeal status, type of diarrhoea and the type of treatment received. Daily rainfall and temperature data for both settlements were obtained from weather stations in each settlement, with data collection starting from the first visit.

To examine the statistical relationship between diarrhoeal cases and environmental factors, we employed two separate Poisson regression models. The first (temporal) model assessed the association between diarrhoeal cases and meteorological time-series variables, specifically rainfall and temperature, incorporating temporally lagged effects up to seven days before each visit to account for potential delayed impacts. The second (spatial) model analysed the relationship between diarrhoeal cases and the spatial proximity of households to flood-prone areas, as well as elevation, to explore the influence of flood exposure on disease incidence. No publications have previously been produced using this dataset.

5.2. Methods

5.2.1. Study site and data

The study covered the Gbegbeyise (GB; latitude: 5.527503, longitude: -0.264258) and Madina Zongo (MZ; latitude: 5.678791, longitude: -0.177108) settlements in Accra, Ghana. Gbegbeyise is a coastal settlement (located 0.7 km inland) with a predominantly Christian population and Madina Zongo is located 13 km inland from the coast and its population is predominantly Muslim (see appendix-3 for site locations). Aerial mapping of both settlements and GPS were used by trained enumerators to assign each household to a unique identification code. Household codes were linked to data collected by the project team and enumerators to assist in navigating through the communities and managing efficient data collection. Households with children under three years old at the start of the survey were specifically prioritized for inclusion in diarrhoeal disease surveillance (DDS) and then monitored for the next 2 years.

This ethically approved study included a participant information sheet and consent form for participants to sign prior to data collection. A data collection form was used to record each child's age, gender, whether they had diarrhoea in the past two weeks, the type of diarrhoea and whether the child was treated at home or required hospitalization. 10 external enumerators were recruited and trained to collect the data. Enumerators recorded diarrhoea data in the field and then transferred them to an excel file. The final dataset was digitised, made available to project partners at Lancaster University and sent to the Council for Scientific and Industrial Research (CSIR) project manager for record keeping.

Precipitation and temperature data were systematically and digitally recorded using two localized weather stations (ATMOS41_ZL6 Logger) installed separately in the GB (5.5255568, -0.2263749) and MZ settlements (5.6753143, -0.1791659). Flooding data, however, were not digitally collected. Instead, they were obtained through direct observations by individuals authorized within the project who possessed extensive knowledge of the area.

Flooding evidence was recorded through protocols that integrated local community knowledge with structured data collection tools. A checklist and area maps were prepared and distributed to individuals authorised to collect flood data, who were familiar with the community context and spatial dynamics of flooding. These individuals identified and localised flood-prone areas, monitored events, and systematically documented observations (see appendix-5). In addition to direct flooding, the protocols also captured information on contributing contamination sources, such as disposal of solid waste and toilet dumping, which often clogged drains and interacted with rainfall patterns. This approach ensured contextual accuracy of the data and promoted meaningful community engagement in the research process. These are evident in the illustrations.

The study sites are informal settlements characterized by fragmented yet existing sanitation infrastructure, including community toilets, open defecation areas, and open drainage systems. Communal sanitation facilities were owned privately by local landlords, and their use was subject to a user fee. These facilities are vulnerable to flooding, which can compromise their functionality and increase risks to public health. No prior engagement between the research team and the communities had occurred, and these sites were selected to provide a representative understanding of environmental and infrastructural conditions in informal settlements of Accra.

Because a population health intervention was implemented in the GB settlement at visit 41 (5 April 2021), we focused exclusively on the first 40 visits for both the GB and MZ settlements. After the 40th visit, an intervention was implemented which included repairing surface drains, removing rubbish and plastics that clogged the drains, and cleaning public toilets at regular intervals. Thus, the importance of environmental factors on diarrhoea prevalence was investigated without the effect of the intervention.

5.2.2. Participant flow

Figure 5.1 shows the temporal trends in the number of children for whom data could not be collected across the 65 household visits in both settlements. In GB (Figure 5.1.a), the number of children with missing data increased steadily during the first year of data collection, reaching a plateau of around 70–80 from mid-2021 onwards. By early 2022, this number stabilised at approximately 80 participants. One child died due to diarrhoea during the study period, while the remaining missing cases were primarily due to household relocations. Occasional short-term declines are attributable to temporary absences, such as children travelling or being away on holidays.

In MZ (Figure 5.1.b), a comparable upward trend was observed, although the absolute number of children lost to follow-up remained lower than in GB. At the beginning of 2021, about 40 children could not be followed, increasing to around 60 by early 2022. Despite this rise, attrition was consistently lower compared to GB. No child deaths were reported in MZ, and the intermittent decreases similarly reflect temporary absences (i.e. children travelling or being away on holidays).

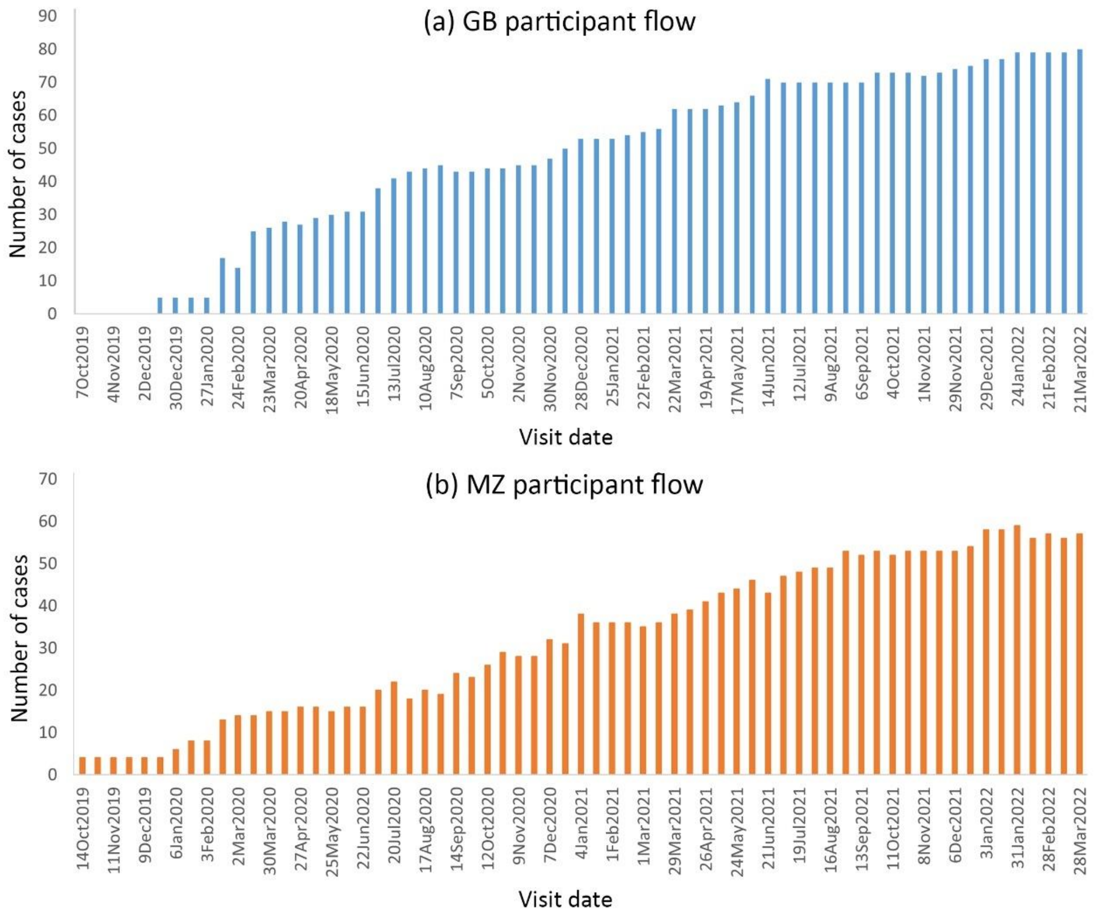


Figure 5.1. Number of children with missing data per visit in Gbegbeyise (GB) and Madina Zongo (MZ).

5.2.3. Gbegbeyise and Madina Zongo household visits

During the pre-intervention period (i.e., the first 40 visits), household-level surveys were conducted every two weeks in the identified households of the GB and MZ settlements. A list of households with children under five years of age was compiled, and listed households were visited (see appendix-2). No random sampling was performed. As the study aimed to cover eligible households, no formal sample size or power calculation was required. Each household was assigned a unique identifier using GPS mapping, which facilitated systematic visits and consistent data collection. Data collection took place between 7 October 2019 and 5 April 2021 in GB and between 14 October 2019 and 12 April 2021 in MZ, covering a total duration of 547 days. Over this period, a total of 228 households in GB and 166 households in MZ were initially visited and surveyed. Enumerators recorded each child's age, gender, incidence of diarrhoea in the past two weeks, type of diarrhoea, and treatment information directly from participants' legal guardians. In cases where participants relocated or passed away during the study, their data were included only for the duration of their availability, maintaining longitudinal integrity while minimizing potential selection bias. Ethical approval for the survey was granted by Lancaster University (FST20014: amendment to FST19026/18055), and informed consent was obtained from all participants' legal guardians

5.2.4. Covariates

Covariates were selected based on their hypothesized relationship with the dependent variable, guided by previous studies [19, 38, 334]. Daily rainfall and temperature data were obtained from weather stations established in the settlements. Flood-affected areas in residential zones were identified through direct field observations conducted by the exploration team and subsequently mapped. These spatial data were then digitized and transferred into ArcGIS Pro 3.0, where buffer zones were generated around the flood-affected areas. The flood exposure status of each surveyed household—determined by its presence within the buffer zones—was recorded and included as a covariate. Additionally, the distance of each household from the nearest flood-affected area was calculated and incorporated into the model as another covariate. Elevation data for both settlements were acquired and processed using a combination of Google Earth Pro, GPS Visualizer (https://www.gpsvisualizer.com/elevation), and ArcGIS Pro 3.0. Initially, specific locations within the GB and MZ settlements were georeferenced in Google Earth Pro and exported as KML files. These KML files were converted subsequently to the GPX file format using GPS Visualizer, with elevation values recorded in meters. The GPX files were then imported into ArcGIS Pro and the elevation value of each household was calculated by averaging the elevation of the surrounding neighbouring households. This approach allowed a detailed spatial representation of elevation, supporting further statistical analyses.

5.2.5. Poisson regression model

Poisson regression is used when the dependent variable represents count data, such as the number of events occurring at a fixed time or location, and the data follows a Poisson distribution [335, 336]. It is typically used when events are rare, independent and have a constant expected rate of occurrence [337, 338] expressed as:

$$\log(\lambda_i) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n + \log(N_i) + \varepsilon$$

where λ is the number of observed cases and β_0 is the intercept. $\beta_1, \beta_2 \ldots, \beta_n$ are the coefficients of the covariates, $X_1, X_2, \ldots, X_n$ are the covariates and ε is an error term. Within the scope of the study, two Poisson regression models were fitted, and both models were implemented using the glm function in the R programming language.

A first Poisson regression model was used to examine the relationship between the time-series number of diarrhoea cases and rainfall and temperature in both the GB and MZ settlements. The dependent variable was the total number of children with diarrhoea recorded at each visit. The independent variables were rainfall, temperature and the expected number of cases (used as an offset). The expected number of cases was calculated by multiplying the overall rate (total number of children with diarrhoea/total number of children) by the total number of children at that visit. Precipitation and temperature values of each day were recorded individually to evaluate any lag effect. For example, the rainfall value of the 1-day lag represented the total amount of rainfall (mm) the day before the visit day. This step was repeated for the preceding days (2-day lag, 3-day lag, ..., 7-day lag). The temperature (°C) was recorded as an average each day. The temperature data of the 1-day lag represented the average temperature value of the day before the visit day and this process was repeated for the preceding days as for rainfall. These lag data allowed the modelling of both instantaneous and time-varying effects of the environmental factors.

In a second Poisson regression model, the statistical relationships between the total count of children with diarrhoea and the spatial proximity of households to flood areas, flood buffer areas and elevation data were analysed. The dependent variable was the total number of children with diarrhoea over the 40 visits and the independent variables were the spatial proximity of households to the nearest flood area, whether the households were located within the flood buffer areas (1 if within the buffer area, 0 otherwise), the average elevation value of the households (i.e. the average elevation value of the nearest neighbouring households to that household) and the expected number of cases (calculated in the same manner as mentioned above and used as an offset in the regression model).

All data used in both Poisson regression models belong to the first 40 visits. In the first regression model which included precipitation and temperature as covariates, statistically insignificant covariates were removed one by one, starting from the most insignificant, until all remaining covariates became significant. Then, variance inflation factor (VIF) analysis was performed to test for any co-linearity between covariates. The covariate with the highest VIF value, if above a threshold of 10, was removed from the model and the model was re-run. The above process was repeated for statistically insignificant covariates and VIF>10. In the final model, all covariates were statistically significant and with VIF<10.

5.3. Results

5.3.1. Exploratory data analysis

5.3.1.1. Age and gender distribution

Some variation in age and gender was found between the GB and MZ settlements for the first visit to households. The total numbers of boys and girls under 5 years living in the visited households in the GB settlement were 135 (52.94%) and 120 (47.06%), respectively (Table 5.1). The largest group among boys consisted of individuals between the ages of 13-18 months, followed by 31-36 months. Similarly, the largest age group among girls consisted of individuals between the ages of 13-18 months, followed by 19-24 months. To further demonstrate the robustness of the dataset, diarrhoea prevalence by child age (pooled across visits) is presented in appendix-4.

Considering the households visited in the MZ settlement, the total number of boys and girls were 93 (48.69%) and 98 (51.31%), respectively. The largest group among boys consisted of individuals between the ages of 13-18 months, followed by 19-24 months. Among girls, the largest age groups were 13-16 and 25-30 months, followed by children aged 27-42 months (Table 5.1).

Table 5.1. Initial age (in months) and gender distribution of children in households visited in the GB and MZ settlements.

Age (months)	GB	Male	Female	MZ	Male	Female
0-6	20	12	8	19	10	9
7-12	31	16	15	29	13	16
13-18	48	24	24	31	16	15
19-24	34	16	18	26	14	12
25-30	36	20	16	23	8	15
31-36	44	27	17	23	12	11
37-42	27	10	17	26	12	14
43-48	13	8	5	11	6	5
49-54	1	1	0	3	2	1
55-60	1	1	0	0	0	0
Total	255	135	120	191	93	98

Changes in the ages of children with diarrhoea in the GB and MZ settlements over the study period are given in Figure 5.2. During the 896-day visit period, it was found that the age ranges of children with diarrhoea in the GB settlement were predominantly between 25-36 and 37-48 months (Figure 5.2). Although these two age ranges were predominant over the full study period, children aged 13-24 months (October 2019-April 2021), 49-60 months (July 2020-December 2021) and 7-12 months (October 2019-June 2020) were also common during long periods. The lowest prevalence across the visits was in children aged 0-6 months.

Similarly, in the MZ settlement, for children with diarrhoea the age ranges 25-36 and 37-48 months were observed to be more dominant throughout the study period. The relatively less dominant age groups were found to be between 7-12 months (October 2019-June 2020), 13-24 months (October 2019-December 2020) and 49-60 months (June 2020-March 2022). As in the GB settlement, the lowest prevalence was in children aged 0-6 months during the visits.

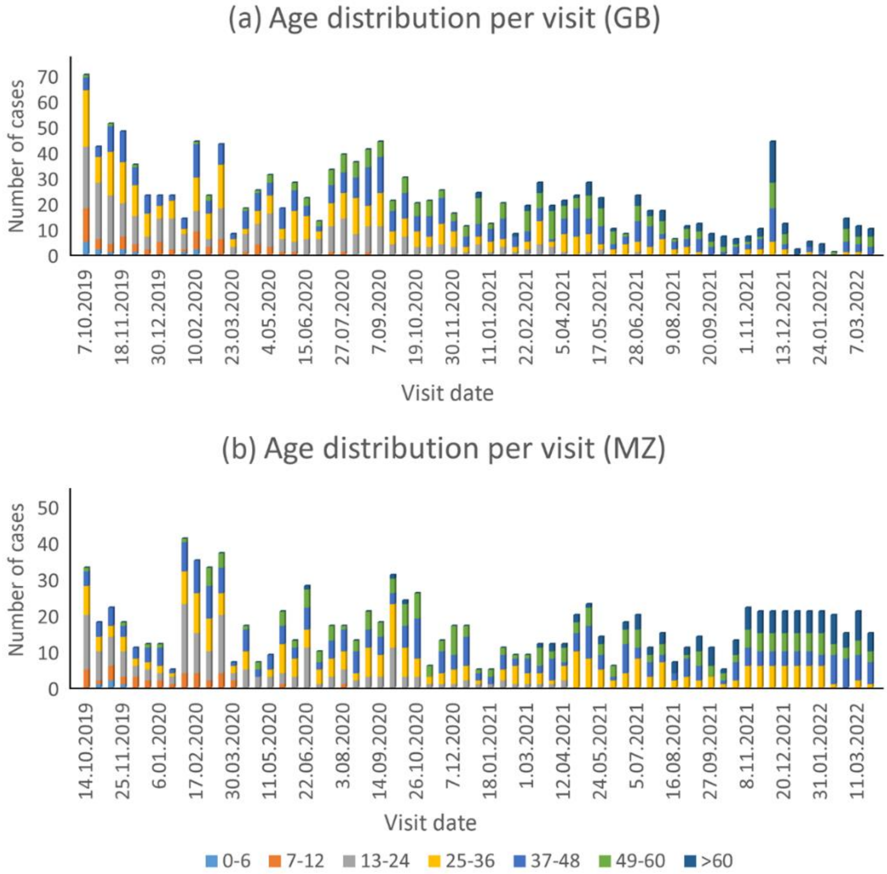


Figure 5.2. Age distribution of children with diarrhoea during visits per month for the (a) GB and (b) MZ settlements.

5.3.1.2. Distribution of diarrhoea types

The distribution of different types of diarrhoea cases over time in children identified in the GB and MZ settlements is given in Figure 5.3. The plots stack the diarrhoea cases identified on each visit date into four different types. Type 1: watery stools (blue), type 2: watery stools and vomiting (green), type 3: loose stools with mucus (yellow), type 4: bloody stools with mucus (red).

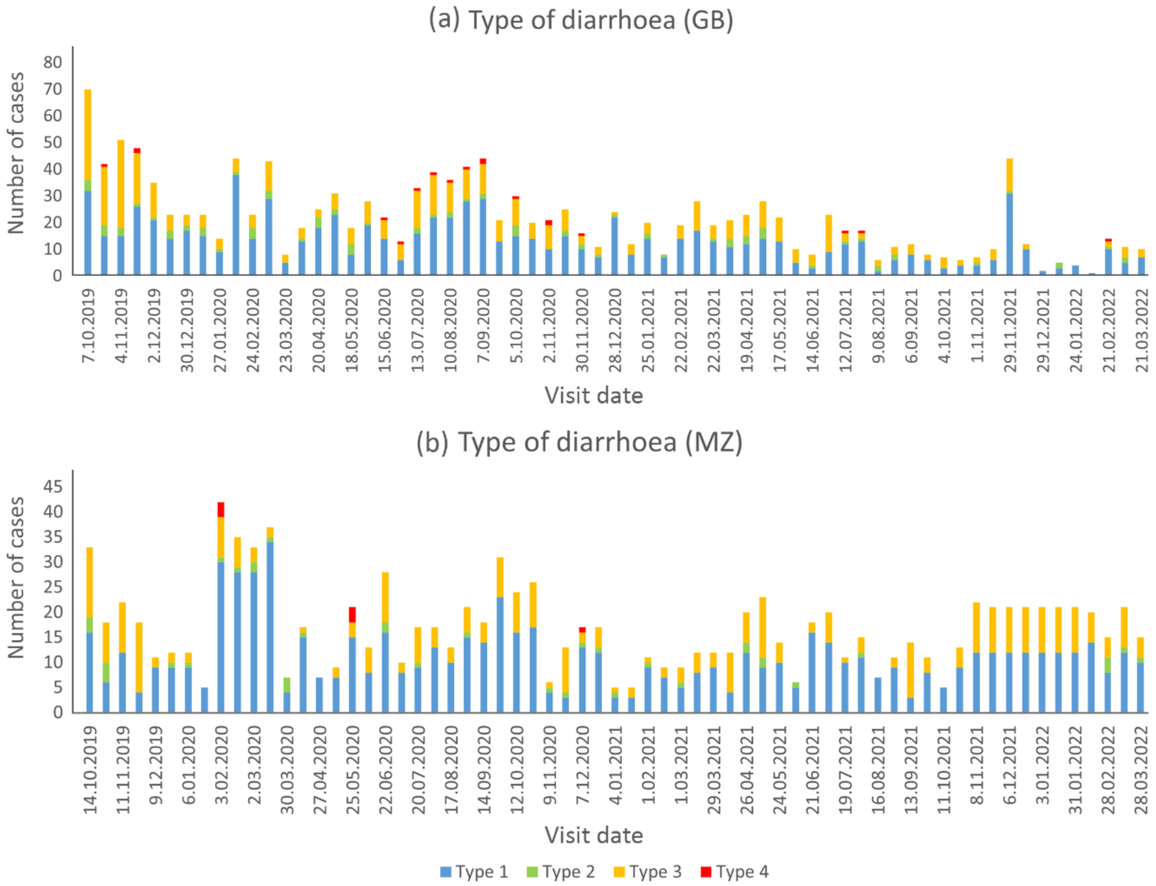


Figure 5.3. Types of diarrhoea recorded in visited households in the (a) GB and (b) MZ settlements. Type 1: watery stools, type 2: watery stools and vomiting, type 3: loose stools with mucus, type 4: bloody stools with mucus.

It is observed that the number of diarrhoea cases was high in the GB settlement in the last quarter of 2019 and early 2020, reaching the highest level in October 2019 (Figure 5.3). There was a significant decrease in the total number of cases towards the middle of 2020, but an increase was observed again between July and September 2020. It is observed that the numbers of cases remained low throughout 2021, but there were small increases in certain periods (e.g. March, May and June 2021). The number of recorded cases peaked again in December 2021. It is noteworthy that the number of cases decreased and followed a stable course from the beginning of 2022.

In the MZ settlement, as with the GB settlement, the number of cases was high in October 2019. There was a decrease in the number of cases in mid-2020, but an increase was recorded again in the February-March 2020 and May-June 2020 periods, and this increase was observed to continue until November 2020. The number of cases remained relatively low throughout 2021, but short-term increases were observed on certain dates (e.g. April, June and November 2021). In early 2022, the total number of cases recorded did not change over the course of a few months of visits but fluctuated in subsequent visits.

When the distribution was examined according to diarrhoea types for both settlements, Type 1 (blue) diarrhoea was the most common type in all time periods (Figure 5.3). The count of Type 2 (green) diarrhoea cases was low and is almost never seen in some time periods. Type 3 (yellow) diarrhoea cases, although less frequent than Type 1 in some periods, have a distinct distribution. Type 4 (red) diarrhoea cases are observed with the lowest frequency and show short-term increases only on certain dates.

5.3.1.3. Distribution of treatment types

The treatment methods applied for the types of diarrhoea recorded in the visits to households in the GB and MZ settlements are shown in Figure 5.4. The treatments comprised: type 1, home care; type 2, traditional heal; type 3, admitted to hospital (kept in the hospital for treatment for more than a day); type 4, Outpatient's Department (OPD) (i.e. visited the hospital for treatment and left on the same day). In both settlements, the most commonly used treatment was type 1, which was predominant throughout all visits. The Type 4 treatment method was the second most common following type 1 treatment. The Type 2 and Type 3 treatment methods were applied less frequently in both settlements; however, their application increased at specific visits.

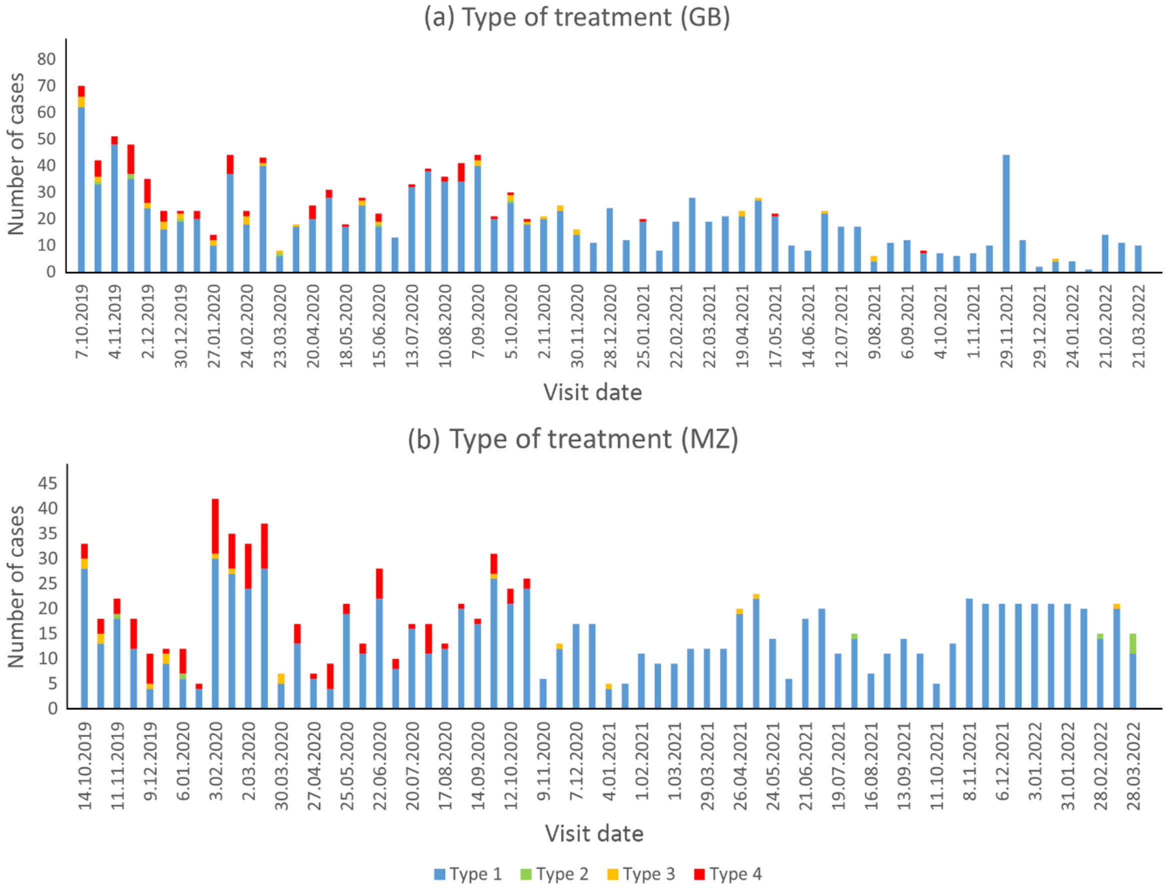


Figure 5.4. Types of treatment applied to diarrhoea cases reported during visits to households in the (a) GB and (b) MZ settlements. Type 1: home care, type 2: traditional healer, type 3: admitted to hospital (kept in the hospital for treatment for more than a day), type 4: Outpatient's Department (OPD) (i.e., visited the hospital for treatment and left on the same day).

Considering the distribution of treatment types in both settlements, type 1 treatment was found to be the most common. This was followed by type 4 treatment, which, although applied during some visits in GB after November 2020, was not applied at all in MZ. Additionally, type 3 treatment was recorded as being applied less frequently than types 1 and 4, but more frequently than type 2 throughout the visits. Type 2 treatment was the least applied method in both settlements and was recorded as being almost never applied during the visits.

5.3.1.4. Distribution of covariates in the GB and MZ settlements

The distributions of total rainfall and average temperature recorded throughout the visits are given in Figure 5.5. In the GB settlement, rainfall peaked in June 2020 and 2021, August

2021 and February 2021, and the average temperature was between 25-30 °C throughout the visits. Although there was no significant fluctuation in rainfall on the days of other visits, there were small peaks in some months. On the other hand, in the MZ settlement, rainfall peaked in early October 2020 and 2021, and fluctuations were more intense with rainy periods observed more frequently than in GB. In MZ, temperature values ranged between 25.9 °C and 35.5 °C throughout the visits, showing minimal variation and similar temperatures to those in GB.

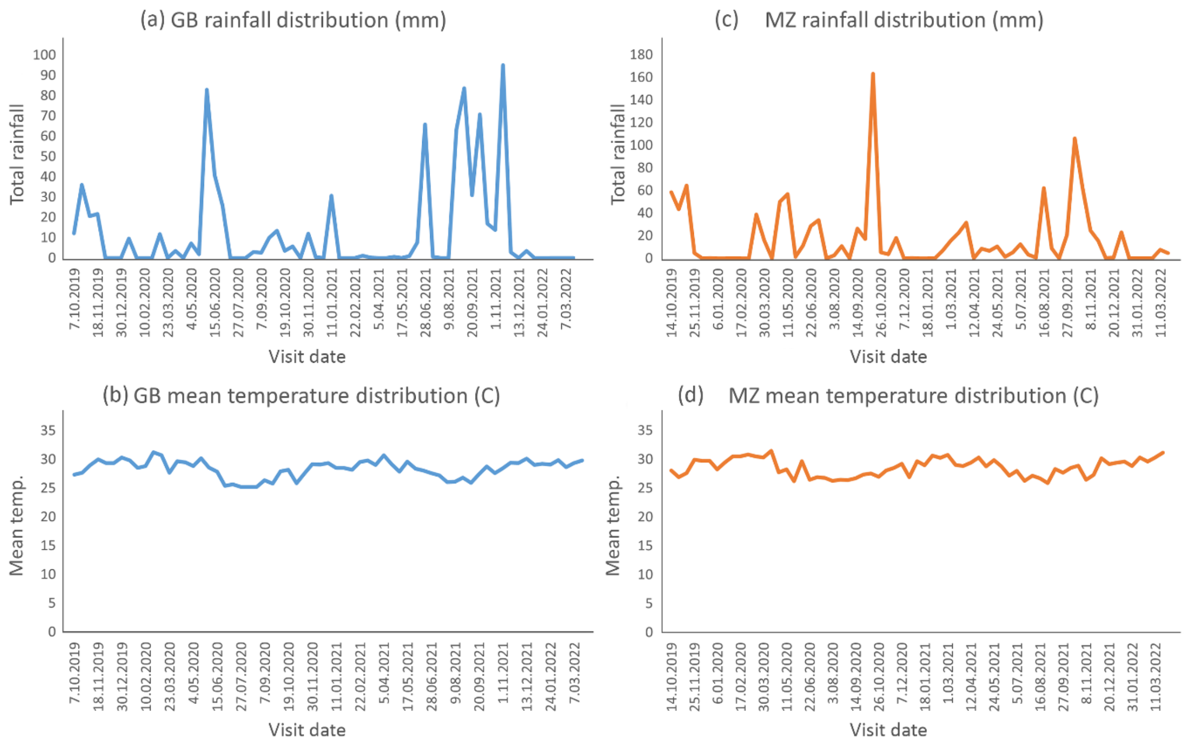


Figure 5.5. (a, c) Rainfall and (b, d) temperature distributions for the (a, b) GB and (c, d) MZ settlements. The specified dates represent the days of visits to households, while the rainfall variable represents the total amount of rainfall recorded during the day of the visit, and the temperature variable represents the average temperature value of the same day.

5.3.2. Poisson regression model

5.3.2.1. Temporal association between diarrhoeal cases and rainfall and temperature

In the final fitted Poisson regression model for GB, the rainfall 1-day (p = 2.66e-05), 2-day (p = 0.00220), 5-day (p = 5.70e-05) and 6-day (p = 8.33e-06) covariates and the temperature 0-day (p = 0.00355) and 7-day (p = 2.52e-09) covariates remained significant

(Table 5.2). It was found that a 1 mm increase in rainfall caused an increase of 15.22% and 9.38% in the number of diarrhoeal cases for the rainfall 1-day and 6-day covariates, respectively, while it caused a decrease of 1.73% and 5.65% for the rainfall 2-day and 5-day covariates, respectively. For temperature, it was found that a 1 °C increase in temperature caused a 10.27% increase in the number of diarrhoeal cases for the temperature 0-day covariate, but a decrease of approximately 21% for the temperature 7-day covariate.

Only the rainfall 2-day (p = 0.00489) and 5-day (p = 5.45e-06) covariates remained significant for MZ. It was observed that a 1 mm increase in rainfall for the 2-day and 5-day covariates caused a 1.2% and 4.4% increase in diarrhoea cases, respectively. No temperature covariate was found to have a statistically significant relationship with the number of diarrhoeal cases for MZ.

Table 5.2. Results of the final Poisson regression model.

Covariates	**GB diarrhoea cases**		**MZ diarrhoea cases**	
	β	p	β	p
rainfall 1-day	0.141754	2.66e-05	NA	NA
rainfall 2-day	-0.017541	0.00220	0.012114	0.00489
rainfall 5-day	-0.058160	5.70e-05	0.043115	5.45e-06
rainfall 6-day	0.089662	8.33e-06	NA	NA
temperature 0-day	0.097775	0.00355	NA	NA
temperature 7-day	-0.235525	2.52e-09	NA	NA

Considering the number of covariates (Table 5.2), and the potential for residual levels of co-linearity, another simpler Poisson regression model was fitted, including only rainfall and temperature covariates, to promote parsimony and test model stability across covariate choices. In the GB settlement, both rainfall 1-day (β = 0.19649, p < 0.001) and temperature 0-day (β = -0.06595, p < 0.001) were statistically significant, and the model produced consistent outputs. In the MZ settlement, rainfall 2-day (β = 0.021515, p < 0.001) was identified as a significant predictor. Overall, increased rainfall prior to visits was associated with higher diarrhoea incidence in both settlements, with a stronger effect observed in GB.

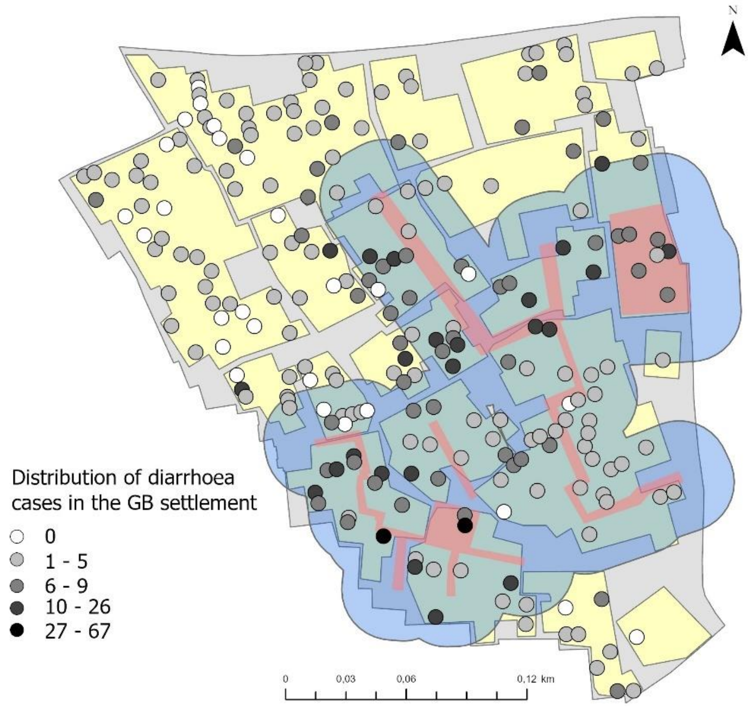
5.3.2.2. Spatial association between diarrhoeal cases and flooding, buffer zones and elevation

The spatial proximity of households to a flooded area and the location of households within a buffer around a flooded area represent different transformations of the same underlying spatial information. The relationships between childhood diarrhoea risk and these two covariates were examined and spatial proximity was found to be the more significant factor and, therefore, was selected as the covariate in our second Poisson regression model. Figure 5.6 illustrates the covariates used in this part of the analysis. Spatial proximity to the flood zone was found to be a highly significant predictor of diarrhoea incidence in both GB (p = 2e-16) and MZ (p = 2.08e-12) (Table 5.3). A 1 m decrease in distance to flood area led to a 1.40% increase in diarrhoea incidence in GB and a 0.32% increase in MZ. These findings show that the incidence of diarrhoea was higher in households closer to the flood area, suggesting the impact of standing water on disease transmission. In contrast, the total number of children with diarrhoea was not associated with the mean elevation, for both settlements. Thus, overall, diarrhoeal risk was found to be significantly affected by flooding and standing water, with more cases occurring in households located closer to flood-prone areas. This finding highlights the critical role of spatial proximity to flood zones in the transmission of diarrhoeal disease

Table 5.3. Results of the second regression model between the number of children with diarrhoea and the distance of households to the flood area and mean elevation. Significant coefficients are given in **bold.**

Covariates	GB diarrhoea cases		MZ diarrhoea cases	
	β	***p***	***β***	***p***
distance to flood	-0.014179	**2e-16**	-0.0031882	**2.08e-12**
mean elevation	0.026672	0.121	0.0355175	0.217

(a)



(b)

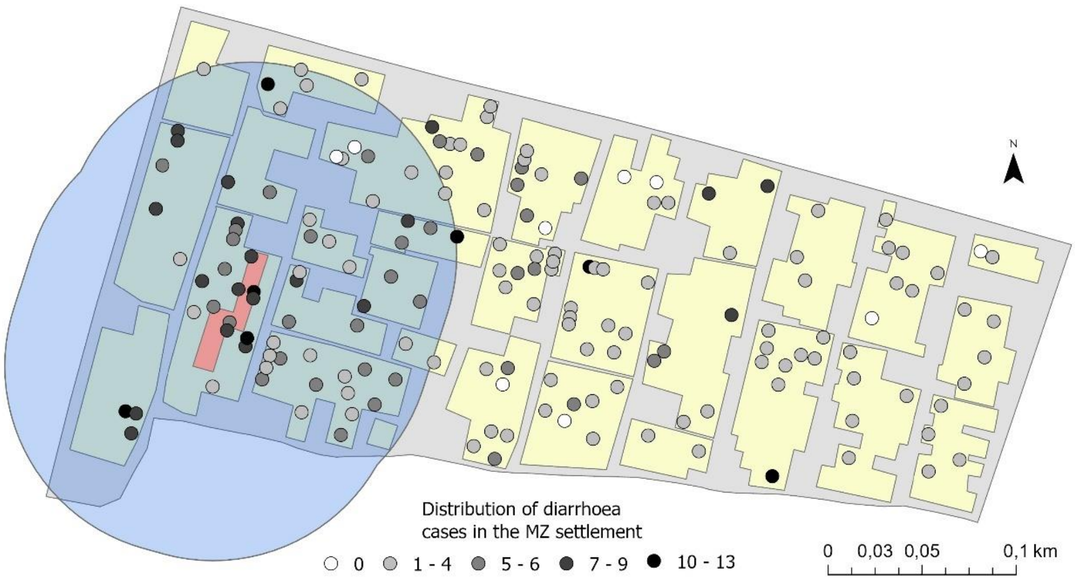


Figure 5.6. Distribution of households in the (a) GB and (b) MZ settlements, together with (white to black gradient circles) total number of diarrhoeal cases recorded during the first 40 visits, (red) flooded area and (blue) flood buffer areas. Households were grouped and marked in yellow to prevent individual identification for ethical confidentiality reasons.

5.4. Discussion

5.4.1. Effect of environmental parameters on diarrhoea cases

The main objective of this research was to determine whether the incidence of diarrhoea in the GB and MZ settlements in Accra, Ghana, was associated with environmental factors. Using data from regular visits to GB and MZ, the statistical relationships between the total number of children with diarrhoea for each settlement and several temporal (rainfall, temperature) and spatial (flooding and elevation) covariates were assessed.

The research encompassed two settlements: GB and MZ, with 228 and 166 households, respectively, and each household was visited biweekly. In the GB settlement, the total number of children observed was 255, comprising 135 (52.94%) boys and 120 (47.06%) girls. Similarly, in the MZ settlement, 191 children were recorded, including 93 (48.69%) boys and 98 (51.31%) girls. During the visits, data could not be obtained from some households because individuals living in those households had moved or the children had died, and these households and/or individuals were subsequently excluded from the analysis. Considering the age distribution of children with diarrhoea across visits, it was found that diarrhoea was more common in children aged 25-36 and 37-48 months for both settlements compared to other age groups (Figure 5.2). In different large-scale studies, the prevalence of diarrhoea was recorded to be high in children aged 18-23 [339], 6-11 and 12-23 [340] and 13-24 months [341].

The most common type of diarrhoea in the GB and MZ settlements was found to be watery stools, followed by loose stools with mucus (Figure 5.3). Watery stools and loose stools with mucus showed a generally balanced trend in GB, but watery stool cases were more common in MZ, especially between February 2020 and March 2020. It has been reported by WHO that diarrhoeal disease is the third leading cause of death in children aged 1-59 months and one of the three clinical types of diarrhoea is <u>a</u>cute <u>w</u>atery <u>d</u>iarrhoea (AWD) [319]. In a large-scale study covering different regions in Africa, approximately 85% of children under the age of 5 were found to have watery diarrhoea [342] and this type is most likely linked to infections from microbial pathogens. On the other hand, loose stools with mucus (stools that are loose or watery in consistency and contain mucus) could be associated with inflammatory bowel disorders which are rare in Ghana [343].

Previous studies have shown that increasing rainfall is effective in increasing the number of diarrhoea cases [19, 206, 326, 327]. Similarly, in our fitted Poisson regression models, it was observed that rainfall and temperature had a significant effect on the occurrence of diarrhoea cases. Individuals with diarrhoea are assumed to be more likely to become ill due to high rainfall before the visits. Rainfall and flooding were both found to significantly influence diarrhoeal risk in the GB and MZ settlements. Increased antecedent rainfall was linked to higher incidences of diarrhoea, particularly in GB. At the same time, it was found that diarrhoeal risk is greater closer to flood areas. This suggests that rainfall increases the risk of diarrhoea, at least in part, by creating flooded areas and surface water which promote pathogen transmission. This finding aligns with existing literature on the link between rainfall and waterborne diseases. It was reported previously that excessive rainfall plays a role in the emergence of waterborne diseases [21], causes an increase in the number of bacteria and viruses in surface waters [22] and increases infection by creating suitable conditions for pathogens (immediate or delayed) [201]. In this context, the statistically significant relationship between the total number of children with diarrhoea and rainfall in GB and MZ is consistent with previous studies.

Antecedent exposures of rainfall and temperature were limited to a 0–7 day lag window for two main reasons. First, previous climate-diarrhoea studies have consistently reported the strongest associations in the weeks following exposure, and many analyses have used weekly lags or averages across lags to capture effects on infection risk [344, 345]. Second, the biological and transmission pathways that plausibly link diarrhoeal incidence to rainfall and temperature—such as contamination of drinking water, increased microbial activity, and heightened exposure following heavy rainfall—typically operate over short time scales, making a short lag structure of 0-7 days both more biologically plausible and parsimonious [203, 346]. Limiting the analysis to this period ensures that the models remain consistent with established practices in climate-health research while also focusing the estimated impacts on an epidemiologically meaningful timeframe.

Although an increase in rainfall is generally associated with a rise in diarrhoea cases, some studies have also reported that a decrease in rainfall can lead to an increase in diarrhoea incidence. Bandyopadhyay et al. (2012) [38] found that inadequate rainfall during the dry season, combined with higher monthly maximum temperatures, contributed to an increased prevalence of diarrhoea among children under three in Sub-Saharan Africa.

Similarly, Lloyd and co-workers (2007) [202] reported that low rainfall was associated with a 4% increase in diarrhoea cases among children under five, potentially due to water scarcity and inadequate hygiene practices.

The Poisson regression model revealed a significant relationship between the incidence of diarrhoeal cases and changes in temperature for GB. This is consistent with previous studies on temperature affecting the transmission of diarrhoeal disease [19, 38, 197, 208, 330]. There are a limited number of studies in the literature in which an increase in temperature causes a decrease in the number of cases [197, 199, 200]. Similarly, several studies reported that the relationship between temperature increase and pathogenic activity is generally positive, that is, pathogens become more active with increasing temperature and, therefore, the risk of infection increases [196]. However, Thindwa et al. (2019) [347] reported that temperature increases can negatively affect pathogenic activity. These findings revealed that temperature factors may have variable effects on the spread of diarrhoeal diseases in different settlements and changing environmental conditions.

The presence of autocorrelation can violate the assumption of independence in statistical tests, necessitating adjustments to ensure accurate inferences [348]. An autocorrelation analysis was performed to test whether there was a pattern among the residuals of the fitted model, calculated as the difference between the predicted and observed case counts. No significant autocorrelation was found, meaning that no further modelling of the residuals (e.g., in a mixed model) was necessary.

The GB settlement is located approximately 720 m from the coastline. Coastal areas, being closer to the sea, tend to have more moisture in the atmosphere. Humid air coming from the sea can turn into rainfall if the temperature and other conditions are suitable. However, the MZ settlement is located approximately 13 km inland from the coastline and its rainfall is relatively lower compared to the GB settlement (Figure 4). Less rainfall may reduce the risk of contamination. However, drought [38, 197, 349] and lack of access to water resources [350–352] may also lead to increased incidence of diarrhoea and hygiene problems.

Gaisie and co-workers (2022) [332] reported that household preparedness against floods was lowest in the GB settlement, and this may result in the recurrence of diarrhoeal cases in this informal settlement in the future. Nevertheless, flooding poses significant challenges for both settlements [353] and it has been reported that households reporting diarrhoeal cases after floods have a high risk of experiencing a similar situation again in future [333]. Unless resolved, the ongoing situation reported here will continue to elevate health risks from flooding, especially in areas where access to clean water and sanitation is limited.

In this research, households located closer to flood-prone areas were found to experience a larger number of diarrhoeal cases, confirming the importance of flooding as a factor contributing to increased disease risk, through spatial proximity to flooding. Flooding contributes to the accumulation of standing water, which can harbour bacteria and viruses, elevating disease risk. In the fitted Poisson regression model, it was observed that the number of diarrhoea cases increased as the distance between households and flood-affected areas decreased. The increase per metre was estimated as 1.40% in GB and 0.32% in MZ. These relationships between the number of diarrhoea cases and flooding are consistent with the findings from previous studies.

5.4.2. Limitations

We acknowledge several limitations in this study. First, the frequency of household visits was fixed at every two weeks. Although respondents were asked to recall diarrhoea episodes from the previous 14 days, there remains a possibility that short-term episodes were forgotten or underreported, which may have introduced bias into the model results [354, 355]. The dependent variable, the number of children with diarrhoea, was derived from household visits every two weeks, where enumerators reported whether a child had diarrhoea in the previous 14 days. This design may have led to underreporting of short-term diarrhoeal episodes that occurred between visits, potentially introducing bias into the model results [355, 356]. In addition, the omission of certain cases may have weakened the relationships between the dependent variable and the covariates. Furthermore, the model did not account for other influential factors that may affect diarrhoea prevalence, such as hygiene practices, water quality or socioeconomic status. To mitigate these limitations, future research could consider increasing the frequency of visits or implementing alternative data collection methods, such as continuous household records, to increase data accuracy and completeness.

Additionally, it should be noted that data were collected from the household head rather than directly from the child's primary carer. This approach may introduce reporting bias, as the household head may be less aware of short-term diarrhoeal episodes or specific treatment practices compared to the primary caregiver. Previous studies have indicated that health utility assessments for children differ depending on whether they are reported by the child or a proxy, with parental reports generally underestimating and health professional reports generally overestimating compared to the child's own assessment [357]. However, parent proxy-reports have been shown to be reliable and valid for measuring children's health-related quality of life, with only 2.1% of item responses missing [358]. Future studies could further increase data accuracy by implementing more rigorous and systematic collection procedures.

In this research, only the data from the first 40 visits were analysed; a period that was not exposed to the effects of the subsequent intervention. However, this does mean that the number of visits was limited to 40. The relatively small number of visits may limit our ability to draw firm conclusions about the links between diarrhoeal disease, precipitation and standing water. It may also limit our ability to assess long-term health outcomes and the effect of potential seasonal changes. Future studies should aim to evaluate health outcomes over longer time-periods, and this would also allow greater consideration of seasonal effects.

There is a strong connection between diarrhoea cases and WASH factors in Africa. Access to safe drinking water is one of the most critical elements of this connection, with children living in households with unimproved water sources being more exposed to contaminants that can lead to diarrhoea [359–361]. Households that rely on shared or unimproved sanitation facilities are more likely to experience diarrhoea cases [360, 361]. Additionally, fewer diarrhoea cases may be reported in households where hygiene practices are improved [359, 362]. In our research, temperature and rainfall data were used as covariates and this included lag effects, but no data were collected regarding WASH practices. Variables such as hygiene habits, water quality, infrastructure status, nutritional level, education level and socioeconomic conditions within the GB and MZ settlements may also significantly affect the incidence of diarrhoea. Including these parameters in the model in future research may allow interpretation from a more comprehensive perspective in addition to environmental factors such as rainfall and temperature and may support more balanced results.

The first Poisson regression model analysed the statistical relationship between the total number of children with diarrhoea and the rainfall and temperature values, including lag. In the first model, statistically insignificant covariates were removed one at a time, starting with the least significant one, until all remaining covariates were significant. Then, the covariate with the largest VIF value was removed, if above a threshold of 10, and the model refitted. This process was repeated with the insignificant covariates removed again. Thus, in this research, the preferred methods for reducing co-linearity [363] were chosen to best suit the current dataset and analysis objectives. In this way, the possibility for co-linearity in the model was reduced. In future studies, the ridge regression model could be used as an alternative to manage the co-linearity problem and improve parameter estimation [364, 365].

Although the model identified significant associations, the final version of the first (i.e., temporal) Poisson model for GB included some statistically significant covariates with both positive and negative coefficients. This is likely due to some residual level of co-linearity in this case. The Poisson models were presented in sequence from initially fitted model including all covariates, to final fitted model using a rigorous covariate de-selection method, to a more parsimonious model choice, to facilitate interpretation by the reader. For example, despite the mix of coefficients in the final version of the first Poisson model for GB, the dominant effect of increases in both rainfall and temperature were to increase diarrhoea risk. The positive effect of the coefficients for rainfall and temperature for GB, was made clearer by selecting only two covariates (rainfall 1-day, temperature 0-day) and re-fitting to create a more parsimonious version of the fitted model, in which both coefficients were positive. For MZ the effect of increases in rainfall was only to increase risk, with temperature having no significant effect.

The demographic and spatial structures of the study regions may differ in terms of hygiene habits. The fact that the Christian population is larger in the GB settlement (evolved from an indigenous settlement with their traditional leaders) and the Muslim population is larger in the MZ settlement (which was a planned relocation of the Muslim population in 1959) suggests possible differences in cultural and religious practices which may impact health outcomes [366, 367]. It has been stated in the literature that religious beliefs may play a determining role in water use, hand washing and cleaning habits [368, 369]. Nevertheless, in this research the objective was not specifically to compare GB and MZ, but rather to investigate the relationship between disease incidence and possible climate drivers both temporally and spatially using the two settlements as exemplars. In future studies, the relationship between religious and cultural factors and hygiene practices and infectious diseases could be examined in more detail.

5.5. Conclusion

This research presents a survey and analysis of childhood diarrhoea in the GB and MZ settlements in Accra, Ghana in relation to environmental covariates. Survey data were described by age, gender, whether children in the visited households had diarrhoea in the last two weeks, type of diarrhoea, and type of treatment applied. Two Poisson regression models were fitted to represent the relationships between (i) the time-series of total number of children with diarrhoea recorded at each visit (i.e. dependent variable) and rainfall and temperature and (ii) the total number of diarrhoea cases across all visits and spatial proximity of households to flooding and elevation. In the first model, it was found that both lagged rainfall and temperature increased diarrhoea risk for GB, and lagged rainfall increased diarrhoea risk for MZ. In the second Poisson regression model, it was found that the number of diarrhoea cases increased for both settlements as the distance of households from flood areas decreased.

In conclusion, we have shown that rainfall prior to each visit increases the risk of diarrhoea in children in GB and MZ in Ghana and shown that spatial proximity to flooded areas also increases risk. Together, these results suggest that rainfall influences disease risk, at least in part, through the creation of areas of standing flood water and ponding, which may harbour bacteria and viruses [22] and, thus, increase diarrhoeal risk, especially for those who are spatially proximate to the flooding. We are not aware of any previous single study that links diarrhoeal disease risk with both antecedent rainfall in a temporal sense and flooding, due to the antecedent rainfall, in a spatial sense.

The observed association of diarrhoea cases with the environmental covariates of precipitation and its temporality, serve as a simple message to duty-bearers as well as the residents of informal settlements. To duty-bearers, the message is that targeted interventions to mitigate flooding and its effects in informal settlements combined with improved sanitation infrastructure and practices can reduce the incidence of childhood diarrhoea. To the residents of informal settlements, the message is to be aware of floodwater's boomerang-style impacts: that rain carries the pathogen released to the environment attributable to poor sanitation facilities and hygiene practices to contaminate the floodwater, and that proximity to this water, in turn, increases the likelihood of diarrhoea.

Chapter 6

6. The Impact of a WASH intervention on Diarrhoea in Children Under 5 Years in Accra, Ghana

Abstract

Diarrhoeal diseases are the third leading cause of death worldwide with a high mortality in children under 5 years of age, particularly in areas with poor sanitation and water quality. Here, we report the results of a water, sanitation and hygiene (WASH)-based intervention in a developing world context. We focused on two communities in Accra, Ghana and, namely, Gbegbeyise (GB) within which the WASH-based intervention was applied and Madina Zongo (MZ) where no intervention was applied and was treated as a control site. A total of 65 visits were made to a selected set of households in each settlement every two weeks, and the number, and several characteristics, of children with diarrhoea were recorded at each visit. At the 41st visit, surface drains in only the GB settlement were repaired and cleared, with additional emptying of communal toilets. The effect of this intervention on diarrhoeal incidence in GB was investigated by calculating the age- and sex-standardized morbidity ratio (ASMR) through time, showing clear evidence of impact after the intervention start date. A Poisson regression model was then used to examine the statistical

relationship between the total number of children with diarrhoea and two meteorological covariates, a dummy covariate representing the intervention, and the expected number of cases (used as an offset). The Poisson model revealed that the number of children with diarrhoea increased with increasing rainfall and temperature. Importantly, in the GB settlement, but not in MZ (which did not have any intervention), the number of children with diarrhoea decreased after the intervention. Specifically, a 39.81% reduction in the number of children with diarrhoea was achieved after the intervention for the GB settlement. In sub-Saharan Africa, a large proportion of deaths are due to inadequate WASH practices, compounded by extreme weather events. This research demonstrates quantitatively the impact of a WASH intervention based on better management of existing sanitation facilities in a developing world context.

In this chapter, Mehmet Akif Veral was responsible for curating the dataset, performing the statistical analyses, creating maps, methodology, interpreting the results and writing – original draft.

6.1. Introduction

Diarrhoeal diseases are the third leading cause of death in children under 5 years [319] and cause approximately 2 billion cases and 1.9 million deaths in children of the same age group each year worldwide [370]. Diarrhoea is a major health concern in low- and middle-income countries, particularly in Sub-Saharan Africa, where a significant proportion of deaths occur among children under 24 months [371, 372]. Unsafe/unimproved drinking water sources [359, 373], poor sanitation facilities such as communal toilets shared by many and/or open defecation [360, 374], poor hygiene practices including poor hand washing and unsafe waste disposal [374, 375] can contribute to increased numbers of diarrhoeal cases. Although diarrhoea continues to pose a serious health threat among children under five years of age in Sub-Saharan Africa, 88% of deaths are reported to be due to inadequate water, sanitation and hygiene (WASH) practices, and these risks are, therefore, preventable [184]. Improving WASH practices in general could greatly reduce the risk of disease which aligns with UN Sustainable Development Goal 6 (SDG6) and, indirectly, SDG3. All too often, improvement is taken to mean building more technically sophisticated toilets, while neglecting to maintain existing sanitation infrastructure such as communal toilets and line drains. This paper, however, demonstrates that interventions that simply involve better management of existing sanitation infrastructure, such as mending line drains, and emptying and making the communal toilets leakproof, can reduce the incidence of childhood diarrhoea.

Climatic factors, particularly rainfall and temperature, can play a significant role in the risk of diarrhoeal disease [186, 208, 325]. Notably, the effectiveness of WASH interventions may be influenced by climatic conditions, with their protective impact becoming more evident during periods of intense rainfall, as indicated in previous research [376]. Increased rainfall has been associated with a higher incidence of diarrhoea, primarily due to its role in facilitating the proliferation and dissemination of pathogenic bacteria responsible for infections. Studies have demonstrated that excessive rainfall contributes to the spread of waterborne diseases [21], increases the presence of bacteria and viruses in surface water sources [22], and creates favourable conditions for microbial pathogen multiplication, ultimately leading to elevated infection rates [201]. Moreover, it has been reported that there has been an increase in diarrhoeal diseases following heavy rainfall and floods [38, 332]. Previous studies have similarly found a significant relationship between diarrhoeal diseases and temperature through the spread of microbial pathogens [38, 377]. In contrast, decreased rainfall coupled with increased temperature, resulting in drought conditions, have also been shown to increase the risk of diarrhoea [38]. In particular, an increase in diarrhoea cases was reported following extreme drought, and this increase was linked to previous climatic conditions [329].

We hypothesize that a WASH intervention comprising a series of environmental hygiene improvements has the potential to significantly decrease diarrhoeal disease incidence in a developing world setting, here exemplified by Accra, Ghana in West Africa (latitude: 5.614818, longitude: -0.205874). Gbegbeyise (GB) and Madina Zongo (MZ), two informal settlements in Accra, the capital of Ghana, were selected as the study sites for this research, with comparable socio-economic profiles. GB is a coastal settlement and is predominantly Christian. MZ, on the other hand, is located approximately 13 km inland and is predominantly Muslim. In both settlements, unplanned urbanization and inadequate WASH practices are known to have negative impacts on public health, making them ideal sites to test the efficacy of a WASH intervention.

We first examined the influence of two meteorological factors (rainfall and temperature) on the incidence of diarrhoeal disease in the two settlements in Accra using Poisson regression. Then using this established system, we tested the hypothesis that a WASH intervention would reduce the incidence of diarrhoeal disease. Specifically, we compared the effects of the intervention in GB to MZ where no intervention occurred which was treated as the control. A total of 65 visits were made every two weeks to two sets of pre-determined households in the GB and MZ settlements. Data on the occurrence of diarrhoea in children under 5 years of age were collected through a questionnaire. At the 41st visit (5 April 2021), a significant and sustained WASH intervention was implemented only in the GB settlement, where all surface drains were cleaned and repaired, and public toilets were emptied over a period of time. Changes in the number of children with diarrhoea before and after the intervention date were assessed in both communities.

6.2. Methods

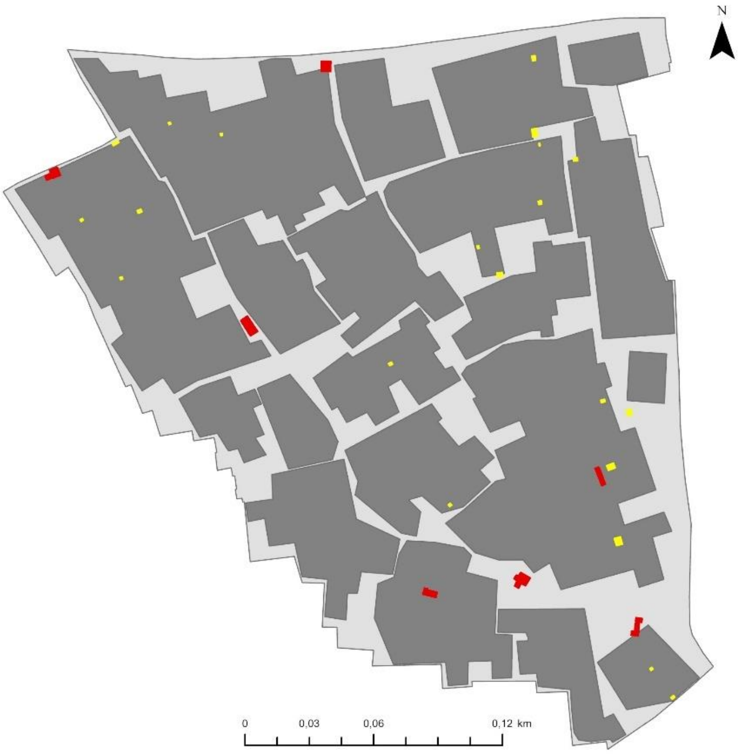
6.2.1. Study site and data

The research focused on the Gbegbeyise (GB) (latitude: 5.527503, longitude: -0.264258) and Madina Zongo (MZ) (latitude: 5.678791, longitude: -0.177108) settlements located in Accra, Ghana. GB is a coastal settlement, while MZ is located roughly 13 km inland from the coast. The study used aerial mapping of both settlements, GIS-based maps to identify a set of households, where each household was assigned a unique identification code. These codes were linked to data collected during the household enumeration process, which was conducted by the project team and trained enumerators. This linkage facilitated effective community navigation and efficient data collection. GB and MZ were selected after an initial assessment of 14 different communities, with the choice based on their similarity in terms of environmental and demographic characteristics. Households were chosen with children under 3 years old at the start of the 2-year survey being prioritized for inclusion in a Diarrhoeal Disease Surveillance (DDS) study as non would be over 5 years old at its conclusion.

A structured data collection form was developed to document each child's age, gender, diarrhoea status within the past two weeks, type of diarrhoea and whether treatment was administered at home or required hospitalization. 10 external enumerators were recruited and trained to ensure accurate data collection. At the beginning of the study, informed consent forms were presented to the household heads to obtain their assent and signature. The diarrhoea monitoring was conducted by an independent team of trained enumerators, while the intervention activities involved direct participation of the community; the monitoring team was separately employed to avoid overlap between implementation and surveillance roles. The trained enumerators conducted a total of 65 bi-weekly visits to the selected households, during which diarrhoea-related data were collected on-site and subsequently transferred to a database. The responses were periodically reviewed, validated and cleaned by the Social Science Team Leader, with updates and checking conducted monthly. The final dataset was shared with project collaborators at Lancaster University and forwarded to the Council for Scientific and Industrial Research of Ghana (CSIR) project manager for archival purposes.

At the 41st visit (5 April 2021), an intervention was implemented in the GB settlement with the aim of improving WASH conditions. The intervention consisted of emptying communal toilets, repairing and clearing surface drainage channels, and removing accumulated waste to reduce blockages. In practice, toilet emptying was undertaken three times, drain repair occurred once, and surface drains were cleared on a monthly basis during the intervention period. Wastewater and faecal sludge were managed by a commercial company and transported off-site by tanker. Implementation was carried out by a local NGO under the supervision of the research team and was financially supported through the RECIRCULATE programme funded by UKRI GCRF. Although the broader project also incorporated an educational component, the present analysis focused solely on monitoring diarrhoeal disease outcomes before and after the infrastructural improvements. From an ethical perspective, the project team maintained contact with the communities after completion of the intervention. Observations of blocked drains and sanitation malfunctions were recorded; however, these did not coincide with the diarrhoea surveillance timeframe. These measures were designed to strengthen sanitation infrastructure and mitigate potential sources of contamination. The distributions of the visited households and toilets in the GB and MZ settlements are given in Figure 6.1.

(a)



(b)

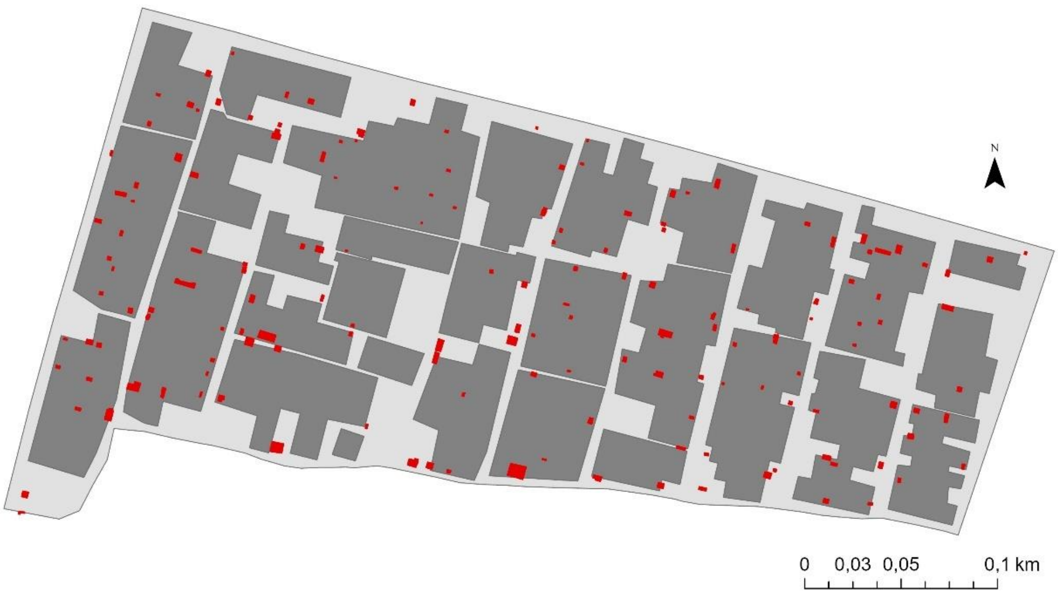


Figure 6.1. Distributions of households in the (a) GB and (b) MZ settlements, along with (yellow) private and (red) public toilets in GB, and (red) public toilets in MZ. Households were grouped and marked in grey to prevent individual identification for ethical confidentiality reasons.

6.2.2. Gbegbeyise and Madina Zongo household visits

A total of 65 bi-weekly household visits were conducted in the GB and MZ settlements. Household-level surveys were carried out in GB from 7 October 2019 to 21 March 2022 and in MZ from 14 October 2019 to 28 March 2022, encompassing a total study period of 896 days. A list of households with children under five years of age was compiled, and listed households were visited. No random sampling was performed. As the study aimed to cover eligible households, no formal sample size or power calculation was required. The surveys included 228 households in GB and 166 households in MZ. Enumerators collected data directly from participants' legal guardians, recording each child's age, gender, diarrhoeal incidence in the past two weeks, type of diarrhoea, and treatment information. In instances where participants relocated or passed away during the study, their data were included in the analysis only for the duration of their availability. Data were managed meticulously to preserve validity and reliability while adhering to ethical research standards. Ethical approval for the study was obtained from Lancaster University (FST20014: amendment to FST19026/18055), ensuring compliance with institutional and research ethics protocols in both the UK and Ghana.

6.2.3. Age- and sex-standardized morbidity ratio

The age- and sex-standardized morbidity ratio (ASMR) is a statistical measure used to assess the prevalence of a particular disease in a region compared to a standard population with the same age and gender distribution. It aims to eliminate the influence of age and gender differences when comparing different populations [378] and is described as:

$$ASMR = \frac{Observed\ num.of\ cases}{Expected\ num.of\ cases}$$

The study populations were classified according to age and sex. The age categories were determined as 0-6, 7-12, 13-24, 25-36, 34-48, 49-60 and >60 months. Each age group was divided into two subcategories of boy or girl. The control community MZ settlement was selected as the standard population and the number of cases and total population values in each age-sex group were recorded. Similarly, the total population values were calculated for each age and sex group in the GB settlement. The rate in the standard population was calculated by dividing the number of cases for each age and sex group by the total population in that group. The rate was then multiplied by the population of the same group in the GB settlement to find the expected number of cases for each category. All values were summed to calculate the expected total number of cases.

An ASMR value of < 1.0 indicates that the number of cases observed in the local population is less than the expected number of cases. Conversely, an ASMR value of > 1.0 indicates that the number of cases observed in the local population is greater than the expected number of cases. In cases where the ASMR is equal to 1.0, the number of cases observed in the local population is consistent with the expected number of cases calculated based on the study population. The ASMR value was calculated for each visit within the scope of the study.

6.2.4. Covariates

Daily rainfall and temperature data were obtained from weather stations located in the GB and MZ settlements. To test whether meteorological parameters have an antecedent effect on the risk of diarrhoea in children, rainfall and temperature up to 1 week before the visit day were also included in the model. For example, the total rainfall value (mm) 1 day before the visit day is expressed as rainfall 1-day and the temperature value (°C) 2 days before the visit day is expressed as temperature 2-day. The intervention parameter was created by assigning a value of 0 to visits 1-40 and a value of 1 to visits 41-65.

6.2.5. Poisson regression model

Poisson regression is a statistical method used when the dependent variable represents count data [335]. This type of analysis is suitable for modelling the number of events occurring in a given time period or space, and where the data follow a Poisson distribution. Poisson regression is generally preferred for the analysis of rare, independent and constant occurrence rate events [338] expressed as:

$$log(\lambda_i) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n + log(N_i) + \varepsilon$$

where λ is the number of observed cases and β_0 is the intercept. $\beta_1, \beta_2 \ldots, \beta_n$ are the coefficients of the covariates, $X_1, X_2, \ldots, X_n$ are the covariates and ε is an error term. A Poisson regression model was fitted using the glm function in R to represent the relationship between the count of diarrhoea cases and several covariates. Rainfall, temperature, the intervention dummy variable, and the expected number of cases (used as offset) were included as covariates. The expected number of cases was calculated by multiplying the overall incidence rate (total diarrhoea cases/ total number of children) by the total number of children at each visit.

In the regression model incorporating the rainfall, temperature and intervention covariates, statistically non-significant covariates were removed one-by-one, starting from the most insignificant, until all remaining covariates retained statistical significance. To assess potential co-linearity among the covariates, Variance Inflation Factor (VIF) analysis was conducted. Covariates with a VIF exceeding a threshold of 10 were excluded from the model, followed by re-estimation. This iterative process was repeated for both non-significant covariates and those with VIF>10. In the final model, all covariates were statistically significant, and all VIF values remained below 10

6.3. Results

6.3.1. Exploratory data analysis

The distribution of diarrhoea cases recorded during household visits in the GB and MZ settlements is shown in Figure 6.2. The largest number of cases (70) in the GB settlement was observed in October 2019. After this date, the number of cases showed a decreasing trend and peaked again between February and March 2020. After a few months of fluctuation, it peaked again, especially between July and September 2020. The next peak (44 cases) was seen in November 2021. The 41st visit, on 5 April 2021, represents the date of the implemented WASH intervention. Before the intervention, the number of cases was relatively high and after the intervention, the number of cases showed a decreasing trend (Figure 6.2).

The largest number of cases (41) was observed in February 2020 in the MZ settlement. After October 2019, the number of cases showed a decreasing trend, but peaks representing an intense increase in the number of cases were seen in the visits made in February-March 2020. One of the smallest number of cases (7) was recorded at the end of March 2020 and an increasing trend was observed until November 2020. After the fluctuation between November 2020 and 2021, the number of cases was recorded to be around 20 on average in the visits made until the end of March 2022.

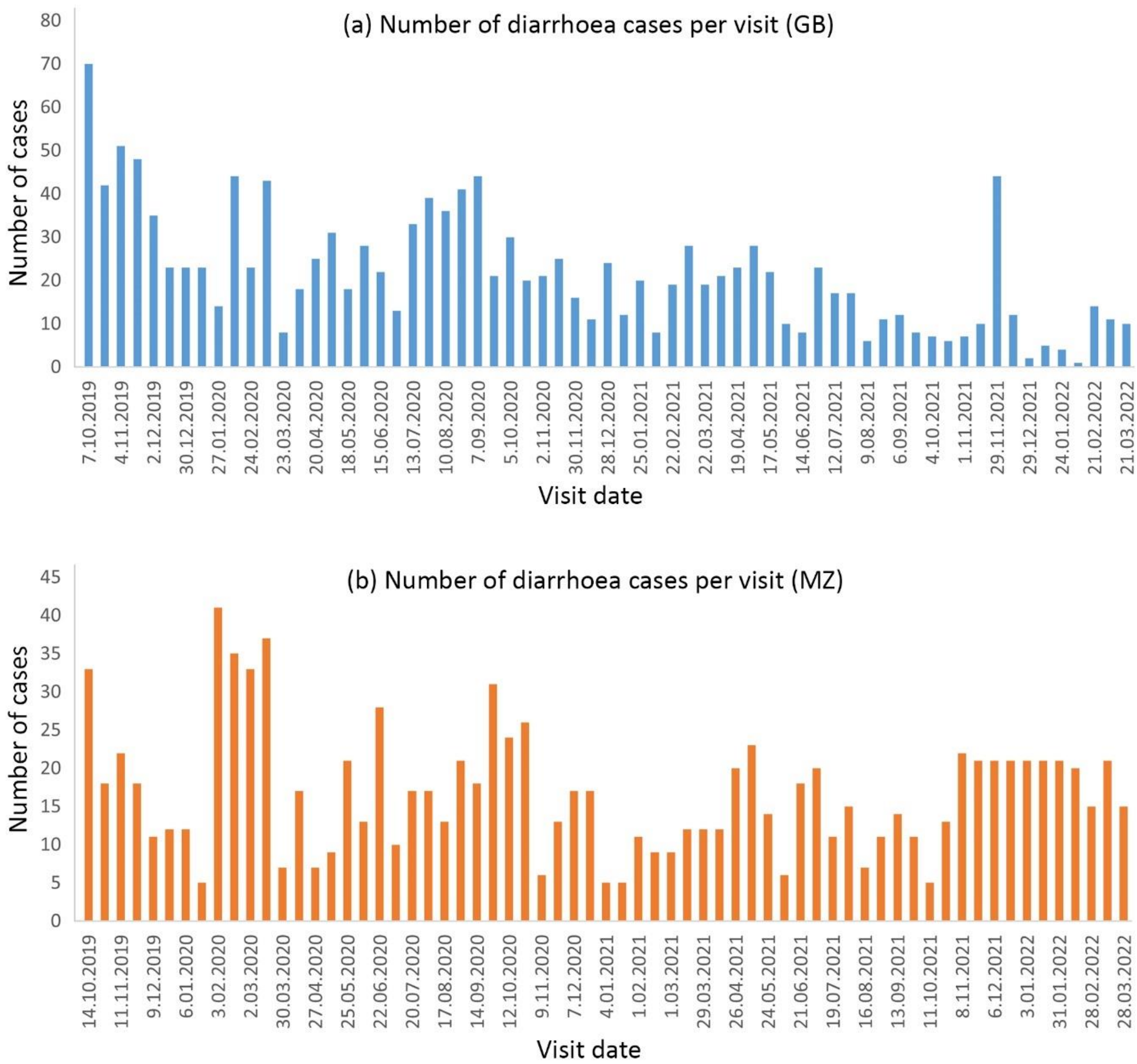


Figure 6.2. Number of children with diarrhoea recorded at each visit in the GB and MZ settlements.

6.3.2. Age- and sex-standardized morbidity ratio

Figure 6.3 shows how the ASMR calculated for the GB settlement changes over time. Initially, the ASMR started slightly above 1 and remained at around 1.5 in the early visits, indicating a higher-than-expected incidence of diarrhoea. Over a short period of time, ASMR fluctuations gradually increased, with the ASMR exceeding 3 on some dates, indicating a significantly higher than expected morbidity. However, these peaks were short-lived, and the ASMR decreased sharply to below 1 for some visits. This indicates that fewer cases were seen than expected in some periods.

It is observed that the ASMR, and variation in the AMSR, both decreased as the visits progressed (Figure 6.3). Especially after the 41st visit, the ASMR was generally below or around 1. This indicates that the number of diarrhoea cases approached or decreased below the expected level in the post-intervention period. ASMR, which rarely exceeded 1 after the 41st visit, generally continued to decrease after visit 41. The trend suggests the important result that the intervention was effective, and that the number of diarrhoea cases, standardised by age and gender, was subdued to at, or below, the expected level.

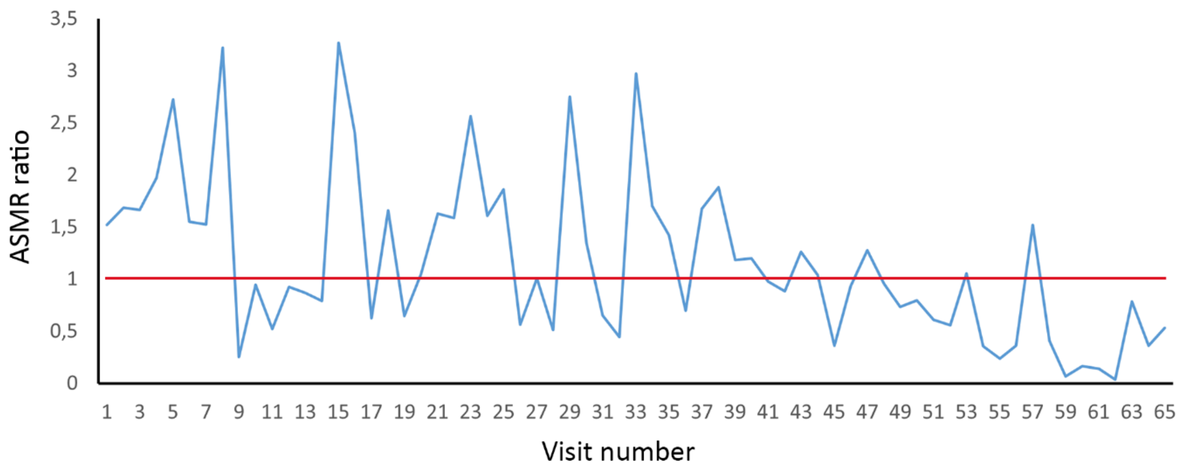


Figure 6.3. Time-series of ASMR calculated for each visit based on age and gender for the GB settlement relative to the MZ settlement. The *x* axis denotes the visits, and the *y* axis denotes the morbidity rate. An ASMR < 1.0 indicates that the number of cases in the study population is lower than expected, while an ASMR > 1.0 indicates that the number of cases is higher than expected. ASMR = 1.0 (red horizontal line) indicates that the number of cases observed is the same as expected.

6.3.3. Poisson regression model

In the GB settlement, rainfall was found to be statistically significant at 1-day (p = 8.05e-07), with a positive estimate, and 5-day (p = 0.0128), with a negative estimate (Table 6.1). These estimates suggest that a 1 mm increase in rainfall is associated with a 17.5% increase and 1.91% decrease in diarrhoea cases for rainfall for the 1-day and 5-day covariates, respectively. Similarly, the temperature covariates were statistically significant for 0-day (p = 0.0183), with a positive estimate and 5-day (p = 1.26e-05), with negative estimate value. The odds interpretation of these estimates is that a 1°C increase in temperature is associated with an 8.24% increase in diarrhoea cases for 0-day and a

14.13% decrease for 5-day lagged temperature. In the final model, the number of cases decreased by 39.81% after the intervention and the intervention covariate was found to be highly statistically significant (p = 3.93e-15).

In the MZ settlement, rainfall was found to be statistically significant for the 2-day (p = 1.42e-05), 3-day (p = 0.005355) and 6-day (p = 0.046204) lagged covariates (Table 6.1). For the rainfall 2-day and 3-day covariates, which had positive parameter estimates, a 1 mm increase in rainfall was associated with increases in the number of diarrhoea cases of 1.95% and 1.05%, respectively. For rainfall with a 6-day lag, which had a negative estimate, diarrhoea cases decreased by 2.01%. The temperature covariate was also revealed to be statistically significant for the MZ settlement (Table 6.1). Specifically, a 1°C increase in temperature with 1-day lag resulted in an increase in the number of diarrhoea cases of 6.94%.

Table 6.1. Final Poisson regression model estimates for the Beta parameters and their probabilities.

Covariate	GB settlement		MZ settlement	
	$\boldsymbol{\beta_1}$	$\boldsymbol{p}$	$\boldsymbol{\beta_1}$	$\boldsymbol{p}$
rainfall 1-day	0.161373	8.05e-07	NA	NA
rainfall 2-day	NA	NA	0.019392	1.42e-05
rainfall 3-day	NA	NA	0.010540	0.005355
rainfall 5-day	-0.019370	0.0128	NA	NA
rainfall 6-day	NA	NA	-0.020404	0.046204
temperature 0-day	0.079251	0.0183	NA	NA
temperature 1-day	NA	NA	0.067160	0.001254
temperature 5-day	-0.152428	1.26e-05	NA	NA
intervention	-0.507736	3.93e-15	0.158308	0.013669

6.4. Discussion

The main objective of this study was to determine whether a WASH intervention implemented in the GB settlement (i.e. repairing surface drains, clearing drains of materials that may cause blockages and emptying public toilets at regular intervals) reduced the number of cases of children with diarrhoea. In this regard, no intervention was implemented in the MZ settlement, which was considered as the control community.

First, considering the relationship between the total number of children with diarrhoea and the rainfall and temperature covariates, statistically significant relationships were identified for both the GB and MZ settlements. It was noted that rainfall 1-day and temperature 0-day produced positive parameter estimates for GB, and the risk of diarrhoea cases increased with increases in precipitation and temperature. These findings are consistent with previous studies in the literature [19, 38, 206, 208, 326, 327, 330]. In MZ, statistically significant associations were obtained for rainfall 2-day, 3-day and 6-day and temperature 1-day. Rainfall 2-day was the most significant and overshadowed the other rainfall parameters. Both the rainfall 2-day and temperature 1-day parameters had positive parameter estimates, meaning that increases in rainfall and temperature, as in GB, increase the risk of diarrhoea cases in this region.

Increased rainfall has been reported in previous studies to cause an increase in diarrhoeal cases [206, 326, 327]. Rainfall creates a favourable environment for the proliferation and spread of diarrhoeal microbial pathogens and can overload waste management systems, particularly in areas with inadequate water and sanitation infrastructure [19, 328], resulting in flooding. Our results are consistent with the literature, but some rainfall and temperature covariates produced negative parameter estimates (Table 6.1). This is a consequence of the rigorous covariate de-selection methodology employed. More parsimonious final models could potentially have been produced by reducing the VIF threshold value, or by selecting an alternative regression modelling framework such as Ridge regression. However, the results stand and are readily interpretable, based on the specific de-selection procedure employed.

Despite the above, there is value in discussing the conditions in which negative parameter estimates may arise. Decreasing rainfall can slow down the replenishment of water resources, increasing the concentration of pollution and negatively affecting hygiene conditions. Furthermore, reduced access to clean water can lead individuals to contaminated water sources. Similarly, lower temperatures can increase the risk of transmission by allowing pathogens to survive longer in water and the environment. In colder conditions, in particular, bacteria and viruses can remain active in water sources or on surfaces for longer periods of time, increasing the risk of contamination and potentially leading to increased cases of diarrhoea. Increases in the number of cases with decreasing rainfall and temperature have been reported previously [38, 199, 200, 202]. Effectively, rainfall and temperature variables may have different effects on the incidence of diarrhoeal diseases under different environmental conditions and this needs to be considered when attempting to generalise the results presented here for Accra, in West Africa.

It has been reported previously that flooding events can increase diarrhoeal disease incidence [196]. Inadequate water and sanitation infrastructure can fail to contain pathogen spread during such flood events, exacerbating public health risks [186]. Observations during household visits in the GB settlement indicated that existing surface drains might be insufficient to manage potential flooding. To mitigate flood risk, enhance WASH practices and assess their impact on diarrhoeal incidence, a WASH intervention, which forms the major focus of this research, was implemented on, and from, the 41st visit (April 5, 2021). This involved repairing drainage systems, clearing blockages, and regularly emptying public toilets.

To evaluate the impact of the intervention, Poisson regression analysis was fitted between the number of cases and the intervention covariate, and a statistically significant parameter estimate was obtained ($p = 3.93e\text{-}15$). After the intervention, a decrease of approximately 40% was observed in diarrhoea cases in the GB settlement (Table 6.1). It has been previously reported that improvements in community hygiene, such as reducing faecal pollution, can lead to significant reductions in the numbers of diarrhoea cases [379]. Considering the strongly significant effect of the intervention, it can be suggested that faecal pollution decreased, thus, decreasing the number of children with diarrhoea. However, it should be noted that diarrhoea outcomes in this study were self-reported by households. As the intervention could not be blinded, there is a possibility that responses were influenced, which may have led to a modest overestimation of intervention effectiveness, as highlighted by Clasen and Boisson (2015) [380]. Additionally, ASMR analysis was conducted to examine the prevalence of diarrhoea in GB and the analysis showed that the intervention implemented at visit 41 resulted in a decreasing trend in

ASMR. In contrast, no intervention was implemented in the MZ settlement, and the number of diarrhoea cases did not show a similar decreasing trend.

Unsafe drinking water sources, inadequate sanitation facilities and poor hygiene practices have been reported to be associated with diarrhoeal diseases in previous studies [360, 373, 375]. The intervention aimed to improve WASH practices in the settlement and to evaluate the impact of these improvements on diarrhoea cases. However, household waste, including toilet waste, is discharged directly into surface drains, which can lead to overflowing sewer systems after floods due to inadequate infrastructure and ineffective waste management, which can increase the risk of infection [381]. This can accelerate the spread of pathogens and lead to increased diarrhoeal cases. Therefore, strengthening WASH practices has played a critical role in reducing such environmental and public health threats. Moreover, effective preparedness and adequate water and sanitation infrastructure are vital in reducing the negative impacts of floods. Gaisie et al. (2022) [332] reported that household flood preparedness was lowest in GB, indicating that the settlement has a high vulnerability to flood events after heavy rainfall. Black et al. (2003) [184] reported that inadequate WASH practices account for 88% of diarrhoeal deaths. This finding highlights the critical role of WASH improvements in public health and suggests that potential interventions can lead to significant reductions in diarrhoeal incidence. Effective WASH practices can not only reduce diarrhoeal cases but also contribute to the prevention of waterborne diseases by improving overall public health.

Autocorrelation in the regression residuals could potentially undermine the assumption of independence in statistical testing, necessitating adjustments to the fitted model [348]. An analysis of autocorrelation was, thus, conducted to examine potential patterns in the residuals of the fitted model, calculated as the difference between the predicted and observed case counts. No significant autocorrelation was found for either the GB or MZ settlements.

We acknowledge several limitations in this study. Household visits in the GB and MZ settlements were fixed at every two weeks, and data on children with diarrhoea, representing the dependent variable, were collected. This visit frequency could have potentially impacted data capture. For example, diarrhoea episodes that occurred for brief durations between visits may not have been recorded, leading to potential underreporting. In this context, the omission of certain cases (if any) could have weakened the observed relationship between the dependent variable and covariates, potentially introducing bias into the analysis. To address this limitation, increasing the frequency of data collection in future studies could enhance the accuracy and reliability of the findings. Additionally, employing continuous monitoring methods, such as household diaries or mobile health reporting systems, may help capture short-term diarrhoeal episodes more effectively.

It is known that there is a significant relationship between diarrhoea cases and WASH practices. Darvesh et al. (2017) [20] reported that WASH practices reduce the risk of diarrhoea in children aged 0–5 years by between 27% and 53%, depending on the type of intervention. Similarly, WASH interventions have been shown to reduce the prevalence of under-five diarrhoea in rural Bangladesh from 13.7% to 3.6% [382]. In our research, rainfall, temperature and intervention data were used as covariates, but no information on household WASH habits were used, which represents a potential limit to our understanding of potential behavioural influences on diarrhoeal incidence. Future studies incorporating detailed WASH-related data, sanitation infrastructure and hygiene practices could provide deeper insights into their role in disease prevention.

In both the GB and MZ settlements, the religious background of the population and settlement morphology may have played a role in the observed frequency of diarrhoeal cases. The GB settlement is predominantly inhabited by Christians, and its planform evolved organically as a dense indigenous settlement, while the MZ settlement has a majority Muslim population and was formed largely as a planned relocation (dense nonetheless) of the Muslim population in 1959 [366, 367]. It has been reported that religious beliefs can significantly influence water use and WASH practices [368, 369]. These factors could potentially impact the incidence of diarrhoeal diseases, as religious teachings often shape public health behaviours, including sanitation practices and water consumption. Given that a larger number of diarrhoeal cases was observed in GB and a smaller number in MZ, it is plausible that these differences may be related to the religious and cultural practices influencing hygiene and water use in each settlement. However, the current data available do not allow for direct conclusions regarding the influence of religious background on diarrhoeal incidence. To better understand this potential relationship, future studies should consider more comprehensive demographic and sociocultural data to explore how religious factors might contribute to the observed patterns of disease prevalence.

6.5. Conclusion

This research examined the effects of a WASH intervention, as well as meteorological factors, on diarrhoeal cases among children in two settlements (GB and MZ) in Accra, Ghana. A Poisson regression model was fitted to reveal a statistically significant relationship between the total number of diarrhoeal cases in both settlements and rainfall and temperature. Generally, increases in temporally lagged rainfall and temperature were associated with increases in the number of cases. During the 41^{st} visit to GB, an intervention was implemented, including repairing surface drains, removing blockages and regularly cleaning public toilets. MZ was not subject to any intervention and was treated as a control settlement. The effect of the intervention was assessed in the same Poisson regression model and showed a reduction of approximately 40% in diarrhoea cases in GB after the intervention ($p = 3.93e\text{-}15$; Table 6.1) which was not reflected in MZ. Moreover, ASMR analysis confirmed the effectiveness of the intervention, producing a significant and sustained decrease in ASMR after the intervention. We conclude that the WASH intervention was successful in reducing the incidence of diarrhoeal disease in children in GB. The findings confirm the effect of meteorological covariates on increasing diarrhoeal cases, while also demonstrating the potential of the intervention to reduce this effect. These findings highlight the importance of continued investment in community-level WASH improvements and suggest that local governments should prioritise the maintenance of drainage infrastructure and public sanitation facilities to help reduce the burden of diarrhoeal disease.

Chapter 7

7. Discussion

7.1. Summary of main findings

The aim of this thesis was to analyze the relationship between disease risk (for two different disorders, IBD and diarrhoea) and several disease-specific environmental factors. To analyze the spatial distribution of IBD cases, and its association with environmental risk factors, a nationwide survey involving 5,452 participants was conducted across the UK. The collected data (i.e., on the distribution of cases) were mapped spatially at a grid scale. Based on these distributions, ASMRs were calculated for Crohn's disease (CD) and ulcerative colitis (UC), and relative risk was assessed using the CD:UC ratio as an internal control. The analyses revealed that CD morbidity rates were particularly higher among women aged 20–59, and that the CD:UC ratio was clustered in North-West England. Shah et al. (2018) demonstrated that the age of IBD onset varies by sex. Their analysis showed that the risk of CD increases in females after the age of 10 and becomes statistically significant especially after age 25. In contrast, UC occurs at similar rates between sexes until age 45, after which it becomes more common in males [255]. Analyses also revealed that among women, the age group with the lowest morbidity rate greater than one for both CD and UC was 20–29 years, while the highest morbidity rate was observed in the 50–59 age group [258–260].

In the second stage of the IBD study, the association between CD risk and environmental factors was examined using a Poisson regression model at the hydrological catchment level. Independent variables included pasture proportion (as a proxy for MAP in hosts and the surrounding environment), urban proportion, average temperature, rainfall, and river width. A statistically significant relationship was found between CD cases and pasture proportion, while no such association was observed for UC cases, which was used as a control. These findings provide epidemiological evidence suggesting that CD risk may be elevated in areas where MAP-infected animals graze on pastureland. Rhodes et al. (2013) reported that MAP is distributed widely across Great Britain, not only in agricultural areas, but also in non-farming environments. While MAP was detected in 10.5% of soil samples, river monitoring revealed a consistent presence of the pathogen over a six-month period. These findings suggest that river monitoring provides a more effective approach than soil sampling for assessing MAP distribution at the catchment level [311]. Similarly, Pickup et al. (2005) reported the long-term persistence of MAP bacteria in both the water column and sediments of the River Taff in South Wales, suggesting a potential link between elevated incidence of Crohn's disease and environmental contamination in surrounding areas [16]. Moreover, MAP originating from infected animal faeces was shown to enter surface waters and persist within river systems, with evidence indicating that, despite water treatment processes, the bacterium may occasionally reach domestic water supplies [17].

To assess the impact of environmental factors on the prevalence of diarrhoeal disease, this thesis examined the associations between diarrhoeal disease incidence among under-fives and climatic and spatial exposures in two informal settlements in Accra, Ghana —GB and MZ. Biweekly household-level data were collected over 65 visits. The initial 40 visits, representing the baseline period, were analysed using Poisson regression models, revealing that antecedent rainfall significantly increased diarrhoea cases in both settlements, while temperature was significant only in GB. Previous studies have reported that the number of diarrhoeal cases increases with increasing rainfall [19, 206, 326]. Additionally, being spatially closer to flood-prone areas was associated with increased case numbers, suggesting that flooding may serve as an important transmission pathway. Levy et al. (2016) reported that heavy rainfall events may lead to flooding which, in turn, facilitates the transmission of pathogenic microorganisms and subsequently contributes to an increased incidence of diarrhoeal diseases [78]. Moreover, Abu and Codjoe (2018) found that households which experienced flooding followed by a diarrhoeal case reported higher perceived risks of future flooding and diarrhoeal outbreaks compared to those that had not experienced such events [333].

At the 41st visit, a WASH intervention was implemented in GB, involving the repair and clearance of surface drains and the emptying of communal toilets. A post-intervention reduction of 39.8% in diarrhoea cases was observed in GB, whereas no comparable decline was recorded in the control settlement, MZ, highlighting the role of the intervention itself. Diarrhoea is known to pose a serious health threat to children under five in Sub-Saharan Africa, with 88% of deaths related to diarrhoea reported to be due to inadequate WASH practices [184]. Furthermore, an effective WASH intervention is likely to reduce these risks. These findings underscore the role of both environmental drivers and basic sanitation infrastructure in shaping diarrhoeal disease risk in informal urban contexts.

The potential impact of environmental factors on the incidence of IBD and diarrhoeal diseases has been addressed at a conceptual level, drawing upon the principal findings of the study. This preliminary discussion aims to frame the broader context of the observed associations. A more thorough and nuanced examination will be presented in subsequent sections, incorporating detailed analyses and consideration of underlying mechanisms.

7.2. Common themes in IBD and diarrhoea studies

Surveys play a crucial role in analysing the relationship between disease incidence and environmental factors, providing detailed individual- and household-level insights [339, 341, 350, 383–385]. In this thesis, both the IBD and diarrhoea studies relied on survey-based data collection, allowing for the analysis of environmental influences on disease incidence. The IBD study gathered participant-reported data via a UK-wide survey, while the diarrhoea study involved periodic household visits conducted in two informal settlements in Accra, Ghana: GB and MZ.

Meteorological and hydrological variables, particularly rainfall, emerged as key drivers of pathogen transmission in both contexts. In the diarrhoea study, intense rainfall and subsequent flooding were shown to increase microbial contamination, thereby elevating diarrhoea risk among children. These findings are consistent with previous studies in the literature [19, 79, 186, 206, 326, 334, 386]. Similarly, previous findings referenced in the

IBD research suggest that heavy rainfall may facilitate the transport of MAP from pasturelands into surface water systems, potentially contributing to CD risk [16, 17]. Moreover, it has been previously reported that aerosols may also be effective in the progression of this condition [16, 281].

Spatial relationships played an important role in both studies, albeit in different ways. Comparative overview of methodological and contextual aspects of the IBD and diarrhoea studies is given in Table 7.1. In the diarrhoea study, the number of cases increased with decreasing distance to flood-prone areas, indicating the role of physical proximity to environmental hazards. In the IBD study, cases were spatially concentrated in catchment areas characterised by high pasture density, suggesting an association with specific land use patterns rather than proximity *per se*. In both studies, these relationships were analysed using Poisson regression models, which are suitable for analysing the distribution of low-frequency events [36], and disease distributions were mapped to identify spatial patterns. Collectively, these findings emphasise a common theme: the importance of environmental context—whether defined by spatial proximity or ecological characteristics—in shaping disease dynamics.

Table 7.1. Comparative overview of methodological and contextual aspects of the IBD and diarrhoea studies.

Category	IBD study	Diarrhoea study	Similarities
Data collection method	a one-time participant-driven online survey	Biweekly household visits survey over a 2-year period	Both studies were survey-based
Timing	One-time data collection	Time series (65 visits)	NA
Study Area	Nationwide (UK)	GB and MZ	NA
Dependent Variable	CD cases	Diarrhoea cases in children under five	Both focused on disease incidence
Independent Variables	Pasture proportion, urban proportion, maximum river width, rainfall, temperature, population	Rainfall, temperature, elevation, proximity to flood-prone areas, intervention	Meteorological variables were common
Statistical Method	Poisson regression	Poisson regression	Same statistical model used
Intervention	NA	WASH intervention	NA
Findings	CD cases associated with pastureland	Diarrhoea cases associated with rainfall and temperature; reduced after WASH	Both found meaningful links between disease and environmental factors
Original Contribution	Grid-level IBD distribution and biogeographic associations	Effect of meteorological variables and spatial proximity on diarrhoea and evaluation of intervention effectiveness	Each study provided novel contributions

7.3. Data related issues

7.3.1. Spatial resolution choices

In the first part of the IBD study, the use of 10 km by 10 km grid cells offered several advantages by enabling the management of geographically extensive data across the UK and allowing spatial patterns to be presented at an interpretable resolution. Given the voluntary nature of the survey data, the use of smaller grid cells would likely have resulted in many cells containing either no cases or only a single case, which could have led to issues with statistical reliability and reduced the interpretability of the results. Conversely, the use of overly large grid cells would have obscured localized clustering and patterns of distribution. Thus, the chosen 10 km^2 spatial resolution provided a balance between spatial detail and case density, allowing for meaningful spatial analyses. Moreover, conducting the analyses at an area level rather than an individual level helped mitigate ethical concerns regarding data privacy, thereby supporting the protection of participant anonymity. This was particularly important for preventing the identifiability of dispersed households in rural areas. A grid-based approach also facilitates future integration with various environmental datasets (e.g., land use or rainfall patterns), enabling more comprehensive spatial epidemiological analyses. Importantly, comparing the spatial distributions of CD and UC using grid cells strengthened the scientific validity of disease risk analyses through the use of consistent controls. In this regard, the spatial resolution employed in this research represents a methodologically reasonable choice, both for the current research and for future studies examining spatial variation in IBD or related health outcomes.

In the second phase of the IBD study, hydrological catchment areas were used as the primary spatial units to investigate the relationship between CD incidence and environmental risk factors, particularly pasture proportion. This approach is justified by the ecology of MAP, the putative etiological agent of CD; MAP is spread to pasture areas with the faeces of infected animals, can persist in the environment for a long time [311], and can be transported to surface waters by the effect of rainfall [16, 17]. Therefore, analysing CD cases at the catchment scale enabled a more ecologically realistic assessment of exposure pathways defined by hydrological connectivity. Unlike arbitrarily defined administrative boundaries, the catchment-based spatial framework more accurately captured MAP dissemination routes, facilitating a more precisely targeted analysis of the contribution of environmental factors to CD risk. Moreover, catchment-level analysis supports the integration of biogeographic features with epidemiological data, allowing robust evaluation of spatial relationships across different scales. The comparison of CD cases against UC cases as a control further enhanced the robustness of this analysis, confirming that the observed associations with pasture exposure were specific to CD rather than general IBD trends.

In the diarrhoea study, collecting household-level data and modelling the spatial relationships with flood-prone areas enabled a more precise and spatially meaningful analysis of the association between environmental factors and childhood diarrhoea cases. The diarrhoea status of children in each household was recorded during regular visits, allowing for individual-level assessments while accounting for temporal variability. In this study, environmental exposure to flooding was modelled in two ways: the spatial proximity of households to flood-affected areas (a continuous variable) and whether households were located within buffer zones drawn around these areas (a binary variable). These two variables represent different transformations of the same underlying spatial information and were analysed comparatively in relation to childhood diarrhoea risk. The results indicated that spatial proximity was the more significant factor and this was, therefore, selected as the covariate representing environmental exposure in the Poisson regression model. Using MZ as a control site strengthened causal inference by distinguishing the effect of flooding and related environmental factors on diarrhoea incidence in GB. This spatially explicit approach highlights the importance of incorporating geographic sensitivity when assessing the health impacts of flooding, particularly in informal settlements where infrastructure is often inadequate.

This research, thus, employed different spatial units—grid cells, hydrological catchments and household coordinates—to examine the effects of environmental factors on health outcomes. Each spatial resolution was selected to be most appropriate to the characteristics of the data and the specific objectives of the corresponding analyses. These choices were guided by a common rationale: to ensure that environmental exposures were represented in an epidemiologically meaningful manner. Presenting these spatial approaches together underscores the sound methodological choices made across the different analyses, aiming ultimately to elucidate the statistical relationships between disease occurrence and environmental exposures. Notably, the use of well-defined control comparisons across all four main analyses—inter-disease (CD:UC), environmental exposure (CD vs. UC controls), diarrhoea and lagged meteorology (GB vs. MZ), and WASH intervention (MZ as a control settlement)—strengthens the scientific rigor and validity of the conclusions of the research.

7.3.2. Uncertainties

7.3.2.1. Model (fitting errors)

Poisson models are based on the assumption that events occur independently and at a constant rate [387] and are suitable for statistically analysing the existing dataset. The most appropriate statistical analysis methods for the datasets used in this study were chosen, but no systematic overdispersion test was performed. In model selection, not only *p*-values, but also covariates that could be associated with theoretical justifications were taken into account and model parsimony was preserved as far as possible. This approach made it possible to establish simple, but conceptually consistent models with which to characterize environmental effects.

7.3.2.2. Data measurement errors

Some independent variables (pasture land, urban land, temperature, rainfall and population distribution) used in the analysis were derived from raster sources or administratively collected data. Such data may contain measurement errors, especially in areas with limited spatial resolution. Relatedly, the dependent variable, the number of diarrhoea cases, was based on biweekly visits to households, and there may be children who recovered, but were not reported during this period. Such uncertainty was carefully taken into account when analysing and interpreting the data in this research.

7.3.2.3. Predictions

The estimates obtained from the models are valid only for the spatial areas within the sample and caution should be exercised when generalizing. Although confidence intervals for the estimate results are not directly presented, the risk of overfitting was minimized by selecting carefully the covariates used in the model. In addition, lag terms were used to capture the lagged effects of some environmental variables. This method is balanced with the aim of preserving the simple structure of the model while taking into account temporal dependencies

7.3.2.4. Other uncertainties

Social determinants such as education level, sanitation conditions and access to health services were not used in the study. This deficiency stems from the study's focus on environmental factors. Therefore, it can be considered that variables outside the model may also be effective in explaining the spatial distribution of diarrhoea cases. In this context, the results obtained should be interpreted within a framework where environmental risks are prioritized. The potential contributions of other social factors can be studied in further studies.

7.4. Limitations

7.4.1. IBD study limitations

We acknowledge that grid and catchment level IBD studies have several limitations. Only a small proportion of IBD cases in the UK could be reached, and some participants may have been misdiagnosed [266, 267]. Data were collected via an online questionnaire, promoted through social media and patient organizations, including CCUK, which has nationwide coverage. However, individuals not engaged with such platforms may have been missed. Of the 3,085 grid cells defined, 73.7% (CD) and 76.9% (UC) had no survey responses, and 9.5% had no population. The 5,452 cases included likely represent just 0.7% of all IBD patients in the UK [263]. Access to national health data or GP records could improve sample size and enable finer-scale analysis in future studies [264]. There may also be a gender-related reporting bias, as ASMRs were higher among females. Accurately distinguishing between CD and UC can be challenging due to their overlapping symptoms, which often complicate the diagnostic process. Since the data used in this study were based on self-reported information, it is possible that responses from individuals without a confirmed or correct diagnosis were included. This may partially explain the similar patterns observed in some results for CD and UC, such as those in the ASMR analysis.

The IBD study conducted at the catchment level investigated potential associations between CD risk and environmental features, such as the distribution of grazing ruminants, at catchment level across England and Wales. This spatial scale allowed for integrating likely sources of MAP with areas of exposure. However, working at this resolution limits the spatial detail of the analysis. While using UC cases as a control strengthens the credibility of the results, findings should still be interpreted with caution. The results are intended as additional supporting evidence for a potential link between human CD cases and JD/MAP in ruminants via hydrological transport pathways [10, 16, 17]. Future research will explore finer-scale associations, for example, through marked point pattern analysis

7.4.2. Diarrhoea study limitations

In this diarrhoea study, the associations between diarrhoeal cases and environmental factors were examined using both temporal (rainfall and temperature) and spatial (distance to flood-prone areas and elevation) analyses. Additionally, changes in case numbers following a WASH intervention were evaluated using statistical methods, including Poisson regression and ASMR analysis. However, the initial phase of the study has several important limitations. First, household visits were conducted at fixed two-week intervals in both settlements, and the number of diarrhoea cases—our dependent variable—was determined based on caregiver reports of whether the child had experienced diarrhoea in the previous 14 days. This design may have missed short episodes occurring between visits, potentially leading to underreporting and introducing bias in the model results. Omission of such cases may have weakened the associations between the dependent variable and the covariates.

In the GB settlement, a WASH intervention—comprising the cleaning and repair of surface drains and regular emptying of public toilets—was implemented starting from visit 41 (5 April 2021). The MZ settlement served as the control area. The present study analysed data from the first 40 visits only, which preceded the intervention period. Limiting the analysis to these initial visits may restrict the ability to robustly assess the relationship between diarrhoea and environmental conditions such as rainfall and standing water. It also limits exploration of long-term health outcomes and seasonal variations. Therefore, future studies should consider extended follow-up periods to better capture seasonal effects and long-term intervention impacts.

In the initial Poisson regression model, non-significant covariates were removed step-by-step, starting with the least significant, until all remaining covariates were statistically significant. Subsequently, covariates with a Variance Inflation Factor (VIF) greater than 10 were excluded to reduce multicollinearity, as recommended by Midi et al. (2010) [363]. This process was repeated until all high-VIF covariates were removed. To further address multicollinearity and improve parameter estimation, ridge regression could be considered as an alternative approach in future studies [364, 365].

Although the model revealed meaningful associations, the final version of the temporal Poisson model for GB included some significant covariates with both positive and negative coefficients. This could reflect residual multicollinearity. To enhance interpretability, model development was presented progressively—from the full model with all covariates to the reduced final version. Despite the complexity in the final model for GB, increases in rainfall and temperature emerged consistently as the dominant factors associated with elevated diarrhoea risk. To highlight this pattern more clearly, a simplified model was re-fitted using only two covariates—1-day rainfall and same-day temperature—both of which had positive coefficients. In MZ, while rainfall increase was associated with higher risk, temperature did not show a statistically significant effect.

The second phase of the study examined the effect of a WASH intervention. In Africa, a strong association between WASH-related factors and diarrhoea incidence is well documented. Access to safe drinking water is a critical component, as children in households relying on unimproved water sources face increased exposure to diarrhoeal pathogens [359, 361]. Studies have also noted that children in households with shared or inadequate sanitation facilities experience more frequent diarrhoeal episodes [360, 361], whereas those in households with good hygiene practices report fewer [359, 362]. While this study assessed a physical WASH intervention, no data were collected on household WASH behaviours, limiting the ability to evaluate behavioural influences on diarrhoea outcomes. Future research should incorporate detailed information on WASH practices, infrastructure conditions, and hygiene behaviours to better understand disease prevention mechanisms.

It is also plausible that differences in the demographic and spatial characteristics of the study areas influence hygiene practices. The GB settlement, which has evolved as a traditional community under local leadership, is predominantly Christian, whereas MZ is largely Muslim, established through a planned relocation in 1959. These cultural and religious differences may contribute to variation in sanitation behaviours and health outcomes [366, 367].

Building on these contextual differences, it is important to note that outcomes observed in controlled trials may not fully translate to real-world settings. Household adherence, frequency of engagement, and local environmental or social conditions—including cultural and demographic factors—can substantially influence the effectiveness of WASH interventions. Moreover, participant reporting bias may occur, as households might provide responses they perceive as desirable or expected, affecting the accuracy of measured outcomes. In this context, it should be noted that diarrhoea outcomes in this study were self-reported by households. As the intervention could not be blinded, there is a possibility that responses were influenced, which may have led to a modest overestimation of intervention effectiveness, as highlighted by Clasen and Boisson (2015) [380]. These limitations highlight the importance of implementation research to evaluate interventions under routine conditions and to inform strategies for improving uptake, sustainability, and public health impact.

7.4.3. Unresolved issues and future research

The global incidence and prevalence of IBD are increasing [242], with around 0.2% of the European population affected [388]. While this research provides valuable information on the spatial distribution of IBD cases and potential environmental determinants of CD risk, several unresolved issues remain. First, as the data were obtained through voluntary survey participation, a more comprehensive dataset across the UK would increase the generalisability of the findings. Increasing the number of participants would provide a more detailed understanding of the spatial patterns of IBD. Although the CD:UC ratio was used to address potential imbalances in participation, the extent to which the observed distribution reflects the wider IBD population is still unclear. Second, the relationship between number of catchment-level CD cases and pasture proportion is innovative in our study. Although a significant relationship was identified, further research is warranted in more diverse geographical contexts with larger sample sizes. Future research should focus on catchment areas with high exposure in the UK and examine case numbers and biogeographical patterns at finer spatial resolution (e.g., smaller grid or postcode level). Moreover, the association between CD cases and pasture areas should be investigated in other geographical settings such as Türkiye to allow for comparative analysis [389, 390].

In terms of diarrhoea studies, although the environmental determinants of diarrhoea cases and the impact of WASH interventions have been assessed, some important questions remain unanswered. First, both studies rely on survey data collected only from selected households, and fixed visit intervals may have led to under-reporting of cases, which may have missed short-term illness episodes. Furthermore, only the physical components of the WASH intervention were assessed, and no data were collected on hygiene behaviour, education level and occupation at the individual and household levels.

This may limit the analysis of the impact of behavioural factors on the disease burden. Given the demographic and cultural differences between the two settlements, it is likely that such behavioural factors may play an important role. Future research should address these gaps through behavioural data integration and long-term follow-up. Moreover, only two settlement areas were examined in the studies. It is important to repeat similar studies in different socio-ecological contexts and compare the results to evaluate the validity and external consistency of the findings. To rigorously assess the effectiveness of the WASH intervention, future studies could implement the same intervention in both communities with high diarrhoea prevalence. By applying the intervention to multiple settings and comparing pre- and post-intervention outcomes across both sites, it would be possible to determine whether the observed reduction in diarrhoeal cases is attributable to the intervention itself rather than to site-specific contextual factors. Such a design would provide stronger causal evidence and support the generalizability of the intervention's effectiveness across similar informal settlements.

In future research, alternative statistical approaches could also be considered for analysing the determinants of diarrhoeal risk. One such approach is the multilevel logistic regression model, which is particularly suited for data with hierarchical structures [391, 392]. This method enables the modelling of outcomes where observations are nested (e.g., repeated measures within individuals or households) and accounts for dependencies within clusters. For example, multilevel logistic regression models might be considered, with the child as a higher-level unit and time or visit as the lower-level unit, or, in catchment-level analyses, the catchment as the higher-level unit and survey respondent as the lower-level unit. While Poisson regression remains appropriate for count data [335, 336] and produced meaningful results in this study, multilevel approaches could offer additional control for socio-economic factors and age-related variation in diarrhoeal risk, potentially refining effect estimates and their interpretation.

Chapter 8

8. Conclusion

This thesis aimed to investigate the association between disease risk (for IBD in the UK and diarrhoea in children in Ghana) and several environmental factors. The spatial distribution of CD and UC cases, and their relationships with potential environmental determinants were investigated in the UK, and the prevalence of diarrhoea in children and its relationship with meteorological and environmental factors were analysed in two informal settlements in Accra, Ghana. More specifically, the thesis aimed to identify the regional environmental and demographic characteristics associated with IBD cases in the UK, and to assess the impact of meteorological variables and WASH interventions on diarrhoea cases in Accra, Ghana. Central to this research was the consistent application of generalized linear models (GLMs) with appropriate controls across all analyses, which strengthened the scientific rigor and validity of the findings. Thus, the research focus was consistently on the use of GLM modelling to investigate the environmental determinants of disease, with the two case studies exemplifying different geographical and socio-ecological contexts, and the different modelling choices required as a result.

This research provided a novel survey-based analysis of IBD cases across the UK, focusing on the spatial distribution and characteristics of CD and UC. By examining case numbers and population data within 10 km grid cells, the findings revealed limited spatial variation in relative risk for both CD and UC, with some localized peaks likely influenced by small sample sizes. Notably, the CD:UC ratio indicated a higher relative risk of CD in core urban areas of North-West England, such as Manchester and Bolton, compared to peripheral and rural regions. ASMR analysis further showed that CD risk was greater among women and spanned a broad age range. Complementing these spatial insights, Poisson regression models identified a significant association between CD cases and the proportion of pasture land, while no such relationship was observed for UC. The use of UC cases as a control revealed the specificity of the association of CD with pasture, reinforcing the plausibility of the ecological link. While noting the many caveats explored in the discussion, the association of CD, and not UC, with pasture proportion provides some evidence for the potential role of ruminants and related environmental and transport factors in influencing CD risk. Overall, these findings contribute to our understanding of the observed regional and demographic patterns of IBD incidence in the UK and establish a foundation for future research on the environmental determinants of CD.

This thesis also analysed childhood diarrhoea cases in the GB and MZ settlements of Accra, Ghana, in relation to environmental factors and the impact of a WASH intervention. To analyse environmental influences on diarrhoea incidence, two Poisson regression models were fitted: one assessing the association between diarrhoea cases and lagged rainfall and temperature, and another examining the relationship between diarrhoea incidence and spatial proximity to flooding and elevation. Results showed that lagged rainfall and temperature increased diarrhoea risk in GB, while lagged rainfall was associated with increased risk in MZ. Additionally, diarrhoea cases rose as household proximity to flood-prone areas increased in both settlements. This latter spatial effect, thus, provided a plausible explanation for the observed temporal influence of precipitation on disease in the GB settlement.

A WASH intervention implemented in GB during the 41st visit, involving drain repairs, blockage removal, and cleaning of public toilets, resulted in an approximate 40% reduction in diarrhoea cases, a change not observed in the control settlement MZ. Crucially, the inclusion of MZ as a control site allowed for clearer attribution of the effect of the WASH intervention, which was restricted to GB only. ASMR analysis further supported the intervention's effectiveness by demonstrating a sustained decrease in diarrhoea incidence in GB, post-intervention. These findings highlight the influence of meteorological and environmental factors on diarrhoeal disease risk and demonstrate that targeted WASH interventions can significantly reduce childhood diarrhoea in informal settlements. The findings underscore the need for continued investment in improved sanitation infrastructure and flood mitigation measures to alleviate the disease burden.

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Appendix-1

IBD survey questionnaire

Participant Information Sheet

Inflammatory Bowel Disease and Its Possible Geographical Influences

Introduction

We would like to invite you to take part in a UK-wide research study. The title of this study is ‘Inflammatory bowel disease and its possible geographical influences’. Please take your time to read through this information sheet and feel free to ask questions at any time. Please take the time to decide whether or not you would like to participate in this study and thank you for reading this.

What is the purpose of the study?

The cause of inflammatory bowel disease (Crohn’s Disease, Ulcerative Colitis, microscopic colitis and indeterminate ‘unclassified’ IBD) is poorly understood. We wish to assess whether the occurrence of IBD is influenced by geographical features in your locality and hence we would like to compare where you live to the surrounding geographical features such as rivers and land use.

Why have I been chosen?

You have been invited to take part in this study because you have been diagnosed with IBD, and we would like to collect information in the form of a questionnaire via our survey website.

Do I have to take part?

No, it is entirely up to you whether you choose to take part in this study.

What will happen to me if I take part?

If you do decide to take part, you will access the survey via the link to our secure website and will be asked to sign a consent form before starting the survey. The study then requires you to fill in a short questionnaire. This will take only 10 minutes.

If you agree to take part, you are still free to withdraw at any stage should you choose to do so within 3 weeks, without any explanation. After that period the information will be anonymised, and it will be difficult to withdraw it. We will provide a link on the website to contact us.

The risks and benefits.

There will be no direct benefits to you as this is not a treatment study. The information provided for this study will help us assess whether geography influences IBD and whether it could be a target for further research. This may discover patterns and also help IBD sufferers in the future.

What happens later?

We will analyse this data and submit the findings of the study for publication in medical/scientific journals by peer review. All publications will be open access. We will publish the anonymised results on our website.

Will my personal and private records be kept confidential?

Your medical records will not be accessed. The postcodes and information you have supplied will be used in Geographical Information System (GIS) mapping. We will use the full postcode in the analysis but from the published results it will not be possible for others to identify you using this information. None of the participants of this study will be identified in any report.

What if I become distressed by my participation?

We do not expect participants to be become distressed, but should this occur we suggest family support, contact with your GP or Consultant or contact with IBD Associations.

Who is organising and funding this research?

Academic scientists at Lancaster University and Gastroenterologists working at Guy's and St Thomas' Hospital in London will be organising the research.

Has this research been approved by all the relevant committees?

This research has been approved by the Lancaster University Faculty of Health and Medicine Research Ethics Committee (FHMREC) on 21/07/2021, reference FHMREC20164.

Who do I contact for further information?

If you have any questions or concerns about this research study, please contact us.

Professor Roger Pickup	r.pickup@lancaster.ac.uk
Professor Peter Atkinson	pma@lancaster.ac.uk

If you have any complaints, please contact:

Dr. Laura Machin - Chair of FHMREC l.machin@lancaster.ac.uk

(Please continue by clicking on the "I have read this and understand." button.)

☐ I have read this and understand.

CONSENT FORM

Title of Project: Inflammatory Bowel Disease and Its Possible Geographical Influences

The Project Team

Professor Roger Pickup (Lancaster University), Professor Peter M. Atkinson (Lancaster University), Dr Glenn Rhodes (NERC Centre for Ecology and Hydrology, Lancaster), Dr Gaurav Agrawal (Honorary Fellow, Kings College London, Clinical Fellow, Guy's & St Thomas' NHS Foundation Trust), Mr Mehmet Akif Veral (Lancaster University), Dr Jeremy Sanderson (Consultant Gastroenterologist at Guy's & St. Thomas' Hospital, Reader in Gastroenterology at the Nutritional Sciences Division King's College London) and Dr Manoj Roy (Lancaster University) (**please make sure to click on the elements listed below to continue with the survey questions**)

- ☐ I confirm that I have read and understand the Participant Information Sheet (dated 21/07/2021) for the above study and have had the opportunity to ask questions.
- ☐ I understand that my participation is voluntary and that I am free to withdraw my data at any time before it is anonymised (which will be 3 weeks after completing his questionnaire), without giving any reason and without my legal rights being affected.
- ☐ I understand that my participation will involve completion of a short questionnaire.
- ☐ I understand that relevant data collected during this study, will be looked at by the project team from Lancaster University and Guy's and St Thomas' Hospital. I give permission for these individuals to have access to this data.
- ☐ I am aware that the information obtained from this study will be stored for more than 3 years but no longer than 10 years.
- ☐ By selecting 'Yes, I agree' means I agree to take part in this study, and this will give me access to the online survey.

Q1 **Please choose one option in order to continue to the survey.**

- ☐ Yes, I agree.
- ☐ No, I disagree.

Q2 **Your answers are very important to us and may help the treatment of IBD patients in the future and make a contribution to the greater understanding of IBD. If you want to leave the survey at this point, please feel free to return at any time in the future.**

- ☐ Yes, I would like to continue.
- ☐ No, I would like to leave.

Inflammatory Bowel Disease and Its Possible Geographical Influences

Participant Questionnaire

The information provided in this questionnaire will be used by Lancaster University to study the association between initial diagnosis of inflammatory bowel disease (IBD) and geographical location. All information will be held securely and only accessed by the research team. **Your name is not required.**

Q1 **If you are under 16, please continue with permission from your guardian.**

- ☐ Yes, I'm under 16 and I got permission from my guardian.
- ☐ No, I'm not under 16.

Q2 **What is your age? (Month/year : xx/yyyy)**

____

Q3 **What best describes your gender?**

- ☐ Male
- ☐ Female
- ☐ Prefer not to say
- ☐ Prefer to self-identify (for e.g. non-binary)

____

Q4 **What is your ethnic group? (Please select the one box that you feel most closely represents your ethnicity)**

- ☐ White
- ☐ Arab
- ☐ Asian or Asian British – Bangladeshi
- ☐ Asian or Asian British – Pakistani
- ☐ Chinese
- ☐ Black or Black British – African
- ☐ Black or Black British – Caribbean
- ☐ Other Black background
- ☐ Gypsy/ Roma/ Traveller
- ☐ Mixed - White & Asian
- ☐ Mixed - White & Black African
- ☐ Mixed - White & Caribbean
- ☐ Mixed – Other
- ☐ Other Ethnic background
- ☐ Other Asian background
- ☐ Prefer not to say

Q5 **Occupation**

____

Q6 **What was your diagnosis?**

- ☐ Crohn's Disease

- ☐ Ulcerative Colitis
- ☐ Indeterminate IBD/ unclassified colitis
- ☐ Microscopic colitis

Q7 **Do you have family history of IBD?**

(After answering this question, please click the "Next" button to proceed to the last stage of the survey.)

- ☐ Yes
- ☐ No
- ☐ Unknown

Q8 **Please specify your family history of IBD (You can choose more than one option.)**

- ☐ Crohn's Disease
- ☐ Ulcerative Colitis
- ☐ Indeterminate IBD/ unclassified colitis
- ☐ Microscopic colitis

Q9 **What is the postcode of your current address (house number not required)?**

____

Q10 What was your postcode/year (house number not required) when first diagnosed with IBD?

	Postcode	**Year**
Postcode and Year		

Q11 **What was the postcode/year of all your previous addresses (house number not required) up to 15 years prior to diagnosis?**

This is the last question. Please try to complete as much as you can. If you are sure that you have written all your addresses correctly, you can complete the survey by clicking the **'Continue Without Answering'** button on the pop-up screen that may appear after clicking the 'Next' button.

	Postcode	Start Year	End Year
Address 1			
Address 2			
Address 3			
Address 4			
Address 5			
Address 6			
Address 7			
Address 8			
Address 9			
Address 10			

Appendix-2

Diarrhoea illness monitoring card

Diarrhoea Illness Monitoring Card

RECIRCULATE WP2: Water for Sanitation and Health, Accra, Ghana

A. Settlement and Household Particulars

Settlement name		Name of Household Head		Household map ID	

B. Children under 5 years old living in this household [Name/ Age (in months)/ Gender (M/F]

1. / /	2. / /	3. / /	4. / /

C. Has any of the children had diarrhoea in the past two weeks? [1 = YES; 2= NO]

Child	Sept'17		Oct'17		Nov'17		Dec'17		Jan'18		Feb'18		Mar'18		April'18		May'18		June'18		July'18		Aug'18	
no.	15th	30th	15th	28th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th

D. If q.C answer is 1, then what kind of diarrhoea was it? [1= Watery stools; 2 = Watery stool & vomiting; 3 = Loose stools with mucus; 4 = Bloody stools with mucus]

Child	Sept'17		Oct'17		Nov'17		Dec'17		Jan'18		Feb'18		Mar'18		April'18		May'18		June'18		July'18		Aug'18	
no.	15th	30th	15th	28th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th

E. Number of days did the child suffer? (in days)

Child	Sept'17		Oct'17		Nov'17		Dec'17		Jan'18		Feb'18		Mar'18		April'18		May'18		June'18		July'18		Aug'18	
no.	15th	30th	15th	28th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th

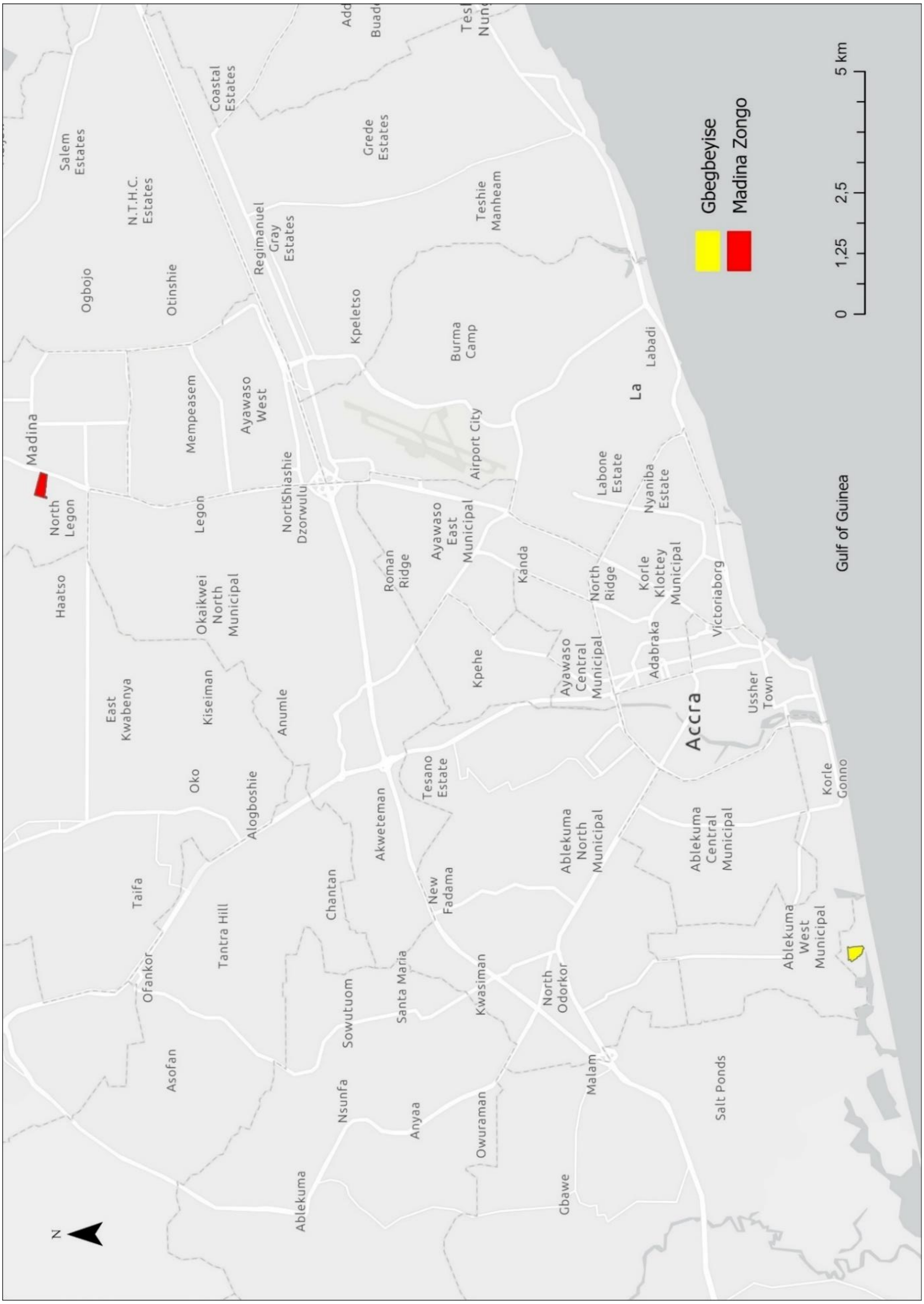
F. What kind of treatment did the child receive? (1 =Home care; 2 = Traditional Healer; 3= Admitted to hospital)

Child	Sept'17		Oct'17		Nov'17		Dec'17		Jan'18		Feb'18		Mar'18		April'18		May'18		June'18		July'18		Aug'18	
no.	15th	30th	15th	28th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th	15th	30th

G. Further comments:

Appendix-3

Location of the GB and MZ settlements in Accra, Ghana.



Appendix-4

Diarrhoea prevalence by child age (in months).

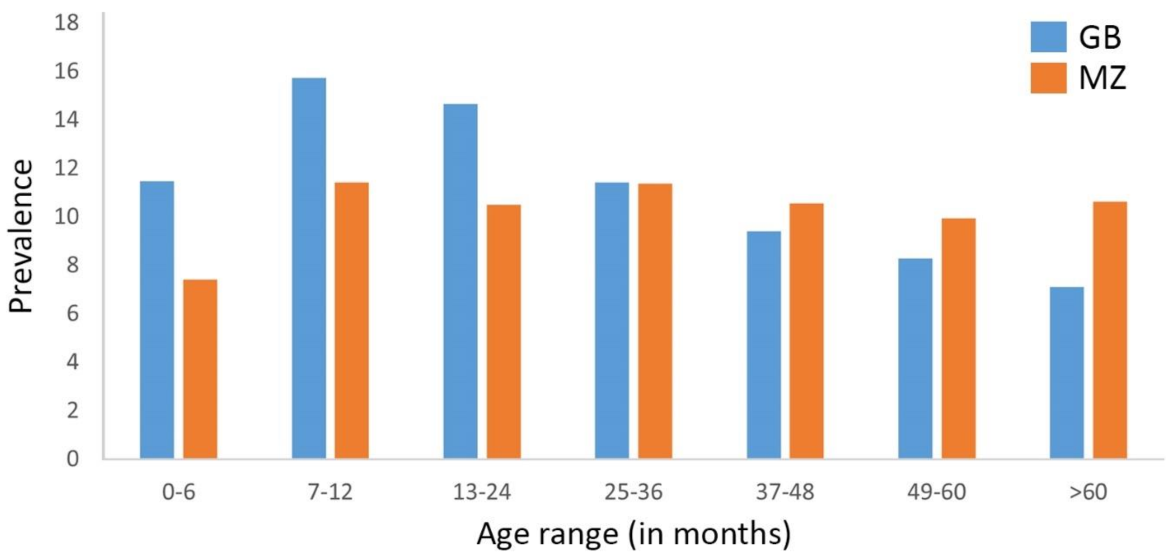


Figure 5.7. Diarrhoea prevalence by child age (in months), pooled across all household visits in the GB and MZ settlements. This figure illustrates age-specific prevalence estimates, providing an overall view of the consistency and robustness of the dataset.

Appendix-5

Flood monitoring form

Date	**Time**	**Researcher**	**Organisation**	**Location/GPS**	**Respondent (Household ID/ name)**	**Observations**	**Actual conversation**