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Human Health: Marine vibrios

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EXECUTIVE SUMMARY

It is estimated that mean air temperature increase of as little as 1 °C in the UK could result in 4.5% increase in foodborne disease in the UK (DOH/HPA, 2008). By 2050 an additional 179,000 annual cases of food poisoning in England and Wales as a result of climate change have been predicted (Bentham and Langford, 1995). Most reports on the impact of climate change on foodborne illness have focused on the potential increase in cases caused by established pathogens like *Salmonella* and *Campylobacter* from consumption of undercooked meat and eggs. However, the burden of foodborne disease may also be impacted by changes in relative contributions of different or emerging pathogens. One such group of potentially emerging pathogens, in Europe at least, are the marine vibrios, predominantly *Vibrio vulnificus* and *V. parahaemolyticus* which can cause seafood associated gastro-enteric or septicaemia illnesses that may occasionally be fatal.

Vibrio vulnificus and *Vibrio parahaemolyticus* are Gram negative halophilic bacteria. They are members of the same genus as the causal agent of cholera (*V. cholerae* O1/O139) however unlike epidemic *V. cholerae* they are not related to poor sanitation but are found naturally in warm marine and estuarine waters (>15 C). In sub-tropical world regions they are the leading cause of seafood-associated bacterial illness. Illnesses, which can be severe and even fatal, are usually reported after consumption of raw oysters or contact with seawater containing pathogenic strains of the bacteria. Increasing seawater temperature and flooding of low-lying coastal areas due to rising sea levels as a result of global climate change are important factors in the proliferation of many bacterially mediated infectious diseases. In Europe and elsewhere *V. vulnificus* and *V. parahaemolyticus* infections have been increasing over recent years, with outbreaks tending to follow regional climatic trends, typically after episodes of unusually warm weather.

There are several well characterised risk factors that may play a significant role in affecting the regional impact of vibrio infections in the UK. Although absolute information regarding many of these variables is incomplete, and are based on predictions, many point towards an increase in these types of infections nationally. Firstly, climate models suggest increases of surface seawater temperature of several degrees Celsius in the coming decades (see Figure 1). Previous studies of disease associated with *V. parahaemolytcius* and *V. vulnificus* indicate that sustained warming events (>15 C) are the most significant risk factor associated with these disease outbreaks. In addition, lower salinity water is another significant risk factor associated with vibrio disease, particularly with *V. vulnificus* which is rarely isolated from seawater with salinities in excess of 30 ppt. Effects are regional, with areas bordering the northeast Atlantic and the North Sea showing a greater reduction in salinity than the Celtic and Irish Sea, based on recent predictive modelling (UK Climate Projections science report: Marine & coastal projections; Lowe et al., 2009). Currently, these models do not indicate a reduction in average salinity to levels below 30 ppt in the UK, thus the risk from *V. vulnificus* remains low (Figure 2). Interestingly, in continental Europe *V. vulnificus* infections have been largely limited to Scandinavian countries where lower average salinities are observed. Localised higher levels of rainfall with consequent flooding causing sporadic periods of low

salinity coincident with higher seawater temperatures cannot be excluded and may contribute to an increase in *V. vulnificus* exposure in the UK. *V. parahaemolyticus* can be isolated from a wider range of salinities within the existing UK range. Relatively small increases in temperatures may also greatly extend the geographical distribution of zooplankton, which act as important global vector organisms for marine vibrios. Given the predicted warming of surface waters in the coming decades a better understanding of the factors driving the virulence, temporal and spatial distribution of these thermodependent bacterial pathogens is critical.

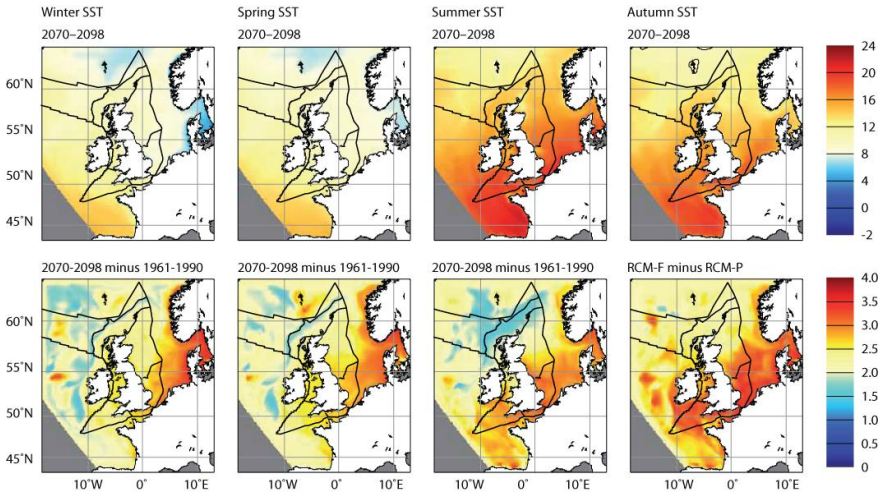

Figure 1 *Seasonal-mean SST (top row) and change (bottom row), relative to model 1961-1990 conditions, in sea surface temperature (deg. C) for 2070-2098 are shown above. As the ocean model was run only once (medium emission scenario), there are no estimates of upper or lower bounds of change. Black lines depict 'Charting Progress' regional borders. (Lowe et al., 2009)*

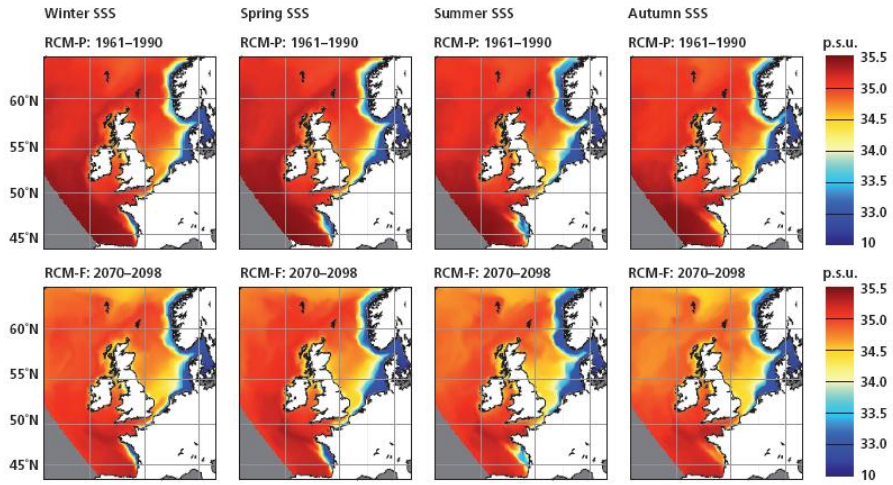

Figure 2 *Seasonal mean sea surface salinity (SSC) for 1961-1990 and predictions for 2070-2098. (Lowe et al 2009)*

FULL REVIEW

It is estimated that a mean air temperature increase of as little as 1 °C in the UK could result in a 4.5% increase in foodborne disease in the UK (Anon, 2008). By 2050 an additional 179,000 annual cases of food poisoning in England and Wales as a result of climate change have been predicted (Bentham and Langford, 1995). Most reports on the impact of climate change on foodborne illness have focused on the

potential increase in cases caused by established pathogens like *Salmonella* and *Campylobacter* from consumption of undercooked meat and eggs. However, the burden of foodborne disease may also be impacted by changes in relative contributions of different or emerging pathogens. One such group of potentially emerging pathogens, in Europe at least, are the marine vibrios, predominantly *Vibrio vulnificus* and *V. parahaemolyticus.*

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This review is adapted from a recent review in Environmental Microbiology Reports (Baker-Austin et al., 2010).

Introduction

Vibrio vulnificus

Vibrio vulnificus is a widespread, halophilic bacterium. It can be isolated from bivalve shellfish and fin-fishes, as well as from sediment and plankton (Aznar *et al*., 1994). *V. vulnificus* can invade humans through existing wound infections or following consumption of raw shellfish (Oliver and Kaper, 2005). The majority of *V. vulnificus* infections are reported during the summer months when warm water (>20 °C) favours bacterial proliferation (Rippey, 1994) although the bacteria has been found in water temperatures as low as 7^{o}C (Motes *et al.,* 1998). In excess of ninety percent of cases occur in men with elevated serum iron levels caused by pre-disposing hepatic disease (Oliver and Kaper, 2005). Within these at- risk groups, mortality rates are one of the highest of any bacterial pathogen. A review of 459 cases in the U.S reported to the Food and Drug Administration indicated that over fifty percent of patients had died as a result of infection (Jones and Oliver, 2009).

Despite the severity of infections there are typically less than 40 reported infections per year in the U.S. The low number of infections relative to its environmental ubiquity and the predicted numbers of ‘at-risk’ individuals indicates that components associated with its pathogenicity have not yet been clearly defined. Although the health of the host is a factor, it is not an absolute determinant of infection or clinical outcome (Shapiro *et al.,* 1998), and despite understanding host-susceptibility risk factors for *V. vulnificus* infections, our knowledge of the pathogenicity associated with this bacterium is still incomplete. Using animal models differences in pathogenicity have been observed when comparing different routes of infection or injection with exotoxins (Gulig *et al.,* 2005). As with other bacterial pathogens, it is likely that a complex yet coordinated transcriptional and proteome-wide response associated with myriad virulence factors is necessary for pathogenesis, and probably involves complex host interactions (Baker-Austin *et al.,* 2010). These factors may be strain dependent, and activated by necessary adaptations for survival in the marine

environment and human host. A variety of specific traits to circumvent innate and humoral host defences, together with virulence and resistance factors are probably involved in the mechanisms of pathogenicity. A number of factors have been implicated in *V. vulnificus*-mediated septicaemia. These include a cytolytic haemolysin (Gray and Kreger, 1985; Kothary and Kreger, 1987), acid neutralization pathways (Kim *et al.,* 2005), elastolytic protease secretion (Jeong *et al.,* 2000), phospholipase A2 (Testa *et al.,* 1984), polysaccharide capsule induction (Hilton *et al*., 2006; Park *et al.* 2006) as well as flagella, siderophore, and pili induction [for a review see Gulig *et al.* (2005) and Jones and Oliver (2009)].

V. vulnificus strains can be characterised by biotypes based primarily on biochemical characteristics, there are currently three reported biotypes. Strains causing human infections belong to biotype 1. Biotype 2 comprises strains responsible for disease predominantly in aquaculture species, most commonly in cultured eel. Biotype 3 can also infect humans and was first discovered in 1996, 20 years after types 1 and 2, after multiple cases of *V. vulnificus* infections emerged in an Israeli fish market. It has been suggested that Biotype 3 is a recombinant clone of two *V. vulnificus* populations (Bisharat *et al.,* 2005). Currently, whilst biotypes 1 and 2 have widespread distribution biotype 3 appears to be geographically restricted to Israel (Baker-Austin *et al.,* 2010). Recently classification schemes based upon pathogenicity utilising molecular methods have been suggested. Among these, a sequence polymorphism of the 16S rRNA gene was originally suggested as a means of distinguishing between the virulence characteristics of strains (Aznar *et al,.* 1994), typing strains into 'A' (highly virulent) and 'B' (less virulent). This polymorphism has been used to develop a restriction fragment length polymorphism (RFLP) method to differentiate *V. vulnificus* strains (Nilsson *et al.,* 2003). Of the isolates tested from clinical fatalities associated with oyster consumption, 94% were 16S rRNA type B, while only 6% of non-clinical isolates were type B (Vickery *et al.* 2006). More recently, PCR primer sets which target the virulence correlated gene (vcg) and accurately distinguish strains of V. vulnificus into 'environmental' (E-genotype, largely non-pathogenic) and 'clinical' (C-genotype, pathogenic) and which appear to offer reliable and sensitive differentiation of virulent and avirulent strains have been reported (Rosche *et al*., 2005).

V. parahaemolyticus

Vibrio parahaemolyticus is a Gram negative, halophilic bacterium frequently present in marine and estuarine environments (Kaneko and Colwell, 1975). Infections are very common worldwide, and this organism is reported to be the leading cause of bacterial illness associated with the consumption of seafood (Joseph *et al.,* 1982). Clinical signs of *V. parahaemolyticus* infections may comprise abdominal cramps, diarrhoea, headaches, nausea, fever, and chills (Honda and Lida, 1993; Hlady and Klontz, 1996) with symptoms usually resolving in less than 3 days. Severe morbidity or mortality fatalities are rare, although in immuno-compromised individuals infections may be prolonged and with more serious sequelae. Most clinically important strains of *V. parahaemolyticus* exhibit beta-haemolysis on specialized blood agar (Wagatsuma agar). This haemolytic activity has been termed the Kanagawa phenomenon (KP) (Miyamoto *et al.,* 1969), and used to differentiate virulent and avirulent isolates. Only a relatively small proportion of *V. parahaemolyticus* isolates (typically <5%) cause gastroenteritis in humans (Oliver and Kaper, 2007). Virulent Kanagawa positive *V. parahaemolyticus* strains produce thermostable direct haemolysin (TDH), however virulent strains may also produce a TDH-related haemolysin (TRH) (Honda *et al.,* 1988) in either the presence or absence of TDH. Genes encoding for synthesis of these haemolysins have been identified and share

several biological properties, including haemolytic activity, enterotoxicity and cytotoxicity (Park *et al.,* 2004). Thus they have been considered excellent molecular screening markers to distinguish virulent and avirulent strains (Oliver and Kaper, 2007). Total *V. parahaemolyticus* levels exceeding 10,000 g^{-1} have been observed frequently in marketable shellfish produce (Cook *et al.,* 2002a), usually less than 1% of strains possess the virulence determinants *tdh* and/or *trh* (Cook *et al.,* 2002b) required to cause disease.

In many parts of the world incidence of *V. parahaemolyticus* infections have increased since the mid 1990s and typically been associated with a new serotype O3:K6 (Chiou *et al.,* 2000; Okuda *et al.,* 1997). The emergence of this pandemic clone is coincident with a rise in food-borne outbreaks compared to the previous more sporadic cases caused by multiple, diverse serotypes. It has been suggested that this novel serotype's ability to cause large food-borne outbreaks may indicate an enhanced capacity for seafood borne transmission and/or ability to cause human infection (Yeung *et al.,* 2002).

Legislative requirements in the UK.

The European Union Regulation (EC) No. 2073/2005 sets out the microbiological criteria for foodstuff (European Communities, 2005). This regulation makes no provision for vibrio controls in seafood traded within the European Community. Thus currently, in the UK there is no legal basis for vibrio testing, consequently there is a lack of systematically generated surveillance data from indigenously produced or EU traded seafood. This is in part due to the recommendations of the EU expert scientific committee on veterinary measures related to public health (SCVMPH), who advised that existing internationally recognised methods were not sufficiently fit for purpose and that available data did not support specific standards for *V. parahaemolyticus* and *V. vulnificus* in raw and undercooked seafood (Anon, 2001a), and, partially due to the observation that the incidence of illness in Europe is reportedly low, and is mainly related to travel to endemic areas (Wagley *et al.,* 2008). In 2009, information gathered from the network of European National Reference Laboratories (NRL) for monitoring bacteriological and viral contamination of bivalve molluscs (www.crlcefas.org) indicated that epidemiologic systems for monitoring vibrio associated illness or occurrence in seafoods was not systematically applied, and that where *ad hoc* testing was in place a range of methods were employed making data comparison problematic. With respect to the development of methodology, a technical advisory group of the Comité Européen de Normalisation (CEN) has recently begun the standardisation process for molecular based methods for pathogenic vibrios and it is anticipated that this initiative will satisfy the need for discriminatory and quantitative methodologies for future applications (Baker-Austin *et al.,* 2010). The SCVMPH also made a number of recommendations with respect to improving the understanding of prevalence of pathogenic vibrios and mitigating consumer risks. Amongst these were that both *V. parahaemolyticus* and *V. vulnificus* should be included in the European Network for Epidemiologic Surveillance and Control of Communicable Diseases (9118/98/CE) and that both pathogens should be included in microbiological sentinel surveillance systems for infectious gastroenteritis (Anon, 2001a). It would seem apparent from the EU NRL network that, for bivalves at least, this is still not being systematically applied throughout the EU (www.crlcefas.org). SCVMPH also recommended that codes of practice should be established to ensure that good hygienic practices were applied at all stages from harvest to the consumer. This final aspect is being addressed at an international level through the Codex alimentarius commission, committee on food hygiene's draft code of hygienic practice for *Vibrio* spp. in seafood (Anon, 2008).

Global climate change and marine vibrio infections.

Increasing water temperature, and flooding of low-lying coastal areas due to rising sea levels as a result of global climate change are important factors in the proliferation of many bacterially mediated infectious diseases (Baker-Austin *et al.,* 2010). By 2050, even relatively conservative estimates suggest an increase in seawater temperature of 2^{o}C in the UK (Hulme *et al.,* 2002) or possibly more in southern UK waters (Hiscock *et al.,* 2004). Coastal flooding may reduce the availability of land for the production of terrestrial crops and livestock potentially resulting in a shift toward aquaculture creating the potential for increased exposure to pathogenic *Vibrio* spp.

Plankton represent a nutrient-rich reservoir capable of enriching *Vibrio* species, which can include human pathogens, at higher densities than the surrounding water column (Turner *et al.,* 2009). Relatively small increases in temperatures may extend the geographical distribution of these vector organisms, with resultant impacts on the timing and severity of infectious disease epidemics (Marsh and Gross, 2001; Kuhn *et al.,* 2005). Reports of marine-related illnesses along the east coast of the U.S. have increased steadily over the last 25 years, in correlation with El Nino events (Harvell *et al.,* 1999). Many bacterial pathogens exhibit marked seasonal dynamics. In the case of *V. vulnificus* and *V. parahaemolyticus* the most significant factor dictating incidence of infection appears to be sea water temperature (>15°C) which impacts equally the abundance and geographical distribution of these bacteria in the environment, and presumably the risk of contact and transmission to humans (Baker-Austin *et al.,* 2010). Accounts of temperature tolerances vary, but it has been suggested that the highest densities of vibrio cells occur in waters ranging from 20°C to 30°C (Tantillo *et al*., 2004; Hsieh *et al.,* 2007). In addition, FAO/WHO and USFDA risk assessments provide clear evidence of increased temperatures and elevated risk (Anon, 2001b; Anon, 2005). The presence of these organisms has traditionally been restricted to warm and temperate regions (Hlady and Klontz, 1996; DePaola *et al,.* 2000), such as the Gulf States in the U.S. The potential impact on the survival, persistence and proliferation of non-cholerae vibrios as a result of climate change has received far less attention than some other thermodependent pathogens (in particular *E. coli* 0157 and *V. cholerae* 01/0139) (Baker-Austin *et al.,* 2010). Currently, there is no global surveillance system to assess temporal and spatial incidence of non-cholerae vibrio infections, thus potential changes in the seasonality and geographic range of these pathogens are based on circumstantial reports in the literature (Baker-Austin *et al.,* 2010). Nevertheless, a number of recent reports have suggested that increases in seawater temperature, potentially as a result of climate change, may be directly responsible for outbreaks of both *V. vulnificus* in Israel (Paz *et al.,* 2007) and Denmark (Dalsgaard *et al.,* 1996, Fouz *et al.,* 2006, Theede *et al.,* 2008) and *V. parahaemolyticus* incidence in Spain (Martinez-Urtaza *et al.,* 2008), Chile (Gonzalez-Escalona *et al.,* 2005) and Alaska (McLaughlin *et al.,* 2005), as well as Oregon, Washington and New York state (CDC, 2005). Mass mortalities in temperate benthic communities in the Mediterranean caused by the *V. coralliilyticus* have been reported to be triggered by climatic anomalies characterised by elevated seawater temperatures (Bally and Garrabiu, 2007). Paz *et al.* (2007) found that pathogenic strains of *V. vulnificus* responsible for disease outbreaks in Israel in 1981 and 1996 were identical based on molecular characterisation. These reports suggest that these pathogens may lie dormant, possibly in marine sediments before re-surfacing to cause disease outbreaks. These findings, when viewed in context of a wealth of data regarding the viable but non-culturable state (VBNC) of many non-cholerae vibrios, indicate appropriate physio-chemical changes, mediated by climate change (i.e. increases in water temperatures, transient decreases in salinity based

on rainfall events) may be important in the disease aetiology (Baker-Austin *et al.,* 2010). Such indirect and less obvious effects associated with global climate change may play a significant role in increasing the abundance and global distribution of non-cholerae vibrios such as *V. vulnificus* and *V. parahaemolyticus*. For example, both pathogens grow preferentially in lower salinity marine and brackish waters (<30 ppt NaCl). Globally, low-level flooding associated with sea-level change is likely to significantly increase estuarine and brackish environments potentially increasing the geographical range over which these pathogens can flourish (Baker-Austin *et al.,* 2010; Figure 1). Twenty-two cases of *Vibrio* spp.-related illness (*V. cholerae, V. parahaemolyticus, V. vulnificus*) and five mortalities were reported directly after the heavy rainfall and tidal surge associated with Hurricane Katrina in August 2005 (CDC, 2005; Hsieh *et al.,* 2007). Taking into consideration the predicted global warming of surface waters of the coming decades, a better understanding of the factors driving the virulence, temporal and spatial distribution and antibiotic resistance capabilities of thermodependent bacterial pathogens such as non-cholerae vibrios will be critical.

Epidemiological risk factors

A range of complex and inter-related epidemiological risk factors may be directly responsible for an increase in both the incidence as well as clinical burden of non-cholerae Vibrio infections in Europe (Baker-Austin *et al.,* 2010). *V. vulnificus* infections are rare; in a population-based analysis of coastal areas in the U.S., the incidence of *V. vulnificus* infections is approximately 0.5/100,000 population per year (Johnston *et al.,* 1985; Klontz *et al.,* 1988,). Globally however, *V. vulnificus* is one of the handful of foodborne pathogens with a reported increase in incidence (Baker-Austin *et al.,* 2010). It is estimated that the mean annual incidence of all vibrio infections increased by 41% between 1996 and 2005 (Bross *et al.,* 2005; CDC, 2005). *V. parahaemolyticus* infections are considerably more common than *V. vulnificus* (~10,000 cases per year in the U.S.) (Mead *et al.,* 1999; CDC, 2005). *V. parahaemolyticus* is not a notifiable illness in the UK or other parts of Europe. Laboratory testing for the organism is not widespread, and as it causes gastro-enteric disease similar to norovirus infection, commonly associated with consumption of raw or lightly cooked seafood (Lees, 2000), the true incidence levels may be obscured. Several risk factors have recently been identified, that will affect non-cholerae vibrio disease incidence (Baker-Austin *et al.,* 2010). A global increase in consumption of shellfish since the early 1970s has been seen. The consumption of shellfish in Europe has risen steadily over the last few decades (Gudmundsson *et al.,* 2006). Recent estimates from the United Nations have suggested that by 2030, maintaining even present-day consumption levels will necessitate an additional 40 million tons of seafood globally. With many marine resources unlikely to meet this demand (Worm *et al.* 2006), the aquaculture industry, particularly in the production of shellfish species, is likely to expand significantly. Such extensive expansion in shellfish consumption is likely to proportionately increase the number of individuals exposed to these pathogens, with the potential to dramatically amplify disease transmission (Baker-Austin *et al.,* 2010). Additionally, some industry practices such as warm water depuration for norovirus and increased summer harvest of triploid oysters may increase vibrio risk. In Europe, as with elsewhere, the numbers of individuals with pre-disposing risk factors have risen significantly, and are likely to further increase in the coming decades, increasing the number of individuals susceptible to non-cholerae vibrio infections, and in particular *V. vulnificus* transmission. For example, recent estimates indicate that almost 33% of the EU population will be aged over 65 in 2050, an increase of 20% from 1950 (UN, 2002). Coupled to this the HIV pandemic, increases in malignancy therapy, such as bone marrow and organ

transplantation, and the longer life expectancy of patients with chronic diseases, will mean that health professionals are confronted with the management of a growing number of immunocompromised patients (Loutan, 1997). Such risk factors (age, underlying liver problems, immunocompetency) are three major epidemiological risk factors in *V. parahaemolyticus*, and in particular *V. vulnificus,* infections. Finally, because many of these infections are relatively rare and require judicious use of appropriate antibiotics (especially in the case of *V. vulnificus*) both clinicians as well as susceptible target groups are less likely to correctly identify symptoms and clinical characteristics in a timely manner (Baker-Austin *et al.,* 2010). A study in north Florida indicated that less than 15% of high-risk patients (i.e. individuals with underlying susceptibilities) were aware of the risks associated with raw oyster consumption (Johnson *et al.*, 1988). These findings emphasize the need for clinicians as well as susceptible target groups to familiarize themselves with the risk factors and clinical characteristics of non-cholerae vibrio infections, particularly now that these disease outbreaks are being reported in previously non-endemic regions.

***V. vulnificus* and *V. parahaemolyticus* in the UK and continental Europe.** In contrast to Asian countries and the U.S., non-cholerae vibrio infections are less often reported in Europe (European Commission, 2001, Su and Liu, 2007). In the UK only 57 cases of *V. parahaemolytcius* infection were reported between 2004 and 2005, and, where information exists, mostly consisted of infections contracted during travel to endemic regions (Anon, 2006, Wagley *et al.,* 2008). One of the first non-cholerae vibrio outbreaks in Europe was reported in the UK in 1973, and involved consumption of locally caught crabs (Hooper *et al.,* 1974). Wagley *et al.* (2008) noted both the seasonality and high frequency of *V. parahaemolyticus*, including TDH positive strains, associated with the Chinese Mitten crab in the Thames estuary in the U.K. although information on illness in the local community, known to harvest crabs for domestic consumption, was not available. In other parts of Europe eight cases of acute gastroenteritis caused by *V. parahaemolyticus* and associated with fish or shellfish ingestion were reported in Spain in 1989 (Molero *et al*., 1989, Su and Liu, 2007). An outbreak involving 64 illnesses associated with raw oyster consumption occurred in 1999, also reported in Spain (Lozano-León *et al*., 2003). Martinez-Urtaza *et al*., (2005) suggested that a unique and specific European clone of *V. parahaemolyticus* was responsible for all of these Spanish infections. It has also been suggested that *V. parahaemolyticus* infections in Spain are far more common than previously assumed particularly in Galicia (northwestern Spain), where most Spanish shellfish are produced (Martinez-Urtaza *et al*., 2005, Baker-Austin *et al.,* 2010). A large outbreak affecting 44 patients in France was related to the consumption of seafood imported from Asia (Lemoine *et al,.* 1999). A more recent outbreak involving 80 cases of *V. parahaemolyticus* infection resulting from consumption of edible crabs was reported in Spain in July 2004; the crabs had originated from the south of the U.K. (Martinez-Urtaza *et al*., 2005). Recently, 03:K6 serotype *V. parahaemolyticus* strains were isolated from a clinical case of gastrointestinal infection in Italy (Ottaviani *et al.,* 2008) and have been detected in waters off the Adriatic coast (Caburlotto *et al.,* 2008). Numerous studies have identified total as well as pathogenic (i.e. *tdh* and or *trh* positive) *V. parahaemolyticus* strains in seafood and water across numerous European countries (Di Pinto *et al.,* 2008, Wagley *et al.,* 2009, Ripabelli *et al.,* 1999).

There are no reported indigenously acquired infections of *V. vulnificus* in the U.K. *V. vulnificus* infections in Europe are rare, sporadic, and have been reported to tend to follow warm weather conditions (Baker-Austin *et al.,* 2010). In 1996 a major outbreak of severe soft tissue infections and bacteremia erupted in Israel among fish market workers and fish consumers (Bisharat and Raz, 1996), which were identified as *V. vulnificus* biotype-3 strains (Paz *et al.,* 2007). During the unusually warm summer in

Denmark in 1994, 11 clinical cases of *V. vulnificus* infection were reported (Høi *et al.,* 1998, Dalsgaard *et al.,* 1996). A recent case of *V. vulnificus* infection acquired from a thermal pool in Turkey was recently reported (Partridge *et al.,* 2009). *V. vulnificus* infections have also been reported in Germany (Hoyer *et al,.* 1995), Sweden (Melhus *et al.,* 1995), and Belgium (Mertens *et al.,* 1979). *V. vulnificus* strains have been identified across Europe in shellfish (Normanno *et al.,* 2006, Ripabelli *et al.,* 1999, Bauer *et al.,* 2006), water and associated with plankton and copepods (Gugliandolo *et al.,* 2005).

1. What is already happening?

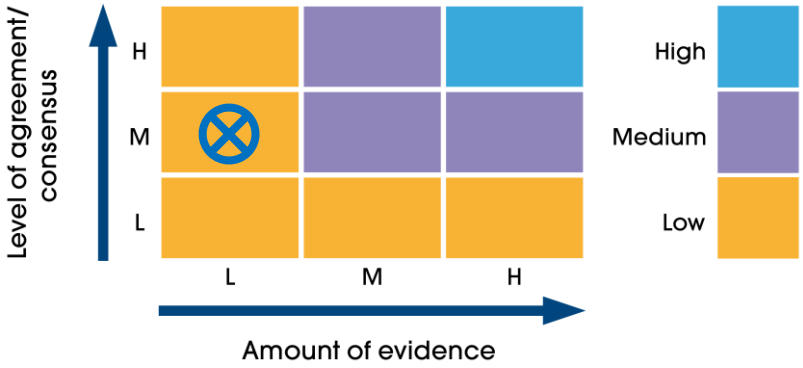
- The disease burden from *V. parahaemolyticus* and *V. vulnificus* in the UK is currently low. However, the incidence of these pathogens in the environment is extremely poorly understood. There exists almost no capacity in the UK to directly test foodstuffs for pathogenic strains in environmental samples such as seafoods.
- It is estimated that because most *V. parahaemolyticus* infections are self-limiting and transient the true clinical burden is unknown.
- No information exists with respect to the antibiotic susceptibility profiles of *V. vulnificus* and *V. parahaemolyticus* from U.K. environments. In other world regions presence of resistance to frontline anti-microbials causes significant problems in treating infections.
- Sporadic cases as well as large outbreaks associated with these pathogens have been reported across Europe over the last 30 years with increasing frequency.
- Disease outbreaks associated with non-cholerae vibrios have been linked to climate change (Paz *et al.,* 2007).

2. What could happen in the future?

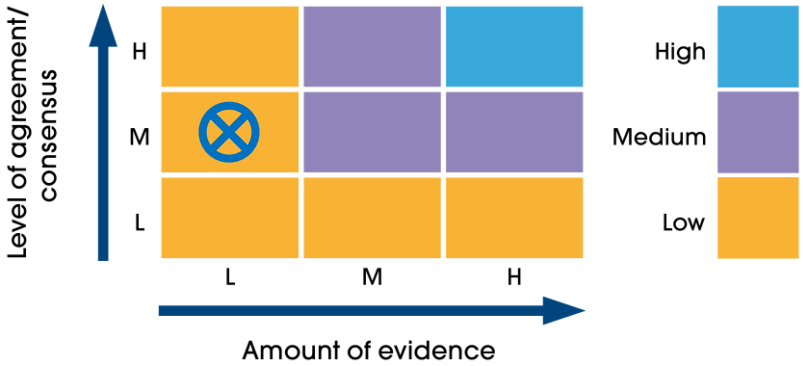
- Rising surface seawater and air temperature are considered likely to increase the numbers and geographical range of the thermo-dependant bacterial pathogens *V. parahaemolyticus* and *V. vulnificus.* This may create conditions in UK coastal waters that will support proliferation of these organisms and increase exposure to shellfish consuming public.
- Transient decreases in estuarine and coastal salinity as a result of flooding may also encourage the proliferation of these organisms.
- Increases in the consumption of shellfish due to the perceived health benefits may increase the numbers of consumers exposed to the pathogens.
- The numbers of individuals with pre-disposing risk factors (age, underlying liver problems, immuno-competency) will rise over the next decade and beyond.

3. Confidence in the science

What is already happening: ***Low***



What could happen: ***Low***



There are several factors leading to low confidence in our predictions regarding current and future risks of vibrio infections in the UK:

1. Uncertainties regarding accurate and regionally specific surface seawater temperatures. These uncertainties are compounded by a lack of predictive capabilities for 'extreme' weather events leading to vibrio outbreaks (i.e. significant rainfall events and droughts/heatwaves).
2. Uncertainties regarding sea surface salinity predictions.
3. Environmental and biological data regarding the incidence, virulence, temporal and spatial distribution of pathogenic vibrios in UK waters.
4. A current lack of accurate surveillance data regarding vibrio infections in the UK, particularly *V. parahaemolyticus*.

4. Knowledge gaps

The top priority knowledge gaps that need to be addressed in the short term to provide better advice to be given to policy makers are:

1. Absence of validated fit for purpose methods that allow real time assessments of non cholera vibrios in foodstuffs and the environment.
2. Prevalence, distribution and seasonal dynamics of pathogenic and non-pathogenic strains of non cholera vibrios in UK coastal waters and shellfish.
3. Fundamental understanding of the virulence mechanisms of these bacteria.

4. Predictive modelling tools that enable identification of risk factors, such as early warning of plankton blooms etc, that enable management strategies to be implemented that mitigate risk.

5. Socio-economic impacts

Recent estimates for UK landings of bivalve shellfish value the industry in the UK at approximately £200 million annually. The perceived health benefits in seafood consumption indicate that this trend will continue. It is likely that a substantial proportion of the demand for bivalve shellfish in the UK will be satisfied by aquaculture. Coastal areas suitable for bivalve aquaculture tend to be located in shallow, estuarine environments which may be subject to greater impacts from climate change (increased surface seawater temperature, salinity fluctuations) than oceanic regions. It is these environs that may favour proliferation of the potentially pathogenic bacteria *V. parahemolyticus* and *V. vulnificus*.

In the US, it is estimated that infections with vibrios increased by 47% between 1996 and 2005, almost all other agents of foodborne disease (bacterial, viral and parasitic) declined over the same period. The annual estimated dollar costs to the US in terms of medical expenses, lost wages and productivity range from $6.5 to $34.9 billion. In the UK there are an estimated 2 million cases of food poisoning annually (3,400 cases per 100,000 individuals). Current trends indicate that the relative contribution of non cholera vibrio infections to the overall burden of food borne illness in the UK will increase.

Additionally this phenomenon may be exacerbated by the greater numbers of susceptible individuals i.e. those presenting with the three major risk factors of advanced age, immuno-incompetence and underlying hepatic disease amongst the UK population.

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