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EXECUTIVE SUMMARY

Executive summary

1. Introduction

Coastal zones are critical ecosystems for human societies, serving as transitional zones between land and sea and offering diverse benefits such as livelihoods, recreational activities and cultural significance. However, the intricate interplay of multiple stressors in these regions poses a risk to humans, animals and the environment. Of particular concern to public health are the pathogens present in coastal waters. This risk may be further exacerbated in the context of climate change, pollution and social disparities.

For the case of coastal pathogens and the associated infectious diseases, we aim to address three key interconnected issues to suggest extensions to the concept of One Health.

First, we recognise the need to conceptualise human health beyond the biomedical paradigm, by exploring which definitions of human health should support an extended vision of One Health. Second, we aim to better capture health-environment connections by studying in detail the environmental context in which pathogens are present. Third, we investigate how to integrate social sciences and socio-economic aspects, especially equity, allowing us to better acknowledge the complex dynamics arising from the interconnections between climate change pollution, social context, individual and population health status, pathogen status and infection risk.

This report aims to support adaptation to climate change from a systems approach illustrated for the case of coastal pathogens.

2. Structure of the report

The report starts with an introduction of the key concepts and the overall objectives. The deliverable is designed so that the reader can freely enter any of the chapters which can be read as stand-alone pieces.

The body of the report is organised into three main modules: Module A (chapters 1, 2, 3), Module B (chapters 4, 5, 6, 7, 8, 9), and C (chapter 10). Module A focuses on the more theoretical aspects underpinning the development of the conceptual framework, such as the concept of health in general, One Health, and other systemic approaches, as well as health imaginaries. Module B analyses the “coastal pathogens and health” system characteristics. The role of multiple factors (climate change, pollution and social context) in determining the risk of infections by coastal pathogens is examined in detail. Module C is the result of distilling the findings from Modules A and B and integrating the two. Through this integration, a conceptual framework supporting an “extended One Health” vision for coastal pathogens is formulated. The framework is summarised through (i) a system map that synthesises the main influencing factors and their complex interconnections, and (ii) a set of principles suggested for considering extensions to the conceptualisation of One Health.

3. Summary of the chapters: key messages

Module A

Module A analyses how the understanding of the connection between humans, animals and the environment has changed throughout history. It examines the concept of One Health in more detail as well as other integrated approaches, and finally introduces the broader idea of health imaginaries.

The One Health framework emerged from the collaboration of human and veterinary medicine in the context of zoonoses. Across recent decades it has integrated a broader set of issues such as antimicrobial resistance (AMR), biodiversity loss, social determinants of health and environmental justice. During the same time, other system approaches have emerged such as Planetary Health, EcoHealth and Ecological Public Health. Despite coming from different backgrounds and differing in nuances, all emphasise the interconnectedness between animals, humans and the environment.

Recent literature on One Health emphasises addressing new challenges with a very broad vision (OHHLEP, 2022), which requires integrating disciplines more thoroughly and identifying new research needs at disciplinary intersections. However, this very broad vision offers little guidance on how to operationalise it. In our report (chapter

10), we aim to conclude with an example of a theoretical framework integrating the pertaining disciplines for addressing the risk of coastal pathogen infections in the context of climate change, pollution, and social inequalities.

One of the research gaps in One Health is the lack of a shared way of understanding human health. Many of the current One Health programs rely on a biomedical model without providing reasons for this choice. Our analysis starts with the question of which health model should underpin an extended One Health vision. For this, we review some of the most recent developments in the understanding of human health. To this end, we dedicate an entire chapter (2) to discuss the evolution of concepts of human health through history.

The Western idea of health originated in ancient Greek culture, which emphasised the importance of the balance between environmental factors and individual behaviours, thus pointing towards an integrated approach. During the Renaissance, infectious diseases were the leading cause of death in the Western world. Advances in science, such as the development of germ theory and the discovery of antibiotics, along with the modernisation of cities, significantly improved people's health. This led to a shift in focusing on the biological aspects of health, resulting in the biomedical model that prevailed until the late 20th century.

As Western societies transitioned from being primarily affected by infectious diseases to dealing with an increasingly elderly population and the rise of chronic diseases there were numerous attempts to define health more comprehensively from the 1960s onwards. Some notable proposals from that time include Engel's bio-psycho-social model (1977) and Antonovsky's salutogenesis (1978). The bio-psycho-social model is a "systems model", which suggests that health and disease are influenced by interactions among different health dimensions, including genetic and biochemical processes, psychological factors and the social context. Consequently, socioeconomic factors and lifestyle conditions can be understood to affect the biological aspects of health according to Engel. On the other hand, Antonovsky investigated the basis of what constitutes "good health" and proposed the "salutary factors" in view of health promotion.

These broader perspectives have converged in recognising that health can be understood as a multi-layered concept characterised by the interconnections between physical, mental, social, and spiritual dimensions, in mutual interdependence with environmental factors. In line with these perspectives and extending the biomedical model of health, the framework proposed in this report views health very much in line with Engel's bio-psycho-social model, which reflects health as a nested system that depends primarily on interaction at multiple scales (biological, psychological, social, etc.).

Going a step further, chapter 3 introduces the notion of health imaginaries. Societies and their sociocultural norms, institutional beliefs and assumptions about health and disease are partly formed by collective interpretation. Imaginaries, which refer to this collective understanding, influence individual and societal behaviours and actions and ultimately affect health outcomes.

The chapter emphasises how scientific paradigms and the corresponding health imaginaries about the microbial world have framed current collective perceptions. It then goes on to show how recent discoveries are setting the foundations to explore new ways of imagining and conceiving what it means to be a healthy human.

One of these emerging health imaginaries is the “holobiont”, which implies that being healthy means fostering stability, resilience and symbiotic mutualistic relationships with multiple microbial species that “inhabit” humans. To embrace new concepts, we need to recognise the powerful role of health imaginaries and how they come into being. The “holobiont” as a new emerging imaginary can help transform assumptions and visions of the general public on how the microbial world collaborates with our human world. This can then have considerable implications on how we intervene in the microbial world. Changing health imaginaries will shape collective behaviour and lifestyle, influence the direction of research, and influence policy and funding, defining which health aspects are valued and prioritised.

Module B

Module B looks at the characteristics of the system “coastal pathogen – human health”. We explore how pressures such as climate change, pollution and societal dynamics impact coastal pathogens’ abundance, spread and virulence. However, the

risk of contracting infectious diseases depends only partly on the exposure to these pathogens. We therefore examine how these different pressures also act on host resilience (i.e. susceptibility and recovery capacity) and the pathways by which they co-determine disease outcome.

The pathogens present in coastal zones (chapter 4) can originate from different places, some inhabiting naturally the coastal ecosystems, while others are introduced from inland sources, such as wastewater discharges, and/or agricultural runoff. When analysing the risks related to coastal pathogens it is therefore important to consider the pathogen sources, survival- and transport dynamics from watersheds to coast. A concise overview of the typology of coastal pathogens related to water-borne, food-borne and vector-borne diseases is conducted and a summary of current policies and monitoring programmes is provided.

In chapter 5 the role of climate change in exacerbating water-borne, food-borne and vector-borne diseases in coastal zones is examined. Droughts, wildfires, environmental heatwaves, marine heatwaves, sea-level rise, heavy precipitation, flooding and storms can trigger favourable environmental conditions in coastal waters for pathogen proliferation, spread and promotion of virulence traits. More and more studies emphasise that climate change also affects other health conditions such as mental health (e.g. anxiety and stress in the face of disasters caused by climate change) and exacerbates pre-existing chronic conditions such as cardiovascular and respiratory symptoms. These health impacts may affect the host's health status making it more prone to infectious diseases.

The next important aspect addressed in the chapter is the cascading effect of climate hazards. The simultaneous or consecutive occurrence of climate hazards generates cascading dynamics that can amplify the impact on both coastal pathogens and host health status.

Finally, this chapter emphasises how social inequalities are exacerbated by climate change. Climate hazards, such as flooding or wildfires, can severely compromise public services and infrastructure, thus further worsening the conditions for vulnerable groups.

Chapter 6 provides an in-depth review of how pollution pressures affect pathogen risk. It specifically analyses the role of heavy metals, persistent organic pollutants (POPs), plastics and microplastics, pharmaceuticals and personal care products (PPCPs), and nutrients (phosphorus and nitrogen). This chapter aims to investigate how contaminants can increase the risk of exposure to coastal pathogens and whether exposure to contaminants can affect the health status of the host, making them more susceptible to infections.

The review shows that pollution in coastal zones can increase the risk of exposure to pathogens because pollutants promote favourable environmental conditions for their proliferation and spread. Additionally, pollutants can enhance pathogen virulence traits and antimicrobial resistance (AMR), rendering them more dangerous to humans. However, the specific effects of pollutants on coastal pathogens depend on the type and level of pollutants, as well as the specific pathogen.

Pollutants present a significant threat to human health, especially by non-communicable diseases (NCDs) and immune system disorders. Even though limited, literature is available on the connection between exposure to pollutants and increased susceptibility to coastal pathogens. The review identifies several studies that focused on coastal populations more exposed to marine or coastal pollution. The studies revealed that exposure to POPs (in particular, per- and poly-fluoroalkyl substances (PFAS) and perfluorinated compounds (PFCs)), particularly in the early stage of life, is linked to increased cases of common colds, gastroenteritis, and respiratory diseases and otitis; being also connected to reduced immune responses to vaccines.

Finally, this chapter reflects that in a context where deaths attributed to NCDs in the European Union (EU) are as high as 91%, NCDs could be additional risk factors in dealing with infectious diseases. The synergies between NCDs and infectious diseases need to be better understood as this collaboration can lead to important implications for health policies.

Although some chronic diseases are recognised as a risk factor for the susceptibility and severity of specific infectious diseases, and some infectious diseases can lead to the development of chronic conditions, the knowledge is still fragmented, and more

research is needed on the interface between pollution, infectious diseases and chronic diseases.

Finally, in the context of marine/coastal pollution, it is paramount to establish rigorous surveillance and monitoring systems as well as proactively implement mitigation measures, such as embracing the precautionary principle for the responsible use of chemicals.

Chapter 7 elaborates on the significant role of AMR when studying coastal pathogens. The chapter provides an overview of AMR in Europe, AMR mechanisms and spread into the environment, and finally, it discusses the resistance profile of key selected coastal pathogens. It shows how AMR is also triggered and enhanced by the presence of pollution and climate change.

Antimicrobial resistance occurs when bacteria develop mechanisms to combat antibiotics, rendering the drugs ineffective in treating bacterial infections. Human activities that lead to the release of pharmaceuticals, antibiotics, and other pollutants, play a significant role in the proliferation and dissemination of AMR among coastal pathogens. The resistance to important antibiotics in coastal pathogens is widespread, encompassing both naturally occurring species and those originating from human or animal sources that have been introduced to estuaries, harbours, and beaches. Experts emphasise the concerning role of coastal and marine bacteria as environmental reservoirs of AMR.

Antimicrobial resistance is a global problem that could cause more than 10 million deaths per year by 2050. This chapter highlights that AMR is not a standalone process that can be tackled by isolated interventions, as other global processes, such as pollution and climate change, can influence it. On the one hand, warmer temperatures trigger the development and spread of AMR. First, because they increase horizontal gene transfer (HGT), and second, the heat stress response can also confer resistance to some antibiotics. Ecological studies in the United States (US) and Europe suggest a significant increase in resistant strains when temperature increases. On the other hand, the relationship between pollution and AMR is complex and has consequences for human health and the environment. Exposure to pollutants, including heavy metals and other compounds, can lead to the development of AMR through a process known

as co-selection. In addition, some pollutants such as microplastics act as hotspots and carriers of AMR. Coastal pathogens can colonise the surfaces of plastic waste, creating hotspots for the exchange of resistance genes, and as plastics persist in the environment, they can easily travel and spread to different locations.

In conclusion, AMR is extremely complex and cannot be addressed independently of other global threats such as pollution and climate change. Therefore, tackling the issue from multiple angles is necessary to promote global multi-perspective actions under a broad One Health approach requiring collaboration between different disciplines and sectors. One of the policy implications of this approach would be to integrate initiatives of health promotion into AMR programs.

Chapter 8, illustrates for a selected pathogen (*Vibrio*) how all the above-introduced pressures come together to alter to infection risk. An in-depth assessment reviews the ecology of *Vibrio*; the impact of climate change on *Vibrio*; the impact of pollution on *Vibrio*; the shared interrelated mechanisms by which climate change and pollution similarly influence *Vibrio* infections, and finally the health impacts on humans.

Then, in the following section of the chapter, the key concepts and mechanisms gathered from the review are integrated within a model based on the Driver-Pressure-State-Exposure-Effect-Action (DPSEEA) framework illustrating the multiple sites for potential intervention. These mechanisms can be summarised as follows; (i) an increase in the proliferation and distribution of *Vibrio* (ii) an increase in the virulence and AMR profile of *Vibrio* and (iii) an increase in the host`s susceptibility to infections due to negative effects on their immune system and gut microbiomes. A key contribution to the methodology of the DPSEEA framework has been to consider the state not only in terms of the environment to which the host can be exposed but also in terms of the host's health status and microbiome.

The DPSEEA approach enables a straightforward pathway for stakeholder engagement and interdisciplinary collaboration. It can facilitate the identification of key health and environmental indicators and serve as a foundation for communicating and exchanging knowledge with a wide audience.

When looking at the complex and interlinked cause-effect dynamics of climate change and pollution-driven *Vibrio* infections in the DPSEEA model, it becomes clear that

actions must be taken under an integrated and systemic approach. Reduction of greenhouse gases, prevention of aquatic pollution, schemes of responsible antibiotic use and health promotion emerge as key areas of intervention.

Chapter 9 highlights the value of an intersectional approach. Intersectionality, a sociological analytical framework, postulates that people's identities and their personal experiences are the product of many overlapping biological, cultural, and social factors. The chapter attempts to analyse how intersecting dynamics in the social context shape the unequal distribution of infectious diseases caused by coastal pathogens in three aspects; exposure, susceptibility and recovery. The term "intersecting dynamics" has been suggested in this chapter as an umbrella term to reflect how social determinants of health intersect with each other to create complex dynamics of social- and health inequalities.

The analysis shows that exposure, susceptibility, and recovery dynamics are unique for each individual and affect different population groups in different ways. For example, regarding exposure, disadvantaged individuals in neighbourhoods with poor water supply infrastructure and sanitation are especially vulnerable. However, advantaged individuals who pursue recreational activities in coastal waters, that consume raw or undercooked food and with extensive international travel may also be strongly exposed. Regarding susceptibility, disadvantaged individuals tend to be more susceptible due to experiencing unhealthy lifestyles and chronic stress, exposure to pollutants or poor healthcare access, lowering their overall health status.

The chapter shows how an intersectional approach is essential to study the social determinants of health by recognising that multiple social, economic, cultural and biological aspects of individuals from advantaged and disadvantaged groups intersect to create unique social dynamics and identities that cannot be understood when they are studied separately. Therefore, risk assessment and disease models should consider the heterogeneity in susceptibility, exposure and recovery. Furthermore, the chapter also shows how adopting a bio-social approach is essential to understanding the dynamic, bidirectional interactions between biological phenomena and social phenomena. It shows how social phenomena that are characterised by intersecting dynamics and the consequent social inequalities have biological pathways.

Module C

Finally, in module C, to address the complexity related to infectious diseases and coastal pathogens, chapter 10 brings together the theoretical findings of module A and the complex system characteristics from module B to suggest a framework supporting an extended One Health vision.

Within the framework, the system map (Fig. 10.1) summarises how key influencing factors associate and interact with each other in determining the final risk of coastal pathogen infections. The influencing factors include climate change, pollution, the social context, coastal pathogens and the host's health status. The three main mechanisms shaping the risk and severity of infectious diseases are “exposure”, “susceptibility” to infection and the “recovery” of the host.

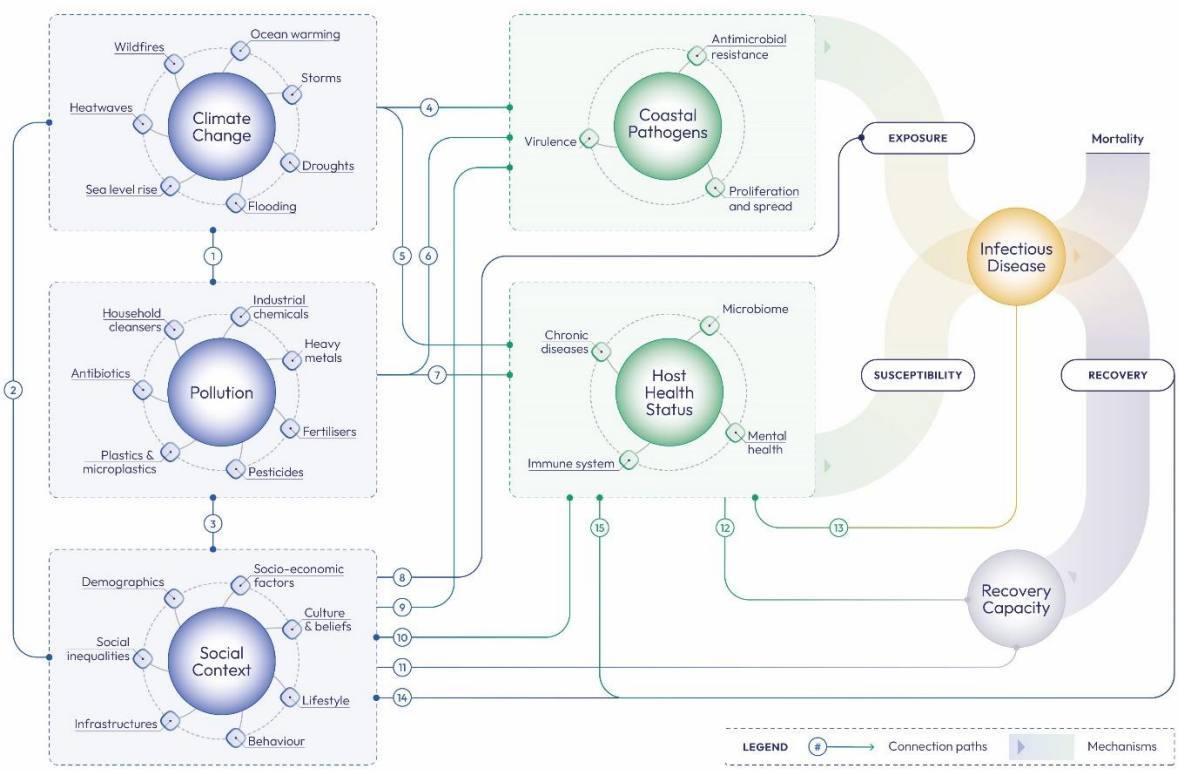


Figure system map. interactions among influencing factors and their impact on the risk of coastal pathogen infections. Each number represents a connection path between different influencing factors in the system (Fig. 10.1).

The system map highlights the significance of the host's health status when individuals and communities face exposure to infectious pathogens. Not everyone exposed to a pathogen will fall ill. Therefore, it is crucial to comprehend how variations in exposure,

susceptibility and recovery capacity can increase the likelihood of infection in specific individuals and populations. Another important aspect of the system map is that the influencing factors and sub-factors themselves interact with each other, resulting in a joint impact on the mechanisms of infectious diseases. Their multiple directional and bidirectional pathways create a causal network with feedback loops and the potential for amplification. Simultaneous stressors from climate change, pollutants and the social system can interact and amplify both the presence of dangerous pathogens (exposure) as well as the susceptibility of the host.

When addressing the risk of infections, a main body of research looks at how climate change, pollution and social factors affect the ecology of pathogens, creating the conditions for pathogens to be more spread, virulent and resistant. For example, the effect of temperature on the proliferation of pathogens is well established, as well as its role in promoting horizontal gene transfer and upregulating virulence genes. Similarly, the presence of pollutants can trigger the co-selection of resistance genes. Lastly, the misuse and overuse of many medical substances contribute to AMR.

These pressures, acting on the pathogens, act at the same time on the host, weakening the host's health status, making it more susceptible, and increasing the risk. For example, heatwaves exacerbate chronic conditions in people in poor health making them more susceptible to infections. Also, exposure to pollutants can impair immunity, the microbiome and mental health, and cause chronic diseases, which can increase susceptibility to certain infections. Finally, lifestyle factors (diet, chronic stress) are also contributing to a weakened host health status.

These factors together with an increased use of recreational water due to climate change (heatwaves), further exacerbate infection risk.

From this integrated perspective, it emerges that the influencing factors can converge to create consequences much greater than any single factor might suggest. This convergence in turn may raise the baseline susceptibility in the population to the risk of infectious diseases. As a result, the host health status might become a major driver for the spread of infectious diseases, triggering a chain of cascading effects on the whole system, with impacts on the social context, in terms of economic impacts,

productivity loss, change in behaviour, overuse of medicaments, impact on the health care system.

The discussion of the system map has led us to question whether any theoretical concepts can be used as recommendations for applying a systemic analysis in other contexts of health and environmental issues. For example, the analysis suggests that a “multidimensional health” understanding, that acknowledges how the social, psychological and biological aspects and their interactions are key in determining the final health outcome, may be a valuable approach. Similarly, we have observed that processes are multiscalar such as encompassing the microbiological, individual, ecological and social scales, etc.

In summary, the principles highlight the interconnectedness and interdependence of humans, animals, and the environment, pointing towards embeddedness rather than mere connections. These three domains engage in ongoing communication and exchange.

The principles were organised at different levels: foundational, operative and adaptive (Fig. 10.2).

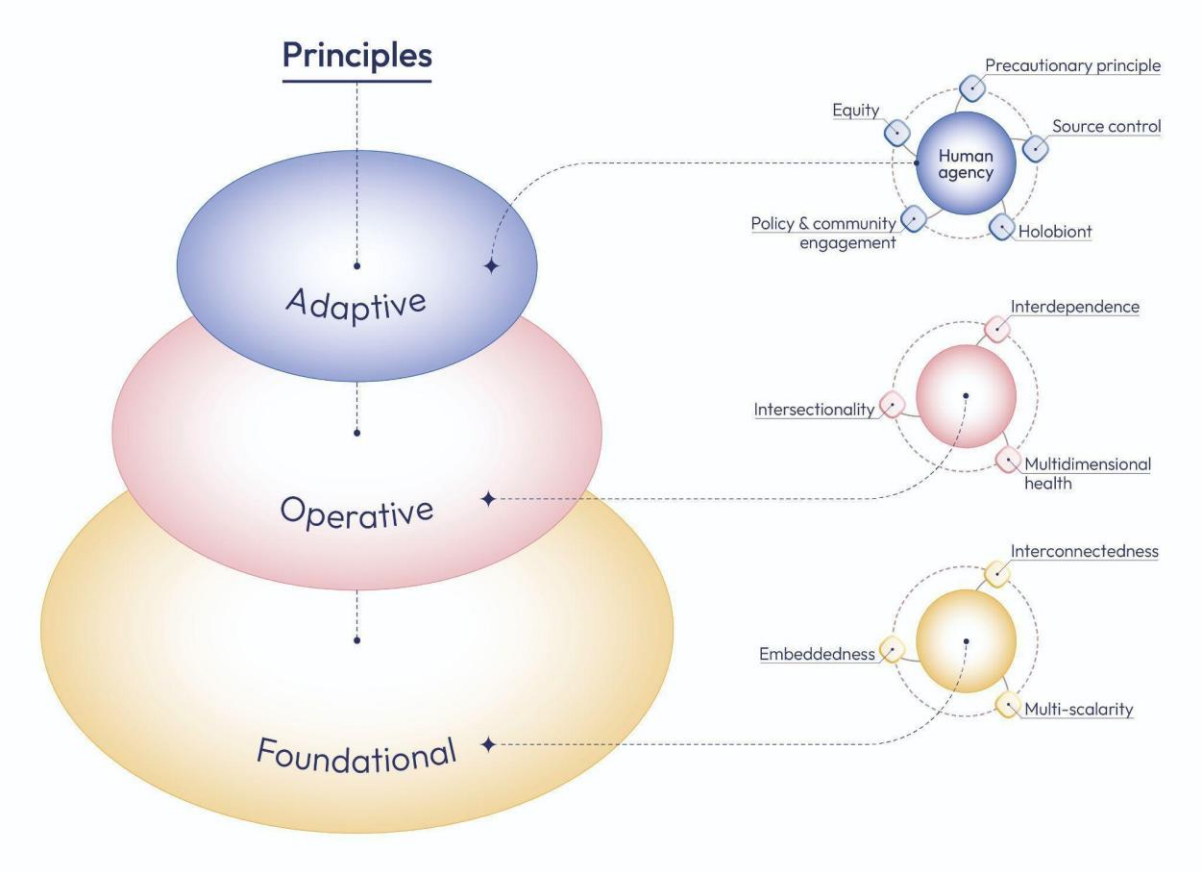


Figure principles. Foundational, operative and adaptive principles supporting an extended One Health framework (Fig. 10.2).

The main implications of our analysis for future research and policy avenues are summarised as the following:

- More research is required on the role of the host health status in infectious disease risk.
- A better appreciation of heterogeneity in exposure, susceptibility, and recovery of individuals and population groups.
- A deeper understanding of the complex interactions between climate change, pollution, and chronic- and infectious diseases.
- Foster preventive instruments such as health promotion policies, in combination with control and surveillance of infectious diseases, and early warning systems.

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Acronyms and abbreviations

ACS	American Chemical Society
AdV	Adenovirus
AMR	Antimicrobial resistance
ARB	Antibiotic-resistant bacteria
ARG	Antibiotic resistance gene
AROPE	At risk of poverty and social exclusion
ASD	Autism spectrum disorder
AstV	Astrovirus
BCE	Before Common Era
C	Carbon
CAMS	Copernicus Atmosphere Monitoring Service
CDC	Centers for Disease Control and Prevention
CE	Common Era
CIMI	Cataline Island Marine Institute
COVID-19	Coronavirus disease 2019
CRED	Centre for Research on the Epidemiology of Disasters
DDT	Dichlorodiphenyltrichloroethane
DNA	Deoxyribonucleic acid
DO	Dissolved oxygen
DPSEEA	Driving Force Pressure State Exposure Effect Action
ECDC	European Centre for Disease Control and Prevention
ECHA	European Chemicals Agency
ECMWF	European Centre for Medium-Range Weather Forecasts
EEA	European Economic area
EMA	European Medicines Agency
EM-DAT	The international disaster database
ENSO	El Niño-Southern Oscillation
EU	European Union
EU/EEAA	European Union/European Economic Area
EURGen-Net	European Antimicrobial Resistance Genes Surveillance Network

EV	Enterovirus
FAO	Food and Agriculture Organisation
FBD	Foodborne disease
GAC	Global anthropogenic change
GAP-AMR	Global Action Plan on Antimicrobial Resistance
GHG	Greenhouse gas
GLASS	Global Antimicrobial Resistance Surveillance System
HAB	Harmful algae bloom
HAV	Hepatitis A Virus
HGT	Horizontal gene transfer
ICF	International Classification of Functioning, Disability, and Health
IPCC	Intergovernmental Panel on Climate Change
IWMI	International Water Management Institute
MDR	Multidrug resistance
MGE	Mobile Genetic Element
MHW	Marine heatwave
MP	Microplastic
MRSA	Methicillin-resistant Staphylococcus aureus
N	Nitrogen
NAPEM	National Academies of Sciences, Engineering, and Medicine
NASEM	National Academy of Engineering and the Institute of Medicine of the United States
NCD	Non-communicable disease
NOOA	National Oceanic and Atmospheric Administration
NoV	Norovirus
OA	Ocean acidification
OHHLEP	One Health High-Level Expert Panel
OIE	World Organisation for Animal Health
P	Phosphorus
PAH	Polycyclic aromatic hydrocarbon
PBDE	Polybrominated diphenyl ether
PCB	Polychlorinated biphenyl

PCBs	Polychlorinated biphenyls
PFC	Perfluorinated compound
pH	Potential of hydrogen
POP	Persistent organic pollutant
PPCP	Pharmaceuticals and personal care product
PTSD	Post-traumatic stress disorder
R&D	Research and development
RV	Rotavirus
SLR	Sea level rise
Spp.	Species
SST	Sea surface temperature
UK	United Kingdom
UN	United Nations
UNEP	United Nations Environment Programme
US	United States
VBD	Vector-borne disease
VGT	Vertical gene transfer
VPH	Veterinary Public Health
WBD	Waterborne disease
WFD	Water Framework Directive
WHO	World Health Organization
WOAH	World Organisation for Animal Health
WWTP	Wastewater treatment plant

INTRODUCTION

Introduction

The objective of this deliverable is to propose an integrated approach to health that could serve as a support for an extended One Health vision, to better account for the complex interlinkages between coastal pathogens, human exposures, health and climate change, including a broader conceptualisation of the upstream factors that influence pathogens in coastal waters, as well as contextual social and economic factors.

Recent literature on One Health approaches acknowledges the need to address emerging challenges with a more comprehensive vision of health. However, how this should be done within specific settings still requires development. For the case of coastal pathogens and associated infectious diseases, we aim to address three key interconnected issues to develop a more integrated approach to health.

First, we recognise the need to incorporate a conceptualisation of human health beyond the current biomedical paradigm, by exploring which definitions of human health should support an extended vision of One Health. Second, we aim to better capture health-environment connections by studying in detail the environmental context in which pathogens are present. Third, we investigate how to integrate social sciences and socio-economic aspects, especially equity, allowing to better acknowledge the complex dynamics arising from the interconnections between climate change – pollution – social context – individual and population health status – pathogen status and infection risk.

In order to respond to these objectives, the work has been organised and structured into three main modules. Module A provides the basis for conceptualising human health and reviews current integrated health frameworks. Module B analyses the factors that influence pathogenic health risks in coastal settings. Module C establishes how health understandings (from module A) can be extended by considering the complexity arising when contemplating the system characteristics and dynamics revealed in module B.

The modules are comprised of several chapters. In module A, chapter 1 studies in detail the origins and evolution of the One Health concept. In addition, it summarises and compares other frameworks that provide integrated perspectives on health that connect humans, animals and the environment. These include Planetary Health, EcoHealth and Ecological Public Health.

Chapter 2 delves into more detail into the conceptualisation of human health itself. The origins and historical evolution of human health concepts are analysed and the emergence of the contemporary understandings of health are presented.

Finally, chapter 3 introduces the notion of health imaginaries showing how visions of health are socially constructed. It describes one of the current imaginaries, the biomedical imaginary and introduces a new, emergent imaginary that shows how the recent discoveries emphasise the central role of the microbiome in regulating processes taking place within ecosystem as well as within humans.

Module B starts with a brief introduction to the system under study encompassing coastal zones and pathogens and associated pressures and responses (chapter 4).

Chapter 5 delves deep into how climate hazards (droughts, wildfires, terrestrial and marine warming and heatwaves, sea level rise, storms, heavy precipitation and flooding) impact coastal pathogens associated with waterborne, foodborne and vector-borne diseases. In addition, the chapter elaborates on how climate hazards affect the health status of humans and indirectly impact pathogenic risks.

Chapter 6 provides an in depth-review of how pollution pressures affect pathogen risk. It specifically analyses the role of heavy metals, persistent organic pollutants, plastics, pharmaceuticals and personal care products, and nutrients. Similar as with climate change, it assesses how each of these pollutants impacts pathogen presence and virulence. It also analyses the relationship between pollutants and human health and how this can affect the propensity towards developing infections.

The role of antimicrobial resistance (AMR) in coastal pathogen risk is discussed in chapter 7. This relates to the fact that resistant pathogens entering the coastal system can significantly amplify health risks as antibiotics lose their effectiveness as treatment options. The chapter provides an overview of AMR in Europe, AMR mechanisms and

spread into the environment, and finally, it discusses the resistance profile of key selected coastal pathogens. It shows how AMR is also triggered and enhanced by the co-presence of pollution and climate change.

Chapter 8, for the case of the bacterium *Vibrio*, illustrates how the above-introduced pressures (climate change, pollution and AMR) come together and potentially also interact to affect the resulting risk of infectious disease. It summarises the findings within a Driver-Pressure-State-Exposure-Effect-Action (DPSEEA) framework illustrating the multiple sites for potential intervention.

Chapter 9 attempts to highlight the importance of the local social context and its intersectionality (i.e. the compounding of factors of inequality) in shaping pathogen risk and disease- and recovery dynamics.

Finally, in module C, chapter 10 makes the effort to synthesise the theoretical findings of module A and the system characteristics from module B within a system map revealing the strong interconnectivity between the different pressures, pathogen status, exposure pathways, host health status and resulting disease dynamics. It then proposes a set of principles that a One Health framework should include based on the consolidated findings from the previous chapters. It concludes with a discussion of findings in light of the existing health frameworks analysed in module A and provides some recommendations to support an extended One Health framework in the context of infectious diseases to guide research and policy action.

The deliverable is designed so that the reader can freely enter any of the chapters that can be read as stand-alone pieces. The deliverable intends to provide rich contextual insight required when studying how climate change may affect pathogen risk. It points to the need for complementing disciplinary approaches, such as the study of how temperature changes may affect the biological processes occurring within a single pathogen with the understanding of complex systems that try and understand how multiple factors act and interact in conjunction to shape disease dynamics. Such a vision also considerably widens the scope for interventions in view of improving overall health of humans, animals and plants understood as interconnected elements within an ecosystem.

CHAPTER 1

One Health and other system approaches

Chapter 1. One Health and other system approaches

1.1. Introduction

The rapid growth of the human population and the associated urbanisation, globalisation, and intensification processes have resulted in a significant imbalance between humans and nature. This imbalance has led to a widespread reduction in biodiversity, the deterioration of ecosystems, and significant migratory movements of both humans and species in general (UN, 2021; UNEP, 2021). These processes have triggered unexpected events, including the emergence of infectious diseases like avian influenza, Ebola, Zika, and most recently, COVID-19 (Lawler et al., 2021; Lindahl & Grace, 2015). These diseases have highlighted the strong connection between humans, animals, and ecosystems (Esposito et al., 2023). In this context, experts have stressed the significance of considering the human-animal-ecosystem interface when addressing public health threats (FAO et al., 2011; WHO, 2019; Zinsstag et al., 2023). Multiple conceptual frameworks have been developed to better understand the interactions taking place between humans, animals, and the environment. One such framework is the One Health framework. It arose in the context of the emergence of zoonoses and has received increasing attention from international organisations such as the World Health Organisation (WHO), UNEP (United Nations Environment Programme) and FAO (Food and Agriculture Organisation), particularly after the COVID-19 pandemic. Today it is promoted as an approach to address complex public health threats (FAO et al., 2022; WHO et al., 2022).

Coastal zones, particularly those in developing countries where the world's most populated regions are located, are strongly impacted by human activity (Xu & Zhang, 2022). The effects of climate change and increasing chemical and biological pollutants amplify the existing pressures. As a consequence, there is a rise in outbreaks of diseases related to pathogenic microorganisms. This situation is alarming as marine and coastal ecosystems sustain human well-being through seafood/fish catching and consumption and recreational activities. In this line, several authors have proposed a One Health approach to address the various emerging public health threats in coastal areas (Aguirre, 2004; Wang et al., 2021).

This chapter aims to achieve two primary objectives: firstly, to provide a comprehensive understanding of the historical evolution of the One Health approach, and secondly, to elucidate the distinguishing nuances that set One Health apart from other approaches that recognise the interdependence between humans, animals, and ecosystems. Addressing these two objectives should enable us to reveal the scope, essential components and principles underlying One Health and other approaches. This will provide the building blocks for suggesting an appropriate framework for addressing health hazards from coastal pathogens in the context of climate change, increasing pollution and growing inequalities (see chapter 10).

1.2. One Health: concept, origin and historical evolution

The One Health approach was established in the early 21st century to tackle emerging public health challenges. However, the foundations of this approach predate the term itself. To comprehend the current meaning of One Health, it is crucial to understand the scientific, political, and health-related ideas from various historical contexts in which some of the concepts that shape today's approach have originated.

In the chapter “One Health in History” from the book, *One Health: The Theory and Practice of Integrated Health Approaches* (2021) (2nd ed.); Bresalier, M., Cassidy, A., and Woods, A. provided a critical analysis of the history of One Health. The authors observed that existing One Health narratives are often linear retellings of historical events and scientific discoveries that justify the One Health approach today (Fig.1.1). However, such accounts fail to understand the historical reasons behind the emergence of One Health and do not provide a historical enquiry into the concepts underpinning the approach. This is recognised by the authors as a gap in the current analysis of One Health.

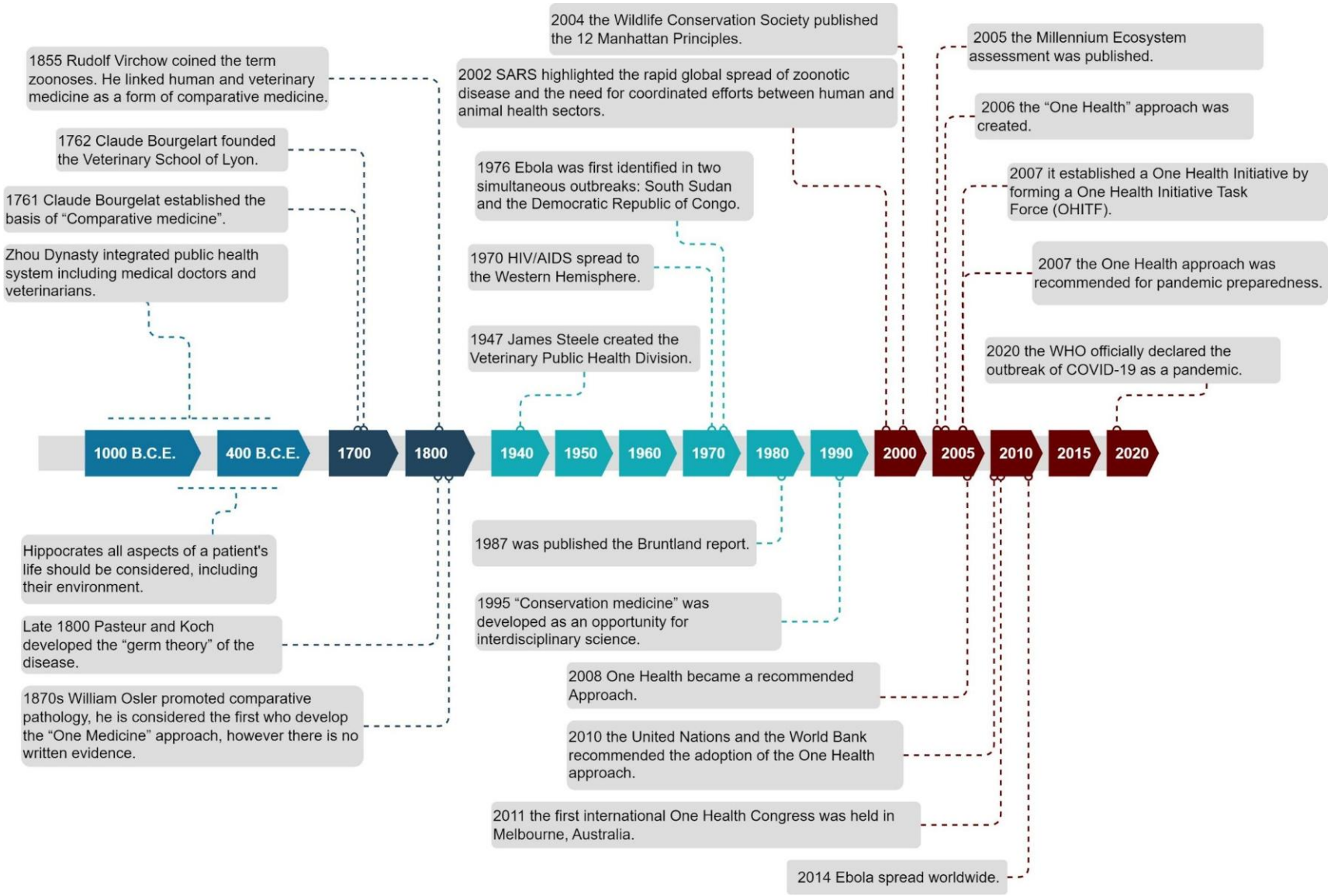


Fig.1.1. Linear representation of the historical events underpinning the concept of One Health.

This section aims to identify the moments in history when health-related interlinkages between humans, animals and the environment were examined more closely. The reviews conducted by Bresalier et al. (2021) and Zinsstag et al. (2011) provide the basis for this analysis.

Ancient cultures such as the Egyptian, Chinese or Indian cultures contemplated human and animal medicine simultaneously. The Zhou Dynasty (1046-256 BCE) had one of the earliest organisations of an integrated public health system including medical doctors and veterinarians (Zinsstag et al., 2011). However, Greek culture, which has had a profound impact on Western society, defended certain distinctions between animals and humans, even if the boundaries between them were often blurred. Greek culture regarded disease as an imbalance of the body rather than a specific pathology. Hippocrates (460-370 BCE), considered the father of modern medicine, in his book *Air, Water and Places* (~400 BCE) advocated for a holistic approach to patient care which included the importance of the environment (Cole et al., 2014). Aristotle (384-322 BCE), a philosopher and disciple of Plato (427-347 BCE), believed that humans and animals were closely related despite humans possessing a rational soul. In his work, he maintained that conducting dissections on animals could provide valuable insights into human anatomy (Bresalier et al., 2021). An influential figure in the development of human and veterinary medicine was Galen of Pergamon (129-216 CE). He followed in the footsteps of Aristotle and applied his findings in animal anatomy to humans because, at that time, performing dissections on human bodies was considered taboo.

During the Middle Ages, Europe experienced various waves of famine, war and plague. The most severe plague epidemic in European history, the Black Death, broke out between 1346 and 1347, killing between 30% and 60% of the European population, the worst demographic catastrophe in European history. There were two main theories to explain the Black Death. The first was related to astrological beliefs and was seen as a kind of divine punishment. The second explanation was related to the miasma theory. According to this theory, miasmas were considered to be a collection of fetid emanations from soil and dirty water (i.e. bad smells) that cause disease (Crawford & Crawford, 2018; Zahler, 2013).

Medicine in the Middle Ages was empirical and strongly influenced by the knowledge of the Greek authors. At that time, medicine was mainly governed by humourism, a theory generally attributed to Hippocrates. According to this theory, the human body contains four humours: blood, phlegm, yellow bile and black bile, and health is mainly determined by the right balance between the four humours. This is why it was common practice to perform bloodletting or provoke vomiting to purge the sick to restore the balance of the humours. This theory of humours was predominant until the 18th century (Lindemann, 2010).

The Renaissance was a time of many scientific discoveries. For the first time, the anatomist Andreas Vesalius (1514-1564) was able to perform a human dissection and document the mistakes that were made when extrapolating animal anatomy to human anatomy. This period saw important scientific discoveries, such as the theory of blood circulation. Later, between 1660 and 1670, the activity known as “comparative anatomy”, which was based on studying animals from colonial conquests, took shape among the elite of the Academy of Sciences in Paris (Bresalier et al., 2021). In parallel, the microbiologist Anton van Leeuwenhoek (1632-1723) claimed to be the first to see a microorganism, although at the time he named these living microscopic organisms as “animalcules”, meaning “little animals”.

The establishment of “comparative anatomy” was crucial at the time, as the differences between humans and animals became increasingly blurred. Key figures of this discipline were George Cuvier (1769-1832), George Buffon (1739-1788) and the naturalist Carolus Linnaeus (1707-1778). For example, Linnaeus placed humans and orangutans in the same genus *Homo*. In 1762 Claude Bourgelat (1712-1779) created the first school of the veterinary profession in Lyon. Bourgelat coined the term “comparative medicine” in 1761 and recommended human clinical training for the veterinary curriculum (Mashkour & Beech, 2017).

Meanwhile, scientific discoveries continued. In 1854, John Snow (1813-1858), a British physician, while investigating the 1854 Broad Street cholera outbreak, hypothesised that cholera was caused by very small cells from contaminated wells and not from bad smell (miasma). A few years later, the discoveries of Louis Pasteur (1822-1895) and Robert Koch (1843-1910) contributed to the development of the germ theory. In 1884, Koch was able to confirm Snow's hypothesis that cholera was caused

by a microorganism, *Vibrio cholera*. In parallel, in 1859 Charles Darwin (1809-1882) published *The Origin of Species*, a book stating that all living organisms had descended by evolution from a common ancestor.

These discoveries in human medicine would not have been possible without the collaboration of many veterinarians who worked on developing diagnostic practices and treatments for animal diseases. Rudolf Virchow (1821-1902), who is known as the father of modern pathology, studied tuberculosis and trichinosis in animals. He is credited with coining the term “zoonoses” in 1855. Throughout his career, he remained interested in the connections between human and veterinary medicine. His research helped to disprove the theory of humourism (Gyles, 2016; Kienle et al., 2013).

Throughout the 20th century, veterinarians and physicians experienced a significant shift in their relationship, as highlighted in the analysis conducted by Bresalier et al. (2021). Multiple reasons contributed to the gradual separation of these two disciplines in the Western world. One of the key factors that triggered this process was the rapid urbanisation that fundamentally changed physicians' perceptions of animals. Previously, animals were ubiquitous in cities—in livestock markets, zoos, in some sports, as a means of transportation, and so on. However, in the 20th century, this started to change, and animals began to disappear from the streets, as a result of changing urbanisation patterns. Rapid urbanisation not only impacted the scientific community's relationship with animals but also led to a broader societal disengagement from wildlife, strengthening in turn the connection with companion animals. Pet owners' increasing concern about their pets' welfare prompted veterinarians to shift focus from using animals to test drugs to treating animals with drugs, e.g. painkillers.

The process of urbanisation and population growth necessitated the provision of protein-rich food sources for the expanding population. As a result, meat and milk became the primary source of protein, leading to new health challenges and increased health responsibilities for Western governments given food hygiene. Differences of opinion between veterinarians and physicians regarding the associated health threats led to the establishment of separate governmental departments. By the close of the century, veterinarians were primarily focused on the care of companion and farm animals resulting in the separation of human and animal health disciplines.

However, not all voices of the time agreed with this division. Among the advocates of further integration of veterinary and human medicine was William Osler (1849-1919), a young Canadian physician who went to Berlin to study under Virchow's supervision. Years later he returned to Canada arguing that there was no fundamental difference between human and veterinary medicine. Although there is no direct written evidence, it is widely believed that Osler was the originator of the concept of “One Medicine” (Zinsstag et al., 2011). However, it was Calvin Schwabe (1927-2006), a veterinary epidemiologist and parasitologist at the University of California, who formally coined the term (Zinsstag et al., 2011). According to Schwabe the human and animal domains share a common body of knowledge in anatomy, physiology, pathology, and the origin of diseases (Schwabe, 1969). The veterinary branch started to gain importance in the United States, and in 1947 James Steele (1913-2013) founded the Division of Veterinary Public Health (VPH) of the US Center for Communicable Diseases (CDC); he is considered one of the pioneers in efforts to prevent the spread of zoonotic diseases.

In the 2000s, there were continuing efforts to merge human and animal medicine. In 2004, the Wildlife Conservation Society and the Rockefeller Foundation organised a symposium in which they proposed the Manhattan Principles on “One World, One Health”. These principles laid out 12 recommendations for a more comprehensive approach to preventing epidemic/epizootic diseases (FAO et al., 2008). Gradually, with the support of international organisations, they began to adopt this broader concept of health that recognised the connection between human beings and the environment. Since then, the One Health approach has become ubiquitous in the vocabulary of international agencies, research funding programmes, and scientific articles.

However, some criticisms of the framework are also encountered in literature, such as the lack of consideration of the role of the environment, the need to include socio-economic factors and equity, the adoption of a too narrow view of health centred on its biomedical characteristics, or the lack of inclusion of social science disciplines (Davis & Sharp, 2020; Destoumieux-Garzón et al., 2018; Gibbs, 2014; Lerner & Berg, 2015; Zinsstag et al., 2011). Rabinowitz et al. (2018) claim the lack of an authentic integration of knowledge from the human, animal and environmental spheres in many

One Health programs, and suggest an analysis of interactions within and across the three realms (human, animal and environment) at multiple scales of hierarchical systems. Zinsstag et al. (2011, 2023) also point towards the need for a stronger analysis of interconnections across scales within a socio-ecological system.

Although in its origins One Health focused more on infectious diseases and in particular on the emergence of zoonoses, the framework has evolved (and continues evolving) to address broader issues such as climate change, environmental damage, or food security. In the next section (1.3) we show how the current One Health approach relates to other approaches that intend to integrate the human-animal-environment domains.

1.3. Human-animal-environment in health approaches

As will be discussed in chapter 2, health is a multifaceted issue which depends on biological, societal, and environmental determinants, and their intricate interplay, giving rise to considerable complexity. As previously mentioned, a variety of approaches have emerged throughout history that seek to capture this complexity.

Of the current system approaches that address human-animal-environment interconnections, three of them have gained significant attention from researchers and policy-makers: One Health, EcoHealth and Planetary Health.

There have also been suggestions from certain authors to combine some of these approaches. For instance, Zinsstag (2012), and Roger et al. (2016) propose merging One Health and EcoHealth, while Castañeda et al. (2023) suggest collaborations between One Health and Planetary Health (Castañeda et al., 2023; Roger et al., 2016; Zinsstag, 2012). On the other hand, in their “Planetary Vision of One Health”, Rabinowitz et al. (2018), propose an integration of the concepts of Planetary Health and EcoHealth within the One Health framework (Rabinowitz et al., 2018).

The three approaches have emerged from different backgrounds and specialisations, even though they may appear synonymous to an outsider, more or less subtle differences exist in each approach. In this section, we aim to compare the characteristics of each approach, looking for similarities and differences. To achieve

this, we start from the theoretical comparison made by Lerner and Berger (2017). Additionally, we include Ecological Public Health in the comparison, an approach that has not received as much attention from international organisations as the other three, as it has been considered by some to be too academic-research based (WHO, 2023). However, it aligns with the other three approaches in addressing the human-animal-environment health connection, as well as supporting systems analysis, so we believe it has significant attributes that should be included in our discussion. Our analysis intends to provide some broad representative characteristics of each approach's definition, focus, disciplines, values and agents. The results from the comparison and discussion are summarised in Table 1.1, which is a modified and extended version of Lerner and Berger (2017). It should be noted that the table presented is not intended to offer a comprehensive analysis of all the current literature but rather an indicative summary and characterisation of the different approaches discussed in the chapter.

The origins and history of One Health are developed extensively in section 1.2 of this chapter. One Health, founded around 2006, emerged from the need for collaboration between human and veterinary medicine in the context of zoonotic diseases. Although in its early days, the concept had a narrow focus, mainly on the emergence of zoonoses, in recent years it has also begun to be understood in a broader sense. In 2022, the One Health High-Level Group (OHHLG)—an expert group established to create partnerships among four organisations: FAO, UNEP, WHO and the World Organisation for Animal Health (WOAH)—proposed one of the most recent definitions of One Health:

> "*One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes that the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent. The approach mobilises multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, acting*

> *on climate changes and contributing to sustainable development*" (OHHLEP et al., 2022).

In their commentary, Castañeda et al. (2023) highlighted that One Health publications tend to cover infectious disease topics more comprehensively than other approaches, particularly focusing on COVID-19, antimicrobial resistance (AMR), and zoonoses (Lefrançois et al., 2023; Velazquez-Meza et al., 2022). While zoonoses have been the mainstay of the One Health approach in the past, it has evolved to include a broader range of disciplines beyond veterinary and human medicine. Critics noted the absence of social sciences in the past; in recent years, significant efforts have been made to integrate specialities such as anthropology, urban planning, and climate change research (Lainé & Morand, 2020; Patz & Hahn, 2013; Sandul et al., 2018).

The concept of One Health has made significant progress in recognising the interdependence of humans, animals, plants, and the environment. However, the underlying values of this approach tend to be utilitarian. That is while recognising the importance of fauna, flora and ecosystems in the overall scheme of things, their preservation is often understood from a perspective of safeguarding human and public health rather than as an objective in itself. This paradox poses ethical and moral questions and highlights the need for a more profound philosophical development of the One Health theory (Davis & Sharp, 2020). One Health's strength lies in its call for multidisciplinary and interdisciplinary collaboration, which enhances information sharing and collaborations across different fields, ideally resulting in a comprehensive and integrated understanding of complex health issues.

The second approach, EcoHealth, is a multidisciplinary approach that strives to enhance health and well-being by prioritising social and ecological interactions. Its origin can be traced back to North America, where it was developed by integrating social disciplines and collaborating with local communities. The term emerged from the EcoHealth Alliance, though its ideas and concepts had been previously developed. One of its predecessor alliances was The Wildlife Preservation Trust International, which was established in 1971, developed into the Wildlife Trust in 1999 and became the EcoHealth Alliance in 2010. As stated in the Encyclopedia of Quality of Life and Well-Being Research (2014):

> "*Ecohealth is a field of research, education, and practice that adopts systems approaches to promote the health of people, animals, and ecosystems in the context of social and ecological interactions. Health is seen as encompassing social, mental, spiritual, and physical well-being and not merely the absence of disease. As a contraction of "ecosystem approaches to health", eco-health emphasizes human agency and systemic thinking to promote well-being and quality of life. As a field of scholarship, eco-health research draws on the natural sciences, health sciences, social sciences, the humanities, and beyond, often working in collaboration with interested parties and community members to address issues at the interface of health, ecosystems, and society*" (Parkes et al., 2014).

EcoHealth considers factors like gender and social injustice, which involve more fields from social sciences and humanities than One Health. EcoHealth also values the inclusion of indigenous knowledge, which is recognised as a source of knowledge beyond Western models. By involving more participatory science, EcoHealth is seen as a more practical approach, promoting the participation of citizens and other stakeholders. Ecologists are the most commonly represented natural scientists, even though the field has become more inclusive and interdisciplinary. Biodiversity and sustainability are among the most important values.

Ecological public health provides a comprehensive outlook on health by acknowledging the intrinsic connection between human well-being, societies, and the environment. While the concepts and ideas behind ecological public health have roots in earlier works, Rayner and Lang (2013) significantly developed the field. Their work notably highlights the strength of ecological thinking in recognising complex and multi-layered connections when addressing public health. In other words, the approach argues that public health should address multiple scales from micro to macro including biological, social, cultural and environmental dimensions of health. Rayner and Lang (2013) posit that ecological public health's key aspects lie in its ability to integrate various models, promote the analysis of complexity and system dynamics, foster knowledge building, assimilate an evolutionary perspective on challenges, and serve

as a comprehensive interdisciplinary and multi-stakeholder model (Lang & Rayner, 2012; Rayner & Lang, 2013).

One of the approaches that has gained attention in more recent times is Planetary Health. This approach was initially proposed by Richard Horton and other collaborators in 2014 and has since been extensively developed by the Rockefeller Foundation (Horton et al., 2014; Whitmee et al., 2015).

> "*Our definition of planetary health is the achievement of the highest attainable standard of health, wellbeing, and equity worldwide through judicious attention to the human systems—political, economic, and social—that shape the future of humanity and the Earth's natural systems that define the safe environmental limits within which humanity can flourish*" (Horton et al., 2014).

Planetary Health aims to understand the impact of human activities such as pollution on global health. While there are publications that focus on zoonoses, most research in Planetary Health has been directed towards larger-scale processes such as climate change. However, it appears to prioritise human interests over those of animals and ecosystems, exhibiting a human-centred perspective that emphasises the need to address threats to sustainability and future human generations, thereby aligning with the Brundtland view of sustainability. Despite this, the approach argues that ensuring human civilisation's survival must be accompanied by improving health for all and equity (Lerner & Berg, 2017).

Planetary Health is an inclusive approach that includes the participation of diverse academic and non-academic disciplines, promoting the co-production of action. This inter- and transdisciplinary approach has been highlighted for its inclusivity of professionals from fields such as policymaking, health care, and economics. Nevertheless, some experts have criticised Planetary Health for failing to represent environmental disciplines, such as ecology and biology (Lerner & Berg, 2015, 2017).

Table 1.1. Indicative summary of the comparison of approaches. Modified from Lerner & Berg, 2017.

Framework features	One Health		Planetary Health	EcoHealth	Ecological Public Health
	Early	**Current**			
Focus	❖ Zoonoses ❖ Antimicrobial resistance	▪ Zoonoses ▪ Emerging infectious diseases ▪ Antimicrobial resistance ▪ Non-communicable diseases ▪ Food safety ▪ Climate change ▪ Biodiversity loss ▪ Ecosystem health ▪ Social determinants of health ▪ Environmental justice ▪ Animal welfare ▪ Occupational health	– Infectious diseases – Vector-borne diseases – Social justice – Health & wellbeing – Climate change – Biodiversity loss – Ecosystem health – Food safety – Land use & urban planning – Sustainable development goals – Environmental justice – Social determinants of health	✧ Infectious diseases ✧ Vector-borne diseases ✧ Climate change ✧ Biodiversity loss ✧ Ecosystem health ✧ Food safety ✧ Social determinants of health ✧ Water & sanitation ✧ Community-based research ✧ Socio-ecological systems	● System thinking ● Intersection between humans and environment ● Biodiversity & human health ● Climate change & health ● Vector-Borne diseases ● Land use & health ● Food systems & agriculture ● Social determinants of health ● Environmental justice ● Governance & health ● Community engagement
Contributing disciplines	❖ Public health ❖ Veterinary medicine	▪ Public health ▪ Human health ▪ Veterinary medicine	– Public health – Human medicine – Economy	✧ Public health ✧ Human medicine ✧ Economy & social sciences	● Public health ● Human medicine ● Economic & social sciences

		▪ Biological & environmental sciences ▪ Economy & social sciences ▪ Ecology	– Energy – Agricultural sciences – Environmental sciences – Urban planning	✧ Agricultural sciences ✧ Environmental sciences ✧ Ecology ✧ Anthropology ✧ Occupational Health ✧ Urban and rural planning	● Agricultural sciences ● Environmental sciences. ● Ecology ● Urban and rural planning
Target	❖ Human	▪ Human ▪ Animal ▪ Environment	– Human	✧ Human ✧ Animal ✧ Environment	● Intersection between humans and environment
Values	❖ Individual health of humans & animals (animal health is addressed for its potential impact on human health). ❖ Encourages multidisciplinary research.	▪ Individual and population health of humans, animals & the environment (still very few studies address animal and ecosystem health for their intrinsic value, they are generally addressed for their potential impact on human health). ▪ Encourages multi- and interdisciplinary research.	– Sustainability (for humans) – Highlights the importance of social justice. – Encourages hands-on, inter and trans-disciplinary research.	✧ Biodiversity and sustainability (for humans, animals and the environment). ✧ Highlights the value of indigenous knowledge. ✧ Encourages hands-on, trans-disciplinary research.	● Complexity and system dynamics as core values (getting into systems rather than individuals). ● Emphasises non-linearity, interactions, variations of scale and feedback. ● Health depends on the successful coexistence of the natural world and social relations. ● Encourages transdisciplinary research.

Agents	❖ Human health professionals ❖ Biomedical scientists ❖ Veterinarians ❖ Public health professionals ❖ Policymakers	▪ Environmental scientists ▪ Biomedical scientists ▪ Agricultural & food safety professionals ▪ Veterinarians ▪ Economics & social scientists ▪ Educators ▪ Community members ▪ Non-governmental organisations ▪ International organisations ▪ Policymakers	– Human health professionals – Environmental scientist – Ecologists – Policymakers – Urban planners – Economists & social scientist – Climate Scientists – International organisations – Indigenous communities	✧ Public health professionals ✧ Veterinarians ✧ Environmental scientists ✧ Economics & social scientists ✧ Educators ✧ Community members ✧ Non-governmental organisations ✧ International organisations ✧ Government institutions ✧ Policymakers ✧ Indigenous and local knowledge holders	● Public health professionals ● Health practitioners ● Environmental Scientists ● Ecologists ● Community members ● Policymakers ● Educators ● Nongovernmental organisations ● Government agencies

1.4. Conclusions

This chapter highlights how the understanding of interconnectedness between animal and human health has evolved. It illustrates times and cultures in history where the consideration of these connections was stronger and times where they were less so.

It reviews various current approaches and frameworks such as One Health, Planetary Health, EcoHealth, and Ecological Public Health for studying the interconnectedness between the health of animals, humans and the environmental. As these frameworks are continuously being developed we sometimes also find different interpretations within a single framework.

Concerning One Health, the most recent literature acknowledges the need to address new challenges with a more comprehensive vision, in line with the newly proposed definitions (OHHLEP et al., 2022). The focus has moved from zoonosis and AMR, to expand to other fields such as emerging infectious diseases, chronic diseases, climate change, biodiversity loss, social determinants of health, and environmental justice, among others. This requires a further integration of disciplines than has been the case so far, as well as the identification of new research needs at the interface between disciplines.

In the next chapters, we focus on some of the acknowledged limitations identified in the literature to support a wider One Health framework, which requires the expansion of the concept of human health, the integration of socio-economic factors and health inequality, and the detailed exploration of interconnections of elements from multiple scales across the human-animal-environmental domains. We illustrate these issues in the case of coastal pathogens and infectious diseases.

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CHAPTER 2

Human health conceptualisation

Chapter 2. Human health conceptualisation

2.1. Introduction

The collaboration between animal and human medicine has led to significant scientific discoveries which have resulted in saving countless lives and contributed to the advancement of modern medicine (see chapter 1). Throughout history, the relationship between human and veterinary medicine has undergone shifts, moving closer and farther apart, depending on the cultural and social context of the time (Bresalier et al., 2015). After a period of distancing between these disciplines, the One Health framework emerged at the start of the 21st century, advocating for the unequivocal interdependence between the health of animals, humans and the environment. In the preceding chapter, we discussed the evolution of One Health and we compared it with other frameworks that also recognise this interdependence (One Health High-Level Expert Panel (OHHLEP) et al., 2022). However, there are broader questions that need to be addressed in this context: What is health? And which definition of human health should underpin a One Health vision? These questions will be contemplated in detail in this chapter.

Health is a complex and ever-changing concept that is shaped by cultural, social, and historical factors (Badash et al., 2017). The definition of health varies widely, ranging from biomedical perspectives that focus on the physical characteristics of individuals to holistic approaches that consider health promotion and multiple determinants of health (Badash et al., 2017; Dahlgren & Whitehead, 2021; Lalonde, 1981; WHO et al., 1986). Throughout history, different ideas about health have emerged as a result of the interaction between cultural and social beliefs and the prevailing scientific paradigms of the time (Huber et al., 2011; Mallee, 2017; Sartorius, 2006; Svalastog et al., 2017). As a result, the definition of health has undergone significant changes over time and continues to evolve.

The purpose of this chapter is to provide an overview of the historical development of the Western perspective on health. Gaining insights into how this concept has evolved over time is crucial for comprehending the current health challenges and formulating research into One Health. Such understanding is essential for guiding policy decisions,

shaping practices, developing healthcare models, and enhancing citizens' awareness and choices.

2.2. Historical evolution of human health

2.2.1. From ancient Greece to the XIX century

The word “health” originates from old English “hælþ” which means “the state of being whole, complete, entire and sound” as analysed originally by Dolfman in 1973 (Boruchovitch & Mednick, 2002). The concept of health used to be related to both physical and mental well-being, including attributes of moral and spiritual aspiration.

All-inclusive approaches to health have been widely used in Western culture and thinking. The Western concept of health has its roots in the earliest culture of ancient Greece, where environmental and behavioural factors were recognised as significant components of individual well-being (Tountas, 2009). Around the fifth century BCE, the school of Hippocrates questioned the transcendental understanding of health concerning magical and religious beliefs. Hippocrates (460-370 BCE), the “father of modern medicine”, in his work *On Airs, Waters and Places* (400 BCE) (Miller, 1962), defined health as a condition of harmony resulting from the interaction of environmental factors (e.g. wind, temperature, water and food) and individual habits related to diet, working condition, leisure, use of alcohol and sexual behaviour (Tountas, 2009). The internal equilibrium in the body rests on the equilibrium of an individual with the external environment. Medical practice included the examination of the entire lifestyle of a person (e.g. diet, physical exercise, sleep, repose and work, among others), as well as the exposure to weather conditions, food, water and soil. Hippocratic schools also recognised the importance of psychological illnesses which were considered in the same way as other physical diseases (Kleisiaris et al., 2014). These ideas represent the roots of our modern conceptualisation of the determinants of health (Rotaru, 2020).

Protagoras (490-420 BCE) suggested “self-reliance” as the basis for patient autonomy, anticipating to some extent the concept of "empowerment" proposed in the Ottawa Charter (1987). Equality was considered as a pre-condition for health, whereas

the lack of equality in a system was deemed as the origin of illness in the population (Tountas, 2009).

As discussed in Rotaru (2020), Platonic philosophy referred to autonomy as the "*knowledge about what is genuinely good for oneself and not the freedom to do what merely appears to be good*". It underlined the difference between choices based on knowledge and wisdom, and choices based on "mere pleasure or appearance". Medicine was cited as "*the arts of resorting to what is true and not what is merely apparent*", revealing the need for combining philosophical principles with the practice of medicine. For Plato (428-348 BCE) "complete care" meant understanding the relationship among "the patient, the illness and the choices", and supporting the autonomy of the individual to make wise decisions. Hippocrates' practice, on the other hand, was determined by the triangle of disease-patient-physician, focusing more on the responsibility of the physician to prevent health risks in the patient, to promote health and to deliver treatments. Platonic philosophy embraced holism and defined healing as "*for the whole of patients, communities and the environment*" (Rotaru, 2020). The basic principles that underpin this approach, such as holism, care, autonomy and individual choices, could be very valuable in current medical practice, as discussed in Rotaru (2020), as "*we might want to recover something our Western culture had back at its roots*".

During the Roman Empire (20 BCE ~ 500 CE), the definition of health provided by Hippocrates was further expanded upon, claiming that the balance or imbalance in the body was governing personality and temperament (Badash et al., 2017). Significant initiatives pertaining to health and sanitation were implemented during this particular period, including the establishment of sewage systems and water pipelines.

During the Middle Ages, Europe endured multiple episodes of war, famine and plague. Christian religion played a prominent role in various aspects of life, including the understanding of health and the treatment of the ill. This led to the sick being isolated and excluded from society. The concept of quarantine can be traced back to the year 1377 and has its roots in the "Black Death" a plague caused by the bacterium *Yersinia pestis*. At that time, the rector of the seaport of Ragusa (today Dubrovnik, Croatia) ordered a mandatory 30-day isolation period, known as "trentina" (derived from the Italian word "trenta"), for ships arriving from infected or suspected infected areas.

Similarly, land-based travellers were required to undergo a 40-day isolation period, known as “quarentina” (quarantine) (Gensini et al., 2004). In the Middle Ages, one of the main explanations for the disease was the miasma theory. According to that theory, miasmas were considered a collection of fetid emanations (bad smell) from the soil and dirty water that caused disease (Crawford, 2007; Zahler, 2013). On the other hand, the humourism theory dominated the understanding of human health. This was an ancient conception dating back to ancient Greek times, developed predominantly by Hippocrates and Galen of Pergamon (129-216 CE), which regained strength in medieval and Renaissance medicine. It was based on the idea that the human body was composed of four humours materialised by four bodily fluids, corresponding to the four elements believed to make up the world: blood (air), phlegm (water), yellow bile (fire) and black bile (earth). Each of these body fluids had distinct physical characteristics and determined the individual behaviour. For instance, blood was considered warm and moist, and thus, a person with an “excess” of blood was regarded as cheerful and optimistic. On the other hand, yellow bile was considered warm and dry, and an excess of it was known to evoke a choleric and irritable temperament. To restore the balance of humours, it was common practice to perform bloodletting or provoke vomiting to purge the sick. This theory of humours was predominant until the 18th century (Lindemann, 2010) (see chapter 1).

The Renaissance period spanning from the 14th to the 17th century in Europe, marked a significant era of transformation in the conception of health. Though humourism remained the dominant medical paradigm, this period witnessed a resurgence in the interest in the natural world and the human body. Consequently, academics and physicians started basing their views of health on a more empirical perspective. Among the epochal thinkers who proposed a new vision of health is Paracelsus (1493-1541), a German-Swiss physician, who described human health as a status of equilibrium between the microcosm represented by the human body and the macrocosm of the entire universe (Conti, 2018). Causes of diseases were classified into natural causes, spiritual causes, poison and planetary causes.

During the Renaissance, two significant revolutions transformed society’s understanding of health: The Scientific Revolution and the Industrial Revolution. The Scientific Revolution spurred advancements in various fields such as mathematics,

physics, astronomy, biology, and chemistry. These advancements contributed to the establishment of a dichotomy between nature and culture (Merchant, 1980). The Industrial Revolution, on the other hand, consolidated industrial capitalism and urban societies, which drastically impacted the landscape of health and well-being. Urbanisation and industrial work led to negative health consequences, prompting social responses that gave rise to public health. This epoch of the co-current Scientific and Industrial Revolution led to the birth of modern epidemiology and the promotion of hygienist policies (Kurtz et al., 2013). The contribution of scientists such as John Snow (1813-1858), Louis Pasteur (1822-1895) and Robert Koch (1843-1910) contributed to the development of germ theory, which postulates that microorganisms, called pathogens or “germs”, were the cause of disease and not miasmas (Lorimer & Hodgetts, 2017). Subsequently, the work of Rudolf Virchow (1821-1902), considered the father of modern pathology, led to the refutation of the theory of humourism (see chapter 1). He introduced the idea that every pathology arises from a damaged cell, paving the way for the development of the first theories of the onset of cancer (Rocca & Anjum, 2020).

2.2.2. The emergence of contemporary health concept

Following the Renaissance, there was a continuing trend towards modernisation and scientific advancement, which accelerated the shift from philosophical to more scientific theories. Advancements in fields such as bacteriology, physiology and anatomy led to focus specifically on the biological factors of disease, thus promoting a biomedical concept of health.

Until the end of the 20th century, the traditional biomedical concept of health dominated Western culture. This perspective defines health as a disease-free state. An individual is considered healthy when there are no symptoms or signs of disease. Health and disease are determined by biological factors, and disease is attributed to biological causes such as mutations or pathogens (Boruchovitch & Mednick, 2002; Conti, 2018). In the biomedical concept, health and disease are considered objective and observable phenomena (Boruchovitch & Mednick, 2002). Unquestionably, this perspective has contributed to understanding and controlling infectious diseases and other health conditions, and to developing appropriate treatments to cure the symptoms. One of the major criticisms of this conceptualisation of health has been

that it created a dichotomy between health and disease when, in most cases, the line between these two states is quite blurred (Boruchovitch & Mednick, 2002). Furthermore, the biomedical approach focuses on biological mechanisms that are manageable and treatable by biomedical interventions, such as drugs (Rocca & Anjum, 2020). In this approach, medical professionals are deemed experts in the patient's health, and it is their responsibility to manage the biological mechanisms that generate disease (Boruchovitch & Mednick, 2002).

The biomedical perspective has certain limitations as it confines health to its biological characteristics alone, without taking into consideration the broader social, economic, and cultural context of individuals. As a result, in the modern era, new definitions of health emerged. The proposal presented by the World Health Organisation (WHO) in 1948 is considered the foundation of modern definitions of health. According to this definition, health is "*a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity*" (Badash et al., 2017). The 1948 WHO definition goes beyond the physical symptoms of a disease to focus on what can define health instead of focusing just on disease. It encompasses the social factors that influence individual health outcomes and quality of life. Additionally, it emphasises the importance of achieving well-being, which is not just limited to the absence of disease, but also includes psychosocial, behavioural, and environmental factors (Badash et al., 2017; Boruchovitch & Mednick, 2002). This perspective acknowledges the idea of an individual as a whole, and also the embeddedness of the biological factors within sociocultural dynamics that influence individual's behaviour, lifestyle and ultimately health. However, this definition has faced some limitations and has not proven to be entirely effective. Many argue that the well-intentioned purpose of the WHO definition lacks clarity and practicality and that it is not equipped to handle complicated, chronic health issues within the context of unequal distribution of resources (Badash, 2017). Other authors such as Huber et al. (2011) also questioned the operationalisation of the WHO's definition of wellbeing. Moreover, they criticised the use of the word "complete" in the definition, as a "*state of complete physical, mental and social wellbeing*" cannot be measured and assessed (Huber et al., 2011). According to these authors, the idea of "complete health" may have also unintended consequences in terms of medicalising society. This definition could potentially benefit the

pharmaceutical industry, which is now able to identify physiological abnormalities and create drugs for conditions that were not previously classified as health issues.

Between the 1960s and 1980s, several proposals challenged the conventional biomedical model of health. Among these propositions, one of the most influential was George Engel's biopsychosocial model (Engel, 1977). Engel was an American psychiatrist who believed that health and disease were the result of complex interactions between different dimensions related to biological, psychological and social factors. He was particularly concerned with the problems faced by psychiatry and overall medicine in that period, arguing that the strict application of the biomedical model was the root cause of this crisis. According to the biopsychosocial model, the dimensions of health and illness involve (i) genetic and biochemical processes (including pharmacological effects), (ii) psychological factors such as attitudes, mood, beliefs and expectations, mental health and (iii) social context such as socioeconomic status, quality of life, cultural and familial factors. This model claims that it is not possible to separate the physical body from the history and emotional state of the patients and that the perceptions of the patients about their illness and distress are also important. As a result, health or disease cannot be explained within a cause-effect model, as they arise from the interaction among different nested systems influencing each other (e.g. biological, individual, family, and cultural systems). For instance, lifestyle factors at the community scale combine with socioeconomic conditions and behavioural choices at the individual scale, affecting ultimately the biology of the individual. Another consequence of this model is that a psychological disturbance can lead to biochemical modifications and disease, or can affect the success of biological treatment. The biopsychosocial model is therefore a “systems model” where multiple interrelating factors combine to cause disease, leading to “circular causality” (i Carrió, 2002). This model of disease allows revealing unexpected interactions, for example between cancer and stress, or personality and cardiovascular diseases, or asthma and family relationships (i Carrió, 2002). Hence, it was proposed as an extension, rather than a replacement, of the biomedical model. In 2002, WHO supported its use as a basis for the International Classification of Functioning, Disability, and Health (ICF), a framework integrating medical and social components to support community-based long-term care related to chronic diseases (WHO, 2022). This model has been extensively used in research related to rehabilitation and disability, and has led later

to the development of the patient-centred care model, which aims at involving actively patients in all decisions about their own health (Wade & Halligan, 2017).

In the 1970s the medical sociologist Aron Antonovsky (1923-1994) studied women survivors of the German concentration camps of World War II. He discovered that many of the survivors had not only survived the concentration camps, but had also been able to live a “good life” and began to investigate the source of this good health. In his search for the answer, he proposed an approach called salutogenesis. Its most common and overall meaning refers to “salutogenic orientation”, which examines health mainly from a positive perspective focusing on factors “actively” conducive to health, rather than the main causes of the disease (Mittelmark et al., 2022). Hewis (2023) discusses the need to develop healthcare strategies to address both risk factors (causes of diseases) as well as “salutary factors” for improving the health of the population. This idea supports a more robust model for health promotion than focusing solely on low-risk lifestyle factors, such as smoking, alcohol consumption, obesity or lack of physical activity. Antonovsky suggests a “continuum model of health” where individuals are positioned “somewhere along a healthy/disease continuum and subject to unavoidable entropic processes”, which justifies the need to move actively towards the healthier side of that continuum. This orientation suggests focusing on “salutary factors” for all individuals, independently of their health status, and should complement the prevailing pathogenic orientation focused specifically on the causes of disease. Antonovsky proposed what he termed the “sense of coherence” as a key factor in supporting the promotion of greater health, defined as the capacity of a person to cope with stressful conditions and undesirable events in life, by perceiving the challenge as “comprehensible, manageable and meaningful” (Antonovsky, 1979, 1987; Hewis, 2023). This capacity in turn depends on a series of factors from family to psychological assets, personal and cultural aspects, etc. As discussed in Lindström and Eriksson (2010), there is an alignment between the salutogenic model and the foundational principles of the Ottawa Charter and health promotion, though this was not specifically cited and acknowledged in the Charter.

In parallel to Antonovsky’s salutogenesis theory, in 1978 the WHO highlighted the importance of health promotion and 8 years later, in November 1986, the first International Conference on Health Promotion was held in Ottawa, Canada, promoted

by WHO, Health and Welfare Canada, and the Public Health Association of Canada. The conference aimed to address the escalating expectations of a new global public health movement. The deliberations primarily focused on the requirements of industrialised nations, while also considering similar concerns in other regions. From the meeting a significant document in public health was developed: The Ottawa Charter. The charter provided a framework for health promotion and outlined key principles and strategies for improving health at the individual, community, and societal levels. The Ottawa Charter emphasises that an individual or group must be able to identify and fulfil aspirations, meet needs, and adapt to changing environments to reach a state of complete physical, mental and social well-being. Health is therefore viewed as a resource that supports daily life, rather than an end goal in itself. The Ottawa Charter's significance lies in its emphasis on the social determinants of health. It recognised that health is affected by various factors, including peace, shelter, income, food security, education, employment, and social justice. Therefore, in the pursuit of good health, it is essential to consider all these factors (WHO et al., 1986).

The principles outlined in the Ottawa Charter had a profound impact on the field of health promotion and since then many authors have reflected on the significance of this manifesto. O'Neill (2012) argued that, while the document has symbolic value, it was written during a time of post-World War II economic prosperity when supportive governments were being elected around the world. However, the turn towards more neoliberal economic visions in world politics during the 1980s-90s, and the prevailing capitalist system of that era, meant that the charter no longer aligns with the values of today's society (O'Neill, 2012).

Other authors, such as López-Fernández (2017), see the Ottawa Charter as a new challenge for action in public health aiming to modify the emerging lifestyle-related risk factors considered at the root of chronic diseases. Approximately from the mid-20th century, especially in developed countries, a gradual shift took place leading to a reduction in mortality rates from infectious diseases, due to improvements in hygiene, water supply and sanitation systems, nutrition, new drugs and medical technologies. This has led progressively to an increase in life expectancy with chronic diseases becoming the main cause of death. This situation has continued to evolve over time

with increasing risk factors for chronic diseases such as progressive urbanisation, migration, pollution, climate change impacts, and social inequalities.

Global changes in the second half of the 20th century led to many socio-cultural changes, including changes in the conception of health. The way in which people imagine health and illness, and their underlying causes, can also be referred to as "social imaginaries" on health, including the influence of social, political and cultural values (see chapter 3).

For example, the rising concerns about the environment led to the emergence of an ecological concept of health. At the beginning of the 20th century, the environment was widely viewed as a threat to public health due to issues such as the effects of pesticides on human health and unsanitary conditions in cities. The field of environmental health emerged as a consequence of the growing concern about the exposure to harmful pollutants, and has gradually evolved to embrace multidisciplinary approaches including epidemiology, toxicology, environmental science and public health, among others.

Mallee (2017) discusses how the concept of health has evolved in relation to risks associated with pollution and new emerging infectious diseases, and the key role of the social determinants of health. In response to these concerns, approaches such as Ecohealth, One Health, and Planetary Health have emerged, integrating knowledge from different disciplines, and showing the increasing contribution of social sciences and humanities to the definition of health (see chapter 1).

2.2.3. Determinants of health

The answer to what constitutes "good health" has varied depending on the social, cultural and historical context as well as the knowledge and beliefs available at the time. These answers have spanned from biomedical definitions to more inclusive definitions such as the one formulated by the WHO in 1948, or the biopsychosocial model of Engel in 1977.

The emergence of these definitions opened up debates about the understanding of health, highlighting it as a dynamic, complex and diverse process, rather than a mere state of presence or absence of disease. Since then, it has been increasingly argued

that health is determined not only by the quality of medical care and scientific advances, but also by many other conditions, both at the individual and community levels, such as genetics, behaviour and socio-economic conditions; today we refer to all these factors as determinants of health.

One of the earliest advocates of health determinants was Canadian Prime Minister Marc Lalonde, who in 1974 proposed a working document: A *New Perspective on the Health of Canadians*. That paper aimed to present a different viewpoint on the health of Canadians and to spark discussions on future health programs for Canada. It did not intend to be an all-inclusive and prescriptive list of actions but rather to spark a debate on the need for new and more holistic perspectives on health. In the paper, while acknowledging the importance of the conventional biomedical view of health, particularly its success in interventions such as population immunisation and advanced surgical procedures, Lalonde stressed that certain aspects of this perspective do not consider other risks arising from environmental factors and lifestyle choices. As a result, in his opinion, the biomedical health definition offered only a limited interpretation of health. Furthermore, the Prime Minister stated that the traditional perspective often equated the level of health with the quality of medical care, placing physicians as the sole authorities on health. This, in turn, tends to direct most health expenditures toward medical care, hospitalisation, laboratory tests and prescription drugs.

The main contribution of this document was the identification of four major determinants of health, which marked an important milestone for both individual and collective health care: human biology, environment, lifestyle and healthcare organisation. The definitions given in the document for each determinant are summarised below:

> *(1) Human biology:* includes all those aspects of health, both physical and mental, which are developed within the human body as a consequence of the basic biology of man and the organic make-up of the individual. This element includes the genetic inheritance of the individual, the processes of maturation and ageing, and the many complex internal systems in the body.

(2) Environment: includes all health-related issues that are external to the human body and over which the individual has little or no control. It can be exposure to contaminated food and water, noise pollution, air pollution, etc.

(3) Lifestyle: consists of the set of choices individuals make that affect their health and over which they have more or less control. Personal choices and habits (e.g. diet, sleep patterns, physical exercise, attitudes, stress and addictions) that are detrimental to one's health can create self-imposed risks. When these risks lead to illness or death, the individual's lifestyle can be considered a contributing factor or the root cause of their health problems.

(4) Health Care Organization: consists of the quantity, quality, arrangement, nature and relationships of people and resources in the provision of healthcare. It includes medical practice, nursing, hospitals, nursing homes, medical drugs, etc. This fourth element is what is generally defined as the healthcare system.

The proposal presented by Lalonde was essential for encouraging reflections on the various factors that contribute to shaping the health of an individual. In the wake of this document, numerous health determinant models were proposed, often with a focus on community health.

One of the most prominent models was proposed by Evans and Stoddart (1990), who expanded the list of determinants and outlined the dynamics and interrelationships between them. In their study, Evans and Stoddart (1990) build their framework by adding components that progressively increase complexity. They start with a model based on the traditional biomedical definition of health and end up with a model consisting of nine interrelated components of interest that represent a set of factors that could be examined in more detail (Fig 2.1).

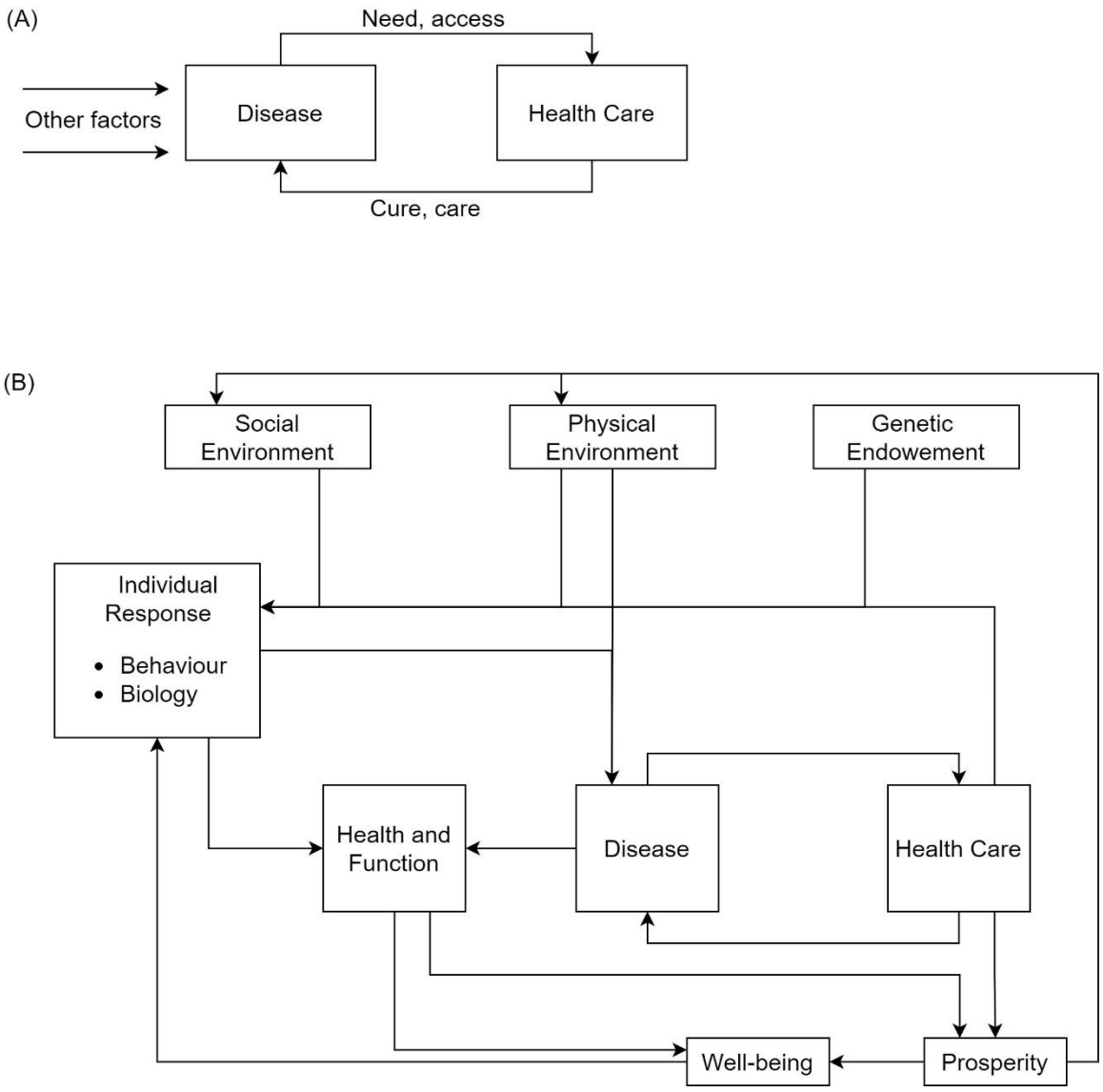


Fig. 2.1. A model of determinants of health. The figure shows two illustrations presented in the paper by Evans and Stoddart (1990). **(A)** shows the model of health based on the traditional definition of health and **(B)** illustrates the expanded model proposed by the authors. Source: Reprinted from Evans, R. G., & Stoddart, G. L. (1990). Producing health, consuming health care. Social Science & Medicine, 31(12), 1347–1363.

Interestingly, Evans and Stoddart (1990) begin by discussing the model based on the biomedical definition of health in which "*people get sick for a variety of unspecified reasons represented by the unlabelled arrows entering on the left-hand side*" (Fig. 2.1.A). According to this model, it is the health care system that defines the patient's needs and provides a response or cure, this response is influenced by: the health professionals' definition of the patient's needs and the set of institutions that a particular society has in place to meet the needs and ensure access to care. The underlying assumption of this model is that providing care to a patient results in a

reduction of illness or a complete cure, thereby leading to an improvement in their overall health. In response to this model, Evans and Stoddart (1990) argue that it oversimplifies the issue and fails to consider other relevant factors that impact health. One of the primary criticisms is that the needs of the patient are determined externally. Consequently, there may be instances where the beneficial effects of the therapy may have negative consequences for the patient. The other main criticism is that it does not consider “the individual's perception of his or her own state”.

Evans and Stoddart (1990) gradually included additional components to create their model (Fig. 2.1.B). The model proposes that disease, health, and well-being can be influenced by individual behavioural and biological responses, which in turn are impacted by social, environmental, and genetic factors that are beyond an individual's control. Shortly after its publication in a report involving the National Academy of Sciences, the National Academy of Engineering and the Institute of Medicine of the United States (NASEM), the committee hailed the model as a starting point for a broad, community-based approach to health (Durch et al., 1997). One of the committee's main observations concerned the effectiveness of the model, which stemmed mainly from its emphasis on interactions between factors (including feedback loops). In Evans and Stoddart's model, health outcomes were the result of intricate interactions between components, rather than individual factors operating independently, and interactions could be as important as a single factor/component. On the other hand, the committee highlighted the model's ability to provide a basis for involving segments of the community not traditionally associated with health, bringing together other stakeholders, such as schools, the media and workers outside the health system, to contribute in the discussion on how to improve health in the community (Durch et al., 1997). This model is also consistent with the biopsychosocial model proposed by Engel in 1977.

One of the most renowned models in the field of determinants of health is the “Dahlgren and Whitehead model”, also referred to as the “Rainbow model” (Fig. 2.2). Developed in 1991 by Göran Dahlgren and Margaret Whitehead, this model has become the most widely used model of its kind for addressing determinants of health. The model provided a visual representation for understanding the various factors that influence health outcomes, commonly represented as a series of concentric circles or

layers, each representing a different level of influence on health. The aim of the model was to provide a framework that includes the broader social, economic and environmental determinants of health.

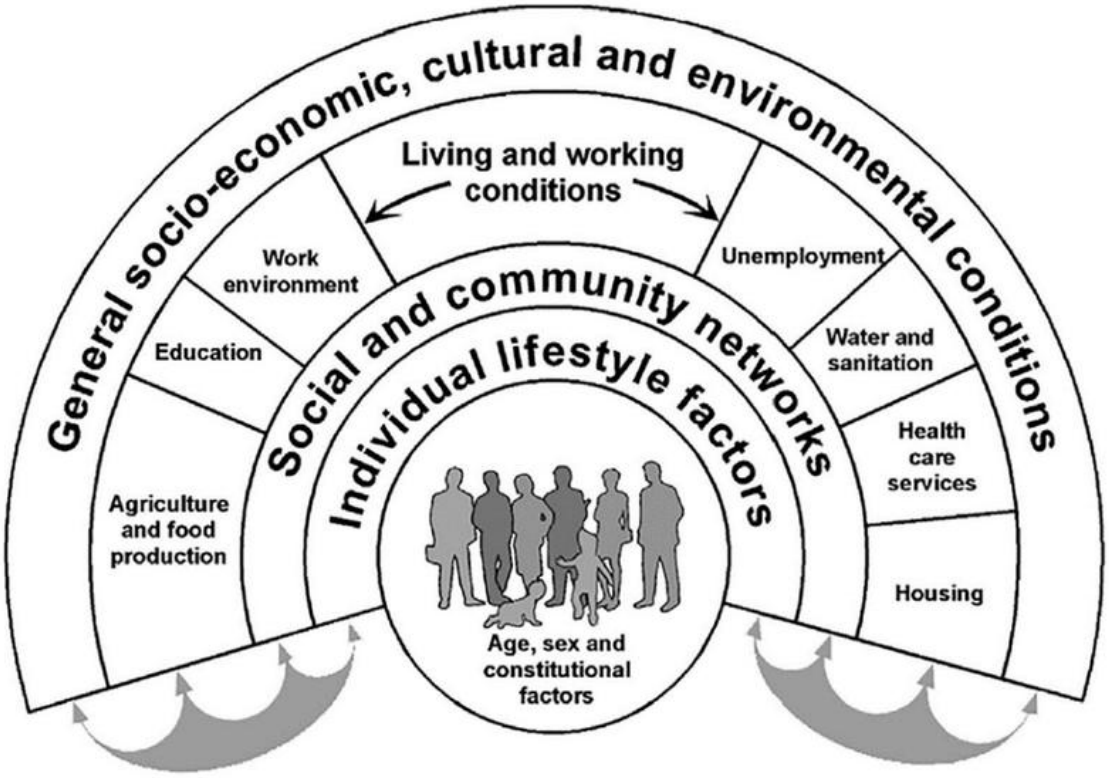


Fig 2.2. The main determinants of health. Source: Dahlgren, G., & Whitehead, M. (1991).

It is worth mentioning that it did not have the expected impact when it was initially developed. The present model was conceived as a contribution to a WHO report on policies and strategies aimed at promoting health equity. However, it was considered too complex by WHO for the targeted audience and it was not included in the final report. Subsequently, the model was published as a supporting document by the Swedish Institute for Futures Studies (Dahlgren & Whitehead, 2021). Gradually the model became popular and gained wide recognition. I even became to be adopted as a representation of public health initiatives in general.

In 2021, Dahlgren and Whitehead published a paper on the possible reasons for the success of their model, three decades after its original publication. They highlight that the model proposes a broad vision of health that extends beyond the domains of the health system, enabling intersectoral collaboration and co-responsibility for improving health outcomes. Its simplicity and holistic perspective make it inclusive and easy to

understand. Focusing on health determinants, rather than the causes of diseases, allows for comprehensive actions that do not fall within the health system's exclusive control. This approach is advantageous because it avoids fragmenting preventive actions when the same risk factor is involved in multiple diseases. Finally, the model offers a theoretical framework for structuring research on health determinants, which can serve as a guide or logic model in systematic reviews.

2.3. Conclusions

The conceptualisation of health has been changing over time, and different views about health have emerged throughout history, influenced by cultural and social aspects, as well as by the dominant scientific model at each epoch. These concepts generate “social imaginaries” about health, which in turn reflect in norms, beliefs, values and language, to create different interpretations of reality which ultimately influence people's behaviour (see chapter 3).

Early conceptions of health up to the Renaissance exhibited quite wide and integrated perspectives but were built on highly empirical explanations. The co-occurring industrial and scientific revolutions brought both an increase in infectious diseases as well as subsequent scientific understanding of the mechanisms and processes involved as well as ways of managing them (hygiene revolution). This led to a predominant view of understanding health through the biomedical lens. The contribution of the biomedical approach to control of infectious diseases and other health outcomes is undeniable.

During the modern era, wider definitions of health began to emerge, such as the proposal of the World Health Organisation (WHO) in 1948. Subsequently, a number of different approaches have been proposed considering a wide range of so-called “determinants of health”, including biological, psychological, social, cultural and environmental factors. These wider perspectives have converged in recognising that health is a multi-layered concept characterised by interconnections between layers. These layers include all aspects related to the fundamental nature of an individual: physical and biological, mental, social, and spiritual dimensions, in mutual

interdependence with external factors related to the environment and the social context.

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CHAPTER 3

Perceptions about health: emerging visions

Chapter 3. Perceptions about health: emerging visions

3.1. Introduction

The purpose of this chapter is to introduce social- and health imaginaries and discuss why they are crucial to understanding how collective values and beliefs of a given epoch influence how humans understand the world and how they engage in it. The imperative paradigms and dominating social- and health imaginaries of any given time permeate all domains of life, shaping opinions and assumptions about health, nature and other forms of life around us. This chapter aims to identify how scientific paradigms and social- and health imaginaries of the microbial world of the last centuries have framed current collective microbial imaginaries and how recent discoveries are setting the foundations to explore new ways of imagining and conceiving what it means to be human and healthy.

3.2. Health imaginaries

3.2.1. Social imaginaries

According to Castoriadis (1997), "*Each society is a construction, a constitution, a creation of a world, of its own world*" (p. 9). He describes this idea as "*the imaginary institution of society*", highlighting how societies are formed by collective interpretation and organising of the world. In essence, "social imaginaries" can be understood as dynamic systems of meaning-making, deeply ingrained in the socio-historical context, and which serve as foundations for creating collective lifestyles (Castoriadis, 1998). This implies that imagination has a social dimension, in addition to the individual dimension, influencing behaviours and actions.

This perspective assigns a creative role to social imaginaries, challenging the idea that social imaginaries are mainly symbolic "imitations" or "descriptions" of the material world and prevailing economic conditions (Vindel, 2020). Far from being simple reflections, they play a pivotal role in shaping practices and institutions, serving as bridges between tangible realities and symbolic representations of society. Through

this mediation, social imaginaries significantly influence shared beliefs, values, norms, languages, and cultural practices, thus shaping the collective consciousness of a society (Castoriadis, 1998; Moutsios, 2013; Vindel, 2020).

"*For society cannot institute itself without instituting itself as 'something' and this 'something' is necessarily already an imaginary signification*…" (Castoriadis, 1998, p.269)

In addition to Castoriadis, other authors have advanced the concept of social imaginaries, illustrating its heterogeneity. Lacan's (2001) approach to the imaginary is rooted in his broader psychoanalytic framework, where he worked on linking three dimensions: the symbolic, the imaginary, and the real. Through these dimensions, Lacan provides an enhanced understanding of how individuals relate to themselves and others, with the social imaginary being particularly connected to elements like narratives, images, and symbols. Ricoeur (1988) developed the interrelated concepts of ideology and utopia, positing that the social imaginary is constituted by ideological imagination and utopian imagination. Ideological imagination implies the self-image of society, or how society conceives its organisation and practices. Utopian imagination encompasses alternative visions of society, which represent the capacity to transcend current realities. These two sources of imagination (ideological and utopian) creatively and dynamically help compose collective values, practices, and beliefs. Taylor (2003) emphasised that "social imaginaries" are crucial to understanding Western modernities, and especially to account for the differences among diverse expressions of modern societies. Thus, his perspective contributes to the understanding of the contemporary epoch. More recently, the notion of social imaginaries has gained special prominence and is applied to the understanding of many diverse subjects. The ecological imaginary, technological imaginary, architectural imaginary or political imaginary are some examples of such breadth. Krummel et al. (2015) note that debate on social imaginaries has progressed so much that it has become a theoretical field of its own.

In more practical terms, recognizing the creative nature of social imaginaries opens the door to envisioning and bringing about change (Porta, 2019). A critical examination of how societies construct and understand themselves provides insight into their functioning and structure (Krummel et al., 2015). And, by understanding and

challenging existing social imaginaries, space is made for new, alternative imaginaries. Social imaginaries are not static, with dominant imaginaries often being contested by emerging ones (Buckles, 2018). Consequently, research into social imaginaries helps to redefine and rearticulate social and political discourse and action (Krummel et al., 2015).

3.2.2. Health imaginaries

Health imaginaries are one expression of social imaginaries. They evolve over time and are influenced by the social and cultural environment, and the emerging scientific discoveries in each epoch, as discussed in chapter 2. They inspire values, beliefs, and directives related to health, including the terminology used to refer to health and illness, and ultimately influencing people´s behaviour. Health imaginaries refer to how people imagine health and illness, and their underlying causes, including the influence of social, political, and cultural values (Link & Phelan, 1995; Solar & Irwin, 2010). This means that how health is discussed in public realms, portrayed in media, or taught in schools and universities influences people's opinions and understandings about health.

Health imaginaries, as an analytical tool, complements other framings that also focus on the social, cultural, and political. For instance, the "social determinants of health", which highlight how social, economic or ecological factors affect the opportunities to be healthy in a given context (Solar & Irwin, 2010; Wilkinson & Marmot, 2003). Additionally, governmental health institutions, alongside the medical and pharmaceutical industries, affect people's health perceptions and play a crucial role in governing life processes, including birth and reproduction (Foucault, 2020). These dynamics resonate with the concept of social imaginaries, illustrating how collective understandings and practices inform and are informed by societal structures and institutions. Understanding this interplay between cultural, societal, and institutional factors offers a comprehensive view of health's multifaceted nature.

Critically engaging with "health imaginaries" involves understanding the underlying paradigms, value systems, and scientific methodologies (Adams, 2016; Horton, 2018). This understanding unveils how health imaginaries not only reflect, but also shape, our perceptions and experiences of health, illness, and well-being. It enables us to

challenge and shape what is considered healthy or unhealthy, normal or abnormal. Some examples of how health imaginaries can be applied are:

- Health imaginaries help to critically analyse and understand the drivers of individual and collective health behaviours. Ultimately, this understanding can help foster health paradigms that may be more inclusive, equitable, and sustainable.
- Health imaginaries influence the direction of research and the creation of new knowledge. They condition the underlying research questions in an experiment, the design of the experiment itself, data collection and analysis, terminologies used and results obtained.
- Health imaginaries have effects on policy and funding, defining what health aspects are valued and prioritized, and who is responsible for health outcomes. This leads to different levels of emphasis on aspects such as: combating infectious diseases, pharmaceutical treatments, public funding vs. private funding of health infrastructure, public health campaigns, urban planning, or lifestyle interventions.

An important health imaginary is the biomedical one, recognized as one of the leading concepts until the end of the 20th century. Biomedical imaginaries support clinical, biological and physiological definitions of health and disease, and emphasise the use of pharmaceutical solutions, epidemiological and technological research, and medical treatment of the symptoms of a disease (Biehl, 2010; Cash-Gibson et al., 2020). Meanwhile, the complex interactions occurring between biological/genetic factors and broader environmental/social/political/lifestyle contexts in determining human health are underrepresented within this imaginary (Biehl & Petryna, 2013; Borowy & Aillon, 2017; Herrick & Reubi, 2017). Exploring and questioning the impacts of health imaginaries, including those rooted in biomedicine, is important for revealing underlying values, perceptions, and aspirations that shape health experiences, behaviours, and policy interventions. By embracing a culturally sensitive approach, health imaginaries offer holistic understandings in which collective and individual constructions of health and illness play pivotal roles in shaping health outcomes. This multifaceted understanding prompts new awareness linked to lifestyle factors.

The next section discusses an emerging health imaginary known as the "holobiont", which aims to broaden our understanding of what it means to be human by emphasizing the importance of microbial communities within our bodies. Also, it diverges from earlier theories like the germ theory of disease, which posited that pathogens or "germs" were the primary drivers of illness. Overall, and as scientific advancements develop, the cultural, social, and dimensions become increasingly significant in comprehending health comprehensively.

3.3. The holobiont: a new concept of the self and a new health imaginary

From the very beginning of the scientific revolution and partly due to Darwin's evolution theory, humans were perceived as single evolutionary individuals of a species (Ayala, 2007). Many different biological standards were used to define what was an individual like morphological, physiological and genetic definitions (Baedke, 2019). Consequently, individual-level perspectives were followed to study anatomy, physiology and development. As Baedke (2019) states *"These and other conceptual frameworks go along with strong ontological assumptions that affect, for example, which units we (do not) investigate and which questions we (do not) pose, how we understand the role of individuals, especially organisms, in development and evolution, and, more generally, how we understand human beings as individuals*".

Furthermore, the process of denominating what it means to be a human from the point of view of biology was shaped by other fields such as immunology and microbiology. The "immune self" model proposed by Sir McFarlane Burnet (1899-1985) in the 20th century, exemplified the immune system as a defensive system to protect the individual (the self) against an uncertain and dangerous exterior world (the other) (Alfred, 2008). This view conveyed the idea that the immune system excludes and attacks anything that is not the self. The immune system was conceived therefore as a defensive machine to protect the individual against possible threats like pathogens. As a consequence, the discipline of immunology, traditionally defined as "the science of self/non-self-discrimination" (Cohen, 2004), has enormously influenced the perception of "the self".

The “immune self” model was reinforced through contributions of scientists and microbiologists such as Robert Koch (1843-1910) whose findings were essential to support the germ theory of disease (Blevins & Bronze, 2010). It was conceived during what has been called the “Golden Age of Microbiology”, where thanks to the microscope, infectious diseases were understood through the notion of microbes attacking humans and their immune defences. These scientific discoveries led to a shared collective belief in that epoch that all microbes were pathogens causing infectious diseases, being the “otherness” and enemies of the human that should be wiped out, giving rise to the Hygiene movement (see chapters 1 and 2).

More recently, in the late 20th century, the revolution in genomics science has also been decisive in the process of shaping the “biological understanding” of the individual. During this “genomic revolution”, geneticists posited that most of the unresolved questions of the human being would be resolved by going deeper into the genetic material and information stored within its cells (Formosinho et al., 2022). In 1992 geneticist Walter Gilbert claimed that one day *“three billion bases of DNA sequence can be put on a single compact disc and one will be able to pull a CD out of one's pocket and say, ‘Here is a human being; it's me!”* (Weatherall, 2012). This quote by this geneticist exemplifies the hope of the genomic revolution and the promises of the Human Genome Project (HGP) in the attempt to define completely what defines a human being biologically.

However, the very same biology disciplines that led to the germ theory of disease and hygiene revolution are currently challenging the notion of a biological individual, and therefore, what it means to be human. Recent advancements in these fields such as nucleic acid analysis, especially genomic sequencing and high-throughput RNA techniques have led to the study of the microbial diversity of the planet creating a new revolution in microbiome research and microbiomics (the study of the genomes of microbiomes) (Parello, 2020). Discoveries in microbiome research have shown that most of the animals and plants of the planet harbour within them trillions of microorganisms from bacteria to viruses and even fungi. All these microorganisms are found spread in specific sites of plant and animal bodies contributing to many crucial anatomical, physiological and developmental functions. Consequently, these new

discoveries challenge the boundaries that until now had characterized the biological individual (Hoffmann et al., 2016).

According to recent estimations, just 43% of the total number of cells that constitute the human body are human cells (somatic and germ cells). Microbes compose the remaining 57% of cells. Therefore, technically, from a cell quantity perspective, humans could be thought of as being more microbial than human (Robinson et al., 2018). Moreover, apart from the realisation that we are comprised of trillions of microorganisms, our own genome, that is, the DNA stored in our cells, are also in part the product of countless genetic material exchanges with microorganisms throughout evolution. In the case of the human genome, the author David Quammen noted in his book *"The Tangled Tree"* that approximately 8% of the human genome is thought to have been acquired horizontally through viral infections. This exemplifies the notion that there is no such thing as the human genome or a unique specific species genome. Instead, the genomes that constitute the living creatures of the planet are an evolutionary product of infinite exchanges among microorganisms like bacteria and viruses (Arnold et al., 2008). In line with this view is the evidence that the organelles –mitochondria and chloroplast– that are so essential for the eukaryotic cells of plants and animals are also of microbial origin (McCutcheon, 2016). Therefore, even our human cells are the symbiotic product of an evolutionary interaction among microorganisms.

In light of these new discoveries the concept of "holobiont" is being increasingly used. The term "holobiont", comes from "holo", a Greek word meaning "whole", and "biont" meaning "life". It was first introduced by the German theoretical biologist Adolf Meyer-Abich in 1943 (Baedke et al., 2020), and then by Lynn Margulis (1938-2011) in her 1991 book *"Symbiosis as a Source of Evolutionary Innovation".* Initially, when talking about the "holobiont", Lynn Margulis was referring to the eukaryotic cell and its prokaryotic microbial partner –the mitochondria or chloroplast– in her endosymbiosis theory (Lazcano & Pereto, 2017). However, nowadays the "holobiont" concept refers to a broader term to refer to an individual plus billions of microbial organisms working symbiotically to form a functional ecological unit. In that sense, the realisation that humans are not individuals but rather a multispecies ecosystem, a product of complex and dynamic interactions with microorganisms, has consequences beyond the

biological disciplines. It brings up an ontological fracture in what it means to be self, making us rethink what it means to be human.

The “holobiont” is challenging the way that biological disciplines such as evolutionary biology, medicine, microbiology, immunology and genetics have until now defined and classified living individuals such as humans. The classical biological explanations of the human individual through the immune system, the genome and the brain among others are being challenged. Microbes are essential for the correct functioning of the immune system, they influence the brain through the gut-brain axis, and they provide genes that provide essential functions of human physiology (Rees et al., 2018). Therefore, the “holobiont” is becoming a new unit of anatomy, development, physiology, immunology, and evolution.

Regarding the immune system, one of the beliefs of the 20th century was that the newborn was fully prepared immunologically to fight all diseases (Dietert, 2021b). However, thanks to the advances in microbiome research, it has been found that the newborn must be exposed to microbes and must co-develop with the microbiome to be immunologically mature and prepared to fight diseases (Zheng et al., 2020). The evidence that a mature healthy immune system requires the presence and functioning of the microbiome revolutionises the way microorganisms have been perceived since the Golden Age of Microbiology and Koch’s postulates about germ theory.

Paradoxically, the immune system that is essential to fight against some pathogenic microbes is functional and effective thanks to other microbes. Therefore, what constitutes the self is dynamic and context-dependent since the immune system has evolved and is still evolving to recognize which species of microbes promote, permit access, and maintain to become the self, and which organisms exclude and destroy to become the other. This perspective promotes and suggests an *“ecological model of immunity involving a multispecies community that includes the proactive recruitment of, and experimentation with, new microbes”* (Droz et al., 2022).

In addition to the indispensable contribution to the immune system, microbial symbiosis appears to be essential and fundamental for the overall health status of the majority of plants and animals on the planet. In the case of humans, the microbial composition and diversity of the human microbiome are key contributors to health

(Ogunrinola et al., 2020). The human microbiome is crucial for metabolic functions such as food digestion and vitamin production and for protection against pathogens that cause disease (Hou et al., 2022). The property of the human microbiome that gives protection against pathogens is generally referred to as pathogen colonisation resistance and it has been considered one of the principal evolutionary advantages provided by the microbiome to the majority of living creatures (Khan et al., 2021; McLaren & Callahan, 2020).

Therefore, one of the main benefits that the microbiome, especially the gut microbiome, provides to humans is colonisation resistance, the ability to prevent colonisation by microbes. The gut microbiome provides protection against infections both by direct inhibition of pathogens and indirect effects on host functions. Direct effects include nutrient competition as well as producing metabolites that inhibit pathogen growth (Vogt & Finlay, 2017). Indirect effects include promoting maintenance of the gut mucosal environment and homeostasis and stimulating innate and adaptive immunity (Vogt & Finlay, 2017). More than two thousand years ago, there was already a notion of the importance of the gut in health and disease, as Hippocrates said, “All disease begins in the gut” (Harkins et al., 2021). With current scientific discoveries, this notion is seconded as the key role of the gut- and intestinal microbiome in influencing health and disease is becoming more and more apparent.

Disruptions of the microbiome have been linked with many negative effects on health. In light of the emergent evidence, studies suggest that early life factors that influence and shape the human microbiome of the newborn have health consequences later in life. Numerous studies have linked a disruption in the human microbiome with impairment in immune system development and subsequent development of many non-communicable diseases including obesity, diabetes, allergies and cardiovascular diseases among others (Bu et al., 2022; Ooi et al., 2020).

Given the recent advancements in the microbiome research field, we are beginning to realise the importance of microbes defining who we are and the essential role they play in our health, and that humans and their microbiomes rely on each other to maintain a stable state of health. Microbiome research challenges us to think more expansively about health and what it means to be healthy. Advances in this field are challenging many philosophical assumptions about health, and the related concepts

of individuality, function and evolution. Since the microbial community in us is an integral and essential part of our health, we should reframe our conceptions and extend our concept of health to cover the “dynamic multispecies functional unit” that represents the “holobiont”. Addressing the human as a “holobiont” can provide for a richer understanding of human health and support the “war no more” reasoning. It seeks to shift the paradigm and discourse that has been traditionally used in infectious disease science. War and catastrophe metaphors and discourses have been applied systemically in public health discourses with enormous impacts on how modern societies conceive the microbial world and pathogens (Nerlich & James, 2009).

As Inkpen (2019) very accurately pointed out “*Rather than treating human health as a war against invading pathogens, it involves seeing a person as an ecological system, and the maintenance of health as a matter of management, restoration, resilience, and sustainability*”. This has significant epistemological and cultural consequences when studying infectious disease dynamics. Rethinking and reframing the biomedical beliefs and perspectives of the last centuries that have shaped our view of the microbial world around us paves the way to reimagine a more collaborative approach to microbes.

“*We perceive only that part of nature that our technologies permit and, so too, our theories about nature are highly constrained by what our technologies enable us to observe*”— (Gilbert et al., 2012). Scientific advancements of this century, in particular molecular methods for studying microbial diversity over the past decade, are opening a new era where the technology available to us is enabling us to develop new epistemological and ontological views of the world that were not available during the last centuries. We are recognizing in detail that all forms of life are interdependent and interconnected, relying ecologically and evolutionarily upon each other. Microbial diversity and microbial mutualistic symbiotic relationships are essential for life on our planet. Only a minority of microorganisms are responsible for causing infectious diseases, however, these and the remaining billion ones are useful and essential to life on our planet, providing many ecological functions (Rappuoli et al., 2023).

Quoting Heather Paxson (Paxson, 2008) *“I suggest that neglect of the microbe (any organism, in the singular, invisible to the naked human eye) continues to distort our anthropological view of the social world. If philosophical attention to microbes – and more, to how microbes and humans have been companion species* (Haraway, 2003)

– might 'lead to a better understanding of how human health, disease resistance, development and evolution have depended and continue to depend on interactions with microbes' (O'Malley & Dupré, 2007:158)*, then anthropological attention to microbes might lead to better understanding not only of certain human cultural artefacts […] but ultimately of the central object of our study: anthropos, the human 'itself' ".*

Viewing the human as a "holobiont", a dynamic ecosystem that requires stability and resilience, opens a broader approach to human health promotion and disease prevention and leads to a more systemic and realistic perspective towards infectious disease dynamics. An ecological understanding of our microbial communities in health and disease replaces the "one germ-one disease" conception of classical germ theory and reinforces the view that biology is mostly governed by symbiotic relationships and a close cooperation with the unseen world that is within us and around us, making us what we are (Sapp, 2016). As Droz et al. (2022) notes *"the relationship that interweaves us with our microbiome and the environment exemplify the porosity and dynamicity of living through the world […] it helps towards a more fluid way of living in the world. Each of us, as embodied individuals, are a part of microbial multispecies societies […] the complexity of multispecies societies and their interrelations could imply a withdrawal of our interventionist urge to control and manage them. Instead of trying to control and manage other species, we could try to understand them better in order to collaborate with them and to nurture the co-dependent relationship that binds us together".*

As Rodney Dietert (2021a) has pointed out: *"Earth is a microbial planet"*. Multicellular life evolved and is continually reborn into a world of microbes. Microbes are the ties that bind all creatures on the planet. In that sense, we have never been individuals since human and microbial worlds are inseparably entangled. Being human involves more than we thought.

3.4. Conclusion

Social imaginaries and by extension health imaginaries are a well-established body of knowledge for investigating how shared beliefs, values, norms, languages, and cultural practices of a given epoch permeate into society's collective thinking and all the scientific disciplines, influencing its paradigms. Culturally specific ways of knowing and understanding the world translate to scientific inquiry, determining how humans engage with their natural surroundings and with other forms of life. The imperative social and health imaginaries of the last centuries towards the microbial world that led to the development of the germ theory of disease and hygiene revolution forged the collective idea that all microbes were enemies of humankind that should be eradicated. These imaginaries arose from the knowledge available at the time and allowed to save many lives and improve public health. However, this has led to unintended consequences where the so essential microbial diversity around us and within us has been jeopardized.

Nowadays advancements in the same fields that led to the germ theory of disease are bringing an emerging imaginary and paradigm towards the microbial world. The emerging concept of the "holobiont" paves the way for a new ontology and health imaginary, where being healthy means fostering stability, resilience and symbiotic mutualistic relationships with multiple microbial species. We still are rooted in a paradigm and imaginary dominated by an antimicrobial perspective where we see microbes as invisible mysterious enemies not pertaining to us. To change this, we need to acknowledge the creative nature of social and health imaginaries. They are not static, with dominant imaginaries often being contested by new and emerging ones. The "holobiont" as a new emerging one can help foster health paradigms that may be more inclusive, equitable, and sustainable towards the microbial world. Changing the way, we perceive and imagine the world will naturally change the way we intervene in it.

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CHAPTER 4

Coastal zones

Chapter 4. Coastal zones

4.1. What are coastal zones?

The term coastal zones refers to geographical areas where the land and oceans meet and interact. Typical examples of these types of areas include estuaries, bays, ports, rocky shores, beaches, mangrove forests and saltmarshes. However, it is difficult to find a unique definition regarding coastal zones (Davies et al., 2004) since these areas may not have precise boundaries, and can be defined differently depending on their context. Recreational water use, or water- or seafood consumption are frequently recognised as ways of getting impacted by coastal pathogens that are present in coastal zones (Asante et al., 2013; Brooks et al., 2016; Völker & Kistemann, 2011). We refer to coastal pathogens in this chapter as pathogens present in a coastal zone. Their origin can be multiple: for some pathogens, the coastal zones are their natural habitat, in other cases, pathogens are washed in from inland waters and can have their origin in water catchments and can be related to treated and untreated wastewater or agricultural activities.

4.2. Coastal pressures

Coastal zones are being impacted by the rise of climatic events and anthropogenic activities (Khatri & Tyagi, 2015; Zhu et al., 2022). Climate change, pollution, antimicrobial resistance (AMR), land use, and human behaviour are among the main stressors of aquatic environments (Economic & Affairs, 2022; Water Europe, 2023). For example, climate change hazards such as flooding, ocean warming, intense rainfall and environmental warming are increasing the propagation of pathogens such as *Campylobacter* and *Vibrio cholerae* (Brandão et al., 2022; Dupke et al., 2023; Mora et al., 2022), which are promoters of waterborne diseases (WBDs) such as cholera (Ajayi & Smith, 2019; Jones et al., 2020). Increased urbanisation and tourism in coastal zones (Arabadzhyan et al., 2021; Moranta, 2020; P. de Alencar et al., 2020) have led to an increase in the prevalence of pathogens and associated infectious diseases (Landrigan et al., 2020; Mora et al., 2022).

The dynamics of coastal zones heavily determine pathogen presence (Bellou et al., 2021). Pathogens can be transported from wastewater discharge and agricultural runoff of livestock manure into coastal zones. Polluted waters can also lead to eutrophication, which can enhance the growth of harmful algal blooms (HABs) creating conditions favourable for pathogens (Bhambri & Karn, 2020).

Other pollution streams such as chemical spills, copper and lead pipe corrosion (Tansel & Zhang, 2022; Wiener et al., 2006), leaking underground storage tanks (Nambi et al., 2017; Wilson et al., 2013), agricultural runoff (Bijay-Singh & Craswell, 2021), septic tank effluents (Lapointe et al., 2017; Sidhu et al., 2023), and toxic industrial waste can also enter surrounding coastal waters. These water contaminants can alter the biological, chemical, and physical composition of aquatic ecosystems (McCarty, 1995; Schiedek et al., 2007), and as a result can favour pathogen propagation, resistance and virulence (Archer et al., 2023; Baker-Austin et al., 2013, 2016).

4.3. Policies and solutions for protecting and improving water quality

To control and improve water quality different policies and strategies are developed. For example, in the European Union (EU), the Water Framework Directive (WFD) and specific supporting directives (Appendix 4.1), models and monitoring tools have been put in place to safeguard aquatic environments.

The goal of this Directive is the prevention and reduction of pollution by the promotion of sustainable water use, protecting and improving the aquatic environment and mitigating the impacts of climate hazards such as flooding and droughts (Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 Establishing a Framework for Community Action in the Field of Water Policy, 2000).

To do so, the Water Framework Directive is supported by other directives like the Marine Strategy Framework Directive (Directive 2008/56/EC of the European Parliament and of the Council of 17 June 2008 Establishing a Framework for Community Action in the Field of Marine Environmental Policy (Marine Strategy

Framework Directive) (Text with EEA Relevance), 2008) (Appendix 4.1). An overall message that these directives have compiled is that currently, 40% of surface water bodies in Europe have a good ecological status, and that 85% of the recreational waters used for bathing show an excellent water quality (European Union, 2023).

4.3.1. Monitoring: rapid tests and predictive models

Different methods can help to examine and forecast water quality, which can help to warn the public when the recreational use is not recommended. Rapid tests can be used by measuring variables such as pH (EU Copernicus Marine Service Information, 2023a), temperature, DO (dissolved oxygen), turbidity, nutrients (N (nitrogen) and P (phosphorus)). In addition, chlorophyll-α (EU Copernicus Marine Service Information, 2023b) is frequently considered for evaluating levels of acidification in European waters. Additional standards and policies can be developed and implemented by local and national authorities. Various approaches exist for examining water quality. For example, the World Health Organisation (WHO) guideline on recreational water quality (WHO, 2021) provides recommendations for the surveillance of waterbodies. An initial water quality assessment is recommended for physical and chemical variables (temperature, pH, DO, turbidity, nutrients (N and P)), followed by a microbiological assessment to asses levels of *E.coli* or enterococci (WHO, 2021). This assessment should be followed by an ongoing and operational monitoring protocol when possible.

Along with rapid tests, predictive models can facilitate water quality forecasting and alert the public with respect to suitability of water for recreational activities (WHO, 2021).

4.4. Coastal pathogens

Pathogens include bacteria, fungi, protozoa and viruses (Alberts et al., 2002). These pathogen groups are causative agents of different infectious diseases, causing detrimental effects on human health. Infectious diseases can be classified as foodborne (FBDs), waterborne (WBDs), or vector-borne diseases (VBDs) depending on their transmission pathway (Anas et al., 2021; Kendrovski & Gjorgjev, 2012; Semenza & Paz, 2021). Whereas FBDs are transmitted mainly through food, WBDs

are transmitted through water (e.g. drinking, recreational waters), and VBD by vector organisms such as mosquitos (Rottier & Ince, 2003; WHO Regional Office for Europe, 2020). Typically, interconnections among transmission pathways can occur. For example, polluted water and standing water are ideal conditions for vector-borne organisms like mosquitoes, which can transmit infectious diseases such as malaria (Fenwick, 2006) (see chapter 5).

Bacteria organisms like *Campylobacter* and *Vibrio cholerae* are promoters of WBD and lead to gastroenteritis and cholera respectively (Ajayi & Smith, 2019; Jones et al., 2020; Kuhn et al., 2020). The survival and proliferation of these and other pathogenic bacteria may be frequently triggered by aquatic conditions as well as upstream sources such as manure (US EPA, 2017). Manure is recognised as a key reservoir, where moisture content, pH and temperature can promote the activity of pathogenic bacteria (Manyi-Loh et al., 2016). Like humans, marine organisms are also prone to WBD. For example, *Streptococcus iniae* and *Mycobacterium* spp. cause Streptococcosis (Meningoencephalitis) and Mycobacteriosis (fish tuberculosis) in fish (Ziarati et al., 2022). Subsequently, fish health, the food web, and therefore indirectly humans are also affected through this pathway.

Along with bacteria, some fungal species are causative agents of WBD (Mora et al., 2022). A recent analysis highlighted the fungi as a currently understudied biological group (Brandão et al., 2021) as well as a group not included within the EU Bathing Water Directive (Directive 2006/7/EC of the European Parliament and of the Council of 15 February 2006 Concerning the Management of Bathing Water Quality and Repealing Directive 76/160/EEC, 2014). Several studies have remarked the importance of infectious fungal genera present on sandy beaches and in polluted waters (Brandão et al., 2021; Moazeni et al., 2023). Among them, the fungal species such as *Candida albicans* (C.-P. Robin) Berkhout and *Candida tropicalis* (Castellani) Berkhout are mentioned. Both of them can be found as part of a healthy human microbiome, but if an invasive infection (invasive candidiasis) occurs, the nervous and cardiovascular system, as well as bones, eyes, and other organs can be damaged (Division et al., 2022). Therefore, these two species have been recently included in the WHO fungal priority pathogens list (Division et al., 2022) where *C. albicans* is

classified within the critical priority group, and *C. tropicalis* within the high priority group (Division et al., 2022).

Among other pathogens, approximately a total of 80 protozoan pathogens are currently recognised (Aronson & Magill, 2020). For example, *Cryptosporidium* and *Giardia* are two protozoan genera recognised as parasites able to impact human health (Alegbeleye & Sant'Ana, 2020; Asokan et al., 2019; World Health Organization. Regional Office for Europe & Europe, 2019). Both parasites are commonly spread in drinking and recreational waters contaminated with faecal sources from animals (CDC, 2019, 2021).

Viruses are recognised for their significant role in WBD (Upfold et al., 2021). Although these microorganisms are causative agents of WBD, they are not frequently used as indicators for monitoring the water quality. More than 150 viruses are classified as enteric viruses. Enteric viruses are viruses mainly transmitted by the faecal-oral route, as well as through contact from person to person or through contaminated water or food (Castro-Mayorga et al., 2016). They are responsible for several human diseases (Upfold et al., 2021). Especially the enteric viruses Adenovirus (AdV), Astroviruses (AstVs), Enteroviruses (EVs), Hepatitis A Virus (HAV), Noroviruses (NoVs), and Rotaviruses (RV) (Gibson, 2014; Sinclair et al., 2009) are recognised for being responsible for different WBD.

Waterborne diseases are driven by the resistance, virulence, abundance and dispersion of all these types of pathogens, which are impacted by climate change and pollution among others. Climate change (see chapter 5) is one of the main risk factors affecting inland and coastal waters, and subsequently, coastal pathogens and public health (Watts et al., 2015, 2021). Climate hazards such as droughts, environmental heatwaves, ocean warming, sea level rise, and storms can increase for example pathogen abundance and virulence, and consequently, human diseases (Dryzek et al., 2011; Holechek et al., 2022). Besides climate change, pollution (see chapter 6) has a significant impact in coastal waters, as its causes detrimental effects on public health. Pollution is a global threat driven by contaminants such as heavy metals, manufactured chemicals (e.g. persistent organic pollutants, plastics, pharmaceuticals and personal care products), and nutrients like nitrogen and phosphorus compounds (Khoaele et al., 2023; Landrigan et al., 2020; Teymourian et al., 2021). All these

contaminants have been suggested to enhance the resistance (see chapter 7) and virulence mechanisms of different coastal pathogens. To illustrate how these different pressures interact it is helpful to study a single species. Therefore chapter 8 explores the convergence of the above stressors for *Vibrio*, and proposes a Driving Force–Pressure–State–Exposure–Effect–Action model (DPSEEA) to capture the complexity of the interactions. Chapter 9 then widens the perspective further to explore how different intersecting social factors affect the host health status and how they modulate disease caused by coastal pathogens.

4.5. Conclusion

This introductory chapter provides a short overview of the elements that need to be considered, i.e. what are coastal zones, what are coastal pathogens? The chapter highlights that pathogens may have different origins such as inland or marine waters. However, their final destiny could be the coastal zone where they interact with the coastal biome and can become initiators of foodborne, waterborne or vector-borne disease. The chapter also highlights the need for policies to safeguard human health and environmental water quality and to monitor the potential presence of pathogens.

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Appendix 1. Water protection and management Directives

Table. App. 4.1. Water protection and management: aims of the Water Framework Directive and specific supporting water directives.

Directive	Aim
Blueprint to Safeguard Europe's Water Resources Communication	To ensure the availability of a sufficient level of quality water for all legitimate uses by better implementing current EU water policy, integrating water policy objectives into other policy areas and filling gaps in the current framework.
EU Water Framework Directive (Directive 2000/60/EC)	To prevent and reduce pollution, promote sustainable water use, protect and improve the aquatic environment and mitigate the effects of floods and droughts.
Drinking Water Directive (Directive (EU) 2020/2184)	To standard and improved access to safe drinking water along the lines of the latest recommendations of the World Health Organization. It furthermore increases transparency for consumers on the quality and supply of drinking water, thereby helping to reduce the number of plastic bottles through increased confidence in tap water.
Bathing Water Directive (Directive 2006/7/EC)	To enhance public health and environmental protection by laying down provisions for the monitoring and classification (in four categories) of bathing water and informing the public about it.
Environmental Quality Standards Directive (Directive 2008/105/EC)	To lays down environmental quality standards (EQS) for priority substances and certain other pollutants as provided for in Article 16 of Directive 2000/60/EC, with the aim of achieving good surface water chemical status and in accordance with the provisions and objectives of Article 4 of that Directive.
Urban Waste Water Treatment Directive	To protect the environment from the adverse effects of urban waste water discharges and discharges from industry. The directive sets minimum standards and timetables

(91/271/EEC)	for the collection, treatment and discharge of urban waste water, introduces controls on the disposal of sewage sludge, and requires the dumping of sewage sludge at sea to be phased out.
Nitrates Directive (91/676/EEC)	To protect water quality across Europe by preventing nitrates from agricultural sources that pollute ground and surface waters and by promoting the use of good farming practices.
Floods Directive (2007/60/EC)	To reduce and manage the risks posed by floods to human health, the environment, infrastructure and property.
Marine Strategy Framework Directive (Directive 2008/56/EC)	To enhancing the sustainable development of its maritime economy while better protecting its marine environment. The objective of the MSFD was to reach 'good environmental status' (GES) of the EU's marine waters by 2020, to continue its protection and preservation, and to prevent subsequent deterioration.
Integrated Coastal Zone Management (2002/413/EC)	To define the principles of sound coastal planning and management to be taken into account by Member States.

CHAPTER 5

Climate change

Chapter 5. Climate change

5.1. Introduction

The detrimental impact of climate change on health is becoming an issue of highest concern (Landrigan et al., 2020; Mora et al., 2022). Climate change is currently recognised as a major driver impacting inland-, coastal-, and marine waters, and subsequently, public health (Danylchuk et al., 2023; Hoberg & Brooks, 2015; Lawrence et al., 2019; Watts et al., 2015, 2021). Thus, a wide range of activities are being conducted by international commissions, research institutions and governmental organisations (Dryzek et al., 2011; Holechek et al., 2022).

These activities include the development of adaptation strategies for a multitude of climate hazards. For example, the European Environment Agency (EEA) recently published a report assessing 16 climate hazards, which were classified according to six different hazard categories (coastal, heat and cold, snow, open ocean, wet and dry, and wind) (EEA, 2021). Similar classifications were shown in Mora´s study, which focused on ten climate hazards linked to human pathogenic diseases, and conducted an in-depth review of transmission pathways and the role of human vulnerability (Mora et al., 2022). The Centre for Research on the Epidemiology of Disasters (CRED) published the Climate Action report taking into account nine weather-related types of disasters (drought, earthquake, extreme temperature, flood, landslide, mass movement, storm, volcanic activity, and wildfire), some of which are strongly related to climate change (CRED, 2022).

Many climate hazards are interconnected, and can occur simultaneously (e.g. droughts and heatwaves) or in sequence (droughts followed by flash-flooding). In this way, hazards are able to have an amplifying effect and produce harmful cascading effects in inland, coastline, and marine waters (Cheng et al., 2022). One of these effects is the increase of pathogen abundance leading to a rise of infectious diseases in urban and rural communities situated along these waters (CRED, 2022; EEA, 2021; IPCC, 2023; Mora et al., 2022; Pörtner et al., 2022; Watts et al., 2021). More generally it has been estimated that 58% of all infectious diseases globally recorded (corresponding to 218 out of 375) are climate sensitive (Mora et al., 2022). This

confirms climate change as a key driver in increasing infectious disease risk (Hoberg & Brooks, 2015; Semenza et al., 2012).

To illustrate the impact of climate change, we analyse in this chapter water-borne diseases (WBDs) and food-borne (FBDs) diseases related to coastal pathogens, as well as vector-borne diseases (VBDs) related to coastal zones. Examples of food- and water-borne coastal pathogens include *Escherichia coli*, *Legionella pneumophila*, *Salmonella* serovar Typhi, *Vibrio cholerae*, and *Vibrio vulnificus*. Our review also comprises VBD because we want to highlight the potential interconnections between different hazards, reservoirs, pathogens and infectious diseases in coastal zones. For instance, the presence of standing and polluted water, or water tanks that store water during droughts may be ideal habitats for vector-borne organisms such as *Aedes aegypti*, *Anopheles* spp. and *Plasmodium* spp.; increasing the risk and exposure to VBD such as dengue and malaria respectively (Nissan et al., 2021; Poveda et al., 2001; Trewin et al., 2013).

The aim of this chapter is to categorise the range of possible pathways by which climatic hazards may influence exposure and/or susceptibility to infectious diseases related to coastal pathogens. This analysis aligns with the climate risk framework outlined in the Fifth Assessment Report of the Intergovernmental Panel on Climate Change (IPCC) AR5 (Estoque 2023, IPCC, 2014), which defines risk as the outcome of the interplay between hazards, exposure, and vulnerability. However, as our focus is on infectious diseases, vulnerability is analysed in terms of susceptibility, defined as the predisposition and sensitivity of developing a disease after exposure to a pathogen (see chapter 10), which in turn is affected also by a series of variables involved in the coping capacity, such as the socio-economic status or the accessibility to public services and infrastructures.

The objective of this chapter is not to be exhaustive but rather to discuss the climate hazards influencing the risk of infection in an illustrative way.

For this purpose, a scoping literature review has been conducted to address the connections between climate change hazards, coastal pathogens and human health. The following climate hazards are reviewed: droughts, wildfires, environmental heatwaves, marine heatwaves, sea level rise, heavy precipitation and flooding, and

storms. Their potential impacts on coastal pathogens and in turn on human health are examined. To do this, two research questions are addressed: (i) How does climate change alter the ecology of coastal pathogens, thus increasing the risk of exposure to humans (section 4.2)? (ii) How might these impacts be amplified by connections between hazards, or by cascading and indirect impacts (section 4.3)? The next sections illustrate for each hazard one specific example of possible interactions.

5.2. Climate hazards and coastal pathogens

5.2.1. Droughts

The severity of droughts is increasing (Dai, 2011; Smirnov et al., 2023), and is further amplified by the current El Niño episode.

With respect to pathogens, malaria outbreaks have been reported after drought events in countries such as Colombia (Poveda et al., 2001) and Sri Lanka (Bouma & van der Kaay, 1996). The main causes of these outbreaks are related to the presence of small pools, as the river water levels and flows are reduced during drought events, promoting the breeding of mosquito populations (Gabaldon, 1949; Nissan et al., 2021). In addition, the decrease of larvae predators during a drought allows vector organisms to proliferate (Kovats et al., 2003), further promoting the spread of VBD.

In Australia, the abundance of mosquitos has been observed to increase during major drought events (Fouque & Reeder, 2019; Trewin et al., 2013). Specifically, the installation of water tanks to preserve water during droughts has caused increased mosquito density (Trewin et al., 2013). As for *Aedes notoscriptus*, the increase of water tanks could promote the dispersion and abundance of other species like *Aedes aegypti*, a mosquito vector of dengue fever (Jansen & Beebe, 2010; Ritchie, 2014).

In addition, water scarcity can imply low flow in rivers, and therefore, low dilution of treated and untreated discharges from urban and agricultural areas, and thus higher pathogen concentrations in general (Gabaldon, 1949; Gude, 2017; Hristov et al., 2021; Nissan et al., 2021).

5.2.2. Wildfires

European Wildfires burnt approximately 260,000 hectares of forest on average per year during the last 15 years (*Europe's Summer Wildfire Emissions Highest in 15 Years | Copernicus*, 2023). As a result, approximately 6.4 megatons of carbon (C) were estimated to have been emitted in the European Union) EU and (United Kingdom) UK during the summer of 2022 (June 1 – August 31) (*ECMWF | CAMS Global Fire Assimilation System*, 2023). The smoke from wildfires has detrimental effects on aerial, terrestrial and aquatic ecosystems due to the polluted particulates emitted and deposited in these ecosystems (Goh et al., 1999). In addition, smoke aerosols emitted from wildfires can carry microbes, in addition to ash and chemicals and can be dispersed across long distances (Kobziar & Thompson, 2020), facilitating the spread of pathogens (e.g. bacteria and fungi) and increasing the risk of infectious diseases for humans, animals and plants (Kobziar et al., 2018, 2022).

A pathway of increasing risk for humans to get into contact with pathogens is through smoke (Kobziar & Thompson, 2020). This has been shown recently by Kobziar´s team, who found a higher composition of bacteria and fungi in wildfire smoke than in ambient air (Kobziar et al., 2022). Among microbial organisms, there were bacterial phylotypes closely related to pathogens like *Acinetobacter ursingii, Escherichia-Shigella coli, Haemophilus haemolyticusinfluenzae*, *Staphylococcus, Streptococcus* spp. Some of pathogens are recognised as causative agents of WBD diseases such as diarrheal (e.g. *Escherichia-Shigella coli*) and gastroenteritis (e.g. *Staphylococcus* spp.) disease. They found 959 phylotypes of bacteria and 101 classifiable fungal genera in wildfire smoke; while only 150 bacterium phylotypes and 92 classifiable fungal genera were present in ambient air (Kobziar et al., 2022). They also found that the ratio of viable microbial cells to total microbial cells was higher in smoke than in ambient air (Kobziar et al., 2022).

As with particulate matter in general, pathogens that are present in wildfire smoke could potentially also travel long distances through wind transport, and get deposited in aquatic ecosystems (Minshall et al., 1989; Smith et al., 2011). The consequences of this deposition, in turn, could imply a higher risk and exposure for humans to infectious diseases.

The microbial community in an aquatic ecosystem could also be altered as the wildfire affects the biological, physical and chemical properties of aquatic systems (Raoelison et al., 2023). For example, the runoff of ash- and carbon particles originating from wildfires can enter inland waters such as streams or rivers, leading to eutrophication and the reduction of water quality (Mishra et al., 2021) and affecting pathogen dynamics. Specifically, researchers have shown that post-fire impacts include the increase of nutrients and metals in inland waters, as well as an increase in turbidity and the promotion of algal growth (Mishra et al., 2021). Consequently, harmful algal blooms (HABs) may occur and pathogen abundance may increase.

This highlights the importance of including potential direct and indirect ways in which wildfires can impact the pathogen dynamics in coastal zones. The novel discipline of "*pyroaerobiology*" may help us to better understand how coastal microbial communities are affected by wildfires (Kobziar et al., 2018). This new field of research connects knowledge coming from microbiology, atmospheric science and ecology of fire.

5.2.3. Environmental heatwaves and warming

Global warming leads to an increase in both mean temperatures as well as temperature variability (Olonscheck et al., 2021; van der Wiel & Bintanja, 2021). To cope with heatwaves and environmental warming, humans are changing their behaviour when using recreational waters.

Heatwaves lead to an increase in the number of users in recreational waters such as oceans, lakes and rivers (Baker-Austin et al., 2013; Ghanchi et al., 2017), as new users are attracted to water-related activities during hot weather (Basagaña et al., 2011; Ellis et al., 1975; Huynen et al., 2001). In addition, the already existing habitual users may increase the number of visits as well as the time they spend in the water (Baker-Austin et al., 2013; Ghanchi et al., 2017; Waits et al., 2018). Consequently, even if the concentration of pathogens remained unchanged, human exposure could increase considerably (number of users; number of visits per user; time spent in water per visit). Thus; cases of human infections within WBD like cholera, gastroenteritis and vibriosis may rise (Baker-Austin et al., 2013; Brehm et al., 2021; Waits et al., 2018).

Besides WBD, the risk and exposure to VBD also increase in coastal areas, as the behaviour and habitat of pathogenic vector organisms are being altered by heatwaves and warming. Vector-borne pathogenic organisms are expanding their geographical range to areas where the temperature was cooler in the past (Biswas, 2022). This is the case for mosquitos and ticks (Fouque & Reeder, 2019; Wallace et al., 2019). Among mosquitoes, the species *Aedes aegypti* is recognised globally as a key mosquito-borne pathogen, being a causative agent of diseases such as dengue, chikungunya, yellow fever, and Zika fever (Piovezan-Borges et al., 2022; Ryan et al., 2019). As a result of heatwaves and warming, the rise of temperature has been identified as a main factor for speeding up the time of larva development (Carrington et al., 2013) and adult emergence (Piovezan-Borges et al., 2020), as well as for reducing the timing of extrinsic incubation (Winokur et al., 2020). Consequently, the abundance of this vector-borne pathogen may start to increase, and the re-emergence of related diseases could also appear. Similarly, other diseases like Lyme disease, which is caused by *Borrelia burgdorferi*, a bacterium hosted by a tick vector (Ebi et al., 2017) is spreading into new ecosystems including coastal areas (e.g. German Baltic coast), which they use as a reservoir (Franke et al., 2011).

This shows the relevance of understanding the ecology of causative agents of infectious diseases and their potential new habitats at the interfaces of aquatic and terrestrial ecosystems.

5.2.4. Marine heatwaves and ocean warming

Sea surface temperatures (SST) reached a completely atypical record in Northern European waters during the strong heatwave of summer 2014, with average ocean temperatures being the highest since 1850 (Vezzulli et al., 2020). Consequently, *Vibrio* infections increased in Finland, Sweden, and reached areas that are at only 160 km distance from the Arctic Circle (Brehm et al., 2021; Montánchez et al., 2019). In August 2023, the global average ocean temperature hit a new record, the warmest in 174 years (NOAA, 2023). The continued increase in marine heatwaves (MHWs) and ocean warming is expected to further alter the dynamics of coastal pathogens and their capacity to live in different habitats (Anas et al., 2021; Brehm et al., 2021). Therefore, the potential risk of diseases such as cholera and vibriosis is rising globally (Archer et al., 2023; Sampaio et al., 2022; Trinanes & Martinez-Urtaza, 2021). Ingesting sea

water during water-related activities or eating seafood (e.g. fish, mussels, oysters) contaminated with coastal pathogens such as *Vibrio* are two of the possible transmission pathways (Lhafi & Kühne, 2007; Ma et al., 2023; Ndraha et al., 2022). These risks and exposures are intensified as the ocean temperatures increase further. The main reason for this is that the metabolism and growth rate of *Vibrio* species such as *Vibrio cholerae* can increase with temperature (Green et al., 2019; Huq et al., 1984).

Subsequently, the risk for humans to be impacted by an infectious disease such as cholera is exacerbated (Green et al., 2019; Huq et al., 1984; Vezzulli et al., 2012). Different studies have demonstrated this effect. However, beyond the direct effect of increased warming on the pathogen, one needs to consider how the surrounding aquatic ecosystem itself is impacted and how this influences the habitat conditions of the pathogens (Vezzulli et al., 2015). The relationship of *Vibrio* organisms with different biotic elements such as plankton and with abiotic elements is well known (Vezzulli et al., 2012). For example, plankton organisms are known for being a nutrient-rich reservoir relevant for the growth of *V. cholerae* (Turner et al., 2009). In addition, the levels of dissolved oxygen (DO) and pH in marine waters could decrease and the ocean would become more acidic (Gobler & Baumann, 2016), potentially promoting the growth of HABs (Griffith & Gobler, 2020), and thus impacting the growth and survival conditions of other species including pathogens.

Therefore, it is important to not only understand the direct effect of ocean warming on pathogens, but also how the ocean warming affects the ecosystem in which the pathogen is niched and how the altered ecosystem in turn affects the spread, abundance and virulence of pathogens.

For the case of *Vibrio*, studies have reported that warm temperatures can potentially enhance the antimicrobial resistance (AMR) and virulence of this pathogen (see chapters 7 and 8). Temperature has been indicated as a crucial factor altering antimicrobial resistance, as high temperatures can increase the resistance and mutation rates in pathogenic organisms like bacteria (Elderd & Reilly, 2014; Rodríguez-Verdugo et al., 2020).

5.2.5. Sea level rise

Out of the approximately one billion people living within 10 meters above current high tide lines, it is estimated that 770 million people live within five meters of this tide line (Kulp & Strauss, 2019). Among SLR impacts, storms, high tides, submersion of land, and saltwater intrusion can potentially occur (Magnan et al., 2022; Stewart, 2023). Saltwater intrusion is known to have detrimental effects on aquatic ecosystems (Ferguson & Gleeson, 2012; Werner & Simmons, 2009). Specifically, the dynamics and ecology of coastal pathogens such as *Vibrio* spp. can be altered (Lipp et al., 2002; Rose et al., 2000). As a result, coastal pathogens are likely to proliferate increasing the transmission of infectious diseases (Sampaio et al., 2022; Trinanes & Martinez-Urtaza, 2021).

The incremental increase of shallow waters (due to SLR) together with temperature rise have been indicated as ideal conditions for *Vibrio* spp. (Dvorak et al., 2018; Froelich & Daines, 2020). It is known that mixed salinity waters and temperature increase are two factors that could promote the dispersion of *V. vulnificus* (Bullington et al., 2022). Some studies have remarked that its resistance to higher levels of salinity and abundance may increase as temperatures rise. Nevertheless, there are still certain discrepancies regarding the relation between *V. vulnificus* and salinity (Froelich & Daines, 2020; Randa et al., 2004) as the physicochemical interactions with the population dynamics of *V. vulnificus* are complex (Randa et al., 2004). For example, Froelich et al. (2015) highlighted the need to be cautious when examining the combined impact of salinity and temperature on *V. vulnificus*. It has been indicated that the optimal levels of salinity for pathogen *V. vulnificus* are similar to the levels of salinity that oysters can tolerate (Froelich et al., 2015). Therefore, the risk of oysters being infected by the pathogen *V. vulnificus* is potentially high and as a result, there is a higher probability of seafood infections (Oh et al., 2009).

In addition, SLR and salinity intrusion may promote the rise of mosquitoes and associated VBD. For example, the potential tolerance of certain mosquito larvae species such as *Aedes aegypti* and *Aedes albopictus* to saline habitats like brackish waters has been shown (Ramasamy & Surendran, 2012). Other vector organisms such as *Anopheles sundaicus* and *Culex sitiens* are also suggested to be able to tolerate brackish waters (Rahaman et al., 2020). The former is defined as a parasite

of malaria diseases, and the latter is recognised as a vector organism of Japanese encephalitis and Ross River viruses (Rahaman et al., 2020). As SLR increases, saltwater intrusion may rise, increasing the risk and exposure to these infectious diseases.

Sea level rise is mostly associated with physical impacts on coastlines (flooding, erosion, sand beach dynamics) and its potential impacts on water quality and ecosystems are generally less examined. Therefore, getting a better understanding of the potential impact that SLR may have on water quality and ecosystems could improve the insights on expected coastal pathogens dynamics.

5.2.6. Storms

Storm events are considered one of the hazards linked to a major number of WBDs (Cann et al., 2013). Rainfall runoff can mobilise and transport pathogens that impact human health (Semenza, 2020). A recent study has highlighted three WBDs that were linked to tropical storms in the US: Cryptosporidiosis, Legionnaires' disease, and *Escherichia coli* infection (Lynch & Shaman, 2023). In the above-mentioned study, cases of *E. coli* and Legionnaire diseases rose steadily following the storm. The number of *E. coli* infections reached the highest point in the week following the storm; while Legionnaire infection cases peaked in the third week following the storm (Lynch & Shaman, 2023).

Legionella is indicated as a pathogenic organism able to replicate in aquatic ecosystems; it is especially well known for its presence within biofilms in water pipes. Abundance and dispersion of *Legionella* can usually increase over time in comparison to pathogens that peak at the start of the infection and dissipate over time (Aurass et al., 2023; Nishida et al., 2019; Winfield & Groisman, 2003). Therefore, as storms are occurring more frequently (Brigmon et al., 2020; Lynch & Shaman, 2022), there is a major concern about the number of individuals impacted by diseases such as Legionnaires.

Legionnaire disease is caused by the bacterium *Legionella pneumophila*, which is a pathogen living in artificial and natural aquatic environments (Fliermans, 1983) and can spread under polluted conditions (Lynch & Shaman, 2022). The abundance of this

pathogen has been shown to increase under stormy conditions (Brigmon et al., 2020). For instance, a recent study has reported that monthly Legionnaires' disease hospitalizations increased 32% in hospitals that experienced a cyclonic storm compared to those that did not (Lynch & Shaman, 2022). A major reason may be the damage of water treatment infrastructures and flooding events happening during storms. These impacts are drivers for creating aquatic niches in stagnant waters (Lynch & Shaman, 2023; Stout et al., 1985).

In addition, terrestrial ecosystems are frequently damaged during storm events, as beaches and dunes suffer erosion perturbations (Gambill, 2017). Consequently, physical and biological processes are altered (Zwart et al., 2017). The related increase in nutrient load (e.g. N and P) can modify ocean conditions, for example leading to a decrease in DO and pH; an increase in turbidity and salinity, and the promotion of HAB growth (Bhateria & Jain, 2016; Klimaszyk & Rzymski, 2013). Consequently, users could be exposed to recreational waters where the diversity and abundance of different coastal pathogens have increased.

5.2.7. Heavy precipitation and flooding

Followed by heatwaves (16,500 deaths), flooding was reported to be the climate hazard with the second highest number of deaths (8,000) in 2022 (*EM-DAT | The International Disasters Database*, 2022). During 2022, a total of 387 disaster events occurred globally, with 176 events being classified as flooding events (*EM-DAT | The International Disasters Database*, 2022). Direct loss of life is a major impact of flooding. However, it is important to acknowledge that potential indirect health impacts following flood events can be also substantial. Increased exposure to polluted waters and coastal pathogens may increase the spread of VBD and WBD (*Flood Diseases*, 2023) with negative impacts on human health (Deaven et al., 2021; Lin et al., 2022).

One source of coastal pathogens is the overflow of sewer systems, which become activated when the capacity of urban wastewater systems is surpassed during heavy precipitation (Liu et al., 2018). Human wastes (e.g. human excreta) and stormwater runoffs (e.g. manure and wastes from domestic herd animals) are diverted to rivers and estuaries; facilitating the spread of pathogens such as *Salmonella* serovar Typhi (Han & He, 2021; Levantesi et al., 2012) in coastal recreational waters (Massinai et

al., 2019). *Salmonella* serovar Typhi (Mogasale et al., 2014) is indicated as being frequently present after heavy precipitation and flooding (Asadi et al., 2023). As this species relies on water for transmission (Kingsley et al., 2018), it has more reservoirs available following flooding. Importantly, *Salmonella* serovar Typhi can also be transmitted between hosts, therefore once a host is infected it can spread rapidly (Wang et al., 2020).

Heavy rainfall can lead to wash-out of catchments and impact water quality including nutrient loads (Paerl et al., 2016), turbidity, DO, and pH (Lindholm et al., 2007). As a result, phytoplankton biomass, cyanobacteria abundance and HABs can increase (Jaegge et al., 2022); being determinants of infectious diseases such as cholera, malaria and typhoid (Lindquist, 2022; WHO Regional Office for Europe, 2023). Furthermore, the washing out of manure from agricultural land and wastewater from combined sewer overflows can increase the loads of bacteria (*Campylobacter* sp., *E. coli*, *Shigella*), parasites (*Cryptosporidium*) and viruses (Hepatitis A, norovirus, rotavirus), thus increasing the risk of gastrointestinal diseases and outbreaks (ECDC, 2021).

5.3. Amplifying impacts

This chapter also intends to highlight the need to not only examine the potential impacts of each type of hazard separately, but to consider how impacts may be significantly amplified when several hazards occur simultaneously or when they appear in sequence. For example, hazards such as heavy precipitations and flooding may occur simultaneously with storms, limiting the use of public services and infrastructures, and in extreme conditions, activating an evacuation protocol. As a result, disruption of water systems, overcrowding of shelters, and poor sanitation can occur, making it easy for pathogens and associated infectious diseases to proliferate. In addition, one specific hazard can also create favourable conditions for the occurrence of a second hazard, intensifying the impacts of these hazards in sequence. For example, a drought increases the likelihood of wildfire events. Consequently, there are cascading risks that increase pathogen exposure and susceptibility.

In addition, unfavourable climate conditions especially weaken the health of vulnerable individuals and communities (Kjellstrom et al., 2010; WHO, 2023). In this way, climate hazards strongly interact with drivers of health inequity such as social and wealth inequities (Gutierrez & Bertozzi, 2020).

For example, exposure to heatwaves can potentially exacerbate non-communicable diseases (NCD) in people in poor health and with pre-existent chronic conditions, and impact them severely (Gutierrez & Bertozzi, 2020; Q. Liu et al., 2020; Remais et al., 2013). For example, an increased risk of asthma and rhinitis has been observed during heat waves in people suffering from chronic respiratory diseases (D'Amato et al., 2007; Q. Liu et al., 2020). Other impacts could include increased heart rate and accelerated blood circulation (Fritz, 2022), which can result in severe health outcomes, especially in people with cardiovascular diseases. Heat exposure can also lead to dehydration and an increment in kidney diseases (Kjellstrom et al., 2010). Prolonged exposure to unusually high temperatures and humidity, especially at night, for these vulnerable groups, might have additional effects on their immune system, thus increasing their susceptibility to infectious diseases. In general, the impact of meteorological conditions on the immune system is acknowledged in the literature (Q. Liu et al., 2020; Mora et al., 2022). Exposure to unusually high night time temperature disrupts sleep patterns, not allowing the body to recover during sleep, increasing general fatigue and ultimately affecting mental health (Bryant et al., 2004). Both effects weaken the immune system and consequently increase the susceptibility to infectious diseases (Asif et al., 2017), which can result in especially severe outcomes in vulnerable groups. In addition to people suffering from NCDs, these include children, old people, pregnant women, manual workers and people who participate in strenuous outdoor activities in hot weather.

Another example of amplifying impacts occurs in disaster situations (e.g. wildfires, storms, flooding events). In these cases, evacuation protocols can be activated, and human displacement and mental health disruption may occur (Hayes et al., 2018). These impacts increase the vulnerability of people at risk, and potentially facilitate the transmission of respiratory infections, and infectious diseases due to overcrowded shelters (Lindquist, 2022). For example, people with a mental condition like autism spectrum disorder (ASD) could experience an exacerbation of the mental disorders

during an evacuation protocol or epidemic, due to communication-, social- and orientation challenges in overcrowded shelters. People with ASD can be uncomfortable in the presence of crowds and the general environment of shelters (Mendis et al., 2023). Furthermore, the levels of stress and anxiety could rise in them and the people who support them, and therefore, they could develop post-traumatic stress disorder (PTSD) (Mace et al., 2018; Mendis et al., 2023). The development of PTSD after a disaster event frequently deteriorates mental and physical health, and thus, may also affect the immune system (Abdurachman & Herawati, 2018; Müller, 2014). Consequently, the susceptibility and exposure to FBD, VBD or WBD may rise. Similarly, people with disabilities can be left behind during an evacuation event (UN, Department of Economic and Social Affairs & Disability, 2024), for example, people with a visual or hearing impairment (Hansson et al., 2020), being disadvantaged under a climate event like flooding (Mace et al., 2018).

Climate change hazards can also cause major disruption to public services (Lawrence et al., 2019) and disrupt essential health services such as medical centres, hospitals and pharmacies (Chang, 2016; Finlay et al., 2012; Seong et al., 2023; Yazdani et al., 2022). Communities “at risk of poverty and social exclusion” (AROPE) are frequently the most impacted, as their financial capacity is limited, and their health and social support systems are easily disrupted (Hajat et al., 2005). They have limited access to primary resources such as water, sanitation and hygienic conditions (Semenza & Paz, 2021). Consequently, their risk and predisposition to infectious diseases such as cholera or salmonellosis are potentially aggravated under severe climate events such as flooding. In addition, civilians can lose their belongings or suffer damage to their properties, increasing their mental stress, and impacting their immune system competence (Ishikawa & Furuyashiki, 2022; Padgett & Glaser, 2003; Thomas et al., 2012), raising their susceptibility to contract an infectious disease.

5.4. Summary of pathways of interactions

Climate hazards and their direct and indirect impacts on coastal pathogens are reviewed in this chapter, indicating also how that, in turn, impacts human health via waterborne, foodborne, and vector-borne disease. Some of the cascading impacts are highlighted, especially those related to pathogens and coastal zones. This review also

reveals the potential synergistic impacts of two or more climate hazards. Climate change can also impact and exacerbate NCDs, thus contributing to a greater burden of disease.

The analysis shows many different pathways of interaction by which climate change can affect exposure and susceptibility to infectious diseases (Fig. 5.1):

- The ecology of pathogens found in coastal zones can be altered under climate hazards; specifically, their abundance and dispersion, virulence, and resistance profile can be impacted by climate hazard events. Consequently, the exposure to coastal pathogens could rise and the risk of civilians being affected by an infectious disease may increase, through different transmission paths (water-, food- and vector-borne).
- Different climate change hazards can impact directly the health status of the host as well as exacerbate the health conditions of people diagnosed with an NCD; consequently, NCD exacerbation may disrupt or alter the immune system of the host. As a result, their susceptibility to infectious diseases could increase.
- The social-economic status of civilians can be altered under a climate hazard event, as their personal and professional properties may be lost or they can be isolated or displaced. As a result, their economic status, as well as their health status (mental, social and physical health), could be impacted, and their susceptibility and exposure to coastal pathogens and infectious diseases could rise.
- Climate hazards impact public services and infrastructures, which can facilitate the dispersion of coastal pathogens and the transmission of infectious diseases. In addition, it may limit medical access, aggravating the medical conditions of affected civilians and increasing their exposure to diseases.
- Behavioural changes may occur under climate hazards. Civilians may be exposed to extreme conditions that influence certain behaviours; increasing their exposure to coastal pathogens and infectious diseases.

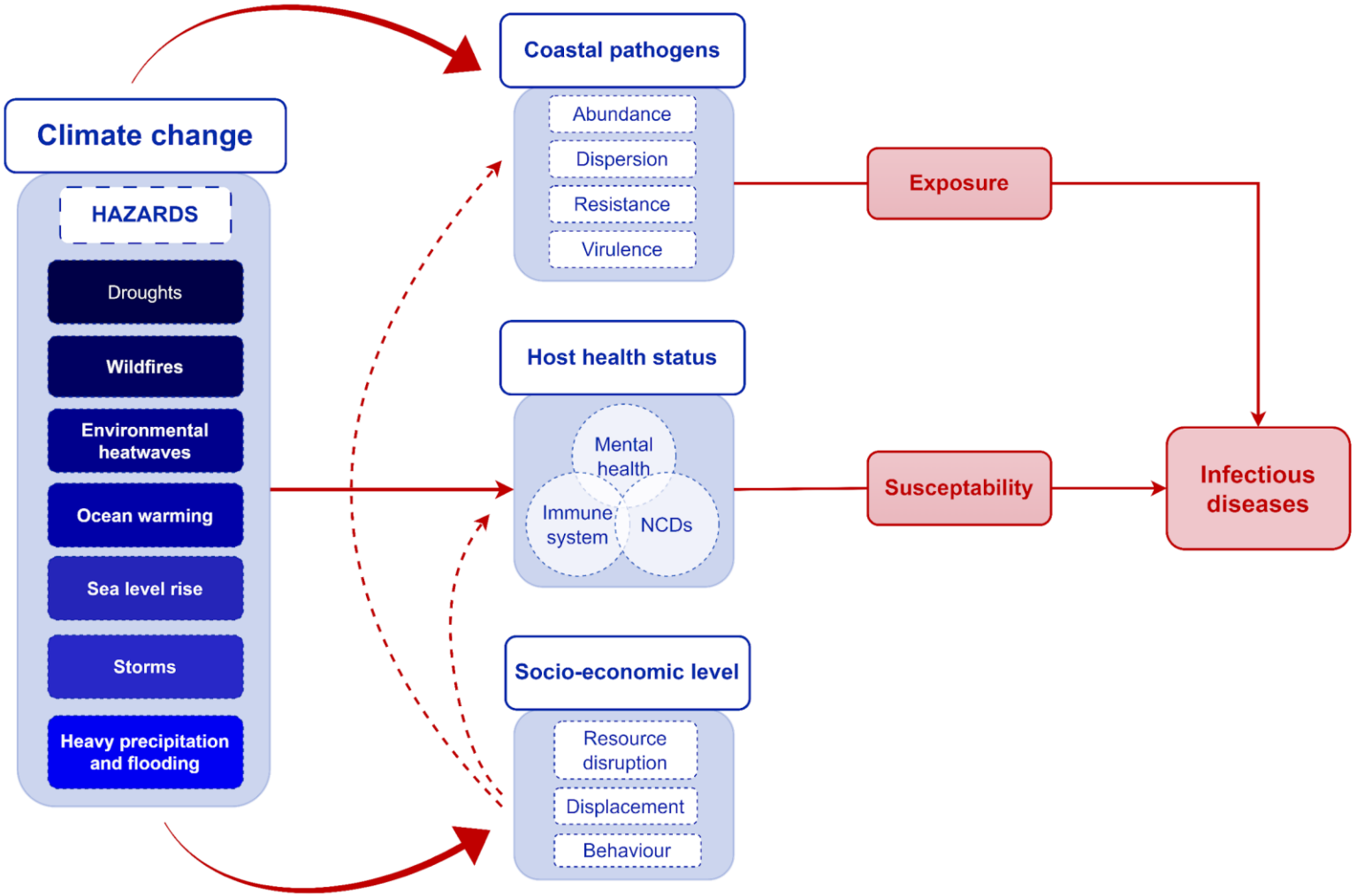


Fig. 5.1. Diagram showing three main pathways (coastal pathogen; host health status; socio-economic level) that can increase the exposure or susceptibility of humans to infectious diseases.

5.5. Conclusions

This chapter has shown the multitude of potential pathways of how a wide range of different climate hazards influence infectious diseases and how favourable conditions are created for the arrival of new diseases. This chapter also elucidates the interconnections among different climate hazards and their potential impacts, not only on coastal pathogens but also on the host health status and their socio-economic situation. The connections among these three components demonstrate that the susceptibility and exposure to infectious diseases arise from a wide range of pathways. Additionally, susceptibility to infectious diseases can be exacerbated due to the interactions between the host's immune system, mental health- and NCD status. Therefore, a multidisciplinary approach that considers all these facets is required when addressing coastal pathogens and their associated diseases.

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CHAPTER 6

Pollution

Chapter 6. Pollution

6.1. Introduction

For decades, our planet has been struggling with pollution (Ukaogo et al., 2020). Pollution is the introduction of materials, substances, or wastes into the environment, which changes its natural qualities and functioning (Champ, 1983). In recent years, this term has expanded to include more specific disturbances such as biological, radioactive, noise or light pollution. Moreover, among emerging pollutants, plastic pollution is gaining more attention as it can take up to 1,000 years to degrade, and even then, it never fully disappears (Kok et al., 2023; Nathanson, 2023; Nations, 2021; Robert et al., 2015; Thompson et al., 2006).

Today, the safe operating space of the planetary boundary for pollutants or novel entities is exceeded, mainly because their production and release have outstripped the capacity to monitor and control them (Persson et al., 2022). Like climate change, biodiversity loss or uncontrolled deforestation, pollution threatens the availability and quality of natural resources essential for thousands of species (Maheshwari et al., 2020; Rockström et al., 2009). From a human health perspective, pollution is now considered the world's largest environmental cause of disease. In 2015 it was responsible for nine million premature deaths (16% of all deaths worldwide) (Landrigan et al., 2018).

Although pollution is ubiquitous, in particular, aquatic ecosystems such as rivers, lakes, wetlands and the ocean have become the global sink for waste (Lovgren, 2021; Parker, 2022). Human activities such as industry, urbanisation, agriculture, aquaculture and tourism release many pollutants into aquatic systems (Zimmer, 2012). Once in the water, pollutants travel through river systems and reach estuaries, coastlines and ultimately the oceans (Nunes & Leston, 2020). In fact, 80% of the pollutants that end up in the sea are released inland (UNEP, 2017a).

One of the most important regions affected by pollution is the coastlines of countries experiencing rapid development (Landrigan et al., 2020). However, pollution in developed coastal areas cannot be underestimated; for example, pollution from toxic metals, industrial chemicals and plastic waste reaches problematic levels in 96% of

the Baltic Sea, 91% of the Black Sea, 87% of the Mediterranean Sea and 75% of the North-East Atlantic Ocean (EEA, 2019b). Furthermore, the European Union (EU) is not on track to meet some of the objectives of the Marine Strategy Framework Directive (Directive - 2008/56, 2008), such as those related to underwater noise, chemicals and eutrophication (EEA, 2022).

Humans can come into contact with pollutants in water through different ways and actions. Coastal pollutants can mainly be encountered through drinking contaminated water, engaging in recreational activities, and consuming contaminated fish and seafood (Landrigan et al., 2020). In particular, the consumption of contaminated seafood and fish is a very important pathway, as many harmful compounds such as methylmercury, microplastics, persistent organic pollutants (POPs) and highly dangerous toxins of harmful algae blooms (HABs) reach humans through the food chain (Friedman & Levin, 2005; Guillotin & Delcourt, 2022; Hong et al., 2012; Smith et al., 2018). For example, the average person ingests (consumption and inhalation) between 74,000 and 113,000 plastic microparticles per year (Cox et al., 2019).

When it comes to exposure to pollutants, especially methylmercury and POPs, it is essential to understand the nature of two crucial processes: bioaccumulation and biomagnification (CIMI, 2021). The first, bioaccumulation, refers to the gradual accumulation of harmful substances in tissues over time, where the tissue concentration can become much higher than the concentration in the environment. For example, it has been observed that methylmercury concentrations in animal tissues can be up to 1,000 times higher than those in the surrounding water (Bełdowska & Falkowska, 2016). The second term, biomagnification, refers to the ability of certain substances to accumulate in tissues as they move up the food chain (EEA, 2018; Winner, 2010). Consequently, the highest concentrations of contaminants are found in long-lived large predators, such as toothed whales, sharks, swordfish and tuna, and therefore consumption of these types of species poses the greatest risk of contaminant exposure to humans (EEA, 2018; McCormack et al., 2020).

Despite the awareness that ocean and coastal pollution can seriously endanger human health and overall welfare (Landrigan et al., 2020), the extent and significance of these effects are still being studied. There are significant information gaps regarding

ocean and coastal pollution (levels, sources, human exposure, health outcomes and impacts of pollutant mixture) (CHEMTrust, 2022; Svingen & Vinggaard, 2016).

There exist several pathways through which pollution can significantly impact human health (Landrigan et al., 2018). For example, research has demonstrated that pollutants can interact with infectious diseases, leading to an increased risk of infection (Board on Life Sciences et al., 2019; Sly et al., 2022). This can occur because contaminants influence the conditions under which pathogens spread and proliferate or because they affect the virulence and resistance profile of pathogens (de Araújo et al., 2019; Su et al., 2022; Zhao et al., 2014). Moreover, pollutants can alter the host's immune response to pathogens, making it more susceptible to infections (Board on Life Sciences et al., 2019). It is noteworthy that there is ample evidence linking contaminants to non-communicable diseases (NCDs) (Prüss-Ustün et al., 2019). For instance, chemicals in coastal and ocean water, such as methylmercury or POPs, have been shown to cause neurotoxic or cardiovascular disorders (Chang, 1977a; Lind & Lind, 2020). Pre-existent multiple chronic conditions may further exacerbate the risks associated with infectious diseases, as observed during the pandemic in patients with COVID-19 (Gimeno-Miguel et al., 2021).

The purpose of this chapter is to examine the intricate connections between pollutants that are pertinent to coastal environments—heavy metals, POPs, plastics, pharmaceuticals and personal care products (PPCPs) and nutrients—and the potential risk of infection by coastal pathogens. To achieve this objective, the chapter has been divided into two sections, which aim to address three fundamental research questions: (1) How do the chosen contaminants interact with coastal pathogens, leading to a possible increase in the risk of infections? (2) How do these selected contaminants weaken the host's immune system, making them more susceptible to infections? (3) Can exposure to these contaminants lead to chronic conditions that worsen the effects of infectious diseases in humans?

6.2. Links between pollutants and coastal pathogens

6.2.1. Heavy metals

The anthropogenic release of heavy metals into the environment started thousands of years ago and increased particularly since the Industrial Revolution (mid-XVIII-IX century) (Nriagu, 1996). Metals are used in various industrial, domestic and agricultural processes and, in many cases, compounds such as mercury, arsenic, cadmium, lead, zinc and copper, end up in coastal ecosystems (Briffa et al., 2020). Heavy metals can potentially mix with water, soil, and air, and living organisms can be exposed to them through the food chain (Mitra et al., 2022).

Concerning coastal pathogens, heavy metals can harm the microbial community and environmental conditions, which can lead to an increase in pathogen proliferation—one of the key mechanisms is the formation of biofilms.

When heavy metals end up in the environment they can cause severe physicochemical alterations (Mok et al., 2023) that change the structure and function of microbial communities (Huang et al., 2021; Yao et al., 2017; Zhao et al., 2014). The effect is that the metal-sensitive microorganisms decline and leave niches for bacteria that are more tolerant to heavy metals (Zhao et al., 2014). Among these metal-resistant bacteria, some species are considered opportunistic pathogens associated with human and animal gastrointestinal infections (e.g. *Enterococcus* spp.) (De La Rosa-Acosta et al., 2015; Fisher & Phillips, 2009). Hence heavy metal contamination could potentially leave more niches and resources available for pathogens.

Biofilms are a good survival strategy for microorganisms (Donlan, 2002). Under environmental stress conditions, such as heavy metal presence, microorganisms form structures to persist in the environment (de Araújo et al., 2019). Metals such as nickel and cadmium stimulate biofilm formation in pathogens such as *Escherichia coli* or *Klebsiella pneumoniae* (de Araújo et al., 2019; Perrin et al., 2009). In biofilms, pathogens can thrive and multiply more effectively than in the free-living form (de Araújo et al., 2019). On the other hand, there are mechanisms by which heavy metals can increase the damaging capacity of coastal pathogens, the most relevant

mechanisms being the up-regulation of virulence factors and the development and spread of antimicrobial resistance (AMR).

Exposure to certain heavy metals (e.g. iron) increases the production of toxins or other virulence factors (such as adhesion and invasion) of some pathogenic bacteria such as *Salmonella* spp., making them more harmful to their hosts (Kortman et al., 2012). In addition, it has been discovered that metals like copper can boost the generation of reactive oxygen species (ROS). These are tiny molecules that occur naturally as a result of metabolism (Sies, 2020). For bacteria, ROS act as essential promoters of horizontal gene transfer (HGT) (S. Zhang et al., 2019); the main mechanism for the spread of AMR (see chapter 7). Thus, metal contamination may contribute to the spread of antibiotic-resistance genes (ARGs) in relevant pathogens. In addition, heavy metals co-select AMR, which means that resistance to heavy metals may, in turn, confer resistance to certain antibiotics (see chapter 7) (Mirzaei et al., 2013; Robas et al., 2021; Rojas Pirela et al., 2014; Su et al., 2022).

6.2.2. Manufactured chemicals

Manufactured chemicals are those developed for use in the industrial processing of chemicals, covering a wide range of chemicals used in inks, plastics, adhesives, paints, glues, solvents, cosmetics, soaps and many other products. In the past 75 years, more than 140,000 new chemicals have been synthesised (Landrigan et al., 2020). More than 60% of chemical production is in low/middle-income countries, where environmental and health protection is often scant (Oxford Economics, 2019). Indeed, some chemicals are not fully tested for safety, in the EU 70% of chemicals placed on the EU market have not been evaluated to ensure safe use (Berggren & Worth, 2023; EEA, 2019a; Maffini et al., 2017).

Although there are many groups and subclasses of manufactured chemicals, in this subsection we will explore how some of the manufactured pollutants—POPs, plastics and PPCPs—affect the spread of coastal pathogens.

6.2.2.1. Persistent organic pollutants

Persistent organic pollutants (POPs) are a group of compounds that have toxic properties, persist in the environment, accumulate in food chains and pose a risk to both human health and the environment (European Commission, 2021b). Due to their persistence in the environment, these chemicals have the potential to be transported far from their source (e.g. through wind, ocean currents and migratory species) (US EPA, 2014). Therefore, banning and reducing the production of POPs is the focus of many international plans for human health and the environment such as the Stockholm Convention (Idowu et al., 2013).

This chemical group is very common in products such as electrical capacitors, hydraulic fluids, pesticides and flame retardants (European Commission, 2021b). A couple of the best-known POPs are dichlorodiphenyltrichloroethane (DDT) and industrial chemicals like polychlorinated biphenyls (PCBs) (UNEP & UNITAR, 2017).

Persistent organic pollutants are very stable chemicals (i.e. able to resist extreme temperature and pressure) that remain intact for a long time in the environment. Many of them are considered legacy pollutants (e.g. PCBs) (UNEP, 2017b). For example, PCBs were used worldwide in electrical transformers and capacitors from the 1930s to the 1970s. Although their production was banned at the end of the 1970s, they are still present in many products today (e.g. paints and industrial machinery), and are ubiquitous in the environment, posing a risk to both human health and wildlife (UNEP, 2017b).

Just as they affect humans and other biotic elements of the ecosystem, POPs can have an impact on coastal pathogens. Although the response of bacteria to POPs depends on multiple factors (e.g. the concentration and structure of the chemical compounds and the taxonomic composition of the microbial community), some POPs are capable of altering the metabolic activity and growth of marine microbial communities (Cerro, 2019). This alteration of the microbial community structure could potentially influence the proliferation of some opportunistic pathogenic species to take the place of the displaced species. On the other hand, POPs can significantly aggravate the growth of certain cyanobacterial species responsible for HABs, for instance by suppressing the competing phytoplankton (Harris & Smith, 2016). The

danger of stimulating HABs is not only due to their dangerous toxins but also because some of these cyanobacterial species can act as a reservoir for coastal pathogens such as *Vibrio cholerae* (Islam et al., 2004).

6.2.2.2. Plastics

Between 4.8 and 12.7 million tonnes of plastics are dumped into the oceans annually (Lebreton et al., 2017). The total amount of plastic waste circulating in the world's oceans is estimated to be 150 million tonnes by 2025 (Geyer et al., 2017; Jambeck et al., 2015). Land-based sources account for up to 80% of marine pollution of which 60-75% is plastic. Most plastics reach the oceans and coasts by being transported downstream, yet there is also some plastic pollution that occurs in the sea and the coast (e.g. waste from aquaculture, fishing and shipping) (Ritchie, 2021).

One of the biggest problems with plastics is that they persist in the environment and can travel long distances, creating problems in areas far away from their point of release (Parker, 2022). In addition, they break down into very small fragments due to weathering, mechanical abrasion and photodegradation resulting in microplastics (<5 mm) or even nanoplastics (<1 µm) (Frias & Nash, 2019; Hartmann et al., 2019). Microplastics are also manufactured for a variety of industrial products. For example, their spherical forms are known as microbeads and are very common in personal care products (e.g. toothpaste or cleanser) and microfibres, which are widely used in the textile industry (ECHA, 2023).

The physical and cumulative effects of microplastics have been extensively studied in marine species, for instance, the obstruction of the intestinal tract or the deleterious effect of microplastics when accumulated in tissues (Naidoo & Glassom, 2019; Sussarellu et al., 2016; Wright et al., 2013; C. Zhang et al., 2017). However, the toxicological impacts of microplastics are hard to elucidate primarily due to their heterogeneity and great complexity (Pirsaheb et al., 2020).

Coastal microorganisms interact with plastics in various ways, primarily through biofilm formation (Harrison et al., 2014; Laverty et al., 2020). *Vibrio* spp., such as *Vibrio cholerae* and *Vibrio parahaemolyticus*, can form biofilms on plastic debris and biofilm-developed microplastics can persist in the environment, providing a favourable

environment for pathogens to thrive and spread (Leighton et al., 2023). Additionally, studies have shown that microplastics, especially those with biofilms, can absorb pollutants like chemicals, heavy metals, nutrients, antibiotic-resistant bacteria (ARB), and ARGs (Chen et al., 2023; Wang et al., 2021). This absorption makes microplastics potential vectors for pollutants and microorganisms entering aquatic environments and organisms. Therefore, microplastics not only create an ideal environment for pathogens and AMR to develop and spread, but they can also release absorbed contaminants into different environments (Wang et al., 2021).

6.2.2.3. Pharmaceuticals and personal care products

Pharmaceuticals and personal care products (PPCPs) are contaminants of emerging concern that are increasing in use and have potential adverse ecological and human health effects (Barceló, 2012; Rosenfeld & Feng, 2011). They are compounds generally used in human and veterinary medicine (analgesics, antidepressants, antiparasitics, contraceptives, antibiotics, *etc.*), beauty, hygiene and cleaning products (facial and hair care products, fragrances, soaps, detergents, toothpaste, *etc.*) (Khalid & Abdollahi, 2021). As PPCPs are used in everyday life, they are continuously introduced into the aquatic media via treated and untreated sewage waters or after being leached from manure from agriculture or waste accumulated in landfills (Ebele et al., 2017; UNESCO & HELCOM, 2017).

The PPCPs enter the environment via several different pathways. For example, after their use in hospitals, veterinary settings, households and industry, many of these products end up directly in the environment, directly or indirectly via wastewater treatment plants (WWTPs) (aus der Beek et al., 2016; Ebele et al., 2017; Huerta-Fontela & Ventura, 2008; Sui et al., 2015). There are more and more effective treatments for the (complete) removal of PPCPs from wastewater such as ozonation, membrane filtration or UV oxidation (Lama et al., 2022; Loganathan et al., 2023; Oliveira et al., 2022; Sauter et al., 2021). However, most of the current treatment processes applied to treat municipal wastewater do not completely remove PPCPs, some of them are released into the environment after passing through these installations. Other relevant inputs of PPCPs into the environment include diffuse (e.g. rainfall-runoff) and point sources from the agri-food industry, leachate from municipal

landfills and the improper disposal of unused or expired products (Loganathan et al., 2023).

Once they reach the environment, PPCPs are highly harmful to living organisms because many of them are designed to produce biological responses at low dosage levels, and therefore, they are a matter of concern in the environment even in low concentrations (Meyer et al., 2019). Another issue is that several PPCPs persist in the environment and accumulate in plants and wildlife, others are slowly degraded by natural phenomena (e.g. solar radiation or the action of water), but as they are constantly released into the environment, their accumulation rates often exceed their degradation rates (Bernhardt et al., 2017). Some common PPCPs found in coastal waters include caffeine, ibuprofen, painkillers, hormones, cancer drugs and antimicrobials such as triclosan and antibiotics. Besides, many PPCPs, in particular cosmetics, contain manufactured nano- and microplastics (Bashir et al., 2021; Kwon & Lee, 2017).

Although the literature on the effects of PPCPs on marine and estuarine organisms is limited, there is growing research on their potential impacts on marine organisms (Arruda et al., 2022; Blue Marine Foundation, 2015). One example of this is the presence of harmful compounds in UV filters commonly found in sunscreen creams, most notably a compound called oxybenzone (Downs et al., 2014, 2016, 2022; Zhong et al., 2019). Oxybenzone has detrimental effects on numerous coral species, resulting in the damage of larvae, an increase in coral bleaching, and the deformation of coral skeletons. Ultimately, marine ecosystems become disrupted by these effects, as corals are crucial for ocean life's refuge and spawning (Downs et al., 2014, 2016, 2022).

In terms of human health, a major current concern is how the release of PPCPs into the environment leads to an increase in AMR (see chapter 7). This is especially the case for antibiotics. However, other types of PPCPs, such as biocides, preservatives and herbicides, can also induce the development and spread of AMR (Barbosa da Costa et al., 2022; Carey & McNamara, 2015; Cen et al., 2020). For instance, the presence of triclosan, a biocide present in several consumer products like soaps, laundry detergents, deodorants, cosmetics, toothpaste, children's toys, and cutting boards, has been linked to the development of resistance in bacteria to triclosan and

clinically relevant antibiotics (European Commission. Directorate-General for Health and Consumers, 2010). In the environment, triclosan can have a significant impact on the composition and diversity of microbial communities (Lydon et al., 2017; Martin et al., 2020). Research has shown that in coastal regions, the presence of triclosan can lead to an increase in the abundance of pathogenic species, such as certain strains of the *Vibrio* genus (Lydon et al., 2017). This may be because some *Vibrio cholera* strains possess an alternative enzyme, which is the target of triclosan. As a result, these bacteria can avoid the effects of triclosan (Massengo-Tiassé & Cronan, 2008).

6.2.3. Nutrients

Rapid urbanisation, changes in diets and food demand have led to changes in agricultural practices that have increased nutrient pollution (mainly nitrogen and phosphorus compounds) in aquatic ecosystems (IWMI & FAO, 2017). Most of this excess nutrient loading comes from human activities such as urban and industrial wastewater, and discharges from farms and agricultural practices, particularly runoff from fields where fertilisers are applied (EEA, 2019c; IWMI & FAO, 2017; NOAA, 2023).

Nutrients are then further transported downstream to estuaries and coastal waters via rivers and groundwater. Nutrient enrichment of coastal waters is considered a relevant pollution problem worldwide and is closely related to the increased frequency of algal blooms (EEA, 2019c; Glibert & Burkholder, 2006).

A major consequence of nutrient enrichment in coastal and riverine water is eutrophication. Eutrophication is a phenomenon responsible for structural and functional changes in aquatic ecosystems, causing environmental problems and reducing the quality of ecosystem services (e.g. fisheries, aquaculture and recreational activities) (EEA, 2019c). This phenomenon occurs when the enrichment of phosphorus (P) and nitrogen (N) in the water increases phytoplankton growth, which in turn reduces the amount of light that penetrates the water column. As a result, the water becomes turbid and algal species living in deeper water die due to lack of light. Bacteria then consume the dead algae and, by decomposing this organic matter the available oxygen (O_2) in the water is rapidly depleted, leading to the mass death of fish and benthic species (Ansari et al., 2010; EEA, 2019c; Jong, 2007).

As previously mentioned, eutrophication triggers the proliferation of algae on the water's surface, so-called algal blooms. Algal blooms are a natural proliferation of microscopic aquatic algae that may float or swim (phytoplankton) or attach to subaquatic surfaces (phytobenthos). Both their growth rate and biomass depend on a combination of physical, chemical and biological factors such as light, nutrients, temperature, salinity, competition with other organisms and predation (Kudela et al., 2015; Shumway et al., 2018).

When algal blooms cause damage (e.g. ecological, health or economic) they are called harmful algal blooms (HABs), whether or not they produce toxins (Shumway et al., 2018). Harmful algal blooms occur naturally, but increasing nutrients, rising surface water temperatures and ocean acidification increase the frequency and severity of HABs, with direct and indirect negative impacts on coastal ecosystems and human health (Gobler, 2020). For instance, certain species of dinoflagellates have been related to mass bird deaths because these algae produce a foam that negatively affects the waterproof properties of bird feathers (Jessup et al., 2009). Another example is the mass mortality of wild animals (turtles, dolphins, manatees, whales, birds) due to microalgae toxins that accumulate in food webs (Starr et al., 2017).

In terms of human impact, the scientific literature to date has focused primarily on the serious effects of the toxins that HABs produce, which can reach humans through contaminated fish or shellfish and can induce gastrointestinal, neurological and respiratory system disorders and even death (Carmichael & Boyer, 2016; Daguer et al., 2018; Landrigan et al., 2020; Watkins et al., 2008). Additionally, chronic exposure to certain toxins, such as microcystins, is of particular concern, as it is associated with the development of tumours and liver damage in humans (Li et al., 2023). However, the long-term effects of these toxins are still largely unknown.

Finally, the proliferation of HABs can be dangerous not only because of the significant harmful effects of their toxins but also because of their association with pathogenic species such as *Vibrio* spp. An increase in nutrient loads promotes both HABs and *Vibrio* ssp. (Glibert & Burkholder, 2006; Liu et al., 2018; Rosales et al., 2022). Harmful algal blooms protect bacteria from predators, creating favourable growth conditions for *Vibrio* (Main et al., 2015). Thus, coastal pathogens, marine organisms, and human

interactions may increase during HAB events, leading to a higher incidence of infections.

6.3. Host health status and susceptibility to infections

Pollutants are a growing concern in terms of their potential impact on human health (Landrigan et al., 2018). Pollution has been linked to NCDs and immune system disorders (Badulescu et al., 2019; Dhimal et al., 2021; Fuller et al., 2018; Glencross et al., 2020; Prüss-Ustün et al., 2019; Schraufnagel et al., 2019; Suzuki et al., 2020). In this section, we will first examine how certain pollutants can weaken the immune system and make individuals more vulnerable to infectious diseases. Secondly, we will provide a summary of chronic diseases caused by coastal pollution and discuss the potential link between NCDs and infectious diseases.

6.3.1. Pollution, immune system and infectious diseases

The impacts of pollutants on humans are manifold (Landrigan et al., 2018), there are multiple examples in the literature showing that per- and poly-fluoroalkyl substances (PFAS)—chemicals classified in the POPs group—can alter the immune system in both animals (DeWitt et al., 2012) and humans (Grandjean et al., 2012; Pennings et al., 2016). In this section, we are particularly interested in the impacts of the pollutants on the immune system because it has important implications for the susceptibility of the host to infections.

In January 2019, the National Academies of Sciences, Engineering, and Medicine (NAPEM) held a workshop and brought together experts in infectious diseases, toxicology, global public health, epidemiology, and political science to discuss the interactions between environmental stressors, infectious diseases, and human health (Board on Life Sciences et al., 2019). One of the key takeaways was the consensus among experts that the fields of environmental health, infectious diseases and NCDs must converge. However, significant silos between these disciplines persist. In addition, the workshop pointed out the importance of taking advantage of the opportunity provided by the One Health, EcoHealth and Planetary Health frameworks to foster the collaboration between biomedical and non-biomedical disciplines to examine the connections between environmental health and infectious diseases.

Finally, the workshop noted the need to study the presence of bidirectional links between exposure to contaminants and exposure to pathogens. Contaminants may bring about changes in the immune system's responses to pathogens and vaccines, while infections can make the host more vulnerable to contaminant exposure. These interactions are believed to be highly influenced by the human microbiome, and this knowledge becomes crucial both for the prevention and treatment of humans and animals (Board on Life Sciences et al., 2019).

In line with the above-mentioned workshop, we aimed to investigate the relationship between exposure to pollution and the risk of infections caused by pathogens. However, there is limited literature available on the connection between exposure to pollutants and increased susceptibility to coastal pathogens. Nonetheless, we were able to identify several studies that focused on coastal populations such as fishing communities or Arctic populations, which are more exposed to marine or coastal pollution due to geographical or socio-economic circumstances. These studies show how these communities are affected in their immune responses due to exposure to pollutants, mainly POPs. For example, Norwegian studies have shown that prenatal exposure to PFAS is associated with increased episodes of common cold and gastroenteritis in children (Granum et al., 2013) as well as respiratory tract diseases (Impinen et al., 2018). According to another study, exposure to organochlorines like PCBs and DDTs during pregnancy is linked to an increased risk of childhood infections in Arctic communities (Dewailly & Knap, 2006). Another study in children in the Faroe Islands found that elevated perfluorinated compounds (PFCs) exposures were associated with reduced immune responses to routine childhood vaccinations in children aged 5 and 7 years, in particular significantly reduced levels of protection against diphtheria and tetanus (Grandjean et al., 2012).

6.3.2. Pollution, non-communicable diseases, and infectious diseases

Non-communicable diseases (NCDs) are chronic health conditions that persist over an extended period and cannot be transmitted from person to person (WHO, 2014). Currently, NCDs make up 72% of all deaths worldwide and this percentage is on the rise (Fuller et al., 2018). The list of NCDs includes cancer, cardiovascular disease, diabetes, and chronic respiratory diseases and can be influenced by a combination of

genetic, environmental, behavioural, and physiological factors (CDC, 2022). In fact, the environment is increasingly being considered a determining factor in the development of NCDs. According to a comment published in The Lancet by Fuller et al., (2018), pollution (in air, water, and soil compartments) is a major risk factor for NCDs. In fact, it is responsible for approximately 16% of all NCD-related deaths. Moreover, it accounts for 22% of all deaths from cardiovascular disease, 26% of ischaemic heart disease deaths, 25% of stroke deaths, 53% of deaths from chronic obstructive pulmonary disease, and 40% of deaths from lung cancer (Fuller et al., 2018).

The impact of coastal and ocean pollution on humans is an active area of research and little remains known about the repercussions of exposure to multiple pollutants (Landrigan et al., 2020). For microplastics, the impacts on humans are just beginning to be understood (Smith et al., 2018). In other cases, such as for methylmercury and POPs, the effects have been extensively studied. For instance, multiple harmful effects of methylmercury have been observed in humans (e.g. cardiovascular diseases and blood pressure problems) (Genchi et al., 2017). Indeed, its neurotoxic effects make it an extremely hazardous compound for the brain (Chang, 1977b). In humans, POPs generate a long list of health consequences, such as cardiovascular effects, developmental neurotoxicity, metabolic diseases, endocrine disruption, cancer, mortality and immune toxicity (Guillotin & Delcourt, 2022; Landrigan et al., 2020). Particularly, the most severe and irreversible damage for both methylmercury and POPs is caused by exposure during the developmental stages of the brain (e.g. in foetuses or growing children) (Boucher et al., 2012; Davidsen et al., 2021; Grandjean et al., 1997; Myers et al., 2003; Myers & Davidson, 1998; Zhou et al., 2023). The impact of pollutants on cognitive development has been extensively studied. However, the impact of pollution on other areas of mental health has been increasingly gaining attention in recent years. It is now well-established that pollution has serious implications on mental health. For instance, residing in areas with high levels of pollution is found to be associated with symptoms such as anxiety and depression (Theron et al., 2022; Zundel et al., 2022). A specific study of coastal areas revealed that marine litter scenes appear to be associated with reduced mood. Moreover, the scenes reduce the psychological benefits that clean coastal areas often provide (Wyles et al., 2016). In addition, new categories of pollution, such as light and noise

pollution, have been identified and linked with stress and irregular sleep patterns (Chepesiuk, 2009; Eze et al., 2020; Hegewald et al., 2020). It has been observed that noise and light pollution are extremely harmful to marine wildlife (Erbe et al., 2019; Marangoni et al., 2022).

While we recognise that making generalised statements about the direct association between NCDs and increased severity of infections or mortality would be inaccurate, as it depends heavily on the specific NCD and the specific pathogen, we believe that the COVID-19 pandemic has emphasised the importance of further research and discussion in this area. As such, we wish to highlight the significance of NCDs as possible risk factors for developing severe illness when contracting infectious diseases.

During the COVID-19 pandemic, the older population and individuals with underlying health conditions such as high blood pressure, diabetes, and obesity have been considered at a higher risk of developing severe symptoms of the virus (Fernández García et al., 2020). Similarly, it has been observed that obesity increases the risk of viral infections such as influenza and SARS-CoV-2, leading to more frequent hospitalizations and complications (Luzi & Radaelli, 2020; Simonnet et al., 2020). In patients with dengue, grade II diabetes has been identified as an aggravating factor, as patients tend to be more prone to bleeding disorders and have worse morbidity and mortality outcomes (Singh et al., 2022). These studies, although they refer to very specific cases, could be very important when considering risk factors for emergency preparedness. For instance, in case of an infectious disease breakout, authorities may be ready to apply measures for better managing patients with underlying health conditions reducing the impact of such an event.

In an article published in 2017, Kostova et al. stated that “the proliferation of NCD risk factors associated with current demographic trends in longevity and urbanisation can raise a population’s baseline susceptibility to infection-related health security risks” and that “integration between initiatives to reduce NCDs and communicable diseases has been recognized as essential for efficient distribution and use of health resources, both human and financial, and can provide a sustainable foundation for emergency preparedness” (Kostova et al., 2017).

Although the synergies between NCDs and infectious diseases need to be better understood. We believe that this collaboration can lead to important implications for the health of our current and future society. We invite academics and experts from different fields to utilise our recent experiences with the COVID-19 pandemic to stimulate discussion and further research on the interactions between NCDs and infectious diseases.

6.4. Summary of pathways of interactions

This chapter provides a comprehensive overview of the impact of coastal pollution on human health, with a particular emphasis on its interactions with pathogens (Fig. 6.1). Pollutants can have a significant impact on the habitat of coastal pathogens, promoting their growth and spread, while also enhancing their virulence and resistance mechanisms. However, the specific effects of pollutants on pathogens depend on the type and level of pollutants, as well as the specific pathogen. Coastal pollution can also alter and disturb the immune system and make individuals more susceptible to infections. Furthermore, ample evidence supports the notion that pollutants can trigger NCDs in humans, thus contributing to a greater burden of disease.

The present findings reveal that pollution poses a significant threat to human health, with consequences that extend from NCDs to potentially infectious diseases. Besides, although significant progress has been made in the fields of environmental health, NCDs, and infectious diseases over the past few decades, the synergies and interplay between these disciplines remain largely undetermined (Board on Life Sciences et al., 2019). Given the incipient growth of deaths attributed to NCDs (91% of deaths in the EU) and the threat posed by infectious diseases as we have recently experienced with the COVID-19 pandemic (European Commission, 2021a; WHO, 2023), to advance towards a society that is more capable to face health challenges, it is imperative that we conduct additional research and encourage collaboration between disciplines that focus on NCDs and infectious diseases. This collaborative approach will enable us to gain a better understanding of the complex interactions between these two areas of focus (Board on Life Sciences et al., 2019).

It is noteworthy that the possibility of the occurrence of a similar scenario in animals cannot be ruled out, although it has not been addressed in this chapter. For instance, it has been reported that pollutants can also alter the response of wildlife to infectious diseases (Sánchez et al., 2020). Therefore, in line with the One Health approach, it is imperative to emphasize the need for further research in this area.

The other main observation from the chapter is that there are still many unknowns about the presence of pollutants in the environment. We know, that pollution is ubiquitous in aquatic ecosystems, both rivers and lakes as well as estuaries, coastal environments and seas are contaminated by a mixture of pollutants. However, knowledge about pollution dynamics in coastal water and its potential impacts on human health is under investigation and much is still unknown about exposure pathways, magnitude of effects and levels of pollutants (Landrigan et al., 2020). Even less is known about the “cocktail effect” of these pollutants when they are combined (Svingen & Vinggaard, 2016). In any case, according to available evidence, the presence of pollutants in the environment poses significant health risks to both the ecosystem and humans. As such, we must address the challenge of public health posed by pollution, despite the prevalence of misinformation and knowledge gaps. Developing effective pollution policies that promote both adaptation and mitigation actions is crucial to this end. We would like to underscore the significance of implementing a precautionary approach that advocates taking measures to mitigate negative impacts on both the environment and human beings, even in the absence of complete scientific certainty.

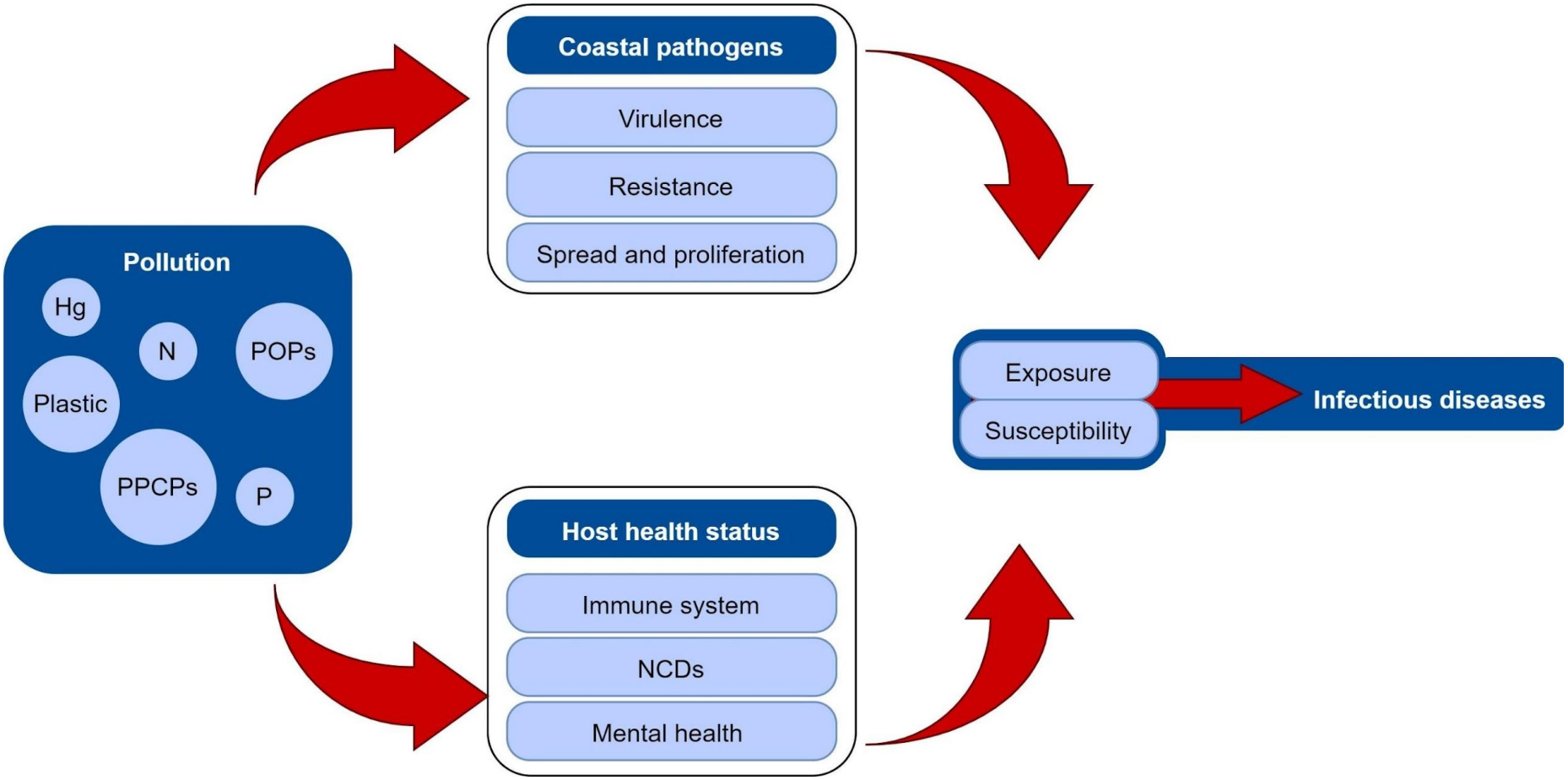


Fig. 6.1. Summary of the key findings highlighted in the chapter. Illustration of how pollution can increase the risk of infectious diseases caused by coastal pathogens.

6.5. Conclusions

In conclusion, it becomes increasingly evident that research into the interface between non-communicable and communicable diseases is imperative. The interplay between these disease categories, often exacerbated by factors like pollution, poses intricate challenges that demand comprehensive research. Particularly in the context of marine/coastal pollution, it is paramount to not only establish rigorous surveillance and monitoring systems but also to proactively implement mitigation measures. Embracing the precautionary principle becomes crucial, signifying the need to act in the face of uncertainty to avert potential harm.

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CHAPTER 7

Antimicrobial resistance and coastal pathogens

Chapter 7. Antimicrobial resistance and coastal pathogens

7.1. Introduction

Antimicrobial resistance (AMR) is one of the leading public health threats of the 21st century (Murray et al., 2022). Antimicrobial resistance occurs when the effective treatment of infection is reduced due to resistant mechanisms developed by bacteria. Although AMR is a natural phenomenon, antibiotics' misuse and overuse have enriched antimicrobial resistance to the point that common bacterial infections may become untreatable by antibiotics (Menz et al., 2021). If urgent action is not taken, AMR could result in over 10 million deaths due to antimicrobial-resistant infections by 2050 (O'Neill, J., 2016).

Human activities, including the discharge of pharmaceuticals and antibiotics, contribute to the development and spread of AMR in marine and coastal bacteria (Singh et al., 2022). The impact of AMR on marine ecosystems is interconnected with human and animal health through seafood consumption and recreational water activities (EMA, 2021). Experts warn that coastal and marine environments can serve as reservoirs of antibiotic resistance genes (ARGs), which can be transferred between bacteria in the environment and those that cause human infections, contributing to the spread of resistance (Hatosy & Martiny, 2015). Therefore, studying AMR in marine or coastal bacterial species is crucial in gaining insights into the risks posed by AMR to human health (Bengtsson-Palme et al., 2023; EFSA Panel on Biological Hazards (BIOHAZ) et al., 2021; Stanton et al., 2022).

This chapter summarises the basis of AMR, the spread of environmental resistance, and its interaction with climate change. Finally, the resistance profile of selected coastal pathogens is discussed in more detail. It is essential to emphasise that throughout this report and this chapter; the term antimicrobial resistance refers specifically to antibiotic resistance.

7.2. General knowledge of antimicrobial resistance

Microorganisms have existed on Earth long before humans (Benner et al., 2020), the oldest evidence of life on Earth are filamentous microfossils (ca. 3,420–4,280 million years old) that have been found in rocks and are thought to have been underwater hydrothermal vents in the past (Cavalazzi et al., 2021; Dodd et al., 2017; Javaux, 2019).

Some microorganisms are pathogenic and can cause infectious diseases in humans, animals or plants (Alberts et al., 2002), although most are considered non-infectious (Y. Zhou et al., 2013). Humans live in a world full of microorganisms, which, under normal conditions, do not threaten us; in fact, they protect us from other potential pathogens, and produce useful compounds such as vitamins K and B (Tortora et al., 2007). Importantly, microorganisms are vital for human survival as they constitute our microbiota, aiding digestion, bolstering immunity, and maintaining skin health (Byrd et al., 2018; Wu & Wu, 2012). Indirectly, they play a crucial role in ecological balance by decomposing waste, nutrient cycling, and supporting plant growth (Gupta et al., 2016). Besides microorganisms' metabolic processes have benefited humans throughout history. For example, it is well known that the production of different biotechnological products, such as antibiotics and other pharmaceuticals, beer, bread, and cheese are among the most common processes where microorganisms are used (Abdel-Aziz et al., 2017).

Among microorganisms, the bacteria domain is very studied. Bacteria are prokaryotic organisms that have lived almost everywhere on Earth for millions of years (Tortora et al., 2007). In nature, bacteria are surrounded by countless compounds. Among these are nutrients or molecules for signalling, necessary for their survival. However, others can be toxic and therefore, bacteria have developed multiple mechanisms to protect themselves from these harmful compounds (Wright, 2012). Bacteria are simple organisms; most have a cell wall and a membrane surrounding the cytoplasm containing the nucleoid with deoxyribonucleic acid (DNA), ribosomes and inclusions. They typically have external structures such as flagella, pilus or capsules, which can facilitate their movement and protection (Tortora et al., 2007).

Antibiotics are natural, semi-synthetic or synthetic compounds that kill bacteria or stop their growth (Bhattacharjee, 2022). These compounds fight bacteria in many ways; for instance, by damaging their DNA and proteins of DNA metabolism or by attacking their cell envelopes (Rosenblatt-Farrell, 2009). Natural antibiotics are produced by fungi, plants and bacteria, particularly those living in soil, for instance, penicillin is generated by fungi of the genus *Penicillium* (Eurotiales: Trichocomaceae), which are classified in the group of moulds (Bhattacharjee, 2022; Garbisu & Alkorta, 2019). Although antibiotics are used in veterinary and human medicine to fight bacterial infections, their role in nature is more complex because depending on the concentration they may act against competitors in the soil ecosystem or as signalling molecules to communicate with other nearby organisms or hosts (Davies, 2006; Traxler & Kolter, 2015).

Regardless of human interference, AMR is a natural and ancient phenomenon (D'Costa et al., 2011; Pinnell et al., 2023). However, the overuse and misuse of antibiotics and the release of contaminants such as metals or disinfectants have enriched AMR to such an extent that the use of antibiotics as a therapeutic tool is compromised (EMA, 2021; O'Neill, J., 2016; Singer et al., 2016; UNEP, 2017). Moreover, the antimicrobials used for destroying harmful microorganisms, which are pathogenic to humans, destroy some beneficial microorganisms at the same time (Ranallo et al., 2021). Consequently, an unbalanced microbiota, e.g. microorganisms that live in our gut and skin, can be developed and may increase the risk of infection, including antibiotic-resistant infections (Ranallo et al., 2021).

One of the most common misunderstandings in the general public when dealing with AMR is that the human body is resistant to antibiotics, while AMR means that the bacteria causing the infection are resistant to the antibiotic.

7.2.1. Brief history of antibiotics discovery

Humans have been using antibiotics since ancient times. In different cultures and periods —Greek, Celtic or Chinese— mould has been used to treat open wounds (Wainwright, 1989). Among moulds, the genus *Penicillium* (Eurotiales: Trichocomaceae) was crucial in the development of the first antibiotic, penicillin (ACS, 1999). This discovery was made in 1928 by Alexander Fleming, who did not ignore what he observed in a Petri dish contaminated with the mould *Penicillium rubens*

(Houbraken et al., 2011). The substance penicillin produced by the mould prevented the growth of bacteria around the fungi (ACS, 1999). Years later, Howard Florey and Ernst Chain would isolate the compound and develop the pharmaceutical (Abraham et al., 1941). All three would win the Nobel Prize for Medicine in 1945 (Lindsten & Nils Ringertz, 2001).

The period between the 1940s and 1960s was considered the “Golden Age of Antibiotics” when most antibiotics were discovered and the relative ease of finding antibiotics led to their overuse (Hutchings et al., 2019). However antibiotic-resistant bacteria (ARB) soon began to appear, and in the case of many antibiotics a few years after their approval for clinical use, resistance was found in patients (Stennett et al., 2022). In 2001, the World Health Organization (WHO) declared AMR an emerging public health threat, and in November 2021, it listed AMR as one of the top 10 global public health threats facing humanity (WHO, 2001, 2021c, 2021a).

Today the need for novel antibiotics is critical, yet very few have been developed in recent years. The WHO warns that novel antibiotics targeting critical WHO priority pathogens are still lacking; in particular, carbapenem-resistant *Acinetobacter baumannii* (Pseudomonadota: Moraxellaceae) and *Pseudomonas aeruginosa* (Pseudomonadota: Pseudomonadaceae) (WHO, 2022a). The explanations for this lack of antibiotic discovery are manifold. One of the main reasons is the high cost of research and development (R&D), coupled with relatively low economic returns compared to other drugs, which has resulted in a reduction in investment in novel antibiotic research (Klug et al., 2021). Additionally, the decreasing efficacy of traditional methods has contributed to the slowdown in the discovery of new antibiotics (Walesch et al., 2023; WHO, 2022a). Historically, antibiotics have been found by screening metabolites produced mainly by soil microorganisms, particularly those of the *Actinomyces* genus (Walesch et al., 2023). Although initially effective and productive, this strategy has progressively slowed down as the species of microorganisms being cultivated are similar, leading to many rediscoveries of antibiotic compounds (Hutchings et al., 2019; Lewis, 2020). In a recent report, the WHO stated that only 20% of newly approved antibacterial agents represent a new class, while more than 80% are derived from known classes (WHO, 2022a).

Ongoing research is dedicated to discovering new methods of addressing bacterial infections (Hegemann et al., 2022; Walesch et al., 2023). One particularly promising avenue of exploration is alternative therapeutic approaches to antibiotics, such as the utilisation of bacteriophages, antimicrobial peptides, and immunostimulatory compounds (Fereshteh et al., 2023; Ghosh et al., 2019; Lin et al., 2017; Pang et al., 2019). Additionally, an increasing number of culture techniques have been developed which allow for the cultivation of previously "uncultivable" organisms (Hegemann et al., 2022). Given that less than 1% of microbial diversity has been successfully cultured (Locey & Lennon, 2016), there is great potential for the discovery of new antibiotics within the poorly studied or even entirely novel microorganism phyla (Walesch et al., 2023).

7.2.2. Overview of antimicrobial resistance in Europe

In recent decades, AMR has emerged as a major public health threat, particularly due to the challenge posed by antibiotic-resistant clinically relevant bacteria (ECDC & WHO, 2022; O'Neill, J., 2016). The most recent report on AMR surveillance in the WHO European Region highlights high levels of third-generation cephalosporin and carbapenem resistance in *Klebsiella pneumoniae* (Pseudomonadota: Enterobacteriaceae), high percentages of carbapenem-resistant in *Acinetobacter* spp. and *Pseudomonas aeruginosa*. In addition, there is a significant growth of resistance to carbapenems in *Escherichia coli* (Pseudomonadota: Enterobacteriaceae) and *K. pneumoniae*, and to vancomycin resistance in *Enterococcus faecium* (Bacillota: Enterococcaceae) during 2016-2020 (ECDC & WHO, 2022).

In Europe, approximately 33,000 patients die annually due to infections of ARB (Cassini et al., 2019), and deaths reached 1.27 million in 2019 worldwide (Murray et al., 2022). However, these data must be considered cautiously as the prevalence of AMR in relevant pathogens is unknown in many regions of the world (ECDC & WHO, 2022). Globally, there are at least 2 billion people that live in countries that lack data, therefore this statistical analysis is potentially underestimating the actual number of cases (Oldenkamp et al., 2021).

Currently, in the European Economic Area (EEA), 85% of countries/areas have developed a national/area AMR action plan and 70% have a national/area AMR

surveillance system for common bacterial infections. However, WHO stresses that effective AMR control in the European Region requires further efforts and investments, as some of the countries, after developing the action plan, have not been able to move to the next phase of implementation of the targets (ECDC & WHO, 2022).

On a global scale, the Global Action Plan on Antimicrobial Resistance (GAP-AMR) and the Global Antimicrobial Resistance Surveillance System (GLASS) have been put into place to ensure that treatment and prevention of infectious diseases remains successful as long as possible (WHO, 2015, 2022b).

7.2.3. Antimicrobial resistance mechanisms

Over thousands of years, bacteria have evolved defence mechanisms to withstand antimicrobial drugs. There are five main mechanisms of antibiotic resistance:

(1) Antibiotic target avoidance: antibiotics often have specific cellular targets, and bacteria can develop new cellular processes that avoid using the antibiotic target (Kapoor et al., 2017).

(2) Inactivation or destruction of the antibiotic: bacteria modify or destroy antibiotics through enzymes, which is a strategy commonly used for aminoglycoside antibiotics such as kanamycin, gentamycin, streptomycin, chloramphenicol, and β-lactams (Egorov et al., 2018; Peterson & Kaur, 2018; Tortora et al., 2007).

(3) Restrict antibiotic access: bacteria restrict antibiotic access by changing or reducing the number of entry routes to the cell (Reygaert, 2018).

(4) Getting rid of the antibiotic: bacteria get rid of antibiotics by pumping out antibiotics through efflux pumps (Kapoor et al., 2017).

(5) Changing antibiotic targets: bacteria change the structure of the antibiotic target, so it cannot associate with it (Peterson & Kaur, 2018). Target modification acts as a self-resistance mechanism against several classes of antibiotics, including β-lactams, glycopeptides, macrolides, lincosamides, streptogramins and aminoglycosides (Peterson & Kaur, 2018).

7.2.4. Selection and transmission of antimicrobial resistance

It is well-known that AMR occurs naturally; however, the misuse and overuse of antibiotics and the release of pollutants into the environment are augmenting the emergence and the spread of resistance (UNEP, 2017). Antibiotic resistance occurs when bacteria are exposed to sub-lethal concentrations of antibiotics (i.e. concentrations that are not sufficient to kill them but are capable of promoting the selection of resistance) (Wright, 2012).

There are two types of antibiotic resistance: intrinsic and acquired (Arzanlou et al., 2017). While the former is characterised by being naturally resistant to specific antibiotics, the latter is caused by the mutations in the bacterial chromosome and by the acquisition of antibiotic resistance genes (ARGs). In this section the types of antibiotic resistance are summarised, the first section describes the inherent type of resistance and the next two sections refer to acquired resistance:

(1) Intrinsic resistance: refers to resistance that certain groups of bacteria have due to their natural traits (Cox & Wright, 2013; Oliveira & Reygaert, 2023). This type of resistance is limited to specific bacterial species and it is transmitted from parental bacteria to progeny (i.e. vertical gene transfer (VGT)) (Coleman & Smith, 2014; Reygaert, 2018). An example of inherent resistance is the one *E. coli* species have to macrolides (Reygaert, 2018).

(2) Mutations in the bacterial chromosome: refer to the resistance obtained through mutational events in the bacterial chromosome (Coculescu, 2009). This resistance is limited to the individual bacterial cell that has undergone the mutation and is transferred vertically to its progeny (Coculescu, 2009). This type of resistance is not very common as mutations tend to disappear in the absence of antibiotic pressure due to their high energy costs (Coleman & Smith, 2014).

(3) Acquisition of antibiotic resistance genes (ARGs): refers to the resistance obtained through the acquisition of ARGs (Coleman & Smith, 2014; Reygaert, 2018). It is the most common type of resistance and the one generating the most significant problems because ARGs can be exchanged between unrelated bacteria through horizontal gene transfer (HGT) (Coleman & Smith, 2014; Dimitriu, 2022), contributing to the spread of AMR among bacterial

communities. Horizontal gene transfer involves mobile genetic elements (MGE) of various types, but the most studied and best understood are conjugative plasmids. Conjugative plasmids are one of the main contributors to ARG transmission (Reygaert, 2018). A bacterium that has a conjugative plasmid, which carries ARGs, can transfer the plasmid to other bacteria through bacterial conjugation. This process needs physical contact between the two bacterial cells (donor and recipient) and it is mediated by a complex molecular machinery called T4S.

7.2.4.1. Co-selection of antimicrobial resistance

Co-selection is a relevant phenomenon for AMR because it maintains and promotes antibiotic resistance in bacterial communities without antibiotics (Pal et al., 2017). Several substances such as pharmaceuticals, biocides, disinfectants, pesticides or metals can favour the co-selection of antibiotics (Baker-Austin et al., 2006; Pal et al., 2015, 2017; Wales & Davies, 2015). In simpler terms, AMR can arise when bacteria are exposed to non-antibiotic substances, such as heavy metals, rather than only antibiotics. There are two main co-selection mechanisms: co-resistance and cross-resistance:

(1) Co-resistance: occurs when genes encoding resistance to a non-antibiotic compound are located on the same genetic element as antibiotic resistance genes, e.g. on the same conjugative plasmid (Baker-Austin et al., 2006; Pal et al., 2015). Example for co-resistance: the resistance genes for the antibiotic and the metal are located in the same genetic element—plasmid.

(2) Cross-resistance: occurs when a single resistance mechanism confers protection against different compounds as they may have the same cellular target or a standard route to cell death (Chapman, 2003). Example of cross-resistance: the bacteria share resistance mechanisms for the antibiotic and the metal that are pumped by an efflux pump.

7.3. The spread of antimicrobial resistance in the environment

Antimicrobial resistance (AMR) can spread in the environment through various pathways and mechanisms (UNEP, 2017). The environment acts as a reservoir and amplifier of resistance genes, allowing them to be disseminated and exchanged among different bacteria (Hatosy & Martiny, 2015; Lepper et al., 2022).

Antibiotics are used worldwide to treat and prevent bacterial infections in humans, animals and even plants (UNEP, 2017). In livestock and aquaculture, antibiotics are commonly used as prophylactic therapy (Manyi-Loh et al., 2018). The difficulty of treating individual animals means that broad-spectrum antibiotics are often administered to the whole herd (EMA, 2022).

After consumption, up to 70-80% of antibiotics (per dose) are excreted in the urine and faeces (Baietto et al., 2014). In the case of human settlements, these residues are frequently transported to wastewater treatment plant (WWTP) plants, where they are partially removed, as WWTPs are not capable of completely removing all antibiotics (UNEP, 2017). However, a large amount of non-treated residues ends up directly in the aquatic environment, such as runoff of manure from agricultural land (UNEP, 2017).

The disposal of pharmaceuticals also is a source of generation of AMR. All kinds of medicines are discarded and collected every day by the solid waste management system and end up in landfills where they accumulate for long periods (Rogowska & Zimmermann, 2022). In addition to the discarded pharmaceuticals, the activated sludge from WWTPs often also ends up in landfills, and is a major source of both chemical and biological contamination (Yadav et al., 2019). Once in landfills, due to leaching, active compounds and contaminants can reach groundwater and surface waters (Hussein et al., 2021). Bacteria coming into contact with these substances can develop AMR.

Aquatic environments are often contaminated with ARB and ARGs from terrestrial effluents (Marti et al., 2014). According to recent reviews, the level of ARB is extremely high in most rivers (up to 98% of the total detected bacteria), followed by lakes (up to

77% of the total detected bacteria) (Nnadozie & Odume, 2019). This can cause a serious public health problem by reaching the human microbiota through drinking and even recreational water reservoirs that are supplied with fresh water containing ARGs or ARBs (Baquero et al., 2008). Even if it is true that dilution and natural degradation decrease the presence of ARGs and ARB in aquatic ecosystems, and although it has been observed that ARBs in freshwater are effectively inactivated by sunlight, their DNA-containing ARGs may still be intact and capable of transferring resistance to non-resistant strains (Anyaduba, T., 2016).

Water can disperse AMR through the different compartments of ecosystems, transporting resistances and enriching itself with the pollution it picks up from the different areas through which it flows and ultimately reaches coastal environments (Marti et al., 2014; Anyaduba, T., 2016). In turn, coastal environments accumulate antimicrobial resistance from activities such as aquaculture or coastal wastewater (Singh et al., 2022). Coastal ecosystems are thus potentially hazardous areas as they are often used for fishing and recreational activities, increasing the risk of exposure to resistant bacteria, including pathogenic bacteria (Hatosy & Martiny, 2015).

7.4. Antimicrobial resistance among relevant coastal pathogens

Most of the research done in the past on AMR has mainly focused on the clinical setting (EMA, 2021). However, this is currently changing due to the growing awareness of antibiotic-resistant infections, and the interconnection between human and animal health through processes such as seafood consumption and recreational water activities (EMA, 2021). In particular, the role of coastal and marine bacteria as environmental reservoirs of AMR is a matter of concern (Hatosy & Martiny, 2015).

Here we summarise the main relevant ARB species present in coastal ecosystems. Some are key species selected for AMR surveillance and others are common species in coastal and marine ecosystems. The species have been selected either because they are significant coastal pathogens where ARGs have been identified or because they are significant ARBs occurring in coastal waters.

7.4.1. *Vibrio* spp. and *Aeromonas* spp.

This section addresses antibiotic resistance in common species in aquatic systems. In particular, it will focus on *Vibrio* spp. (Pseudomonadota: Vibrionaceae) and *Aeromonas* spp. (Pseudomonadota: Aeromonadaceae), which are genera that include species considered waterborne pathogens, and consequently, vehicles of waterborne diseases of importance to humans (Cabral, 2010). Note that a more comprehensive discussion on *Vibrio* spp. is provided in chapter 8 of this deliverable.

Vibrio species are naturally occurring bacteria found in coastal and marine waters, marine algae, and animal tissues (Thompson et al., 2004). There are over 100 species that have been determined within the genus *Vibrio* (Jones, 2017), and only three species of *Vibrio* (*V. cholerae, V. parahaemolyticus*, and *V. vulnificus*) are considered pathogenic and responsible for causing vibriosis (Thompson et al., 2004). Some typical signs of vibriosis include diarrhoea, abdominal pain and vomiting fever (Baker-Austin et al., 2018). The main ways to get vibriosis are by eating raw seafood (like oysters, crabs, and shrimp) that have been cross-contaminated, or by eating raw fish (like sushi or sashimi). Direct contact of open wounds with seawater can also spread the disease (CDC, 1993; European Commission, 2001).

The prevalence of AMR in *Vibrio* species is concerning as the emergence of *Vibrio* strains resistant to clinically prescribed antibiotics has raised concerns in the health sector and may hinder the effective treatment of severe vibriosis (Banerjee & Farber, 2018; Onohuean et al., 2022). An increasing number of studies are beginning to focus on the presence of ARGs in isolates of *V. parahaemolyticus* and *V. vulnificus* from environmental and seafood samples (Dutta et al., 2021; Mohamed Hatha et al., 2020). The main cause of antibiotic resistance in the genus *Vibrio* is the excessive and indiscriminate use of antibiotics in human agricultural and aquaculture systems (Cabello, 2006).

A meta-analysis of antibiotic-resistant marine bacteria isolated from marine bivalves revealed high resistance rates in *Vibrio* spp. to multiple antibiotics including carboxypenicillins (92%), glycopeptides (77%), first/second-generation cephalosporins (62%), lincosamides (83%), penicillins (83%), polypeptides (72%), rifamycins (84%), and macrolides (57%) (Albini et al., 2022). Another study on bivalves

from California (USA) showed a predominance of phenotypic resistance to ampicillin (47.27%) and cefoxitin (35.45%) (Hirshfeld et al., 2023).

Another opportunistic pathogen causing a range of infections and widespread in various aquatic environments, including freshwater and marine ecosystems are *Aeromonas* species. The genus *Aeromonas* is a type of bacteria that can be found in various water sources, including irrigation water, river water, brackish water, freshwater, spring water, surface water and groundwater, estuarine and seawater, and chlorinated and non-chlorinated drinking water (Kivanc et al., 2011). Recently, the human pathogenicity of *Aeromonas* spp. has been increasingly detected, causing septicaemia, wound infections, diarrhoeal diseases and severe respiratory disease (Batra et al., 2016). Humans are exposed through drinking contaminated water, ingestion of raw or improperly cooked contaminated food, and close contact with infected animals (Hoel et al., 2019; Igbinosa et al., 2012).

Understanding the prevalence and mechanisms of AMR in *Aeromonas* spp. present in coastal and marine waters is critical for assessing the potential impact on public health. In marine bivalves, Albini et al., (2022) observed that *Aeromonas* spp. have very high resistance to rifamycin (89%) and first/second generation cephalosporins (75%), and complete resistance to penicillin.

Similar results were found in a study on antibiotic resistance in *Aeromonas* spp. in *Mugil cephalus* (flathead grey mullet) from the Mediterranean Sea. All tested strains were completely resistant to ampicillin, penicillin, and sulfamethoxazole-trimethoprim (100%) and highly resistant to oxytetracycline (90%), with a considerable percentage of resistance (62.22%) to streptomycin (Eid et al., 2022).

One of the most worrying facts about these two genera is that in comparison to other species of terrestrial origin (e.g. *E. coli* or *Salmonella* spp.), there is evidence that *Vibrio* spp. and *Aeromonas* spp. are the major reservoirs of AMR in coastal waters (Albini et al., 2022; Eid et al., 2022; Gabashvili et al., 2022; Jeamsripong et al., 2022; K. Liu et al., 2019). This makes surveillance of these species essential when combating the spread of AMR.

7.4.2. *Escherichia coli* and *Salmonella* spp.

This section will address antibiotic resistance in common human and animal gut bacteria that have been detected in coastal/marine waters or tissues of fauna living there. In particular, it will focus on *Escherichia coli* (Pseudomonadota: Enterobacteriaceae) and *Salmonella* spp. (Pseudomonadota: Enterobacteriaceae), which are bacteria commonly used as indicators of faecal contamination in environmental waters or as sanitary indicators in food of animal origin intended for human consumption (Directive (EU) 2020/2184; Directive 2006/7/EC; Regulation (EU) 2016/429; Commission Regulation (EC) No 2073/2005).

Escherichia coli is a bacterial species widely distributed in the gut of warm-blooded mammals (humans, livestock, domestic animals and wildlife) (Kaper et al., 2004; Savageau, 1983). That is precisely why, it has been extensively used as an indicator of faecal pollution in water (Denissen et al., 2021; Hubbart et al., 2022; Islam et al., 2021; Manzanas et al., 2023; Masindi & Foteinis, 2021; Nowicki et al., 2021; Petculescu et al., 2022; Sruthi et al., 2023; H. Wang et al., 2022; Wen et al., 2020).

One of the main reasons for studying AMR in *E. coli* is the fact that these bacteria are significant carriers of ARGs and therefore relevant contributors to AMR spread (Collis et al., 2022; dos Anjos Adur et al., 2022; Jalil et al., 2023; Rafiq et al., 2022; Xedzro et al., 2023; Y. Zhou et al., 2022). Although in most developed countries wastewater is treated before being discharged back into the environment, WWTP effluents are still heavily contaminated with antibiotic-resistant *E. coli* (Coleman & Smith, 2014). Water released from WWTPs travels down rivers and into coastal waters, contaminating areas where fisheries and aquaculture sites are located (Peterson, 2021). That is why resistant *E. coli* is widely studied in seafood (Albini et al., 2022; Giacometti et al., 2021; Jeamsripong et al., 2022). For instance, in shellfish farms in Thailand, *E. coli* isolates detected were mainly resistant to ampicillin (39%), tetracyclines (36%) and multi-drug resistant (25%) (Jeamsripong et al., 2022). Another recent study on antibiotic resistance in marine bivalves from Italy found that for *E. coli* the most commonly observed resistances were towards ampicillin (56%), streptomycin (52%), sulphonamides (30%) and ceftiofur (24%) (Giacometti et al., 2021). High levels of resistance are also found in aquatic samples. Seawater has been detected as a relevant reservoir of antibiotic resistance in *E. coli,* the study showed the most

prevalence resistance toward streptomycin (83-100%), tetracycline (48%) and cephalothin (42%) (Alves et al., 2014). In coastal sediments from Kuwait, *E. coli* resistance patterns to five antibiotics tested showed resistance to ampicillin (95%), cefpodoxime (67%), ciprofloxacin (50%) and ceftriaxone (41%) (Al-Sarawi et al., 2022).

Salmonella is a highly diverse bacterial genus that can be found in both human and animal intestinal tracts. These bacteria are prevalent in water, soil, and food (Talib et al., 2022). In 2021, salmonellosis was the second cause of zoonoses in the European Union (EU), there were 60,050 confirmed cases, 14.3% more than in 2020 (EFSA & ECDC, 2022).

The classification of the genus *Salmonella* is complex. In practice, only one species of *Salmonella* is considered: *Salmonella enterica*. This species has 2,400 serovars or serological variations (Talib et al., 2022; Tortora et al., 2007). Five serovars are identified as the most relevant for human infections: *Salmonella enteritidis* (54.6%), *Salmonella typhimurium* (11.4%), monophasic *Salmonella typhimurium* (8.8%), *Salmonella infantis* (2.0%) and *Salmonella derby* (0.93%) (EFSA & ECDC, 2022).

Most cases of salmonellosis are caused by the consumption of contaminated food (eggs, milk, meat, vegetables, raw meat/seafood etc.) (Talib et al., 2022). The most common is the development of enteric disease, causing symptoms such as stomach pain, fever, nausea, vomiting and diarrhoea, but in case of complications, septicaemia and death can occur (*Salmonella* | *EFSA*, 2022). In some cases, salmonellosis can have long-term consequences, such as chronic arthritis, appendicitis, irritable bowel syndrome, meningitis and pneumonia (*Salmonella* | *EFSA*, 2022).

Similar to *E. coli*, *S. enterica* reaches different aquatic systems (rivers, lakes, coastal waters, etc.) via waste streams containing animal and human faecal residues (Baudart et al., 2000; H. Liu et al., 2018).

Results on the prevalence of antibiotic resistance in *S. enterica* from bivalves or seawater samples vary between studies. For instance, in their study, Giacometti et al. (2021) reported that among the 102 *S. enterica* isolates, a total of 83 isolates (81.37%) showed resistance to, at least, one antimicrobial agent and 45 isolates (44.12%) were multidrug resistance (MDR). The most common resistances in *S. enterica* isolates

were streptomycin (58.8%), ampicillin (52%) and tetracyclines (45.1%) (Giacometti et al., 2021). However, in a recent meta-analysis Albini et al, 2022 concluded that the prevalence of antibiotic resistance is low, it was serovars-specific. A high prevalence of resistance for first/second-generation cephalosporins (60%), tetracyclines (47%), nitrofurans (35%), and quinolones (22%) (Albini et al., 2022). Another study on the Sicilian coast also observed a low prevalence of *S. enterica* (1.7%) and a low incidence of phenotypic resistance in *S. enterica* (Gambino et al., 2021).

7.5. Antimicrobial resistance and other relevant public health threats

7.5.1. Antimicrobial resistance and climate change

The issue of climate change is a global concern that has a significant impact on human health (WHO, 2021b). The effects of climate change are diverse and include heat-related deaths, food insecurity, increased transmission of infectious diseases, cardiovascular morbidity, and mortality related to wildfires (Watts et al., 2021). However, the relationship between climate change and antibiotic-resistant infections remains understudied. Hence, further research is necessary to understand the intersection between these two critical challenges (Burnham, 2021).

Climate change is triggering AMR in multiple ways (Burnham, 2021). For instance, warmer temperature increases HGT, which is the main mechanism of resistance transmission (von Wintersdorff et al., 2016). In addition, the physiological response of microorganisms to heat stress is similar to the response to certain antibiotics. As a consequence, the resistance to heat stress may confer resistance to some antibiotics (Rodríguez-Verdugo et al., 2020). A recent study suggests that there is a significant increase in resistant strains for every 10°C increase in minimum temperature in the US (223 facilities in 41 states) (MacFadden et al., 2018). Specifically, 4.2%, 2.2% and 2.7% for *E. coli*, *K. pneumoniae* and *S. aureus* respectively (MacFadden et al., 2018). Over 17 years, a study conducted across 28 European countries found similar results (McGough et al., 2020).

It is well-recognised that changes in temperature and precipitation have a crucial impact on food and waterborne diseases (Mora et al., 2022). Nevertheless, causative agents such as mosquitoes can also affect the habitat distribution of vector-borne diseases. For example, mosquitoes are more ubiquitous due to climate change, and therefore, they are more likely to transmit infectious pathogens to more people including resistant pathogens (Caminade et al., 2014).

In addition to the direct effects of climate change, it can also contribute to the spread of ARB indirectly (Burnham, 2021). For example, extreme weather events such as drought or flooding increase the risk of waterborne infectious diseases (Yavarian et al., 2019). Extreme precipitation can cause an overflow of sewage from sanitation systems, spreading ARGs, ARBs and pollutants throughout the environment (Ahmed et al., 2021; Ratajczak et al., 2010). These meteorological phenomena are also linked to overcrowding of people in non-flooded or less flooded areas which facilitates the transmission of infectious pathogens including ARB (Yavarian et al., 2019).

7.5.2. Antimicrobial resistance and pollution

The relationship between pollution and AMR is complex and has consequences for both human health and the environment (Landrigan et al., 2018). Pollution provides an ideal breeding ground for the evolution and spread of AMR, which poses a significant public health concern (EFSA Panel on Biological Hazards (BIOHAZ) et al., 2021). Additionally, contaminants like heavy metals can lead to the onset of various non-communicable diseases (NCDs) in humans and animals. Furthermore, contaminants can contribute to the proliferation and spread of coastal pathogens. This issue is discussed in more detail in chapter 6 of this report.

One crucial mechanism that influences the development and spread of antibiotic resistance in microbial communities is co-selection (Pal et al., 2017). The mechanisms underlying this phenomenon are detailed in section 6.2.4.1. Exposure to pollutants, including heavy metals and biocides, can lead to the development and spread of antibiotic resistance in microbial communities. The widespread use of non-antibiotic substances applies selective pressure on bacteria, allowing the survival and proliferation of strains with intrinsic or acquired resistance traits. This phenomenon

increases the resilience of bacteria making them adept at not only the pollutants but also antibiotics crucial for human and animal health (UNEP, 2023).

Moreover, the role of plastics in the dissemination of AMR adds another layer to this complex issue. Plastics, ubiquitous in our environment, act as both a source and a carrier of ARGs. Microorganisms can colonise the surfaces of plastic waste, creating hotspots for the exchange of resistance genes (Y. Liu et al., 2021; Meng et al., 2021; J. Wang et al., 2021). Additionally, the persistent nature of plastics allows them to accumulate in water bodies, becoming reservoirs for AMR dissemination (Y. Liu et al., 2021).

It is imperative to recognise that the fate of AMR is inextricably linked to the health of our ecosystems, emphasising the urgency of mitigating pollution and embracing sustainable practices to safeguard both human health and our environment.

7.5.3. Antimicrobial resistance and the COVID-19 pandemic

One of the biggest public health events in recent history is the COVID-19 pandemic caused by the SARS-CoV-2 virus (WHO, 2020b). Even though the first cases were reported in Wuhan (China), in a very short time a global pandemic was declared due to the COVID-19 outbreak on March 11 2020 by the WHO (WHO, 2020b, 2020a). The main reasons for this declaration were due to the size, infection speed and severity of the problem (WHO, 2020b). Emergency measures were put in place worldwide to combat the virus, including lockdowns, social distancing and the mandatory use of masks in many places (Ayouni et al., 2021). All these actions generated huge pressure on healthcare settings, completely overturning their functions and priorities, which inevitably also affected other health issues such as AMR (Knight et al., 2021; Lobie et al., 2021; Lucien et al., 2021). Consequently, during this period, the coronavirus had both effects, direct and indirect, on the use of antibiotic therapies and AMR spread-related behaviours:

> *(1) Direct effects:* antibiotics were used extensively in COVID-19 patients at the beginning of the pandemic. At the beginning of the pandemic, more than 70% of patients with coronavirus received antibiotics (Langford et al., 2023). There were two main reasons for the use of antibiotics: (1) the symptoms of COVID-

19 resembled those of bacterial pneumonia (Knight et al., 2021) and (2) more than half of the patients who died from COVID-19 also had secondary bacterial infections (Chen et al., 2020; da Costa et al., 2022). Therefore, healthcare professionals (particularly at the beginning of the pandemic) prescribed antibiotics as a preventive measure. However, the rate of confirmed bacterial coinfections was very low (1-10% according to estimates) (Rawson et al., 2020; F. Zhou et al., 2020).

(2) Indirect effects: there are multiple examples of how the pandemic has indirectly altered patterns of antimicrobial use and AMR. Below some of the most relevant are described:

(2.1) The disruption of antibiotic manufacturing and transport. As a consequence, during the pandemic, the use of broad-spectrum antibiotics increased in the absence or shortage of specific or recommended antibiotics (Lucien et al., 2021).

(2.2) Prolonged hospital stays and invasive interventions required in patients with COVID-19, may have promoted the risk of acquiring resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA), which are common in hospital settings (Despotovic et al., 2020; Kariyawasam et al., 2022; Opatowski et al., 2021).

(2.3) Permanent sequelae (e.g. lung damage in patients recovered from coronavirus) required prolonged antibiotic therapy in some patients, favouring the development of AMR (Augustine & Bonomo, 2011).

(2.4) Social distancing significantly reduced the transmission of resistant pathogens in schools, leisure centres or workplaces (Brueggemann et al., 2020); however, an increase in the transfer of resistant bacteria between household members was observed (Maillard et al., 2020).

COVID-19 is also believed to have led to changes in healthcare-seeking behaviour (Arora & Grey, 2020), as it seems that the pandemic contributed to prescribing antibiotics through phone calls (Han et al., 2020). Although the total number of face-

to-face medical appointments decreased significantly in 2020, the number of antibiotic prescriptions was 6.71% higher than expected (Armitage & Nellums, 2021).

In addition, the excessive use of different types of biocides (for disinfection) in households and hospitals, and their subsequent release into the environment, may have led to an increase in antibiotic resistance (Rezasoltani et al., 2020).

The resulting impact of the COVID-19 pandemic on antimicrobial resistance is still unclear (van Duin et al., 2020). Experts caution against the need to highlight the synergistic and multiplicative impacts on AMR management practices to prevent and control COVID-19 (WHO, 2021c, 2021d).

7.6. Conclusions

Antimicrobial resistance is a major global health concern. It is estimated to be one of the leading causes of death worldwide. This problem is extremely complex and cannot be addressed independently of other global threats such as pollution and climate change. Therefore, it is necessary to tackle the issue from multiple angles to promote global multi-perspective actions under a broad One Health approach that allows collaboration between different disciplines and sectors.

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CHAPTER 8

The case of *Vibrio*

Chapter 8. The case of *Vibrio*

8.1. Introduction

Vibrio is one of the most abundant genus of Gram-negative bacteria found naturally in coastal waters and is a fundamental part of the marine microbiome, where some of its roles are crucial for the correct functioning of the marine and coastal ecosystem (Sampaio et al., 2022). However, some *Vibrio* species can cause severe infections in humans and other *Vibrio* species can cause severe infections in many marine organisms (Baker-Austin et al., 2018). Moreover, there is evidence that during the last decade, infections are on the rise globally due to many reasons (Vezzulli, 2023). The coastal aquatic environment is especially vulnerable to many global anthropogenic changes (GACs) like climate change and pollution. Since *Vibrio* naturally inhabits the coastal aquatic environment, these GACs have complex effects on the ecology and physiology of *Vibrio*, being one of the main causes behind the rise of *Vibrio* infections globally.

The purpose of this chapter is to (i) identify and analyse the interaction mechanisms or cause-effect processes by which climate change and pollution influence infectious diseases related to *Vibrio,* and (ii) propose and explore how a model based on the Driving Force–Pressure–State–Exposure–Effect–Action (DPSEEA) framework can help in the analysis of these complex interactions. To achieve this objective, the chapter has been organized into six sections. The first analyses the ecology of *Vibrio* and the main environmental parameters that govern the ecology of *Vibrio*: habitat, environmental reservoirs, environmental preferences, association with other organisms, etc. The second and third sections identify and discuss the main mechanisms of interaction by which climate change and pollution alter the ecology of *Vibrio* and how this is associated with *Vibrio infections*. The fourth section identifies and summarises the similarities in the interaction mechanisms. The fifth section analyses the main health impacts and health inequalities of *Vibrio* infections in humans distinguishing between cholera and vibriosis and the main routes of transmission. Lastly, the sixth section proposes a DPSEEA model for *Vibrio* infections.

8.2. The ecology of *Vibrio*

Vibrio is one of the most abundant heterotrophic bacteria found widely distributed in natural aquatic environments from freshwater, and estuarine to coastal aquatic environments. They naturally inhabit all ocean environments, with some species particularly adapted to coastal waters due to the low salinity and higher temperature conditions (Johnson et al., 2012). *Vibrio* proliferation and physiology are strongly governed by environmental parameters, proliferating immediately when environmental parameters such as temperature, salinity, and dissolved oxygen are favourable (Sampaio et al., 2022).

The abundance and density of *Vibrio* in the water are mainly related to temperature. They cannot grow outside of a certain temperature window and when the temperature is optimal, they proliferate abundantly (Jacobs et al., 2015). Studies show an exponential relationship between the growth rate and an increase in temperature in some species of *Vibrio* (Kirschner et al., 2008). In addition to temperature, salinity is one of the main environmental parameters intrinsically associated with the abundance and distribution of *Vibrio* (Vezzulli et al., 2015). The growth of different *Vibrio* species is then mainly affected by specific salinity and temperature ranges. However, in tropical waters, where temperature and salinity do not vary much throughout the year, other factors such as nutrients, dissolved oxygen, phytoplankton and zooplankton abundance gain more importance (Padovan et al., 2021).

Vibrios are ecologically very relevant since they play an important role in nutrient cycling in coastal aquatic environments by taking up dissolved organic matter and remineralising it (Zhang et al., 2018). Moreover, *Vibrio* has been observed to provide essential polyunsaturated fatty acids (e.g. Omega-3) to the aquatic food web (Estupinan et al., 2020).

Regarding their habitat, vibrios can be found in the coastal aquatic environment in several ways. These include i) a free-living way suspended in the water, ii) attached forming biofilms in the sediments, on rocks or the surfaces of marine coastal organisms and iii) in association with marine coastal organisms in their gut microbiota, sometimes just temporally until they are excreted or sometimes longer time with more complex relationships (Sampaio et al., 2022). When physical-chemical conditions

such as high temperatures and nutrient abundance are optimal, vibrios can grow and proliferate naturally since they can obtain nutrients from organic matter dissolved in the water or from particulate matter. Then, they are naturally found living freely in the water column in the coastal aquatic environment (Bernáldez-Sarabia et al., 2021). When physical-chemical conditions are not favourable, and they cannot grow and proliferate naturally due to a lack of nutrients or low temperature, they employ different survival and growth strategies. They can associate with marine coastal organisms to seek shelter and food sources or persist in the environment by colonization of biotic or abiotic surfaces and subsequent biofilm formation. The abiotic surfaces they can possibly attach to are sediments and rocks or solid surfaces of anthropogenic industrial origin like microplastics (Kirstein et al., 2016). The biotic surfaces they can attach to are for example the exoskeleton rich in chitin, a carbohydrate, of some marine coastal organisms that they use metabolically as a food source. *Vibrio cholerae*, for example, has been found to form tight associations with copepods (small crustaceans) and to form biofilms on their body surfaces that have a chitin-rich exoskeleton (Huq et al., 1983). Moreover, there is evidence that living within these biofilms is highly beneficial for them. It can cause them to become more infectious and virulent than when free-living (Silva & Benitez, 2016) since in the biofilm environment horizontal gene transfer (HGT) is increased and favoured.

Vibrio can be found in commensal, mutualistic or parasitic symbiotic relationships with marine coastal organisms from the microscopic ones like phytoplankton and zooplankton to the macroscopic ones like fish, shellfish and crustaceans (Takemura et al., 2014). Among the several marine coastal organisms that have been found to be in association with *Vibrio*, special attention must be paid to the plankton community, both phytoplankton and zooplankton. Several studies have shown that *Vibrio* can be found attached and in association with micro- and macroalgae and with phytoplankton (Main et al., 2015; Rehnstam-Holm et al., 2010). Phytoplankton produces dissolved organic matter and polymeric substrates during photosynthesis that *Vibrio* uses as a food source, providing a nutrient-rich environment. Moreover, dead or live phytoplankton cells and particles can act as surfaces for biofilm formation, providing protection and giving access to nutrients. All in all, phytoplankton has been suggested as one of the main environmental reservoirs for *Vibrio* (Sampaio et al., 2022).

Chitin-rich copepods among the zooplankton represent one of the main reservoirs for *Vibrio* due to the combination of copepods´ feeding behaviour, surface attachment and subsequent biofilm formation and intestinal colonization (Huq et al., 1983; Rawlings et al., 2007). In addition to the body surface colonization and subsequent biofilm formation, since copepods are filter feeders and consume a variety of particles, including bacteria and algae, while they actively feed on suspended particles in the water column, they ingest *Vibrio* bacteria present in the surrounding water. Once ingested by copepods, *Vibrio* bacteria can colonize their digestive system. The copepod´s intestines provide a favourable environment for their growth as they offer nutrients and protection from external stresses.

Furthermore, copepods and other species of zooplankton have been suggested to act as vehicles and carriers of *Vibrio* through long distances in the coastal area by ocean currents, transporting *Vibrio* species with them and transporting them to distant regions and habitats (Martinez-Urtaza et al., 2012).

In summary, *Vibrio* can be found in the aquatic environment in a free-living state in the water column, attaching and forming biofilms on several biotic and abiotic surfaces and in association with other organisms in commensal, mutualistic or parasitic symbiotic relationships (Fig. 8.1).

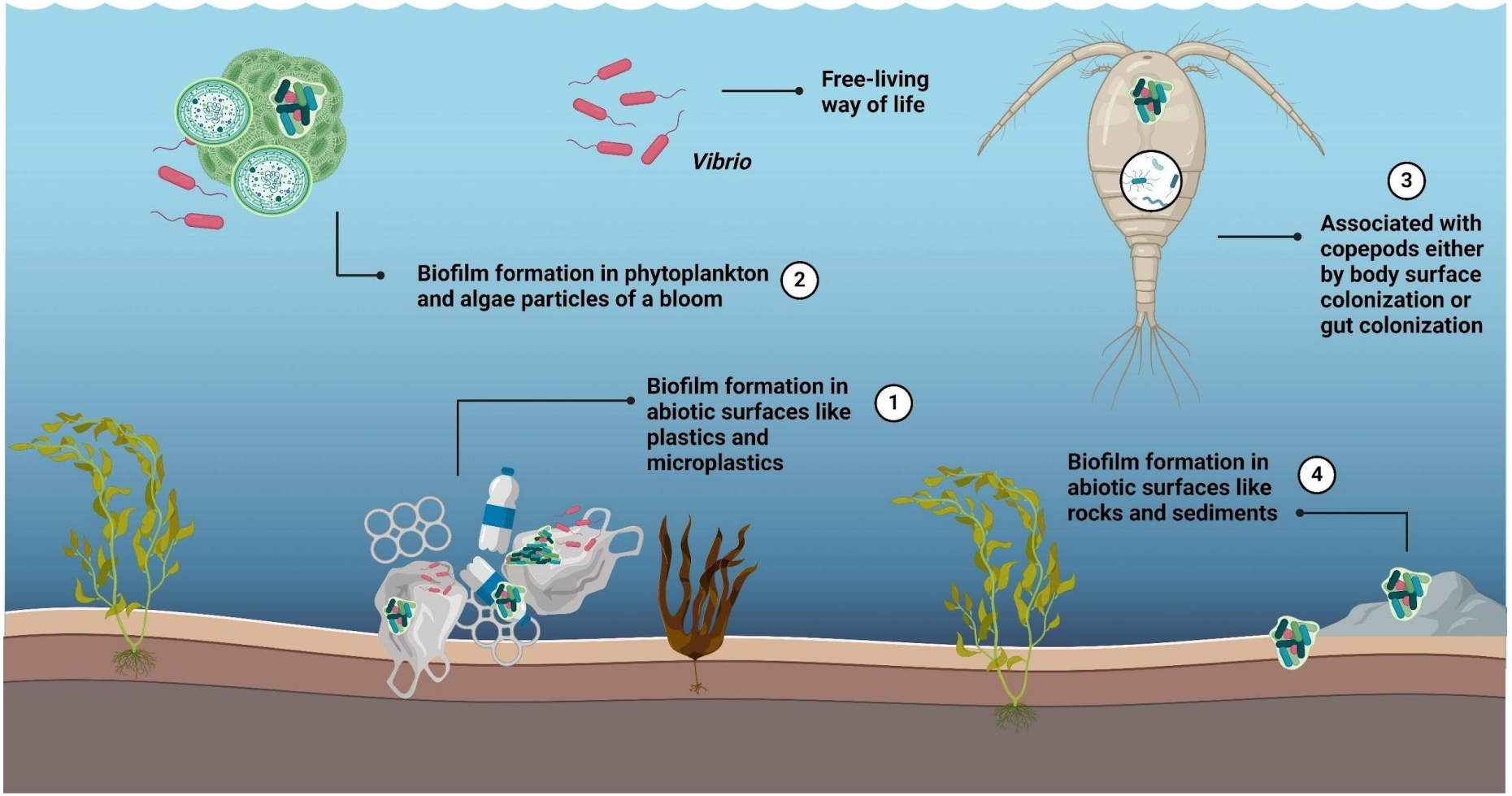


Fig. 8.1. States in which *Vibrio* can be found in the coastal aquatic environment. Created with Biorender.com

8.3. Climate change and *Vibrio*

Global climate change is one of the most visible and concerning global anthropogenic changes that the coastal ecosystem is subjected to (Toimil et al., 2020). The correct functioning of the coastal aquatic ecosystem is directly related to the environmental parameters such as the sea surface temperature, the pH and salinity of the water. *Vibrio,* as part of the coastal aquatic ecosystem, is subjected to many changes and impacts of climate change. There is substantial evidence in the literature that *Vibrio* infections are increasing worldwide with climate change and this is why it has been considered in the literature as a "microbial barometer" of climate change (Baker-Austin et al., 2017).

One of the mechanisms by which climate change influences *Vibrio* infections is through altering the environmental parameters that increase the abundance and distribution of *Vibrio*. If climate change leads to a higher abundance of *Vibrio*, this automatically leads to higher exposure of the hosts to the pathogen and an increase in the number of infections. At the same time, climate change can affect the behaviour of the host. For instance, in the case of humans, hot summers are expected to make people use the coastal zone for bathing and recreational activities more often. Therefore, there will be more humans in the water available to get exposed and infected by *Vibrio*.

The main environmental parameters that alter the distribution and abundance of *Vibrio* are extreme weather events, temperature, salinity, ocean acidification and the ecological state of the environmental reservoirs of *Vibrio*. Changes in global weather patterns due to climate change and the El Niño-Southern Oscillation have been suggested as important drivers in the abundance and spread of some *Vibrio* species, like *V. cholerae* (Moore et al., 2017). Along with El Niño-Southern Oscillation, other extreme weather events including heat waves and hurricanes have also been associated with an increased risk for vibriosis infections (Rhoads, 2006).

Moreover, ocean warming and reduced salinity due to increased precipitations or flooding in the coastal waters due to climate change have long been associated with geographic expansion and increased cases of *Vibrio* infections (Baker-Austin et al., 2012). An example of this, is the increase in *Vibrio* infections in humans in Northern

European countries around the Baltic Sea (Vezzulli et al., 2016; Amato et al., 2022), during the last decades and in other European countries like Spain (Martinez-Urtaza et al., 2005), France (Deter et al., 2010), and Portugal (Santos et al., 2017). Pathogenic species of *Vibrio* were not detected in these geographical areas until very recently and most infections are caused by swimming in coastal waters during hot summers and heat waves. All in all, there is evidence to state that the geographical shift observed in the last decades is directly linked with climate change and ocean warming that increases the suitability and distribution of pathogenic *Vibrio* species at higher latitudes.

Temperature is an important factor in the abiotic and biotic surface colonization and subsequent biofilm formation of *Vibrio*. *Vibrio* attaches and forms biofilms on the body surface of some marine organisms. There is evidence that higher temperature increases the persistence of *Vibrio* in the aquatic environment by promoting colonization of biotic surfaces of zooplankton especially in the case of copepods by influencing the expression of proteins that help the *Vibrio* to better adhere and attach (Stauder et al., 2010) (Fig. 8.2). Therefore, the attachment of *Vibrio* bacteria to copepods facilitated by higher water temperatures due to climate change increases the abundance, survival, and transmission of *Vibrio.*

Since phytoplankton and zooplankton are one of the main reservoirs of *Vibrio*, alteration in the state of their abundance and diversity by environmental parameters affected by climate change will have effects on the abundance and distribution of *Vibrio*. It has been observed that ocean warming, ocean acidification, eutrophication from agricultural runoff and extreme weather events have increased the frequency and abundance of phytoplankton and algal blooms (Gobler et al., 2017; Trainer et al., 2020; Wells et al., 2015). These blooms are favourable for *Vibrio* for several reasons: (i) a high quantity of nutrients, especially nitrogen and phosphorus, is available providing an abundant food source, (ii) there is an increase in the availability of surfaces for bacterial attachment and biofilm formation, (iii) the dense and complex structure of the bloom provides shelter and protection providing a physical barrier against predation and other environmental stresses.

Another mechanism by which climate change influences *Vibrio* infections is by increasing *Vibrio* virulence and its antimicrobial resistance (AMR) profile (Fig. 8.2). In

pathogenic bacteria like *Vibrio*, changes in environmental parameters, such as temperature, nutrients, pH, and oxygen levels are the most common environmental signals to express virulent factors. Among them, temperature changes are one of the most frequently used environmental signals (Konkel & Tilly, 2000). *Vibrio coralliilyticus,* a *Vibrio* species that infect corals, for example, presents temperature-dependent virulence whereby at higher temperatures genes involved in its virulence are up-regulated and consequently, there is more expression of proteins involved in its virulence (Ben-Haim et al., 2003; Kimes et al., 2012) (Fig. 8.2). This has also been observed in *Vibrio anguillarum*, a *Vibrio* species related to infections in some fish species (Lages et al., 2019). In the case of *V. vulnificus*, temperature has also been identified along with iron availability as one of the two main external signals to express its virulence (Hernandez-Cabanyero et al., 2020; Oh et al., 2009). In the case of *V. parahaemolyticus*, temperature up-regulates genes involved in its virulence and adhesion and biofilm formation on abiotic surfaces like microplastics (Billaud et al., 2022). Therefore, temperature increase by climate change will facilitate the adhesion and biofilm formation of some *Vibrio* species to microplastics and other surfaces increasing their environmental persistence, distribution, and virulence. Temperature also increases *Vibrio* virulence and AMR profile by increasing HGT (Fig. 8.2). Temperature accelerates the frequency of HGT of virulence factors and antibiotic resistance genes (ARGs) in bacteria by increasing the transfer rate of plasmids (MacFadden et al., 2018). Moreover, thermal stress due to high temperatures activates stress response pathways that induce the expression of genes involved in HGT (Fuchsman et al., 2017). Although this has only been proven for some bacteria, *Vibrio* is expected to show similar results.

The final mechanism by which climate change influences *Vibrio* infections is by increasing host susceptibility, both for humans as well as marine organisms. Host health status is one of the main factors determining the susceptibility to any infectious disease. Climate change may influence host health status in different ways. One of them is by altering and diminishing the immune system and the capacity of the host to fight against infections of *Vibrio* (Fig. 8.2). It has been suggested that one of the reasons for the increasing disease burden from infectious diseases in humans is closely linked with the effects of global anthropogenic changes on immune functions (Martin et al., 2010).

Moreover, the immune system has been proposed *"as an interface across which many climate change-sensitive exposures will affect health outcomes"* (Swaminathan et al., 2014). Global temperature increase exerts thermal pressure and stress on marine organisms leading to thermal stress-induced immunosuppression and consequent susceptibility to opportunistic pathogens like *Vibrio* (Mason, 2021; Neuman et al., 2016). For example, it is known that corals bleach in response to different environmental stresses (Yee & Barron, 2010). Long-term exposure to high temperatures leads to physiological stress in corals increasing the frequency of opportunistic pathogens like *Vibrio* (Munn, 2015; Rubio-Portillo et al., 2014; Vezzulli et al., 2010) (Fig. 8.3). The most well-known species involved in coral bleaching at high temperatures are *Vibrio coralliilyticus* (Gibbin et al., 2019) and *Vibrio shiloi* (Rosenberg & Falkovitz, 2004).

Concerning *Vibrio* infections in humans, the human gut microbiome has been found to play a key role in preventing and resisting infections by pathogens like *Vibrio*. The human gut microbiome helps maintain the host health status and provides resistance to pathogen colonization and fighting infectious diseases, including diseases from some species of *Vibrio* (Barrasso et al., 2022; Sun et al., 2022; Midani et al., 2018).

Changes in the environmental parameters by climate change such as temperature increase, ocean acidification increase, and changes in the concentration of dissolved oxygen can act as stressors affecting the gut microbiome of certain marine organisms. For example, low pH, low dissolved oxygen, and increased temperature alter the microbial community of the microbiome of marine mussels towards pathogen-dominated microbial communities and increase susceptibility to pathogen invasion such as *Vibrio* (Khan et al., 2021) (Fig. 8.2). It has also been observed in some species of fish, where an increase in the temperature was associated with an increase in *Vibrio* numbers in the gut microbiome (Neuman et al., 2016). Therefore, *Vibrio* can be part of the resident gut microbiome of some marine organisms in small quantities that do not cause disease. However, changes in environmental parameters in the coastal waters can induce the growth and invasion of *Vibrio* in the gut microbiome of marine organisms increasing the probability of infection.

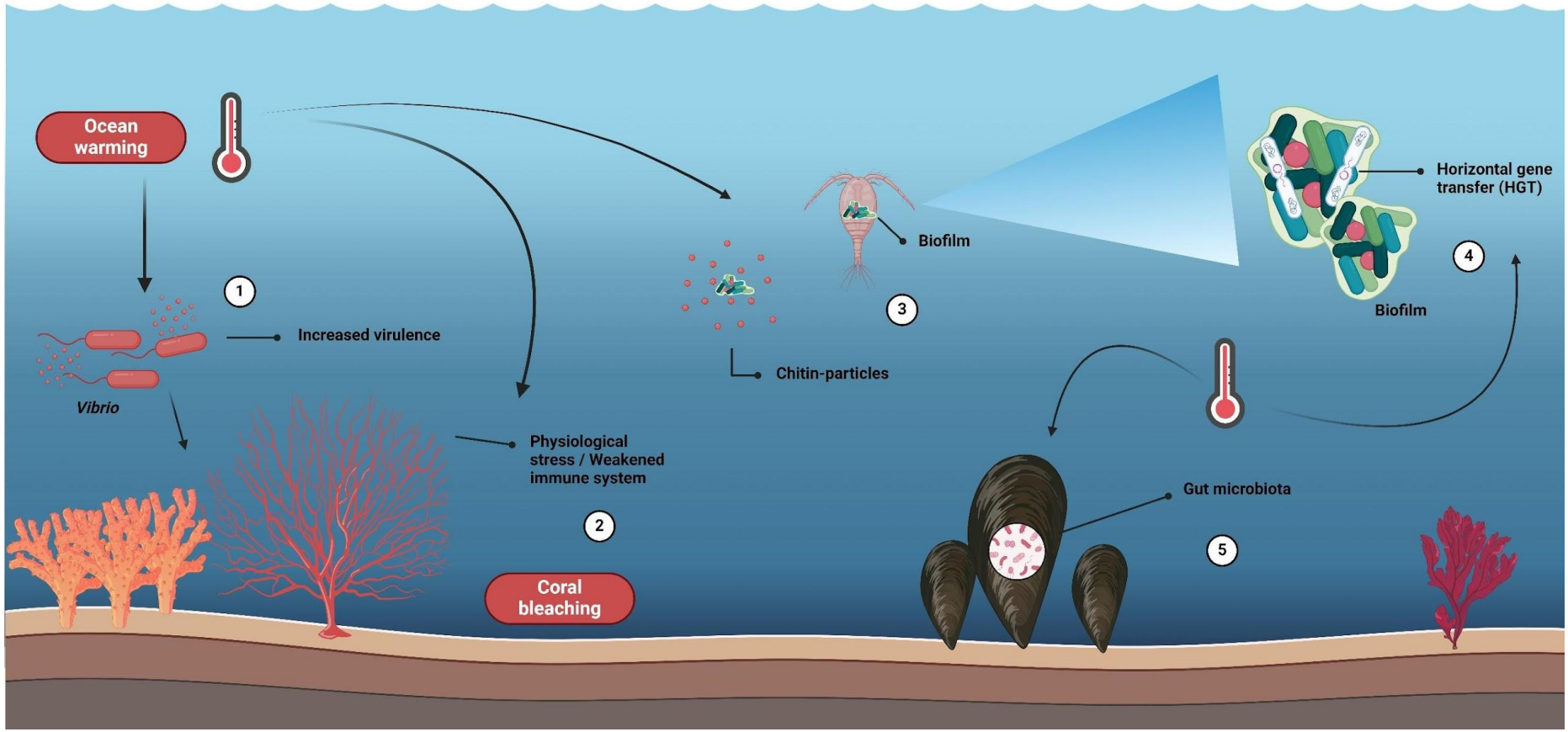


Fig. 8.2. Effects of ocean warming caused by climate change in *Vibrio* infections. A temperature increase in the coastal waters affects *Vibrio* infections in several ways; **(1)** it increases *Vibrio* virulence by up-regulating genes involved in virulence. *V. coralliilyticus* has been observed to present temperature-dependent virulence when infecting corals; **(2)** it produces physiological stress in corals and other marine organisms causing a more weakened immune system and therefore making them more susceptible to infections; **(3)** it increases the ability of *Vibrio* to form biofilms on various surfaces like chitin-particles and body surface of copepods by increasing the expression of proteins involved in adhesion and attachment; **(4)** an increase in temperature has also been observed to promote HGT within the biofilms that are formed and therefore increase the virulence and resistance profile of *Vibrio*; **(5)** ocean warming alters the microbial community of the gut microbiota of marine mussels and other marine organisms towards pathogen-dominated microbial communities and increases susceptibility to pathogen invasion such as *Vibrio***.** Created with Biorender.com.

8.4. Pollution and *Vibrio*

Because of massive population growth and industrial activity increase, large amounts of newly manufactured and synthetic materials have been developed and released into the environment (Hatje et al., 2021). The coastal aquatic environment is one of the most polluted environments in the world (Vikas & Dwarakish, 2015). Therefore, along with climate change, pollution is one of the main anthropogenic global changes that the coastal aquatic environment is subjected to.

One of the mechanisms by which pollution influences *Vibrio* infections is through altering the environmental parameters that increase the abundance and distribution of *Vibrio* (Fig. 8.3). Pollutants can change the physicochemical properties of coastal waters such as pH, and nutrient availability which can favour the growth and survival of *Vibrio* since there is more available food sources and more favourable conditions to grow. Eutrophication by organic pollutants and nutrients from agricultural runoffs and sewage water severely affects coastal ecosystems (Vigiak et al., 2023) and leads to algal blooms, which can provide a favourable environment for *Vibrio* to grow (Greenfield et al., 2017; Thickman & Gobler, 2017) (Fig. 8.3).

Another mechanism by which pollution influences *Vibrio* infections is through increasing its virulence and antimicrobial resistance (AMR) profile. Iron contamination has been observed to increase the virulence of some species of *Vibrio* like *V. cholerae* (Patel & Isaäcson, 1999). However, there are very few studies examining this link, highlighting a knowledge gap in this topic.

Regarding the AMR profile of *Vibrio*, the increase in antibiotic contamination in aquaculture settings and wastewater treatment plants (WWTPs), has led to an increased AMR profile in *Vibrio* (Elmahdi et al., 2016; Pan et al., 2013; Sahilah et al., 2014). WWTPs are considered giant reservoirs of AMR bacteria and *Vibrio* (Mohammadali & Davies, 2017; Mukherjee et al., 2021) since they collect sanitary and domestic sewage that has a high concentration of antibiotics, human pathogens, high nutrient content and other pollutants (Lapointe et al., 2015; Rorat et al., 2019). Moreover, climate change is expected to increase precipitation in many regions, which puts more pressure on wastewater infrastructure and will result in more frequent sewage water overflows (Giakoumis & Voulvoulis, 2023; Hughes et al., 2021),

promoting the growth of some species of *Vibrio* (Conrad & Harwood, 2022) and increasing their resistance and virulence profile.

Aquaculture settings that are mainly constructed in coastal areas have also been identified as hotspots for the spread of AMR *Vibrio* (Brunton et al., 2019) since all the antibiotic pollution that comes from inland and especially from the water that is released from WWTPs ends near these settings. Furthermore, in aquaculture settings, vibriosis is the most prevalent bacterial disease, then, antibiotics are widely overused to treat infections that cause disease in fish and shellfish (Fig. 8.3).

In addition to the antibiotics, several different pollutants promote the genetic transfer of ARGs and virulence genes in *Vibrio* through HGT and therefore contribute to the increase in the AMR and more virulent profile of *Vibrio*. There is evidence that organic pollutants such as polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs) (Chen et al., 2017), herbicides (X. Li et al., 2022), preservatives used in food and personal care products (Cen et al., 2020), commonly prescribed pharmaceuticals (Wang et al., 2020), natural sphalerite nanoparticles (G. Li et al., 2020), copper nanoparticles and ions (Zhang et al., 2019), placlitaxel (B. Yang et al., 2022) and chloroxylenol (Guo et al., 2022) promote HGT of plasmid-mediated ARGs. These studies are not related directly to *Vibrio*, but similar results are expected since the mechanisms of horizontal transfer of plasmid-mediated ARGs are quite conserved across the bacteria domain.

Another mechanism by which pollution influences *Vibrio* infections is by increasing host susceptibility. Pollutants can weaken and disturb the immune system of marine organisms and humans. Exposure to pollutants causes immunotoxic effects in marine organisms such as histological changes in immune system tissues and alteration or reduction of immune cells (Kataoka & Kashiwada, 2021). In marine bivalves, exposure to heavy metals, pesticides, PAHs, PCBs, polybrominated diphenyl ethers (PBDEs), pharmaceuticals and nanoparticles disrupt the immune system (Renault, 2015) (Fig. 8.3). In humans, air pollutants (Glencross et al., 2020; Tingskov Pedersen et al., 2023), heavy metals (Zheng et al., 2023), POPs (persistent organic pollutants) (Corsini et al., 2014) and several other pollutants disrupt the immune system.

Moreover, similar to climate change, pollutants also disrupt the healthy gut microbiome of marine organisms and humans, a key component in their capacity to fight and resist infections by *Vibrio*. Pesticides (Giambo et al., 2021), heavy metals (X. Li et al., 2019), microplastics (Qiao et al., 2019) phthalate esters (Deng et al., 2020) and endocrine disruptors (Mousavi et al., 2022) induce gut microbiome disruption in humans and marine organisms reducing pathogen colonization resistance to pathogens like *Vibrio*.

Special attention must be paid to plastics and microplastics. They offer an optimal surface for microbial colonisation and biofilm formation by *Vibrio. Vibrio* has been identified particularly in summer months to colonise plastics and microplastics (Caroline A. De Tendera, 2015; Du et al., 2022; Laverty et al., 2020). Since studies have shown that *Vibrio* is more likely to attach to microplastics in warmer temperatures special attention must be paid to the effects of warming due to climate change. Additionally, changes in precipitation patterns and storms caused by climate change could lead to increased runoff and flooding, which can increase the number of microplastics that can be colonized by *Vibrio* in coastal areas (Nakajima et al., 2022). Therefore, increased plastic pollution with continued warming and precipitation increase due to climate change amplifies the potential risk of exposure of humans and marine organisms to *Vibrio.* Moreover, HGT of virulence genes and ARGs occurs more frequently within microplastic biofilms than among free-living *Vibrio* (Laverty et al., 2020), causing some species of *Vibrio* such as *Vibrio vulnificus*, *Vibrio parahaemolyticus* and *Vibrio cholerae* to become more infectious and resistant than when free-living (Schulze et al., 2021). Consequently, microplastics represent a highly important environmental niche for the development, retention, and spread of antimicrobial-resistant *Vibrio*.

Moreover, there is evidence that microplastics disrupt the immune system of both marine organisms and humans (Bhuyan, 2022; Hirt & Body-Malapel, 2020; Sharifinia et al., 2020; W. Yang et al., 2022). Microplastics ingested by shellfish and fish will have detrimental and additive effects concerning *Vibrio* infections since, on the one hand, they will act as carriers of *Vibrio* and, on the other hand, they will make the host more immunocompromised and susceptible to infections (Fig. 8.3).

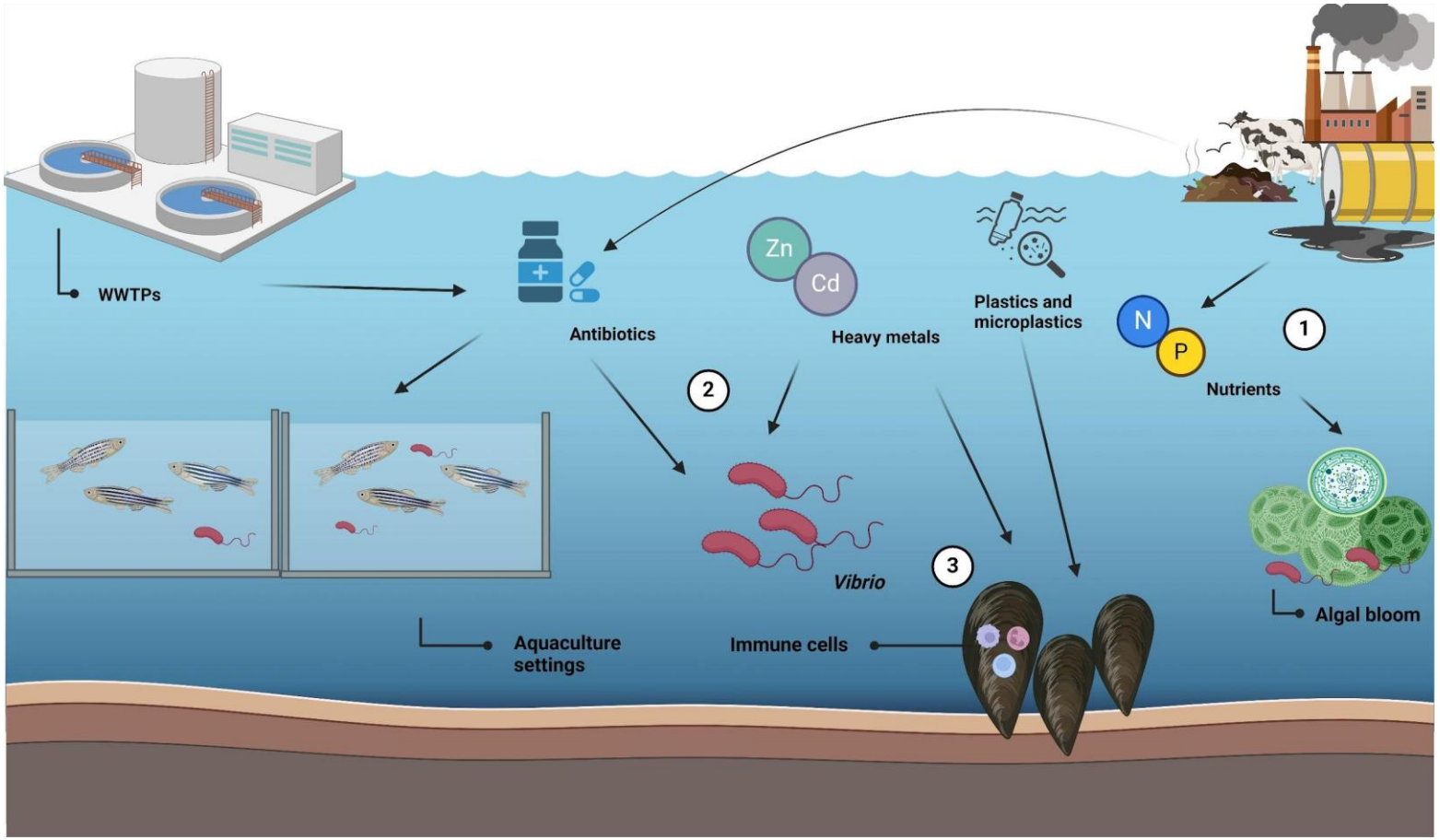


Fig. 8.3. Sources, distribution, and interactions of some pollutants with *Vibrio* infections. Many pollutants are released around the coast from industrial activity, agriculture, and wastewater treatment plants (WWTPs); **(1)** nutrients and organic pollutants that are released to the coastal waters from agricultural runoffs promote the growth of phytoplankton and algal blooms by a phenomenon called eutrophication. These blooms have been associated with an increase in the abundance and distribution of *Vibrio* since it provides a favourable environment for *Vibrio* to grow; **(2)** large amounts of antibiotics are released to the coastal waters from WWTPs and agricultural runoffs. Moreover, antibiotics are often overused in aquaculture settings to treat infectious diseases such as vibriosis. Consequently, the high pressure of antibiotic pollution coupled with other pollutants such as heavy metals that co-select for ARGs has led to an increased resistance profile in *Vibrio;* **(3)** several pollutants, among them heavy metals and microplastics, have been observed to produce immunotoxicological effects in many marine organisms making them more susceptible to *Vibrio* infections. Created with Biorender.com.

8.5. Similarities in mechanisms induced by climate change and pollution

The previous sections have discussed how climate change and pollution affect the coastal aquatic environment and how this influences *Vibrio* infections. In doing so, similar interaction mechanisms and processes have been identified for both climate change and pollution. These mechanisms can be summarized as follows.

The first mechanism identified is the alteration of the environmental parameters that increase the abundance and geographic distribution of *Vibrio*. An increase in the temperature and a reduction in the salinity in the coastal waters by climate change and an increase in nutrients by pollution likely will make some species of *Vibrio* proliferate and become more abundant and geographically distributed, interacting more with the host, such as humans and marine organisms and being environmentally more present to infect them (Fig. 8.4; 8.5).

The second mechanism is the increase in the virulence and AMR profile of *Vibrio*. A temperature increase caused by climate change and some pollutants can increase the mechanisms of virulence of *Vibrio*. Furthermore, temperature increase and several pollutants increase HGT leading to an increased virulence and resistance profile of *Vibrio* (Fig. 8.4; 8.5).

The third mechanism is the increase of the host's susceptibility to infections due to alteration of the immune system and the gut microbiome and therefore the capacity of the host to fight against infections. An increase in the temperature and ocean acidification caused by climate change can immunosuppress the host by direct effects on the immune system or indirect effects on the gut microbiome, making it more susceptible to *Vibrio* infections. Similarly, pollution can alter the correct functioning of the immune system and alter the gut microbiome of the hosts. All this results in a highly unfavourable scenario where *Vibrio* is more abundant and distributed, as well as more virulent and more resistant and where the hosts (marine organisms and humans) are more immunocompromised and therefore more susceptible to infections by *Vibrio* (Fig. 8.4; 8.5).

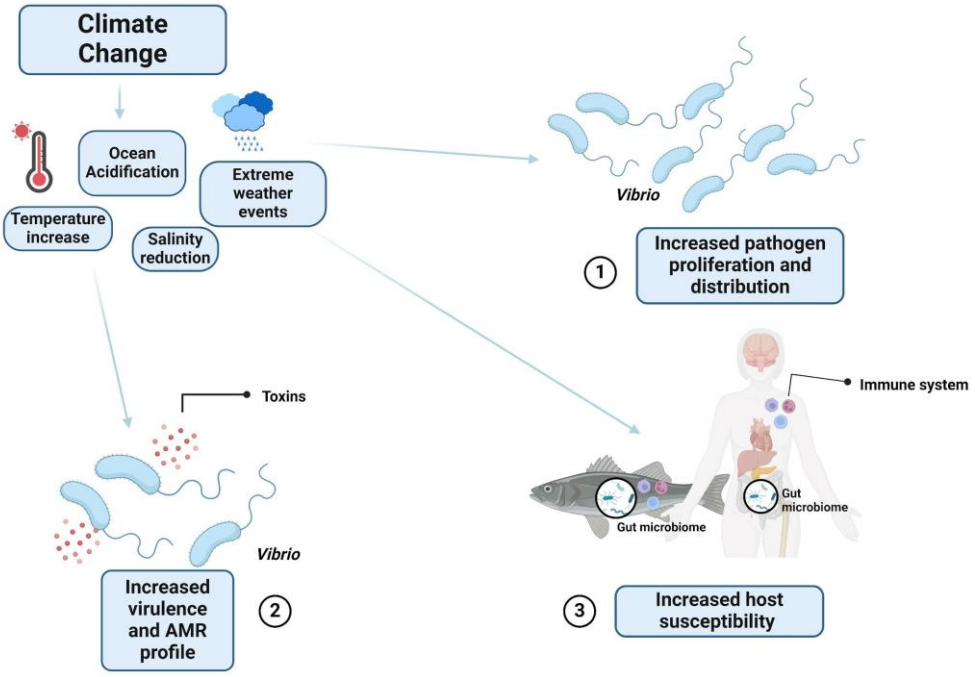


Fig. 8.4. Mechanisms by which climate change interacts with *Vibrio* infections. The effects of climate change on environmental parameters on the ecology of *Vibrio* such as an increase in the temperature, an increase in ocean acidification and a reduction in salinity will influence *Vibrio* infections by three main mechanisms; **(1)** by increasing the pathogen proliferation and distribution; **(2)**; by increasing *Vibrio* virulence and antimicrobial (AMR) profile **(3)** by increasing host susceptibility. Created with Biorender.com.

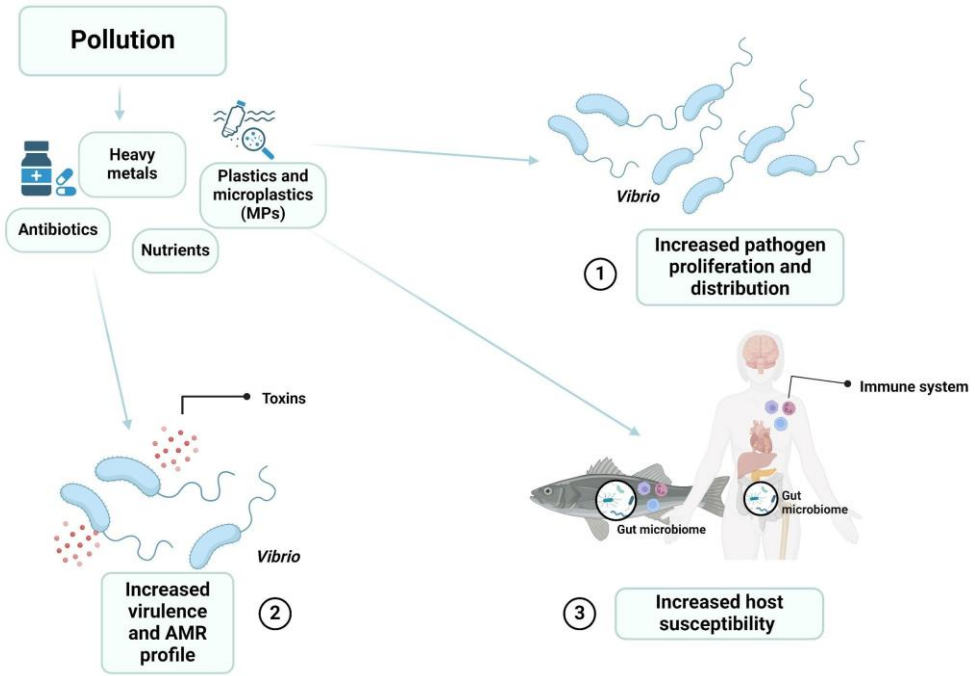


Fig. 8.5. Mechanisms by which pollution interacts with *Vibrio* infections. The increase in the abundance and distribution of pollutants caused by pollution will interact with *Vibrio* infection by three main mechanisms; **(1)** by increasing the pathogen proliferation and distribution **(2)** by increasing *Vibrio* virulence and antimicrobial (AMR) profile; **(3)** by increasing the host susceptibility. Created with Biorender.com.

8.6. Health impacts on humans

Of the 147 identified *Vibrio* species, around 12 have been detected to cause infections in humans. The most common human pathogens are *Vibrio cholerae*, *Vibrio parahaemolyticus* and *Vibrio vulnificus*. Subsequently, human diseases caused by pathogenic *Vibrio* can be divided into two major groups: cholera and non-cholera infections or vibriosis.

Although cholera is rare in high-income countries, it continues to represent a major cause of mortality worldwide, especially in low- and middle-income countries where *V. cholerae* is endemic (Baker-Austin et al., 2018). In these countries, there is a high number of people living in big cities where hygiene is not good and reliable drinking water sources are low, increasing the incidence (Baker-Austin et al., 2018). Around 3–5 million people get cholera worldwide annually, and about half of the deaths occur in children below 5 years of age (Ali et al., 2015). Children are more susceptible to cholera than adults (Deen et al., 2008) for several reasons, which include an underdeveloped immune system (Leung et al., 2012), lack of immunity due to lack of previous exposure and malnutrition (Nuzhat et al., 2022).

Regarding the clinical symptoms, approximately one in five individuals who get infected by *V. cholerae* exhibit symptomatic cholera, so, 90-95% of infected individuals do not develop symptoms (Baker-Austin et al., 2018; Montero et al., 2023). Typical symptoms include severe diarrhoea, but most individuals have no symptoms or only mild diarrhoea, indistinguishable from other mild diarrhoea diseases. The susceptibility and severity of the infection depend on many factors including local intestinal immunity (from previous natural exposure or vaccination) (Montero et al., 2023), the gastric-acid barrier of the patient (Sack et al., 1972), the patient's blood group (Harris & LaRocque, 2016), age, and nutritional, immune system and gut microbiota status (Midani et al., 2018).

Typical treatment includes rehydration and replacement of lost fluids, antibiotics in severe cases and nutritional supplements. In the majority of cases, rehydration is sufficient. That is why, rehydration is considered the cornerstone of cholera management (Guerrant et al., 2003). Antibiotics have been shown to reduce the duration and severity of the infection, but they are not considered to be a "life-saving"

treatment. Therefore, the use of antibiotics in cholera treatment must be used only when needed and alternatives should be investigated.

Cholera vaccines have been shown to be highly effective in preventing cholera (Wierzba, 2018). Moreover, it has been observed that one contributor to variance in human populations in cholera vaccine efficacy is the gut microbiome (Weil et al., 2019), suggesting that the gut microbiome status at the time of infection or vaccination is critical for providing correct immunity in the gut and resist and fight infections (Macbeth et al., 2021). That is why, the status of the gut microbiome in humans is being recognized as an important factor in driving susceptibility to infection by *V. cholerae* (Cho et al., 2021). Recurrent strong diarrhoea caused by cholera results in the expulsion of the healthy gut microbiome (Cho et al., 2021). Moreover, the use of antibiotics to treat all types of infections disrupts too the gut microbiome (Patangia et al., 2022). Therefore, the overuse of antibiotics in treatment, malnutrition in some individuals and recurrent severe diarrhoea leads to gut microbiome immaturity, increasing susceptibility to future infections (Macbeth et al., 2021) and reducing vaccine efficacy.

Regarding non-cholera infections or vibriosis, *V. parahaemolyticus* and *V. vulnificus* are the most common ones. *Vibrio parahaemolyticus* is a major human pathogen and a global public health concern (Martinez-Urtaza & Baker-Austin, 2020) since it has been observed that some serogroups have caused pandemic outbreaks (Martinez-Urtaza et al., 2013; Nair et al., 2007). Regarding the clinical symptoms, the infection usually leads to acute gastroenteritis that is self-limiting and does not require hospitalization. The symptoms of the disease include mild diarrhoea, vomiting and low fever (Ottaviani et al., 2012). In addition, if individuals have open wounds in their bodies, these wounds can be infected and in individuals with immunodeficiency or some chronic diseases, this infection causes septicaemia (bloodstream infection), which is associated with a high mortality rate (Ghenem et al., 2017). The treatment for an infection caused by *V. parahaemolyticus* typically involves rehydration, antibiotics, and rest.

Regarding *V. Vulnificus*, on the contrary to *V. cholerae* and *V. parahaemolyticus*, it is not considered a pandemic vibrio. Moreover, unlike *V. cholerae* and *V. parahaemolyticus*, it is an opportunistic pathogen since most cases happen in

immunodeficient individuals already with an underlying disease (Baker-Austin & Oliver, 2018). The most common risk factors are liver diseases (such as cirrhosis or hepatitis) but there are others such as diabetes mellitus and immune disorders. Studies highlight that individuals with chronic liver disease such as cirrhosis are more likely than healthy individuals to develop *V. vulnificus* severe infections (Chuang et al., 2019). Infections are typically most prevalent in individuals 45–60 years of age and men. Given that middle-aged men make up the majority of vulnerable cirrhosis patients, this partly explains the age and sex specificity of this pathogen infection (Baker-Austin & Oliver, 2020). Typical symptoms are gastroenteritis, severe wound infections, and septicaemia. Treatment for an infection caused by *Vibrio vulnificus* typically involves a combination of antibiotics, rehydration and rest. Regarding prevention, those people with a weakened immune system or underlying medical conditions, specifically liver diseases such as cirrhosis, should take extra precautions to avoid exposure.

Regarding the routes of transmission, in cholera, the main route is the faecal-oral route by ingesting contaminated water, however, the bacterium can also be transmitted person-to-person in some cases (Baker-Austin et al., 2018) as well as through contaminated food (Rabbani & Greenough, 1999). For vibriosis, the main routes are consumption of seafood or direct contact with contaminated water by swimming or bathing, particularly in areas with poor sanitation.

Overall, cholera and vibriosis cases are increasing and causing considerable health impacts. In the case of cholera, most deaths can be resolved by investing in the good management of the water supply and supportive medicine. The symptoms may not be very severe, and with the correct rehydration therapy, most of the infections can be treated. Children, however, represent an important susceptible group. They do not have immunity to previous exposure events and in underdeveloped countries many of them are malnourished. Water sanitation, malnutrition and supportive medicine should be improved for the correct management of cholera.

Furthermore, vaccines are effective in the prevention of cholera infections. The status of the gut microbiome is an essential susceptibility factor and becomes crucial to fight infections and to create immunity after infection and after vaccination. Therefore, nutrition and the promotion of a good health status by targeting the gut microbiome

are key in fighting cholera. In the case of vibriosis, infections are different. In the case of *V. parahaemolyticus*, the symptoms are very mild, usually causing self-limiting gastroenteritis. In the case *of V. vulnificus*, which is considered an opportunistic bacterium, symptoms are more severe and middle-aged immunocompromised men with liver disease are of special concern. Consequently, contrary to cholera, in the case of vibriosis, older adults and immunocompromised people with chronic diseases are especially susceptible.

8.7. DPSEEA model for *Vibrio* infections

Originally the DPSEEA framework was developed by the WHO in 1995 to support decision-making and identification of areas of intervention regarding human disease burdens (Briggs, 1999) since it can bring together professionals, practitioners, and managers from both environmental and public health fields to help orient them in the larger scheme of the problem. It allows complex phenomena, including impacts on ecosystems, to be visualised as a linked series of processes so that the connections between these components constitute critical control points for intervention or mitigation.

Therefore, a model based on the DPSEEA framework has been developed to capture and show the complex interaction mechanisms regarding *Vibrio* infections since it provides a useful tool for understanding and predicting complex human-environment and ecosystem interactions. It is also a tool to guide management and policy responses regarding the emergence and re-emergence of infectious diseases.

The model consists of six parameters: drivers or driving forces, pressures, state, exposure, effects, and actions. The main GACs that the coastal aquatic environment is subjected to, climate change and pollution, have been suggested in this model as the drivers or driving forces. The identified interaction mechanisms by which climate change and pollution interact with *Vibrio* infections are proposed as the pressures on the state. The mechanisms are: 1) altering the environmental parameters that increase the pathogen proliferation and distribution; 2) increasing the virulence and antimicrobial resistance (AMR) profile of *Vibrio* and 3) increasing host susceptibility by negative effects on the immune system. Consequently, changes in the environmental

parameters and the concentration of the pollutants will act as a pressure through the different mechanisms mentioned resulting in an altered state of the environment where *Vibrio* is more abundant, distributed, virulent and resistant and the hosts that can be infected are more immunocompromised and therefore more susceptible to infections (Fig. 8.6)

This altered state of the environment regarding *Vibrio* infections will have adverse effects on human health and some marine organism's health. Therefore, through the main routes of exposure to getting infected by *Vibrio*, the more abundant, distributed, virulent and resistant *Vibrio* will come more frequently into contact with more immunocompromised and susceptible humans and marine organisms (Fig. 8.6).

Increased virulence and resistance profile of *Vibrio* will cause infections to be more difficult to treat since currently used antibiotics will be less effective, increasing mortality and severity of *Vibrio* infections. Consequently, it is essential to strengthen reduction policies for antibiotic use and to search for alternatives to antibiotics for treating vibriosis outbreaks in aquaculture settings and infections in humans (Fig. 8.6). As mentioned above, antibiotics are not considered to be a "life-saving" treatment in *Vibrio* infections in humans, although in some cases their use is essential. Moreover, their overuse has adverse long-lasting effects on the hosts such as gut microbiome imbalance and immaturity. Therefore, their use should be limited only when truly necessary.

Some alternatives have been already suggested. For example, probiotics, postbiotics, prebiotics and synbiotics have been used to control vibriosis in fish in aquaculture settings (Abdel-Latif et al., 2022; Yilmaz et al., 2022). They are considered as immunomodulators that enhance fish immunity, thereby increasing resistance against vibriosis. Bacteriophage therapy has also been considered as one of the best alternatives for antibiotics in cholera treatment although currently studies have been carried out with only animal models and not in humans (Bhandare et al., 2019; Yen et al., 2017).

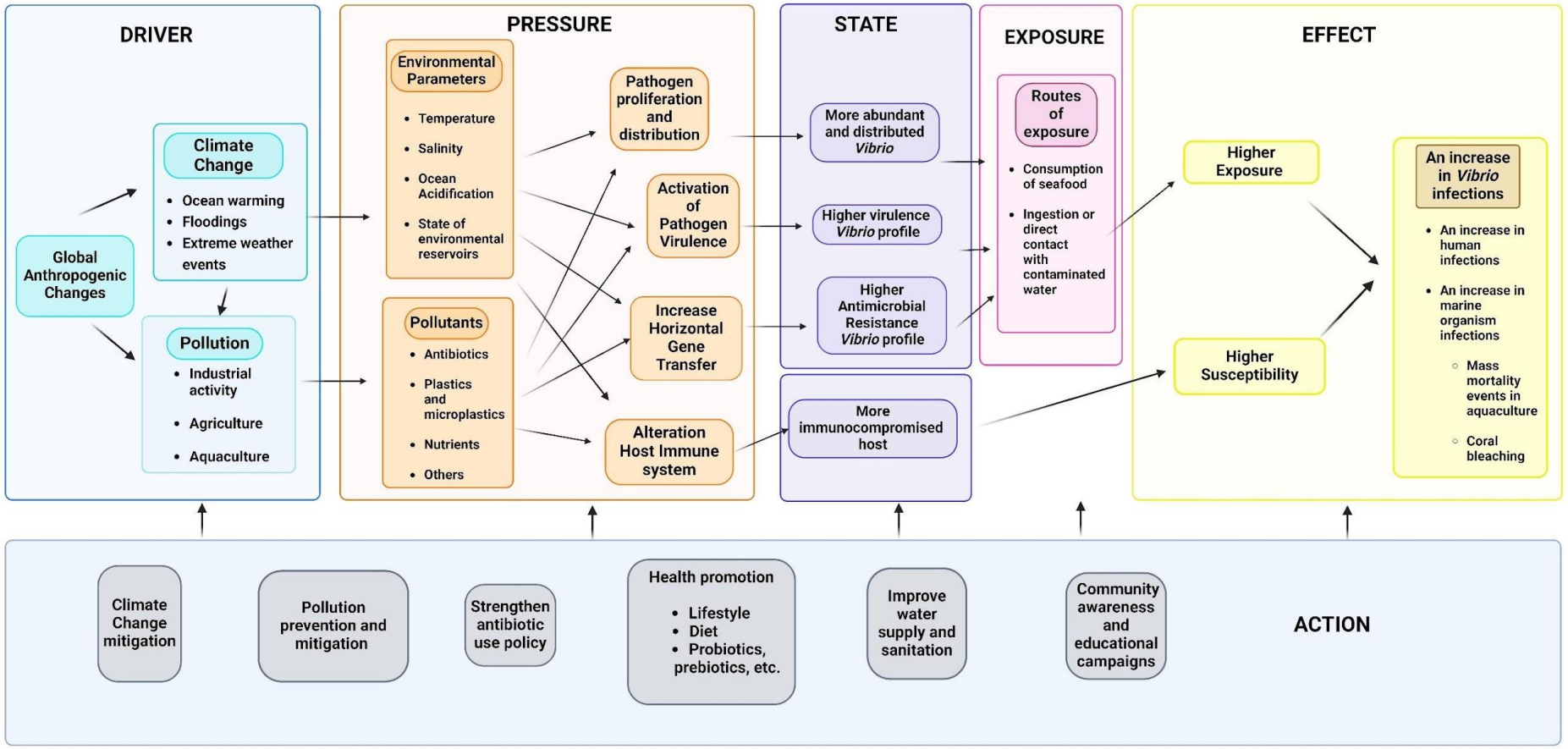


Fig. 8.6. DPSEEA model for *Vibrio* infections. Created with Biorender.com.

In a climate change and pollution scenario, marine organisms and humans are expected to be more immunosuppressed and therefore more susceptible to infections caused by coastal pathogens like *Vibrio*. Future predictions are leading to a scenario where the human population is becoming older with more chronic diseases and immunodeficiency disorders caused in part by lifestyle and environmental hazards coming from climate change and pollution. Therefore, for future adaptation and prevention strategies, it is essential to consider the reinforcement of the immune system and other factors of the host health status with “health promotion” policies (Fig. 8.6).

The microbiome and especially the gut microbiome of the hosts is essential in their capacity to fight against infections, but also for the overall health status. Therefore, acting on the improvement of the microbiome and the gut microbiome is a key area of intervention to strengthen the capacity of hosts to fight against infections. Diet and a healthy lifestyle lead to a mature and healthy gut microbiome (Rinninellaa, 2023). Likewise, the negative effects that climate change will have on global food production, ultimately leading to human malnutrition (Fanzo et al., 2018) and consequent negative effects on the healthy development of the gut microbiome (Catania et al., 2021) must be addressed as one of the main possible factors leading to the increase in the susceptibility of humans and especially children to *Vibrio* infections in the future.

In the effort to integrate the knowledge of the complex interaction mechanisms of *Vibrio* infections, the microbiome appears as the key component connecting all elements of the picture. How the environmental microbiome, from which *Vibrio* and other pathogens are part of, is altered by global anthropogenic changes like climate change and pollution is essential in the dynamics and processes of the infections. In addition, it is equally essential to understand how the status of the microbiome - both human and marine organisms is altered and pressured by these global anthropogenic changes.

8.8. Conclusions

When looking at the complex and interlinked dynamics of climate change and pollution-driven *Vibrio* infections, we can see that actions must be taken under an integrated and systemic approach. Climate change mitigation, pollution prevention and health promotion for humans and marine organisms emerge as key areas of intervention. Regarding health promotion, maintaining healthy lifestyles and improving the gut microbiome of humans and marine organisms appear as promising strategies. In addition, improving water supply, sanitation and food safety and investing in infrastructure and community awareness campaigns are crucial in reducing the risk of *Vibrio* infections in the future.

The chapter proposes a key methodological contribution to the DPSEEA model by including the host health status and the microbiome in the state.

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CHAPTER 9

The social context

Chapter 9. The social context

9.1. Introduction

Traditionally, many different fragmented and separated determinants have been proposed to understand what influences human health (see chapter 2). In the last decades, researchers have highlighted that among the conventional health determinants, social factors can greatly impact human health, thus contributing to health inequalities (Braveman et al., 2011; Marmot & Bell, 2019a). For example, Braveman et al. (2011) argue that factors such as income and education can impact health in different ways "through complex, biologically plausible pathways that do not always involve medical care". As a result, these findings have attracted more and more attention to addressing the specific roles of social determinants in public health.

Nevertheless, some scholars have pointed to the fact that the "social determinants of health" concept may unintentionally ignore the root structural and systemic causes generating health inequalities. They criticise the concept *"for adopting a truncating logic that elides the complex, multidimensional, and interrelated processes that characterise social reality and focuses instead on discreet "factors" that can be isolated and placed within a Cartesian, linear, causal chain linking abstracted social conditions with health disparities […] incapable of capturing the holistic social totality that more accurately depicts the social dynamics responsible for the production of health, disease, and their distribution […] insisting that epidemiological tools of analysis cannot be allowed to divorce the empirically observable from their generative social processes. These must be analysed as part of one holistic social, political, and economic totality that is sensitive to intersecting social forces…"* (Harvey et al., 2022).

Therefore, more and more scholars are proposing an intersectional approach to study the role of social factors able to reduce health inequalities. The term "intersecting dynamics" has been proposed in this analysis as an umbrella term to reflect how traditional social determinants intersect to create complex dynamics of social and health inequalities. Intersecting dynamics ultimately result in structurally advantaged or disadvantaged unique and heterogeneous identities in the social context. Being *structurally advantaged or disadvantaged refers to the fact that certain individuals or*

groups in society are privileged over others due to benefitting from advantages, opportunities, or privileges due to the way that societal, political, and institutional systems and structures are organised. Multiple social, economic, cultural and biological aspects of advantages and disadvantages such as sex, gender, age, ethnicity, socioeconomic position, education, lifestyle and behaviour have been considered in this analysis.

The analysis of the social context builds partially on the INHERIT model, represented as a complex and dynamic system of interactions between health, behaviour, lifestyles, social inequalities and the environment (Staatsen et al., 2017).

All these aspects of a person's identity overlap among them to create unique social dynamics that cannot be understood when the impact of each factor is studied separately.

In the case of infectious diseases, many overlapping aspects of a person's identity differently influence the risk and incidence of disease across the population. For example, gender has been found to play an important role in the differential exposure routes to zoonotic diseases, in some low and middle-income countries women are at higher risk due to household tasks and animal care duties (Oruganti et al., 2023). In this particular case, many aspects of a person's identity are intersecting to create a unique exposure dynamic. Because being a woman implies culturally influenced behaviours, culture, behaviour and gender intersect to create unique health inequalities.

The purpose of this chapter is to apply an intersectional approach to understand how intersecting dynamics within the social context influence the differential distribution, prevalence and risk of infectious diseases caused by coastal pathogens in all three aspects: (i) exposure, (ii) susceptibility and (iii) recovery. The chapter has been organized into three main sections, respectively, applying the intersecting dynamics approach to analyse (i) *exposure* to coastal pathogens, (ii) *susceptibility* to develop an infectious disease once an exposure event has occurred, and (iii) *recovery* after the development of an infectious disease.

9.2. Exposure

Exposure to a certain pathogen that can cause disease refers to a host's encounter with an infectious agent (van Seventer and Hochberg (2017). This encounter of a host with an infectious agent creates the possibility for the pathogen to invade the host and establish an infection (Sweeny & Albery, 2022). Exposure is, therefore, referred to "the frequency and intensity at which an individual comes into contact with an infectious agent" (Noppert et al., 2023a). There is evidence that social and cultural factors influence disease transmission (Buckee et al., 2021). Therefore, in the social context, intersecting dynamics can deeply influence how individuals and communities interact with their surroundings and with each other. This influences pathogen exposure patterns and probabilities through the main routes of transmission differentially across structurally advantaged or disadvantaged individuals and communities.

Exposure is strongly influenced by the time individuals and communities spend in social spaces such as the house, the neighbourhood, the working environment, and public transport (Egede & Walker, 2020; Noppert et al., 2023b) Humans spend most of their time in these spaces of the social context, where they relate to each other. However, as the social context is within the broader ecological context of the biosphere and inextricably entangled with it, how different spaces of the social context merge and mix with other ecological spaces of the biosphere will strongly influence exposure patterns and probabilities, especially to pathogens with environmental reservoirs such as some coastal pathogens like *Vibrio*.

Within sociocultural spaces of the social context, the house is very important since it is the space where individuals and families spend most of their time. The house is a principal source of exposure to pathogens for many people, primarily by direct contact with family members or contact with contaminated surfaces, water, and food (Baker et al., 2022). Intersecting dynamics that generate structural disadvantages like poverty influence the quality and characteristics of the places and houses individuals and communities live in and how they interact and engage with those environments. A poor housing infrastructure increases exposure to pathogens. For example, cracks in roofs, floors, and walls, as well as a lack of windows have been observed to increase the risk of vector-borne diseases (WHO, 2024). Other housing factors such as poor ventilation,

temperature and humidity also increase the probability of exposure to pathogens (Wolkoff et al., 2021).

In the case of waterborne and foodborne infectious diseases caused by coastal pathogens in low- and middle-income countries, the quality and sanitation of the water supply and wastewater infrastructure at the household and neighbourhood level is one of the most important factors in the unequal distribution of the exposure across disadvantaged individuals and communities (Ondieki et al., 2022).

In the case of legionellosis, *Legionella* bacteria are naturally found in freshwater environments like lakes, but they sometimes proliferate in the water infrastructure system of some buildings (CDC, 2023a). Structurally disadvantaged families and communities that live in neighbourhoods with poor housing infrastructure are more likely to be exposed to *Legionella*, with studies showing a higher frequency of infections in poor and non-white populations (Gleason et al., 2017). In addition to *Legionella*, disadvantaged ones are exposed to many other pathogens such as those causing cholera, dysentery, hepatitis A, and typhoid fever present in drinking water supplied using poor infrastructure (Adelodun et al., 2021; WHO, 2023a).

In addition to the higher intensity and frequency of exposure to pathogens due to poor water supply infrastructure, intersecting dynamics also influence sociocultural food and water handling practices and hygiene practices (Negassa et al., 2022). Poverty and low levels of education influence improper methods of disposing and handling food and water which are potential sources of exposure to coastal pathogens (Ferronato & Torretta, 2019). Disparities in food handling knowledge and practices, a lack of access to basic sanitary supplies, and a lack of awareness of preventive measures have all been linked to the increase in exposure to many coastal pathogens such as *Shigella* and *Salmonella* (Ehuwa et al., 2021; Libby et al., 2020).

As mentioned, exposure to a pathogen is essentially an encounter in the environment between the pathogen and the host. Therefore, intersecting dynamics will influence the incidence of these encounters. However, in the case of human hosts, since humans have a sophisticated and cultivated knowledge regarding their surroundings, and consequently the possible hazards on it and how to avoid or handle them, exposure to a coastal pathogen is something that can be actively avoided or reduced.

So, even if there is a higher probability of being exposed to a higher load of pathogens in disadvantaged contexts, knowledge and health literacy can reduce these exposures. That is why, educational and awareness campaigns are essential to promote and disseminate knowledge about possible exposure routes to pathogens. For example, disadvantaged individuals belonging to communities of Southern Ethiopia with higher education and health knowledge were found to be associated with a lower incidence of foodborne and waterborne infectious diseases (Seboka et al., 2023).

In the case of structurally advantaged individuals and communities, mediating pathways by which intersecting dynamics increase the exposure to coastal pathogens differ slightly from those of disadvantaged ones. One of the main pathways is by higher incidence of carrying out recreational activities in coastal waters. Socioeconomically advantaged individuals are more likely to spend more time on the beach or carry out aquatic sports in coastal waters like surfing (Currie, 2016), where they can be exposed to many coastal pathogens. International and national travels are another factor by which these individuals can be more exposed. In high-income countries, those belonging to a high socioeconomic position have the material and temporal capacity to travel long distances to countries where there is a higher incidence of infections caused by coastal pathogens, being like that more exposed to contaminated water and food (Mavridou et al., 2018). Another mediating pathway is a higher incidence of contaminated food consumption. There is a tendency for higher consumption of raw or undercooked seafood and meat, one of the principal sources of exposure to many coastal pathogens such as *Vibrio*, *Salmonella* and *E. coli* (Adams et al., 2019; Iwamoto et al., 2010).

The mediating pathways by which exposure to coastal pathogens is increased might be some of the plausible reasons behind the conflicting results in the literature regarding infection incidence. In a recent systematic review that studied the association between socioeconomic status and waterborne and foodborne infectious diseases in developed countries, (Adams et al., 2018), inconsistent results were observed among studies, where some report a higher probability of infections in low socioeconomic-status individuals, but others report the opposite.

In the case of Shigellosis, conflicting results are also observed in the literature. Most affected are children younger than 5 years of age and transmission is particularly common in rural areas where structural disadvantages such as poor water quality and inadequate sanitation are common (Badr et al., 2023). Moreover, in developed countries, disadvantaged poor individuals belonging to oppressed ethnicities have a higher incidence too (Libby et al., 2020). However, other studies are showing the opposite results. In a study carried out in Denmark, it was found that shigellosis incidence was correlated with higher income and education, suggesting that differences in international travel and diet could be some of the plausible explanations (Simonsen et al., 2008).

Similarly, in the case of Shiga toxin-producing *Escherichia coli* infections, the relationship between infections and socioeconomic status is not very clear since some studies are showing that low socioeconomic status is associated with a lower risk of infections, but other studies are showing the opposite pattern and other studies showing no clear association (Adams et al., 2019).

In summary, an unequal exposure to coastal pathogens might be plausibly explained by some cause-effect mediating pathways that operate differently in structurally disadvantaged and advantaged individuals and communities. In the first group, higher exposure can be explained partly due to: (i) household overcrowding and poor housing and neighbourhood infrastructure especially water supply and sanitation infrastructure (ii) sociocultural food and water handling practices and hygiene practices and (iii) lower education and health literacy. In the second group, higher exposure can be explained partly due to: (i) greater accessibility to get involved in recreational activities in the coastal waters such as surfing, sailing, and swimming, ii) sociocultural practices such as higher consumption of raw or undercooked food in restaurants and (iii) higher incidence of international and nationals travels (Fig. 9.1).

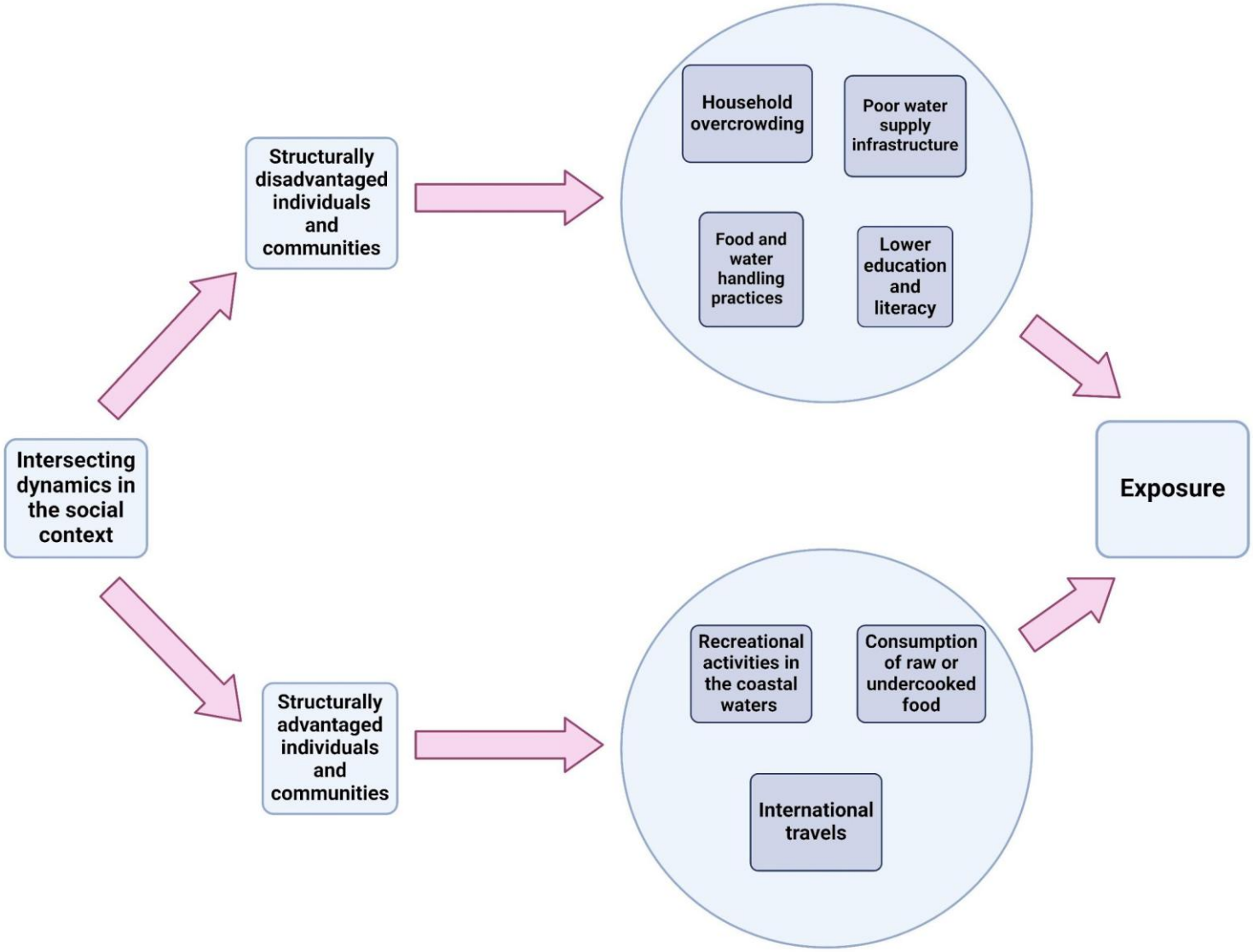


Fig. 9.1. Mechanism pathways by which intersecting dynamics in the social context increase exposure. Created with Biorender.com.

9.3. Susceptibility

Regarding infectious diseases, susceptibility refers to the predisposition and propensity of developing a disease after an exposure event to a certain pathogen (Pooley et al., 2020). When an exposure event occurs, a pathogen must infect host tissues to cause disease (van Seventer & Hochberg, 2017). Infection might cause some negative effects on the host, but it does not always result in disease, since an infection can be resolved or neutralized by the host defences without developing major symptoms.

Therefore, an exposure event to a pathogen does not automatically translate to the development of a disease from a biomedical and symptomatic perspective (van Seventer & Hochberg, 2017). Furthermore, even if an infection leads to the development of some symptoms of the disease since disease or the perception of being ill is also sociocultural, the development of some symptoms might not be understood and perceived as being ill.

Susceptibility is a crucial element in infectious disease dynamics. However, it is often disregarded or not given the importance it deserves. As Beldomenico and Begon (2010) note, traditionally in epidemiology and public health, an automatic assumption is made attributing the cause of infectious disease to the pathogen only. Nonetheless, placing susceptibility at the centre suggests that the host health status of individuals and communities might be the cause too for the disease. Beldomenico argues that the infection dynamics might partly be a reflection of the host health status, as “populations in poor average condition might exhibit higher prevalence of infections, increasing the risk of further infections, with further deterioration in condition”; “observational studies can demonstrate associations but cannot establish causality”; and “the interpretation of such associations has tended to see the pathogen as the putative cause”. Therefore, infectious disease dynamics might reflect an underlying dynamic of the hosts’ susceptibility (Beldomenico & Begon, 2010).

Regarding susceptibility, the integrity of the host's health status is fundamental. For infectious diseases, four main categories of the host health status have been found to play a key role in susceptibility; (i) chronic diseases (ii) immune system (iii) microbiome, and (iv) mental health. Intersecting dynamics within the social context

influence the four main categories of human hosts' health status through many pathways. Intersecting dynamics within the social context influence the four main categories of human hosts' health status through many interconnected and entangled pathways. This section aims to summarise and illustrate some of the main pathways that result in an unequal distribution of the susceptibility to coastal pathogen infections across structurally advantaged and disadvantaged individuals and communities.

9.3.1. Chronic diseases

The presence of a chronic disease at the time of infection is a very important susceptibility factor since it can significantly increase a person`s risk of severe disease after an infection. According to the WHO *"the main types of chronic diseases are cardiovascular diseases, cancers, chronic respiratory diseases and diabetes"* (WHO, 2023b).

Although it cannot be generalized that having chronic diseases makes people more susceptible to infectious diseases, there is evidence that some of them operate as important susceptibility factors for the predisposition and development of some specific infectious diseases (Remais et al., 2013). The role of some chronic diseases in shaping the susceptibility towards some infectious diseases depends to a large extent on the type of pathogen and its mode of infection in the body (Clohisey & Baillie, 2019). A clear example of the heterogeneity of mode and place of infection within the host's body is viral tropism. Viral tropism is the ability of different viruses to infect specific different cell types or tissues ultimately producing an infection (McFadden et al., 2009). If the pathogen, being a bacterium or a virus, infects a tissue or an organ that is not compromised by a chronic disease, it might not necessarily influence or aggravate the outcome of the infection. However, if the pathogen infects a tissue or an organ already compromised or disrupted by a chronic disease, it might aggravate the outcome of the infection. For example, having asthma or a chronic respiratory disease might not act necessarily as a susceptibility factor to an infection caused by an enteric pathogen like *E. coli* but in contrast, it might act as a susceptibility factor for respiratory viruses like SARS-CoV-2.

In the case of infectious diseases caused by coastal pathogens, some specific chronic diseases have been found to act as key factors in susceptibility. In the case of

infections caused by *Vibrio vulnificus*, middle-aged men with chronic liver disease are especially susceptible since a higher prevalence of liver disease is found in older males (Nazir et al., 2016). This is explained because the pathogen, *V. vulnificus*, needs iron to proliferate and it enhances its cytotoxicity and virulence. Therefore, patients with elevated iron stores due to hepatic chronic diseases are especially susceptible to *V. vulnificus* infections and develop severe symptoms after the infection (Haftel & Sharman, 2023).

In infections caused by *Legionella pneumophila*, according to CDC, *"most healthy people who are exposed to the bacterium do not become ill and those that are more susceptible to getting sick are people of 50 years old or older, smokers, and people with chronic lung disease (such as chronic obstructive pulmonary disease or emphysema)"* (CDC, 2023a). Therefore, since *L. pneumophila* targets lung tissues causing pneumonia (Chauhan & Shames, 2021), already existing lung complications due to chronic diseases act as an important susceptibility factor. In the case of *E. coli* infections, some studies suggest that some chronic diseases like diabetes, chronic lung disease, cirrhosis and heart disease, may increase the susceptibility (Laupland et al., 2008).

To better understand who is at risk, there is a need to explore which parts of the population exhibit a high prevalence of chronic diseases. Epidemiological studies have confirmed a strong association between socioeconomic inequalities and a wide range of chronic diseases (Lawlor & Sterne, 2007). Studies have shown that in most countries regardless of being a low, middle or high-income country, poor people belonging to a low socioeconomic status have a higher risk of dying from them (Cesare et al., 2013).

Marmot and Bell (2019), have identified four main pathways and mechanisms by which social inequalities increase the probability of developing chronic diseases; (i) by differentially distributing the four main behavioural risk factors—that is, unhealthy diet, physical inactivity, tobacco smoking, and excess alcohol consumption—(ii)by increasing psychosocial stress affecting mental health and increasing unhealthy lifestyle choices and behaviours (iii) by increasing environmental exposure to pollutants linked to specific chronic diseases and (iv) by affecting health care access

and influencing prevention, diagnosis and treatment, including the affordability of drugs.

Consequently, intersecting dynamics unequally distribute susceptibility to infectious diseases across structurally disadvantaged individuals and communities by increasing the prevalence of chronic diseases (Fig 9.2). This increased prevalence might be explained to a large extent by the four main pathways already identified by (Marmot & Bell, 2019). However, many interconnected unexplored pathways might additionally exist.

9.3.2. Immune system

The robustness of the immune system and its correct functioning at the time of the infection is essential to neutralize the pathogen and not develop a severe infection. That is why, immunosuppressed or immunocompromised patients and individuals belong to the susceptible group for almost all of the infectious diseases (Dropulic & Lederman, 2016). In the case of the majority of infectious diseases caused by coastal pathogens such as *Vibrio*, *Legionella* and *Shigella*, immunodeficient and immunosuppressed individuals belong to the most susceptible group (CDC, 2019, 2023a, 2023b).

Close relationships between many chronic diseases with an immunodeficient state of the host at the time of the infection have been observed (Bates et al., 2015). Many cancers and chronic diseases debilitate the immune system and in addition, the medical treatments for those cancers and chronic diseases also weaken the immune system (Cancer Research UK, 2014). Therefore, the four pathways that have been described in the previous section through which intersecting dynamics operate by increasing the prevalence of chronic diseases are inextricably entangled with deleterious effects on the immune system. Hence, structurally disadvantaged individuals and communities are more likely to develop and live with various chronic diseases that simultaneously further debilitate the immune system, increasing the susceptibility to any infectious disease.

Even if the disruption of the immune system might be caused partially by chronic diseases, there are exclusive pathways by which intersecting dynamics alter or disrupt

the immune system of a healthy individual without chronic diseases. Recently, “social immunology” has been proposed to understand how social and cultural factors of the social context “get under the skin” to produce inflammatory responses and impairments in the immune function of individuals and communities (Shattuck, 2021). The metaphorical concept of “getting under the skin” is increasingly been used to convey the idea that sociocultural aspects of our everyday life manifest as embodied biological processes and dynamics. These new ideas try to understand how intersecting dynamics in the social context translates into biological dynamics such as stress responses, mental conditions and immune system disruptions.

Advancements in fields like psychoneuroimmunology and medical anthropology are helping to delineate more accurately the mechanisms by which socioculturally shaped behaviours and relationships influence immune functions. For example, there is evidence that isolation, social stress and low socioeconomic status are associated with negative effects on the immune system (Mattos Dos Santos, 2020). Psychosocial stress has been observed to increase the susceptibility to infectious pathogens in structurally disadvantaged individuals and communities (Cohen, 1994). Therefore, it seems that structurally disadvantaged individuals experience more stressful and adverse life events (such as losing jobs or being in a war context) that influence negatively their immune functions making them more susceptible to infectious diseases (Fig 9.2).

Another mechanism by which intersecting dynamics in the social context affect the immune system is malnutrition. The impairment of the immune function by malnutrition, known as nutritionally acquired immunodeficiency syndrome (Elizabeth, 2020), plays a key role in the susceptibility to any infection. Many studies show that malnourished individuals and communities have a higher risk of developing infectious diseases since they lack a strong immune system (De Vita et al., 2019; Fan et al., 2022). Consequently, many intersecting dynamics in the social context influence individuals and communities of low- and middle-income countries to be more susceptible to generic infections and infections caused by coastal pathogens due to a diminished immune system caused by malnutrition. Moreover, malnutrition is especially of concern in enteric and gastrointestinal infections caused by coastal pathogens since it disrupts the gastrointestinal mucosa increasing susceptibility to

infections caused by pathogens such as *E. coli* and *Vibrio* (Guerrant et al., 2008; Ibrahim et al., 2017; Tickell et al., 2020).

9.3.3. Microbiome

The status of the human microbiome is influenced by numerous biological factors such as genetics, sex, age, and diet (Hasan & Yang, 2019). Geographic location, psychological situation and exercise also affect the human microbiome (Yang et al., 2021). Additionally, from a very early age onwards, many social and cultural factors like ethnicity, socioeconomic position and lifestyle choices and behaviour influence it strongly (Bowyer et al., 2019; Dowd & Renson, 2018). All these varied geographic, demographic, social, biological and behavioural factors intersect to create unique individual dynamics and experiences that result in the alteration of the human microbiome.

The host's microbiome is an essential factor in determining the host's health status. Advancements in microbiomics have shed light onto the complex entangled ways by which the microbiomes of humans and other animals contribute significantly to the correct and healthy functioning of their physiological functions (Hou et al., 2022). Regarding infectious diseases caused by coastal pathogens, the status of the host's microbiome—composition and diversity—is a key susceptibility factor that operates through two main pathways; (i) by influencing the other susceptibility factors and (ii) by differential pathogen colonisation resistance capacity.

Regarding the first pathway, there is evidence that the immune system of humans must potentially co-mature with the microbiome in early-life stages so that the individual is immunologically strong and prepared to fight diseases (Zheng et al., 2020). Therefore, if the microbiome is affected and depleted at early life stages due to unfavourable intersecting dynamics in the social context, the immune system of the individual will be impaired and unmatured, becoming a susceptibility factor for future possible infections that the individual will undergo in its lifetime.

Furthermore, the disruption of the maturation, composition and diversity of the microbiome at early life stages might be the root cause of many chronic diseases including obesity, diabetes, allergies, cardiovascular diseases (CVDs) and intestinal

diseases such as inflammatory bowel disease (IBD) later in life (Bu et al., 2022; Ooi et al., 2020).

Consequently, all the mechanisms outlined in Sections 9.3.1 and 9.3.2 by which intersecting dynamics in the social context exacerbate or cause chronic diseases and alter the immune system across structurally disadvantaged individuals and communities are also operating through influencing the status of the microbiome. This highlights that the host health status is a complex interconnected system where all parts are connected and must work in harmony to ensure the integrity of the host and its defences to fight against pathogens. Moreover, it highlights that alterations in one component of the host health status alter the other components. For example, an alteration in the microbiome might alter the immune system and chronic diseases. Similarly, a chronic disease might influence the immune system and the microbiome.

Regarding the second pathway, there is evidence that one of the key roles of the microbiome is the protection against pathogens. This property of the microbiome is generally referred to as "pathogen colonisation resistance" and it has been considered as one of the principal evolutionary advantages to the majority of living creatures (McLaren & Callahan, 2020). As a consequence, if the microbiome status is altered and disrupted by intersecting dynamics, the colonisation resistance capacity of the microbiome will be diminished increasing the susceptibility to colonisation and infections by coastal pathogens.

The establishment of a mature status of the microbiome is divided into three main stages: *"1) the developmental period (at 1 year old), where the child's microbiota is influenced by breastfeeding, geographics, maternal and/or fetal diseases, and the use of antibiotics; 2) the transitional period (at 2 years old), where exposure to the environment, such as pets, siblings, other household related-acquaintance, and chronic pathologies, among others, increases and affects the microbiota; and 3) the stable period (at 4 years old), which will remain throughout life and can be slightly modified by lifestyle and diet"* (Nobre & Alpuim Costa, 2022).

Intersecting dynamics in the social context affect significantly all these three stages. To elucidate some of the main pathways, the following sections unpack some of these in more detail.

9.3.3.1. Breastfeeding and mode of delivery

During the developmental period, lifestyle choices and behaviour regarding breastfeeding practices and mode of delivery affect the human microbiome. These choices and behaviours are associated with individuals' socioeconomic position and sociocultural factors (Motee et al., 2013). Breastfeeding is more beneficial for the maturation of the microbiome than other alternatives such as formula feeding (Ma et al., 2020). According to UNICEF, babies are much more likely to be breastfed at least once in low- and-middle-income countries like Bhutan (99%), Madagascar (99%) and Peru (99%) than those born in Ireland (55%) the United States (74%) or Spain (77%) (UNICEF, 2018).

Regarding the mode of delivery, caesarean section delivery has been shown to negatively impact the development of the human microbiome since there is a lack of good exposure to the vaginal microbes of the mother (Ríos-Covian et al., 2021). Although there are conflicting results, there is evidence that caesarean section delivery is a preferred mode of delivery among women belonging to a high socioeconomic position and with higher education compared to poor women with lower education (Carlotto et al., 2020). Therefore, evidence indicates that those in higher socioeconomic positions have a higher chance of perpetuating some deleterious behaviour and lifestyle choices like formula feeding and caesarean section delivery for the correct acquisition and development of the human microbiome at early-life stages.

9.3.3.2. Behavioural risk factors and diet

Deleterious behaviour and lifestyle choices such as the four main behavioural risk factors of chronic diseases identified in section 9.3.1; unhealthy diet, physical inactivity, tobacco smoking, and excess alcohol consumption have been observed to also influence the microbiome (Capurso & Lahner, 2017). Therefore, the contribution of these behavioural risk factors to the higher mortality due to chronic diseases can be explained in part by the adverse effects these behaviours have on the microbiome since they might be the root cause of many of these diseases.

Of special concern is malnutrition and an unhealthy diet. After the establishment of the microbiome after the first three years of life, the main modulators of the human gut

microbiome are diet and the nutritional status of the individual (Leeming et al., 2019). Furthermore, the most significant changes in gut microbial composition at the individual level are associated with malnutrition (Bixby et al., 2022). There is evidence that intestinal microbiome impairment due to malnutrition results in the disruption of intestinal immune and barrier functions increasing the risk of infections by pathogens of the order Enterobacterales, including *E. coli*, *Klebsiella pneumoniae* and *Salmonella* species (Holowka et al., 2023). Hence, malnourished individuals especially children residing in low- and middle-income countries are among the most susceptible to coastal pathogen infections due to a disrupted microbiome (Williams et al., 2018).

9.3.3.3. Antibiotics and other pharmaceuticals

The differential usage pattern of antibiotics and other pharmaceuticals is one of the main influences in early life stages for the disruption of the human microbiome and especially the gut microbiome (Huang et al., 2024). Antibiotic use can indiscriminately target both pathogenic and benign bacteria, disrupting ecological niches that are responsible for many metabolic and physiological functions (Fishbein et al., 2023). These antibiotics-dependent alterations in the microbiome have been linked to the development of many other diseases such as allergies, asthma, and inflammatory and autoimmune diseases (Kesavelu & Jog, 2023). Hence, antibiotic-induced changes in the human gut microbiome can have a negative impact on the host's health status, influencing susceptibility to coastal pathogens.

9.3.3.4. Vaccine efficacy

There is a clear link between structural disadvantaged contexts and susceptibility to infection due to persistent disparity of vaccine coverage (Zimmerman et al., 2010). In the case of cholera, vaccines are highly effective in preventing cholera. However, they are disproportionally distributed (WHO, 2022). Moreover, one determinant of vaccine efficacy is the gut microbiome, suggesting that gut microbiome composition at the time of vaccination is critical for providing strong immunity (Macbeth et al., 2021). Therefore, structurally disadvantaged individuals and communities that are malnourished and have an altered microbiome are more inclined to vaccine failure and consequently to be susceptible to coastal pathogen infections.

9.3.3.5. Harmful or beneficial exposures

Another important aspect in the adequate development of the microbiome is how individuals and communities interact with each other and with their surroundings from early life stages. The microbes that colonise individuals' gut and other parts of the body come from the exposures and interactions individuals engage with the environment and with other individuals (Johnson, 2020). People with more social relationships have a richer microbiome, suggesting that social interactions may shape the microbial community of the human gut due to direct exposure to microbes (Dill-McFarland et al., 2019; Johnson, 2020). Consequently, intersecting dynamics within the social context strongly influence how individuals and communities interact with each other and their surrounding environment, ultimately influencing harmful or beneficial exposure patterns for their microbiomes.

Social phenomena like urbanisation are profoundly changing and shaping the microbial landscape around humans, influencing microbial exposure dynamics. Urbanisation alters the human microbiome by altering the patterns of exposure to beneficial microorganisms associated with green spaces (Zuo et al., 2018). Differential access and exposure to green areas in urban environments and big cities are determined by intersecting dynamics, where structurally disadvantaged individuals and communities have limited access to green areas and therefore are less frequently exposed to beneficial microbes (Rigolon et al., 2021). Soil microbial diversity loss due to land-use changes such as urbanisation has been already suggested as a public health threat due to its negative effects on the human microbiome (Tasnim et al., 2017).

Furthermore, disadvantaged individuals and communities are more exposed to polluted environments (Cushing et al., 2015). This exposure to a wide range of pollutants and xenobiotics alters the status of the human microbiome. Pollutants including airborne particulate matter, mercury, and phthalates among others have been linked to human microbiome disruption (Prescott et al., 2018). Moreover, there is evidence that various pollutants alter the human microbiome with subsequent effects on the physiological functions and systems that it regulates, like the immune system and the intricate microbiome-gut-brain axis, impairing overall mental health and the immune system (Singh et al., 2022). Therefore, pollution is directly and

indirectly increasing susceptibility to infectious diseases caused by coastal pathogens. Namely, it acts directly by decreasing the quality of the microbiome and indirectly by affecting physiological functions, immune system and mental health that are so important for the overall health status of the host.

Although some studies indicate that structurally disadvantaged individuals and communities are especially at risk of suffering harmful effects on their microbiomes, other reports suggest that they might have favourable exposures and interactions among each other and with the environment. A recent study reports that living in poor rural villages and crowded households could be associated with a better status of the microbiome (Lapidot et al., 2022). Furthermore, there is evidence that living in rural areas close to nature and farm animals is beneficial for acquiring a healthy microbiome and consequently increasing individuals' protection against infectious diseases caused for example by some coastal pathogens (Panthee et al., 2022). In a study assessing gut microbiome changes by acute diarrheal disease in urban versus rural settings in Northern Ecuador, the authors have found that the microbiome of rural populations is more resilient to acute diarrheal disease (Soto-Girón et al., 2021).

In summary, similarly to what has been mentioned about how intersecting dynamics "get under the skin" and manifest biologically as disruptions in the immune system and cumulative physiological responses of stress (Schulz et al., 2012), intersecting dynamics also "get into the gut". Harmful influences that lead to a disrupted microbiome are not randomly and equally distributed across the population. Although there are some negative lifestyle and behaviour choices among structurally advantaged individuals and communities, most of the evidence points to the fact that disadvantaged individuals and communities experience a higher degree of psychological and physiological stress, unhealthy diets, exposure to contaminated environment, etc. (Fig 9.2). The impairment of the human microbiome by all these negative factors has been described as the "*dysbiotic drift hypothesis"* (Logan, 2015). The *"dysbiotic drift hypothesis*" goes beyond a scientific explanation of the numerous factors that influence microbiome disruption. It is a metaphor used to describe how the social context pushes microbiome disruption more intensively in structurally disadvantaged individuals and communities (Prescott et al., 2018).

9.3.4. Mental health

Mental health and the integrity of the cognitive and psychological capacities are essential to ensure the overall health status of the host (Jokela, 2022). Many important public health organisations such as the EU Council of Ministers, the Pan American Health Organisation, the UK Royal College of Psychiatrists, and the World Federation of Mental Health have supported the WHO statement that there can be "*no health without mental health*" (Prince et al., 2007). Mental health can be impacted by many biological, social and cultural factors such as sex, gender, sexuality, age, ethnicity, disability and poverty (Babalola et al., 2017). Intersectionality helps understand the dynamics in which mental health inequalities are not only the outcome of individual elements like biology or behaviour but are also the result of intersecting social dynamics such as poverty, isolation and discrimination (Funer, 2023).

These mental health conditions due to intersecting dynamics that influence the other three main categories of the host health status, the immune system, chronic diseases, and the microbiome, might be in turn exacerbating these exact mental health problems by bidirectional iterative routes. An example of this is the "gut–microbiota–brain axis". It is a complex system comprised of connections that allow bidirectional communication between gut microbiota and the brain (Morais et al., 2021). Consequently, a disruption in the gut microbiota caused by psychological stress might in turn influence mental health and further influence susceptibility to infectious diseases caused by coastal pathogens (Fig. 9.2).

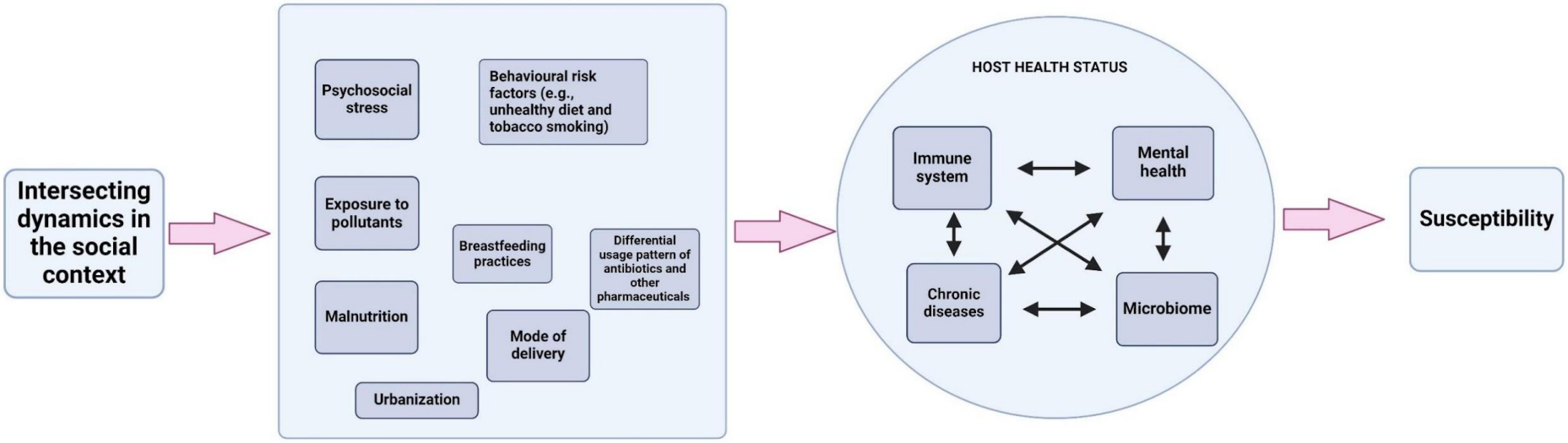


Fig. 9.2. Mechanism pathways by which intersecting dynamics in the social context increase susceptibility. Created with Biorender.com.

9.4. Recovery

In modern Western medicine, recovery from an infectious disease in biomedical terms involves the disappearance of symptoms, that is the acute phase of the disease, and the return to normal physiological functions (Nash et al., 2015). A recovered state means conventionally that the acute disease has been resolved, although the pathogen may remain in the body, for example as opportunistic pathogen or in a dormant state.

However, there are more connotations in what it means to be recovered, strongly influenced by social and cultural perceptions and practices. Friedman (2021) has defined recovery as a function of three key aspects: 'curing', 'healing', and 'habilitating'. Curing means curing the symptoms and removing the cause of the disease from a biomedical perspective. Healing is a personal experience and an individual perception of well-being and involves broader health outcomes, such as good mental health and the ability to take responsibility for one's health. Habilitating refers regaining the ability to function in society, contributing to society and to maintaining social relationships.

While susceptibility and recovery are related concepts within the context of infectious diseases, they are distinct. Susceptibility is about the likelihood of getting the disease and is relevant before the infection occurs. In contrast, recovery consists in overcoming the disease and therefore it becomes relevant after the infection and development of the disease have occurred (Noppert et al., 2023b). Intersecting dynamics influences significantly the recovery of individuals and communities after outbreaks of infectious diseases. Cultural beliefs and structural social disadvantages such as poverty and social exclusion prevent individuals and communities from recovering effectively and slow down the recovery process through many different pathways.

9.4.1. Health-seeking capacity and behaviour

One of the main pathways by which intersecting dynamics might be interfering with or preventing a correct recovery is by influencing the health-seeking behaviour and the health-seeking capacity of individuals. In the literature, both concepts are commonly included by the umbrella term health-seeking behaviour. However, even if both

concepts are intertwined, we propose that they should be considered separately since some nuances and differences exist. Health-seeking behaviour refers to the sociocultural practices and beliefs regardless of the material and temporal capacities of getting access to a treatment or a health-positive intervention (Abuduxike et al., 2020). On the contrary, health-seeking capacity refers to the material and temporal capacities of individuals and communities to get adequate treatment and recover properly from an infectious disease.

Regarding health-seeking capacity, it is strongly shaped by social and cultural factors, where structurally disadvantaged individuals and communities have less material and temporal capacity to have access to treatments and recover properly from health-related problems and infectious diseases. For example, the chance for disadvantaged individuals to opt for paid sick leave is lower and therefore, they need to work even if they are sick (Clemans-Cope et al., 2008). Consequently, people with lower sick leave option, are more at risk of not recovering properly from infectious diseases and therefore they are more prone to develop more severe symptoms caused by persisted diseases.

Regarding health-seeking behaviour, all cultures have health beliefs to explain what causes disease or what it means to be ill and how and by whom should the disease be treated (EuroMed Info, 2024). Therefore, health-seeking behaviour is strongly influenced by sociocultural perceptions and practices. For example, family, friends, culture, beliefs and education have been found to influence the incentive of African American men when seeking healthcare (Eley et al. 2019).

In another study, it was revealed that Southern Pakistan rural mothers' access to healthcare and treatment is hindered by many factors such as geographical isolation, poverty, illiteracy and cultural scepticism (Ahmed et al., 2023). Similarly, in KIlombo District, Tanzania, they found that health-seeking behaviour during some infectious diseases such as malaria and typhoid fever was influenced by individual and sociocultural factors (Mburu et al., 2021). Age, income and perceptions of disease severity were some of the factors contributing to an improper health-seeking capacity and behaviour and consequent prolongation and increased severity of the infection (Mburu et al., 2021).

In the case of cholera, treatment normally consists of rehydration, administration of antibiotics in some severe cases, and nutritional supplements if patients are malnourished (Baker-Austin et al., 2018; Hsueh & Waters, 2019). If oral rehydration solutions are timely provided, nearly all deaths are avoided, thus pointing to the key role of rehydration in cholera treatment (Guerrant et al., 2003). However, structurally disadvantaged individuals and communities are especially vulnerable regarding the recovery process because they lack the healthcare infrastructure to maintain adequate rehydration therapy (CDC, 2022). Indeed, many children in rural communities of low- and middle-income countries die after they have been infected because of the lack of access to adequate treatment (Ilic & Ilic, 2023). Furthermore, sociocultural health-seeking behaviours have been observed to delay recovery from cholera and increase its severity due to individual and community characteristics including inadequate knowledge and inappropriate attitudes and practices (Elimian et al., 2020; Yakum et al., 2017).

9.4.2. Host-health status recovery capacity

Another pathway by which intersecting dynamics might be interfering or preventing recovery is by the host health status recovery capacity. Previously, host health status has been defined as a susceptibility factor. However, host health status also gains relevance during recovery, since recovery can vary widely depending on individual factors such as immune response and overall health status. Indeed, infections can boost the host's health against future infections. For example, V. cholerae infection often induces long-lasting immunity after recovering from the infection (Harris, 2018; Levine et al. 1981). On the other hand, if the health status of an individual is negatively affected by immunodeficiency, chronic diseases, an unhealthy microbiome and compromised mental health, then it can impair recovery.

9.4.3. The impact of antibiotic-resistant coastal pathogens on recovery

One important factor that hinders the correct and rapid recovery is being infected with antibiotic-resistant coastal pathogens. In general, the recovery from the diseases caused by antibiotics-resistant and antibiotics-sensitive pathogens can proceed differently. If an individual gets infected by an antibiotic-resistant coastal pathogen and develops a severe infection that needs to be treated with antibiotics, those

antibiotics will not work effectively, preventing the rapid recovery of individuals and communities.

Structurally disadvantaged individuals and communities are especially at risk of getting infected by antibiotic-resistant pathogens for many reasons. They are more likely to live closer to polluted environments that are hotspots of antimicrobial resistance reservoirs (Ikhimiukor et al., 2022). In a study where scientists have assessed antimicrobial-resistant *E. coli* infections in children living in rural and poor communities of Quito, Ecuador, they found that infections in children are influenced by exposure to domestic and commercial poultry and cattle (Kurowski et al., 2021). Therefore, neighbourhood and housing risk factors expose individuals and communities to antibiotic-resistant bacteria by living in rural areas close to animals, water and food contaminated with faecal material. Another reason for the higher risk of infections caused by antibiotic-resistant pathogens is behavioural and sociocultural factors related to lower education. Some of these factors include misuse of antibiotics, unhygienic conditions and inadequate disposal (Okeke et al., 1999).

Nevertheless, other studies are showing that advantaged individuals and communities can likewise be infected by antibiotic-resistant bacteria. In one study, the authors found that rich children have more probability of infection with antimicrobial-resistant (AMR) *Shigella* of faecal origin compared to those from the poorest families (Gruninger et al., 2017). Similar results have also been obtained in a study conducted in the Amazonian region of Peru, where young children from rich families were more likely to be infected with AMR *E. coli* (Kristiansson et al., 2009). Furthermore, surfers in high-income countries show a higher risk of exposure to and infection with clinically important antibiotic-resistant *E. coli* (Brunton et al., 2019).

Furthermore, structurally advantaged individuals and communities have greater access to healthcare facilities, where they can get exposed to multidrug-resistant pathogens since hospitals and other healthcare facilities are hotspots of antimicrobial resistance (Chokshi et al., 2019; Hocquet et al., 2016). Moreover, children from high-income families tend to have a higher consumption of antimicrobials (Nilsson & Laurell, 2005). Explanations include higher accessibility and use of antibiotics and greater consumption of food produced by using antibiotics.

Disruptions of the human gut microbiome favour the colonisation of antibiotic-resistant bacteria (Casals-Pascual et al., 2018). In a recent study of adults from Wisconsin, USA, it was shown that low socioeconomic status is associated with poorer gut microbiome composition due to food insecurity and that this increases the prevalence of antibiotic-resistant infection and colonisation (Zuniga-Chaves et al., 2023). Therefore, the increased chance of being infected by antibiotic-resistant coastal pathogens due to gut microbiome disruption (Garcia et al., 2022), hinders the proper and rapid recovery after the infection if antibiotic treatment is needed.

In summary, intersecting dynamics might be preventing recovery from infectious diseases caused by coastal pathogens according to the two main scenarios. The first one is related to health-seeking capacity and behaviour, and implies that structurally disadvantaged individuals and communities have less material and temporal capacity to recover properly. They cannot access health facilities and proper treatments, and these conditions impede their rapid recovery. Moreover, some sociocultural perceptions and beliefs act as obstacles in the process. The second scenario is related to the host health status recovery capacity. The integrity and health of individuals and communities shaped substantially by intersecting dynamics are essential to recover rapidly. For example, mental health integrity is essential during all three dimensions of recovery: curing, healing and habilitating (Fig. 9.3).

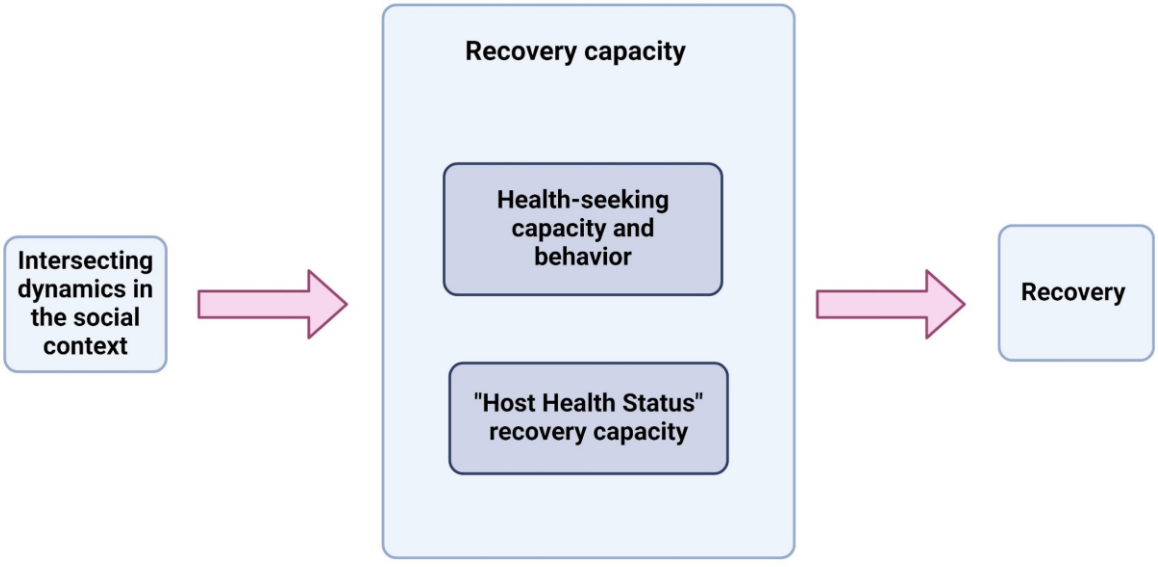


Fig. 9.3. Mechanism pathways by which intersecting dynamics in the social context influence recovery. Created with Biorender.com.

9.5. Summary of interaction pathways

In summary, intersecting dynamics in the social context influence the three main aspects of infectious diseases caused by coastal pathogens: (i) exposure, (ii) susceptibility and (iii) recovery.

Regarding exposure, many different mediating pathways have been found in both structurally disadvantaged and advantaged individuals and communities. A poor water supply infrastructure and poor water sanitation are the main reasons for exposure in disadvantaged neighbourhoods and families. Furthermore, individuals and communities living in these deficient infrastructure contexts are especially vulnerable to many intersecting dynamics of poverty, lack of education and culture that manifest as unsafe food and water handling and hygiene practices. Structurally advantaged individuals and groups may also have higher exposure for reasons that differ significantly from those of disadvantaged ones. In these groups, the main exposure pathways are related to social and cultural practices such as higher recreational activity in the coastal waters, higher consumption of raw or undercooked food and higher incidence of international and national travel. Therefore, in these advantaged social contexts, culture, behaviour and income among others intersect to create unique exposure dynamics (Fig 9.4).

Regarding susceptibility, the social context greatly influences the health status of individuals and communities through many intersecting dynamics. The health status is a complex interconnected system where all parts influence each other and must work in harmony to ensure the integrity and capacity to fight infectious diseases. Disadvantaged individuals are the most susceptible since many factors such as income, gender, culture, behaviour and lifestyle among others intersect to create unique dynamics of psychological stress, exposure to pollutants, unhealthy lifestyle choices, and poor healthcare access that affect the immune system, the microbiome and mental health and cause many chronic diseases (Fig 9.1).

Higher susceptibility is also observed in a dvantaged groups since culture, income, gender and behaviour among others intersect to create dynamics such as urbanization, mode of delivery, stressful and hectic jobs, unhealthy diets and overuse

of antibiotics that negatively influence the microbiome and the other aspects of the health status of individuals and communities (Fig 9.4).

Regarding recovery, intersecting dynamics in the social context influence recovery in both disadvantaged and advantaged groups by influencing health-seeking capacity and behaviour and the host health status recovery capacity. Disadvantaged ones are the most affected since poverty, gender, culture and behaviour among others intersect to create unique inequality dynamics where they lack basic healthcare infrastructure and treatment programs, their health status is in poor condition slowing down recovery and some cultural and social beliefs act as barriers when seeking treatment (Fig. 9.4).

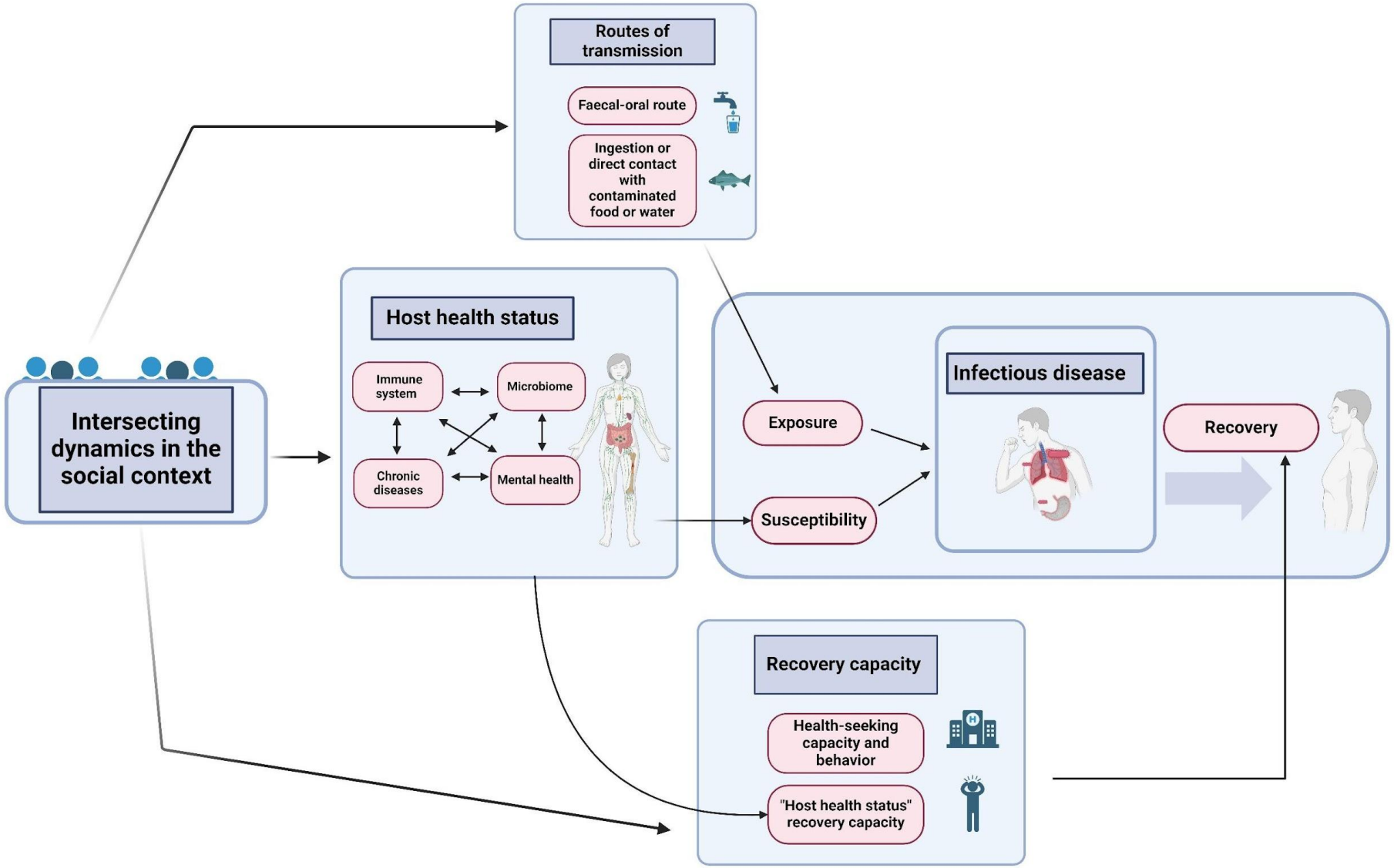


Fig. 9.4. Summary of interaction pathways. Created with Biorender.com.

9.6. Conclusion

Intersecting dynamics in the social context significantly influence which groups of the population are exposed, and susceptible, and how well they can recover from infectious diseases caused by coastal pathogens. Even if some dynamics increase the risk of disease in structurally advantaged individuals and communities, structurally disadvantaged ones in low-, middle- and high-income countries are still the ones bearing the higher risk of coastal pathogen infections. However, exposure, susceptibility and recovery dynamics are very unique and heterogeneous for each individual regardless of their structural advantage or disadvantage.

People's identities are the product of many biological, cultural and social factors. Gender, income, ethnicity, culture, and behaviour among others intersect to create unique identities of health inequalities affecting the risk of infectious diseases from coastal pathogens. As a consequence, intersectionality is essential in future research to elucidate in more detail the mechanisms and dynamics underlying health inequalities in the population that give rise to unequal distribution of infectious diseases.

Although the analysis in chapter 9 dicusses examples of pathways specific to coastal pathogens (as defined in chapter 4), the overall framework linking exposure, susceptibility and recovery is applicable to infectious diseases in general.

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CHAPTER 10

Conceptual framework supporting an extended One Health vision for coastal pathogens

Chapter 10. Conceptual framework supporting an extended One Health vision for coastal pathogens

10.1. Introduction

Pathogenic health risk in coastal zones is an area of growing concern due to the complex interaction of multiple influencing factors.

Coastal zones are critical ecosystems that provide essential benefits to human society, such as food (e.g. fish and seafood), recreation and cultural values. However, the complex interactions of multiple stressors in these areas pose a significant risk to both humans and the environment. In particular, pathogenic microorganisms found in coastal waters can pose a major threat to human health, especially in the context of climate change, increasing pollution levels and social inequalities.

To address these complex challenges, a conceptual framework is proposed to understand the risks associated with these stressors, as well as to outline a pathway to good health by highlighting the role of host health status as a key component for acquiring and developing severe infectious diseases.

The conceptual framework draws on the extensive analytical literature review conducted in modules A and B of this deliverable. The framework consists of (i) a system map that synthesises the main factors and their complex interconnections, and (ii) a set of principles that are suggested for considering extensions to the conceptualisation of One Health. The simultaneous consideration of the system map (Fig. 10.1) and the principles (Fig. 10.2) lays the theoretical foundation for an in-depth comprehensive understanding of the complex landscape of risk for coastal pathogens infection.

10.2. System map

The first aspect of the conceptual framework is illustrated in figure 10.1 and depicted as a system map showing the intricate interactions among key components or influencing factors in the coastal pathogen infection network. The figure emerges from the analysis done in module B, which aimed to identify the components and pathways that determine the system behaviour. Each pathway could entail thousands of specific mechanisms; however, the figure is not intended to be an exhaustive assessment of all potential mechanisms, but rather an illustrative map to identify, highlight and unravel the system's complexities.

The system map could inform how to couple phenomenological models, such as climate models, with pathogen behaviour models and host models as it reveals which system components need connecting. Alternatively, the map could also serve as a basis to develop more conceptual models, such as ones based on conditional probabilities (e.g. Bayesian Belief Networks), fuzzy cognitive mapping or population dynamics (e.g. with simple ecological models like the Lotka Volterra model). Such models would serve more illustrative purposes in showing the propagation of information or how an intervention might affect the network. It could also serve for geospatial models: e.g. identify areas and regions where climate change, pollution pressures, population pressures, poor host health status, and high inequalities coincide.

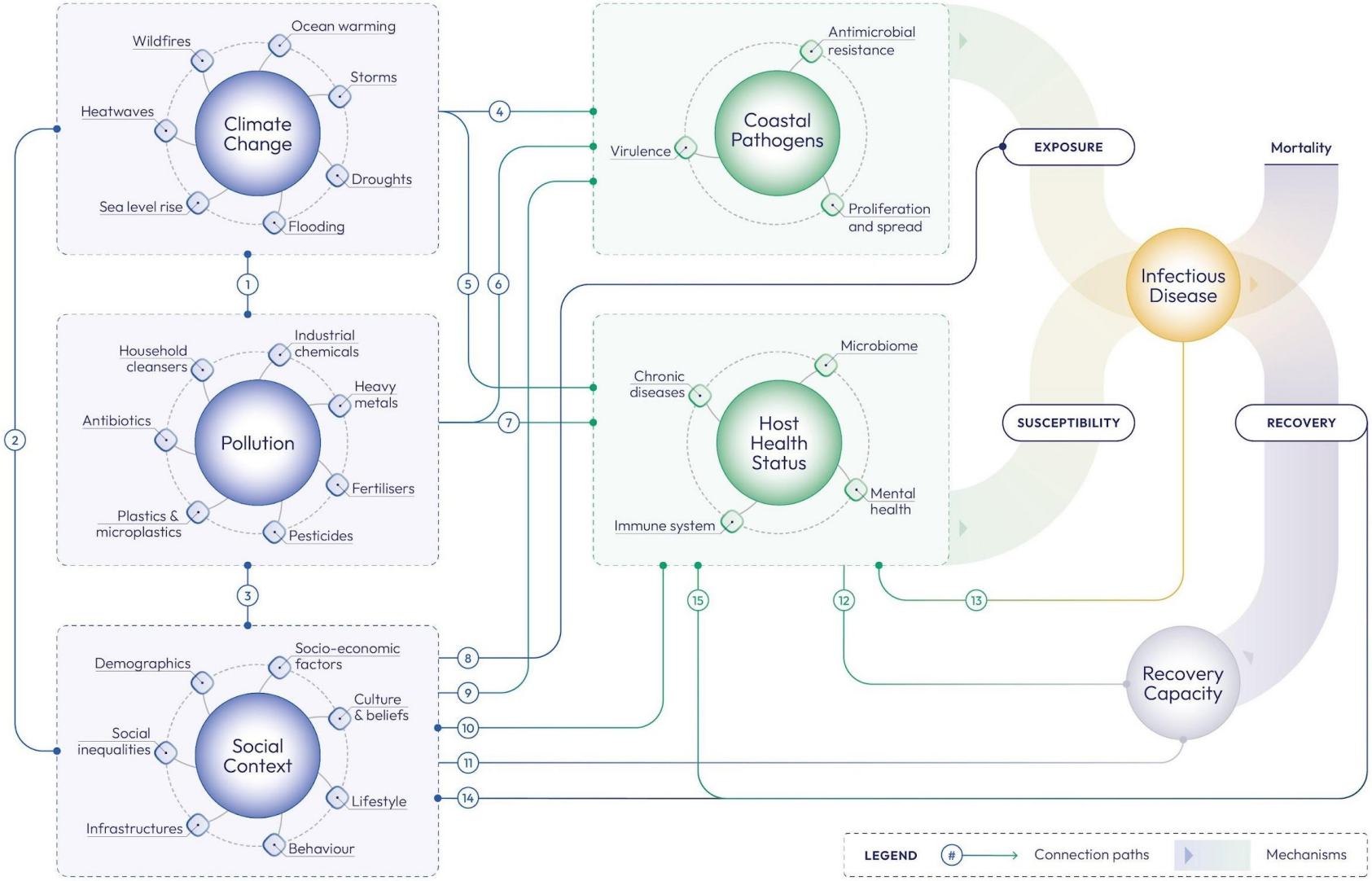


Fig. 10.1. System map: interactions among influencing factors and their impact on the risk of coastal pathogen infections. Each number represents a connection path between different influencing factors in the system (see Table 10.1). For a higher resolution of the system map, see Appendix 10.2.

The system map presents how the analysed components or influencing factors of the system associate and interact with each other in determining the risk of coastal pathogen infections (Table 10.1). The components or influencing factors include climate change, pollution, the social context, coastal pathogens (virulence, antimicrobial resistance, proliferation and spread), and the host's health status (mental health, underlying chronic diseases, microbiome, immune system). The three main mechanisms shaping the risk and severity of infectious diseases are “exposure”, “susceptibility” to infection and the “recovery” of the host. The system map aligns with the climate risk framework outlined in the Fifth Assessment Report of the Intergovernmental Panel on Climate Change (IPCC) AR5 (IPCC, 2014), which defines risk as the outcome of the interplay between hazards, exposure, and vulnerability. Vulnerability, in this context, encompasses sensitivity and coping/adaptive capacity (Estoque et al, 2023; IPCC 2014). However, given our focus on analysing infectious disease risk, we have chosen to use the terms “susceptibility” (equivalent to sensitivity in the IPCC definition) and “recovery capacity” (equivalent to coping/adaptive capacity in the IPCC definition) as these terms are specifically relevant to disease and health.

Table 10.1. Summary of the main pathways and feedback loops identified in the system map (see Fig. 10.1).

Path number	Title of the pathway
1	Bidirectional link between climate change and pollutants
2	Bidirectional link between climate change and the social context
3	Bidirectional link between pollution and the social context
4	Climate change impact on coastal pathogens
5	Climate change impact on host health status
6	Pollution impact on coastal pathogens
7	Pollution impact on host health status
8	The impact of the social context on exposure
9	The impact of the social context on coastal pathogens
10	Bidirectional link between the social context and host health status
11	The impact of the social context on recovery capacity
12	The impact of host health status on recovery capacity
13	Self-reinforced susceptibility loop
14	Structural inequalities and recovery loop
15	Health reinforced loop

To facilitate a clear and comprehensive discussion of the system map, we have divided the analysis into two subsections. The first section elaborates on the three main mechanisms of infectious diseases: exposure, susceptibility and recovery. The second section focuses on synergies and feedback loops. However, it is essential to note that as the discussion is focused on the entire interconnected system, the observations made in one part are inextricably linked to other parts and *vice versa*.

10.2.1. Mechanisms of infectious diseases

Exposure, susceptibility, and recovery are the pivotal elements shaping the dynamics of infectious diseases. Understanding how individuals encounter pathogens, the

determinants of their susceptibility to infection, and the processes that underlie their recuperation is fundamental to both preventing and managing infectious diseases.

To aid in the comprehension of our analysis, we first provide a brief definition of exposure, susceptibility, and recovery.

Exposure to infectious diseases is “the frequency and intensity at which an individual comes into contact with an infectious agent” (Noppert et al., 2023). This encounter of a host with an infectious agent creates the possibility for the pathogen to invade the host and establish an infection (Sweeny & Albery, 2022). In the context of infectious diseases, *susceptibility* is the propensity of an individual who has been exposed to become infected (Noppert et al., 2023; Pooley et al., 2020). Beyond this, we conceptualise susceptibility in terms of host health status using four key aspects: the presence of an underlying chronic disease, mental health condition, the microbiome and the immune system. We highlight that the susceptibility considered in the analysis pertains not only to the general likelihood of contracting an infectious disease. We acknowledge the heterogeneity in susceptibility and the influence of certain factors that may render some individuals more or less susceptible than others to a specific disease (Beldomenico & Begon, 2010). Finally, it is important to note that although susceptibility and exposure relate to the individual, they have their roots at the social (Noppert et al., 2023) and even planetary levels. This means that macro-level social and environmental processes, such as climate change, release of pollutants into the environment, and social inequalities, can increase exposure to pathogens as well as aggravate the susceptibility of hosts.

The remaining mechanism, *recovery,* can be defined as “cure” which refers to the elimination of infectious agents and the alleviation of symptoms (Nash et al., 2015). However, we recognise that recovery is a complex process that cannot be reduced to its biological components but that there are more dimensions at play. Friedman (2021) argues that recovery is composed of three dimensions the “cure”, “healing” and “habilitating”. The first refers to the biomedical process we have already referred to. The "healing” refers to the restoration of the individual’s physical, mental and emotional well-being and the “habilitating”, refers to the recovery or acquisition of the ability to function in society, for example, to be productive at work or to be able to interact socially (Friedman, 2021).

To understand the dynamics of coastal pathogen infection risk and health outcomes, and to identify the root causes, we summarise and analyse the main factors discussed in Module B that influence exposure, susceptibility and recovery. For each mechanism, we illustrate a subset of pathways that have been identified in the previous chapters.

10.2.1.1. Factors influencing exposure

Our analysis uncovers numerous pathways leading to higher exposure, linked to climate change, pollution, and the social context. These three factors can create environmental conditions that may lead to an increased risk of coastal pathogens by favouring their spread, abundance, virulence and antimicrobial resistance profile.

Climate hazards such as drought, wildfires, floods, and heatwaves can affect coastal pathogens (Fig. 10.1, path 4). For example, ocean warming and marine heatwaves can directly impact the growth, spread, virulence, and antimicrobial resistance profile of certain pathogenic *Vibrio* species. As a result of rising ocean temperatures, pathogenic *Vibrio* species like *Vibrio cholera* can proliferate and shift their distribution to higher latitudes. However, increased water temperature can also contribute to the development of antimicrobial resistance (AMR) and its transmission. In addition, ocean warming may also indirectly affect pathogens, as it may favour the proliferation of plankton and harmful algal blooms (HABs), which can act as nutrient reservoirs and refuges for coastal pathogens (see chapter 5).

Pollution can also create favourable conditions for coastal pathogens to proliferate and create virulence and antimicrobial resistance mechanisms (Fig. 10.1, path 6). For example, plastics and microplastics that end up on the shore and in the sea can act as a surface for the formation of biofilms or attached microbial communities. These formations protect pathogens from adverse environmental factors such as desiccation or ultraviolet radiation, allowing pathogens to persist in biofilms of plastics and microplastics and be transported by the currents. In addition, biofilms can adsorb and concentrate chemical pollutants and nutrients in the aquatic environment, which act as resources for pathogens and favour their proliferation and the development of antimicrobial resistance. Finally, the presence of microorganisms in biofilms makes them ideal sites for the exchange of antibiotic resistance genes (ARGs) (see chapter 6).

There exist multiple routes by which the social context potentially increases the likelihood of exposure to coastal pathogens. First, we highlight how individual and community lifestyles and behaviours can favour the conditions for coastal pathogens to develop antimicrobial resistance profiles (Fig. 10.1, path 9). Misuse, overuse and improper disposal of antibiotics are principal behaviours causing an increase in antibiotic-resistant pathogens in coastal environments. Other pathways in the social context that may increase exposure to coastal pathogens are related to certain social and cultural behaviours (Fig. 10.1, path 8). It is important to note that underlying these behaviours there are often structural inequalities, such as different levels of education or income. For example, structural inequalities themselves may influence behaviours that increase exposure to coastal pathogens; for example, lack of accessibility to adequate information may lead to poor hygiene or food handling practices and a lack of risk perception to bathing in inappropriate conditions. On the other hand, advantaged groups such as those of high socio-economic status, may also be more exposed to infections due to certain social and cultural attitudes. For instance, these groups tend to consume more raw foods, like oysters or raw fish, travel internationally more frequently, and participate in recreational activities that increase their risk of exposure to coastal pathogens, such as surfing (see chapter 9).

10.2.1.2. Factors influencing susceptibility

Our analysis of susceptibility has focused primarily on the variability of host health status, which we have determined through four main aspects: microbiome, immune system, mental health and underlying chronic diseases. Although it is inaccurate to make generalised claims about a direct link between chronic diseases and susceptibility to infectious diseases, it is becoming increasingly evident that certain chronic diseases can impact the body's ability to resist and handle infections.

Exposure to pathogens does not necessarily translate to an infection. Its occurrence is the result of the interplay of multiple factors happening at the individual level, which might converge at the community level to create specific dynamics leading to a higher risk for some groups to be infected. On the other hand, an infection does not always translate into disease, since it can be counterbalanced by the immune system of the host. Hence, understanding how heterogeneity in susceptibility can exacerbate the risk of infection in certain individuals and populations is key (Beldomenico & Begon,

2010). This section aims to emphasise the importance of host health status in situations where individuals and communities are exposed to infectious pathogens.

In Module B, we have examined how climate hazards, pollution and the social context can impact the host's health status. We summarise here some of these dynamics.

Climate hazards, such as heatwaves, can damage the health of individuals and communities by triggering physiological and psychological stress, thereby increasing their susceptibility to infectious diseases (Fig. 10.1, path 5). For example, heatwaves can exacerbate pre-existing chronic diseases in people in poor health, which may have additional effects on their immune system and susceptibility. In addition, rising temperatures at night can disrupt sleep patterns, leading to fatigue and mental health problems in people in good health. Other extreme events, such as floods, wildfires or storms can have a huge impact on the mental health of the affected population and aggravate the effects on those already suffering from mental disorders, with consequent impacts on the immune system (see chapter 5).

We have found many examples that demonstrate how pollutants can deteriorate the health condition of the host (Fig. 10.1, path 7). Pollutants present in coastal zones can accumulate in the tissues of marine organisms, and when humans consume these organisms, they can get exposed to high levels of pollutants. For instance, heavy metals and industrial chemicals can harm health; leading to a range of chronic illnesses such as cardiovascular diseases, neurotoxic diseases, and cancer. Furthermore, these pollutants can weaken the immune system, rendering individuals more susceptible to infections, as detailed in chapter 6.

The social context has a significant impact on the health status of the host and it is closely related to the intersection between variables such as income, gender, age, education, and living conditions (Fig. 10.1, path 10). The dynamics arising from these intersections can create unfavourable conditions that can hinder or impair the health status of the host and can result in unequal distribution of the susceptibility to infectious diseases across structurally advantaged and disadvantaged individuals and groups.

An example of how social context leads to poor health is that of unhealthy lifestyles (e.g. unhealthy diets, physical inactivity, smoking and substance abuse), which can lead to the development of chronic diseases related to the respiratory or vascular

system. These chronic diseases combined with other risk factors can increase susceptibility to infections. For instance, middle-aged men suffering from chronic liver disease might be more susceptible to *Vibrio vulnificus* infections. Similarly, people with chronic lung diseases might be more susceptible to *Legionella* infections. (see chapter 8 and 9).

However, the key insight into how social context affects susceptibility to coastal pathogens is that several attributes (age, gender, income, education, housing conditions, etc.) intersect, affecting host health so heterogeneously that the resulting susceptibility is almost unique for each host.

An example that helps to understand how these complex dynamics work is the case of the microbiome. The microbiome is a highly relevant component of the host's health status, as it affects the other components of susceptibility (mental health, chronic diseases and the immune system). Intersecting dynamics within the social context uniquely shape the host's microbiome and therefore shape a unique susceptibility profile. For example, in structurally disadvantaged communities, factors such as unhealthy diets, high exposure to pollution and high stress (e.g. due to job instability) can alter the microbiome by first influencing the ability to resist pathogen colonisation and secondly influencing the other susceptibility factors. Alternatively, in structurally advantaged groups some overlapping behaviours impact the microbiome. These behaviours may include the overuse of antibiotics (possibly due to easy access to antibiotics), a higher frequency of caesarean sections, less frequent instances of breastfeeding, and increased stress. These factors may alter the microbiome and consequently also increase the susceptibility in structurally advantaged groups (see chapter 9).

10.2.1.3. Factors influencing recovery

Recovery is a multifaceted process that depends on multiple factors. In this analysis, but more specifically in chapter 9, we have looked at two crucial factors that play an important role in achieving successful recovery: healthcare-seeking capacity and -behaviour and the health status of the host. The first is an umbrella concept that refers to physical and temporal resources and health-related behaviours necessary to achieve adequate treatment and recovery (Fig. 10.1, path 11). The social context plays

a significant role in the recovery process, and it is therefore essential to consider it. In disadvantaged communities, factors such as inequalities, geographical isolation, poverty, and illiteracy can impede access to proper healthcare or treatment programs. Similarly, socio-cultural beliefs surrounding health can influence an individual or community's motivation to seek care and achieve recovery.

The second crucial element in the recovery process is the health status of the host at the time of infection (Fig. 10.1, path 12). It is noteworthy that poor health at the time of contracting an infectious disease can impede recovery. For instance, the presence of chronic diseases, compromised mental health, microbiome and immune system can diminish the capacity to manage an infection and lead to a more complicated recovery. It is crucial to comprehend that, as illustrated in the susceptibility section, climate hazards, pollutants, and social factors can impact host susceptibility by modifying health status. Likewise, these influential factors can also impede recovery by worsening the host's health status (see chapter 9).

10.2.2. Interaction pathways, synergies and feedback loops

One of the most remarkable aspects of the behaviour of the system map is that the influencing factors themselves interact with each other, resulting in a joint impact on the mechanisms of infectious diseases.

Climate change, pollution, and the social context are interrelated and have mutual impacts. Certain interaction pathways have been identified between these factors that demonstrate their interconnectedness.

First, the bi-directionality between climate hazards and pollution is illustrated in figure 10.1 through path 1. Climate hazards such as wildfires can emit particulate matter into the air, which can eventually reach the oceans and coasts via wind and precipitation, contributing to pollution in those areas. Similarly, severe storms can cause infrastructure damage, leading to the release of stored pollutants. Flooding, for example, can cause pollutants stored in industrial facilities and wastewater treatment plants (WWTPs) to be released, contaminating different environmental compartments. On the other hand, some persistent organic pollutants (POPs) commonly used in industrial processes, such as perfluorinated compounds (PFCs), are potent

greenhouse gases (GHGs) and significant contributors to climate change (Kostyuchenko & Smolennikov, 2020).

Second, the bi-directionality between climate risks and the social context is illustrated in figure 10.1 through path 2. Climate change can have a significant impact on the social context by exacerbating social inequalities. For instance, the occurrence of extreme weather events like floods can result in the destruction of crucial public services and infrastructure, including roads, hospitals, schools, places of worship, and homes, as well as vital assets such as water-supplying infrastructures, crops, and livestock farms. Conversely, human activities shaped in the social context, such as lifestyle choices and patterns of production and consumption, can increase climate change. For example, lack of climate change and pollution awareness, overconsumption and intensive food production patterns contribute to GHG emissions.

Third, in figure 10.1, we illustrate the bi-directionality between pollution and social context through path 3. The dynamics occurring in the social context can affect pollution in various ways. Communities of lower socioeconomic status or with specific demographic characteristics are often more exposed to pollution (e.g. communities living in coastal areas are more exposed to certain pollutants due to their location and dietary patterns). In addition, social expectations can promote certain behaviours that can contribute to increased pollution, for instance, the use of single-use plastics. Contrarily, pollution can also lead to increased inequalities in the social context, particularly in terms of health. Pollution-related health problems can increase health costs and reduce productivity, which can put job stability at risk and contribute to economic inequalities.

Finally, in figure 10.1, we illustrate the bi-directionality between host health status and social context through path 10. As explained in section 10.2.1.2 the social context can affect the status of the host’s health influencing its susceptibility to infections. Considering the opposite direction, the host health status can also impact the social context, for instance, health problems can reduce work productivity and exacerbate economic inequalities between social groups.

When considering the interplay of influencing factors, the bidirectionality alone indicates the complexity of the system's functioning. However, the intricate nature of

the system further adds to the complexity of its behaviour. Moreover, the synergistic mechanisms between these factors compound the issue, as climate change, pollutants, and the social context or health status of the host all play a role in increasing exposure and susceptibility to coastal pathogens.

There are numerous cases where several influencing factors can interact and affect each other, leading to synergistic effects. An example is the effect of frequent heavy rainfall in combination with heatwaves, pollution and risk increasing behaviours. On the one hand, extreme rainfall puts additional pressure on sewage and WWTPs, which can lead to overflows. This overflow can increase people's exposure to pollutants, which can weaken their immune systems and encourage the development of chronic diseases, making them more susceptible to infections. At the same time, contaminants that reach the coast, such as nutrients, antibiotics and plastics, may also favour the growth and proliferation, as well as the development of virulence and resistance mechanisms in coastal pathogens. On the other hand, climate change may alter social and behavioural patterns, increasing the use of recreational waters (in terms of frequency, intensity and number of users) during heatwaves, thus, increasing exposure to pollutants and pathogens. Finally, a health status weakened by exposure to pollutants or sanitary infrastructures damaged by extreme weather events can reduce the recovery capacity of the host. As a result, exposure, susceptibility and recovery of individuals may be affected by multiple hazards occurring simultaneously or sequentially and therefore it is important to address the risk of coastal pathogen infection from a risk-associated approach.

To finalise the characterisation of the system map operation, we have identified examples of feedback loops through pathways 13, 14 and 15 as illustrated in figure 10.1. Although the identification of the loops has not been carried out comprehensively, the aim of highlighting their presence is to emphasise their role in introducing complex dynamics that can amplify or dampen the effects of the influencing factors.

The feedback loop indicated through pathway 13 refers to infections that can compromise the overall health status of the host, making it more susceptible to new infections. This is because certain infectious diseases can cause tissue and organ damage, alter the functioning of the immune system, or even trigger the development

of chronic diseases. However, it is important to note that the relationship between infectious and chronic diseases is intricate. The importance of this feedback loop is that it can perpetuate and exacerbate the weakened health status of populations with pre-existing health conditions, leading to increased incidence of infections and consequent deterioration in overall health.

The feedback loop designated by pathway 14 (Fig. 10.1) is characterised by a pattern in which structurally disadvantaged individuals and communities have difficulty recovering from infections, further exacerbating existing social inequalities. This means that contracting infections may lead to an increase in their inequities, for instance, by losing employment if they lack sick leave options. This, in turn, can worsen their economic disparity and increase their risk of future infections.

Small disturbances can have a significant impact on a system's equilibrium due to non-linear dynamics. It is crucial to comprehend how feedback loops can either stabilise or destabilise the behaviour of the system to identify critical intervention areas.

Finally, the feedback loop shown by path 15 (Fig. 10.1) pertains to acquired immunity following exposure to an infectious disease. This immunity protects against subsequent infections by bolstering the host's resilience in case of reencountering the pathogen. The duration of this immunity varies, lasting for months in some cases and for years or even permanently in others.

10.3. Principles

The purpose of this section is to establish a set of principles that could support an extended One Health framework. This is done by integrating the theoretical concepts related to the framing of health that have emerged from module A with the findings of system characteristics in module B, which investigated the complexity that arises when trying to understand how climate change interplays with other pressures to determine the dynamics of infectious diseases caused by coastal pathogens.

These principles could serve as a basis to guide interventions and decision-making. The principles have been organised into three levels: foundational principles, operative principles, and adaptive principles (Fig. 10.2).

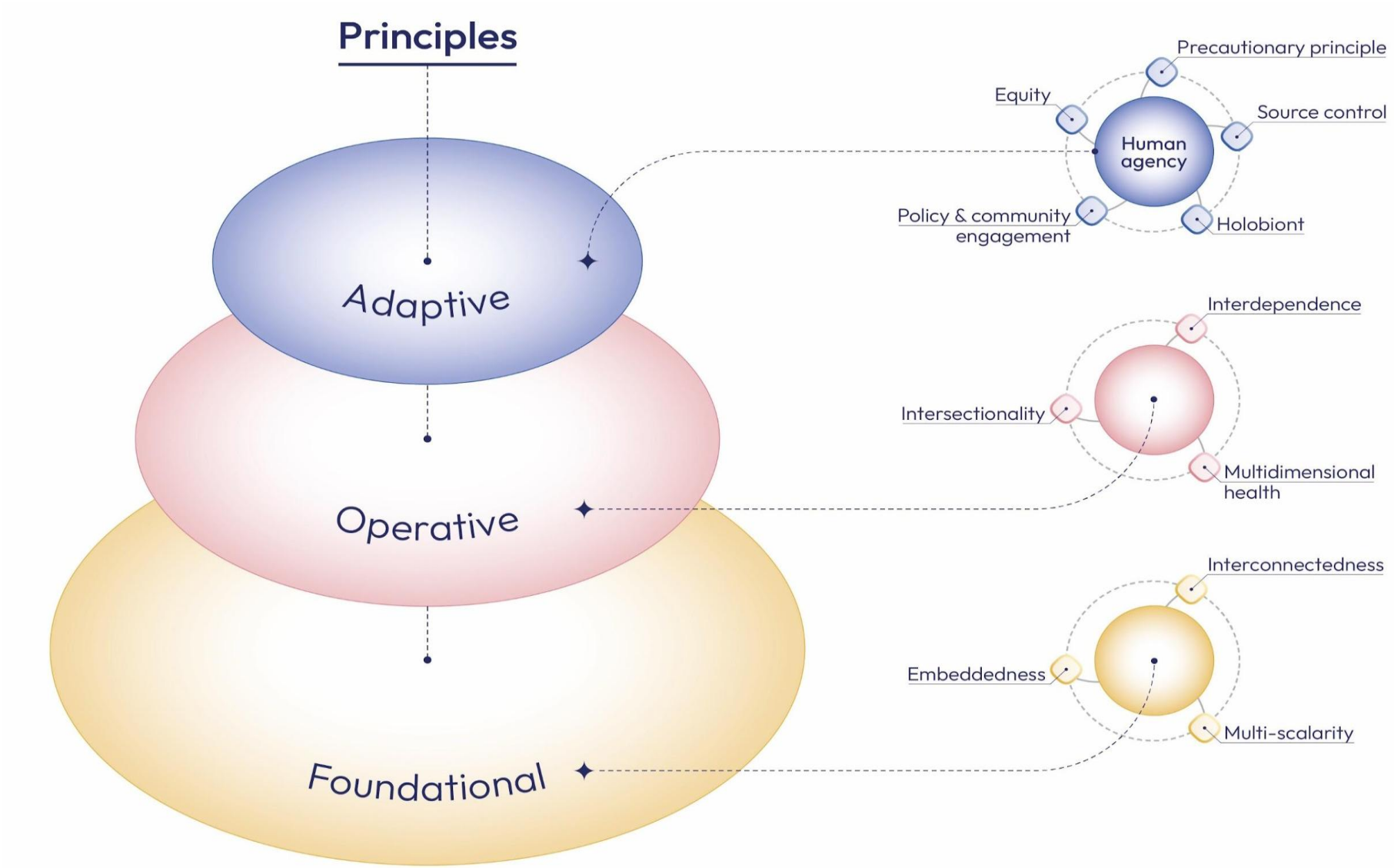


Fig. 10.2. Principles supporting an extended One Health framework.

10.3.1 Foundational principles

Foundational principles are related to the fundamental concepts that underpin the structure and functioning of a given system. Within our conceptual framework, we have identified three foundational principles based on the characteristics of the system we have studied and summarised in section 10.2 of this chapter (see system map in Fig. 10.1). These foundational principles are (i) interconnectedness, (ii) multi-scalarity and (iii) embeddedness.

The dynamics of infectious diseases caused by coastal pathogens are rooted in a foundational matrix of interactions of an interconnected, multi-scalar and embedded nature. Our lives are in constant dialogue and exchange with multiple physical, chemical, microbial and ecological interconnected and multi-scalar dynamics. Authors such as Zinsstag et al. (2011) and Rabinowitz et al. (2018) have already proposed that health and disease dynamics in the One Health framework are characterised by systemic interactions among ecological, microbial, social, cultural, economic, and political interconnections across scales from pathogens to individuals to populations and the global scale.

i. Interconnectedness: Our analysis has revealed how multiple pressures operate and interact through multiple interconnected pathways that increase the risk of coastal pathogen infections. Disregarding these interconnected pathways leads to underestimating the potential compounding of factors.

ii. Multi-scalarity: Across our work, we find that we need to conceive and analyse processes that are active at multiple interacting and overlapping scales from micro to macro levels: e.g. biochemical, microbiological, individual, family, community, habitat and ecosystem, global dynamics (Appendix 10.1).

iii. Embeddedness: The dynamics or processes happening in a given scale are inextricably interconnected and situated inside another bigger scale or context where other dynamics and processes happen. The cells and microbes composing our organs and gut microbiomes are embedded in the body. The body that constitutes a human is embedded in a community or society where it relates to other humans through social relationships. The community or society is embedded in a global population and in the biosphere, where other forms of

life especially microbes are the main characters. Life in a broad sense is, therefore, a continuum of the integration of different embedded scales that increase in complexity. Moreover, those scales are interconnected and effects in upper scales have cascading effects in lower scales and vice versa. For example, as analysed in module B, what happens at the social scale of the community has impacts at the scale of the health of the individual, and the individual's behaviour in turn, shapes processes of health resilience at the community level.

10.3.2. Operative principles

Operative principles determine how something operates or functions. While foundational principles are more directed towards the explanation of system characteristics, the operative principles explain how the emergent dynamics under study operate. Three main operative principles have been identified throughout our study: (i) interdependence, (ii) health and disease multidimensionality and (iii) intersectionality.

i. Interdependence: It refers to the condition of being in reciprocal dependence. It highlights how each living organism depends on other organisms. When elucidating the dynamics of infectious diseases caused by coastal pathogens, the complex interdependent and mutualistic nature of the entanglements of the microbial world and humans has emerged as a still understudied field highlighting this interdependence between organisms.

ii. Health and disease multidimensionality: We have seen how multiple dimensions of health and disease can explain many of the interconnections in the system map, in line with the biopsychosocial approach proposed by Engel (see chapter 2), where processes are rooted in a system with the foundational characteristics of interconnectedness, multi-scalarity and embeddedness. It means that the multiple dimensions of health operate in a interconnected and nested way, such that the health dimensions can't be addressed separately. This interaction between multiple dimensions itself becomes a driver of health outcomes.

iii. Intersectionality: It acknowledges that various biological, cultural and social aspects of an individual's identity intersect and interact with each other in complex heterogenous dynamics, producing unique identities, with social and health inequalities that cannot be understood by looking at just one isolated aspect. Therefore, in the field of public health and epidemiology, intersectionality becomes a powerful approach to examine and elucidate in detail the rise of health inequalities in both advantaged and disadvantaged individuals and communities.

10.3.3. Adaptive principles

In complex systems, a disruption in one component of the system due to external or internal interferences can lead to a cascade effect that impacts the entire system (Alfaqiri, 2020). Then, to dynamically change and adapt to these interferences, these systems need to be flexible and adaptive. Humans are just one element of these complex systems; however, they hold significant agency in guiding and adjusting their adaptation. Six main adaptative principles have been identified throughout our study which highlight the role of humans: (i) human agency, (ii) holobiont, (iii) precautionary principle, (iv) source control, (v) policy and community engagement and (vi) equity.

i. Human agency: Humans have evolved to a degree of awareness and knowledge which has enabled them to participate in processes that have significantly altered the dynamics of the planet, strongly impacting other life forms, intensifying interspecies encounters and altering the microbial world. Understanding the capacity of humans to actively influence these dynamics, highlights a responsibility to avoid or mitigate negative impacts.

ii. Holobiont: Social imaginaries permeate all scientific disciplines, influencing their paradigms (see chapter 3). Culturally specific ways of knowing and understanding the world influence scientific research and inquiry. This strongly shapes the way human beings relate to and influence their natural environment and other forms of life. Consequently, in the attempt to change the dynamics of infectious diseases, one of the crucial aspects is the transformation of social- and health imaginaries towards the microbial world. Our greatest challenge is to learn and imagine new ways of inhabiting the

planet according to its systemic characteristics. For this, innovative public health measures, discourses and approaches must be formulated and implemented. As a new emerging health imaginary, the “multi-species ecological dynamic unit” represented by the “holobiont” aims to pave the way for a more holistic public health approach to microbes (see chapter 3).

iii. Precautionary principle: when there is no sufficient evidence about the hazardous effects of a man-made technology or products, preventive actions must be taken. It enables decision-makers and policymakers to adopt precautionary measures to safeguard public health and the environment. Some of the current public health threats have been partially caused by the application and production of multiple technologies and products, e.g. the AMR crisis. The development of AMR is caused not only by antibiotics and drugs, but also by many other compounds, such as heavy metals, herbicides, household cleaning products, etc. (see chapters 6 and 7). While adopting the precautionary principle is vital for managing uncertainty around pollution and other hazards, its application presents challenges. It is therefore essential to invest research efforts in determining how this principle can be effectively implemented.

iv. Source control: Climate change and pollution on the coast are the two main global anthropogenic changes that are influencing current health and disease dynamics of infectious diseases caused by coastal pathogens. The royal road to addressing environmental problems in general is “source control”, which means reducing the problem at its initial source. At the other end of the spectrum, the so-called “end-of-pipe solutions” are “quick fixes” that often provoke new problems in new places (unintended consequences). Reducing the pressures at source typically is associated with the largest amount of co-benefits in other areas. A good example of this is microplastics, a health threat in themselves, and that we have seen act as an ideal carrier and habitat for pathogens, amplifying their proliferation and spread, virulence and AMR (see section 10.2.1 and chapter 6).

Source control consists of preventing plastics from entering the water environment in the first place and/or limiting plastic production for essential

usage. The “source control” to “end-of-pipe solutions” extends on a spectrum starting with policies that reduce or limit their production and use to intermediary solutions such as adding additional treatment steps or filters at WWTP and preventing them from entering the waterways to unfeasible and expensive clean-up activities following their release and dispersal into natural environments.

With regard to climate change, we have seen that most climate hazards amplify risks associated with pathogens, also in unknown and unpredictable ways (e.g. increased risks of zoonosis and the emergence of new pathogens). In addition to elaborating collaborative adaptation and disaster risk plans the emphasis needs to return to preventing high and mid-level CO_2 emission pathways from occurring (source control).

v. Policy and community engagement: As we have seen in the operative principles, health is multidimensional. Therefore, actors influencing the different levels of health provision are essential in shaping individual, community and global health. All relevant actors at multiple fields and scales—community members, policymakers, researchers, health practitioners, educators, urban planners, and local companies— must be involved equally through all the research and decision-making process, recognising the unique strengths that each of them brings. All members of the community, especially structurally disadvantaged groups must be represented, bringing their unique needs and experiences to the fore.

vi. Equity: Fairness and just distribution of resources and opportunities should be pursued for all, including access to health, education, housing, and a clean environment, as they address the underlying determinants that influence health, including risks to infectious diseases. With regard to this, an approach based on intersectionality should be adopted both in research and decision-making processes, to develop actions promoting collaborative and just policies.

In addition, an intergenerational and interspecies approach to environmental and social equity is necessary, meaning that equity and

justice should not only be for current generations and humans, but also for future generations and other forms of life. These two aspects of equity are intrinsically linked, as future generations will require intact and functioning ecosystems to be able to prosper.

To achieve this objective, it is necessary to promote the development of ethical considerations to support an extended One Health vision by incorporating disciplines such as environmental philosophy or anthropology among others.

10.4. Conclusions and outlook

The purpose of this prospective section is to discuss key outcomes that have emerged from the analysis of modules A, B and C, to outline future directions, potential implications for research and policy, and related recommendations. We aim to propose some final reflections that can guide next steps and support the operationalization of an integrated approach to health in real contexts.

10.4.1 Implications for research and policy

Ecological Public Health and links with other system approaches

The first step has been to compare the outcomes of the three modules with the analysis carried out in chapter 1 on the characterisation of the different system approaches to health. Although having One Health as a point of departure, our findings turn out to align more closely with some of the fundamental principles and concepts found in Ecological Public Health (Table 1.1). What emerges in our analysis as a central theme are the interconnections and interdependencies between health, environment and societies, requiring a system perspective and evidence-based research. This is highlighted by the resulting system map (Fig. 10.1) that identifies and discusses unique processes and pathways by which the intersection of biological, environmental, behavioural, socio-economic, infrastructural, cultural and beliefs-related dimensions determine health outcomes. This acknowledges the broader context influencing health- and disease dynamics and emphasises the nexus of environmental- and social determinants of health. Our approach highlights the need

to better capture complexity, with its intersecting dynamics, interconnectedness of elements, processes that are active across scales from micro to macro, non-linearity and feedback mechanisms. Emerging themes shared with Planetary Health include social inequalities and impacts of large-scale processes like climate change. Themes shared with EcoHealth are the emphasis on human agency, and a need for systems thinking, and a stronger inclusion of social sciences. Our findings point towards a more generic approach that is not bound to the more formalised frameworks. Indeed, the approach chosen in our work could be supportive of any of the integrated frameworks such as One Health, Planetary Health or EcoHealth.

The system map has been developed specifically for human health, in order to address the research question in Task 2.3 of the BlueAdapt project related to coastal pathogens and infectious diseases. However, the work carried out in module B could be quite naturally adapted to identify pathways of interaction affecting animal health, as similar influencing factors are affecting infectious diseases in animals, especially concerning climate change and pollution.

Knowledge integration underpins an integrated approach to health

The multiple interactions emerging from the system map emphasise the importance of knowledge integration as a key pre-condition to integrated approaches to health. In our analysis, we have identified at least 50 disciplines that support the analysis of coastal pathogen infections from an integrated perspective (Appendix 10.1). The disciplines identified are cross-scalar (e.g. microbiological, individual and community). We highlight that more emphasis should be given to the intersection with the social sciences. Future research should focus on the interface between disciplines, recognising the interconnectedness and interdependence among different research fields as a basis to create new knowledge. The interface between social science and microbiology, or between infectious diseases and non-communicable diseases, represents some key examples of research gaps. Working on the intersection between disciplines would pave the way towards more robust approaches for interdisciplinary and transdisciplinary modes of study.

Multi-hazard approaches require a complex systems perspective

Our analysis integrates multiple dimensions related to coastal pathogens and infectious diseases: climate change, pollution, the social context, coastal pathogens (proliferation, spread, resistance, virulence) and the host's health status (mental health, underlying chronic diseases, microbiome, immune system), each one containing multiple sub-factors that also interact among each other. Understanding how these factors interact to create multiple pressures on the dynamics related to exposure, susceptibility and recovery of the host is key for identifying preventive actions for infectious diseases. This aligns with the climate risk framework outlined in the Fifth Assessment Report of the Intergovernmental Panel on Climate Change (IPCC) AR5 (IPCC, 2014), which defines risk as the result of the interaction between hazards, exposure, and vulnerability.

The results show the necessity of integrating these multiple risks under a unified and cohesive framework for both research and policy to facilitate a common multi-hazards risk evaluation, which is also in line with previous requirements from the IPCC (IPCC, 2012).

Any disturbance in one of the factors in the system can trigger cascading effects that ripple through the system, with unintended consequences. Conversely, it is also true that any deliberate action to mitigate one of the disturbances within the system can trigger indirect positive or stabilising effects with ripple effects capable of initiating a virtuous cycle. Understanding these connections within a multi-hazard framework therefore has huge potential in broadening the entry points of action.

Another implication of a multi-hazard approach is the need to consider heterogeneity in susceptibility, recovery and exposure of the host in health models.

Emphasising the importance of the host health status

Traditionally, the main focus has been the analysis of how the host is exposed to the pathogen. In our analysis, the role of the host health status emerges as a fundamental factor strongly interconnected to many other factors (Fig. 10.1). Considering the susceptibility and the recovery capacity of the host (in addition to the exposure) allows to evaluate more accurately the infection risk. It allows to identify groups at higher risk

of infection and severe outcomes, underlying risk factors, tailored interventions and response strategies, with increased overall effectiveness.

Putting the host at the centre balances the need for exposure reduction with strategies oriented towards an active promotion of salutary factors. This could lead to more robust public health strategies for health promotion, which becomes especially important in a context of multiple pressures and hazards stemming from climate change, pollution, antimicrobial resistance, population ageing, and increasing prevalence of chronic diseases and mental health problems.

Improving host health status has many co-benefits in terms of reduction of infectious and chronic disease burden, including mental health, as well as socio-economic benefits associated with reduced costs for the health care system, increased work productivity or improved wellbeing.

We recommend therefore that the focus on host health status and the supporting salutary factors should become key components to support any integrated assessment of infectious diseases in public health.

Emphasising human agency and the role of imaginaries

The third group of principles (so-called “adaptive principles”) proposed in our framework (see section 10.3.3) highlights the role of agency in initiating positive changes capable of breaking the perpetuation of vicious cycles. From a public health perspective, working with a multidimensional health concept, allows widening the scope for action considerably. Small steps towards any improvement in any of the components of the system can be decisive in triggering change and amplifying the signal through the interconnections in the system. Emphasising human agency is a precondition for empowering individuals and communities, initiating behavioural changes, developing community-driven policy advocacy, and co-producing knowledge with communities and citizens.

This implies both providing narratives and health imaginaries, that spark such changes. As well as settings where these changes can take place and be fostered. One example of this is Living Labs, which bring together all the relevant actors within their unique local socio-cultural context.

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Appendix 1. Internal workshop held among BC3 research team of BlueAdapt.

1.1 Introduction to the exercise

An internal workshop was held among the BC3 research team of BlueAdapt, to discuss and identify the disciplines that could be useful to address the risks of coastal pathogens and their impacts on humans, animals, and the environment, under an extended One Health vision. The discussion was based on the analysis performed under modules A and B.

The exercise was carried out by using the classification of Rabinowitz et al. (2018), where multiple scales for different One Health interactions are proposed from micro scales (molecules, cells) to macro scales (individual, community, population, nation. The three realms, human, environment and animal are represented in columns (Fig. App. 10.1). Participants were asked to identify disciplines by scale within the three realms.

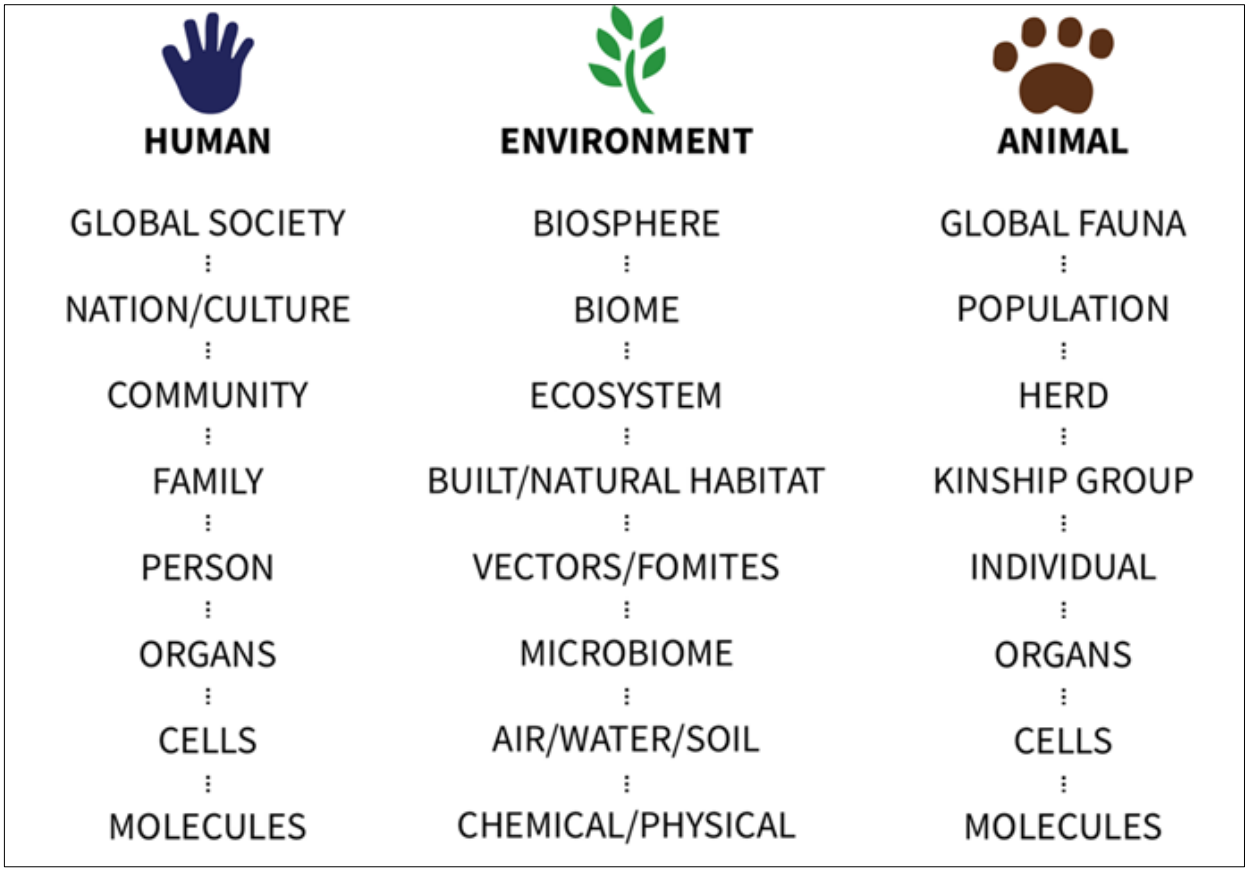


Fig. App. 10.1. System levels proposed by Rabinowitz et al. (2018).

1.2. Results

Answers from all the team members were compiled and analysed. To obtain just one term per discipline, we followed the Simple Knowledge Organization System (SKOS) – the UNESCO nomenclature for fields of science and technology (UNESCO, 2024). This classification system is widely used and is categorised into three different categories according to the expertise (fields, disciplines, subdisciplines). In our case, we used the discipline category, which includes the main disciplines adopted in science and technology. We used this code as an indicator for integrating similar disciplines cited by different participants to obtain one single consistent terminology.

After compiling the answers from all participants, a total of 50 disciplines were identified as being useful for the extended One Health framework. Out of the 50 disciplines, the human category was the realm where more disciplines were included. Overall, a total of 33 disciplines were included within the human realm, 20 within the animal realm, and 22 disciplines within the environment realm (Fig. App. 10.2). Some disciplines such as biochemistry, epidemiology, nutritional sciences, and plant biology (botany) were indicated within all three realms. However, other disciplines appeared only within a realm. For example, general economics, and occupational and personnel psychology were indicated only within the human realm. “Human” was the realm with the widest range of disciplines among different fields; including disciplines such as anthropology, epidemiology, food technology, general demography, internal medicine, geography, national law and legislation, philosophy, and toxicology.

Different disciplines were cited depending on the micro and macro-scale (Fig. App. 10.3). For example, within the animal realm, the microbiology discipline appeared in seven of the eight scales proposed by Rabinowitz et al. (2018). In the case of the environment, the biosphere was the scale that comprised more disciplines; among them, atmospheric sciences, geography, and geology disciplines. Among human scales, the micro-scale “cells” comprised only two disciplines, inorganic chemistry and pharmacology. However, the macro-scales “community” and “nation” included 17 disciplines each; being these 17 disciplines from a wide range of fields.

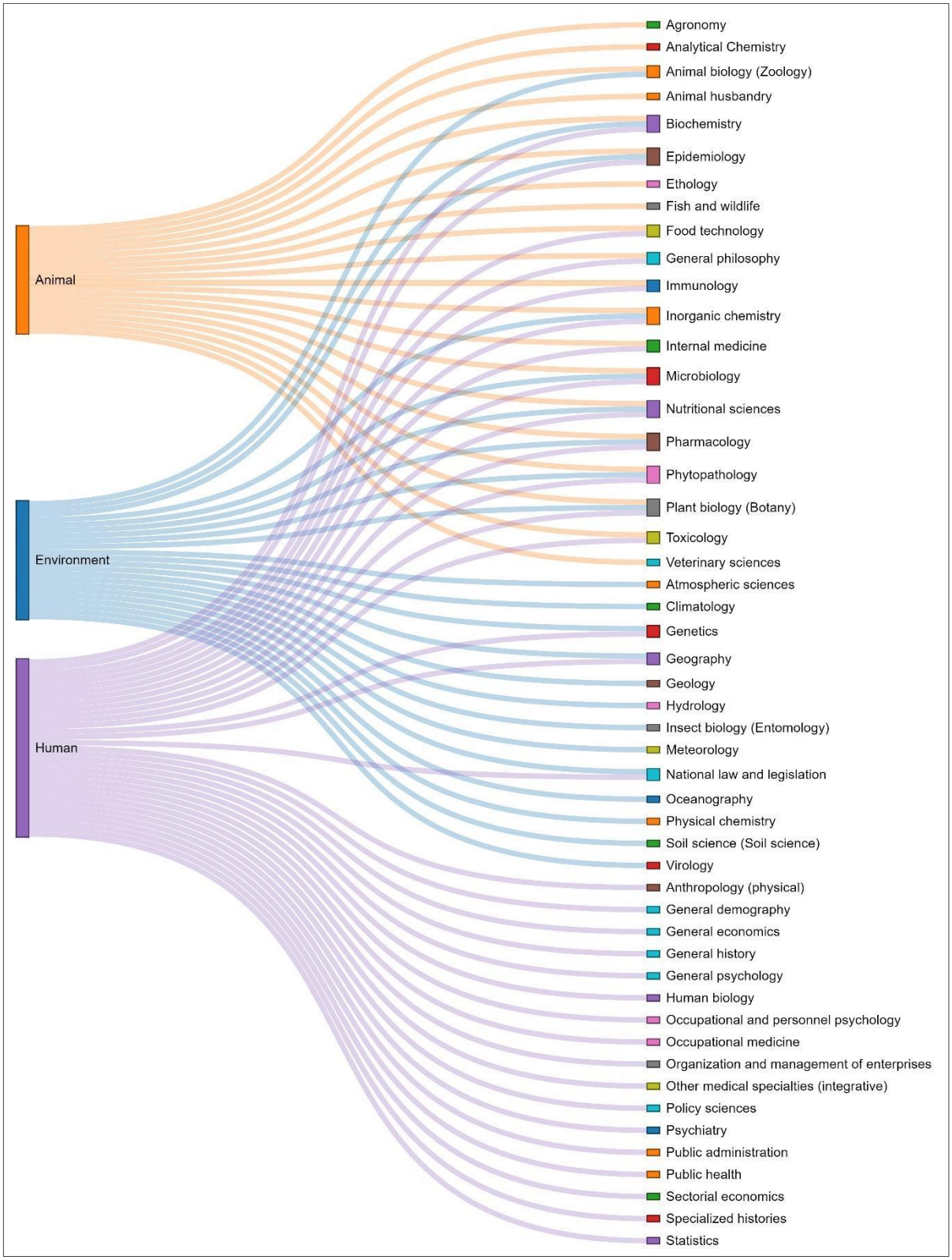


Fig. App.10.2. Disciplines obtained after compiling the answers from all participants present at the workshop. The disciplines are linked to the realms proposed by Rabinowitz et al. (2018): animal; environment; and human.

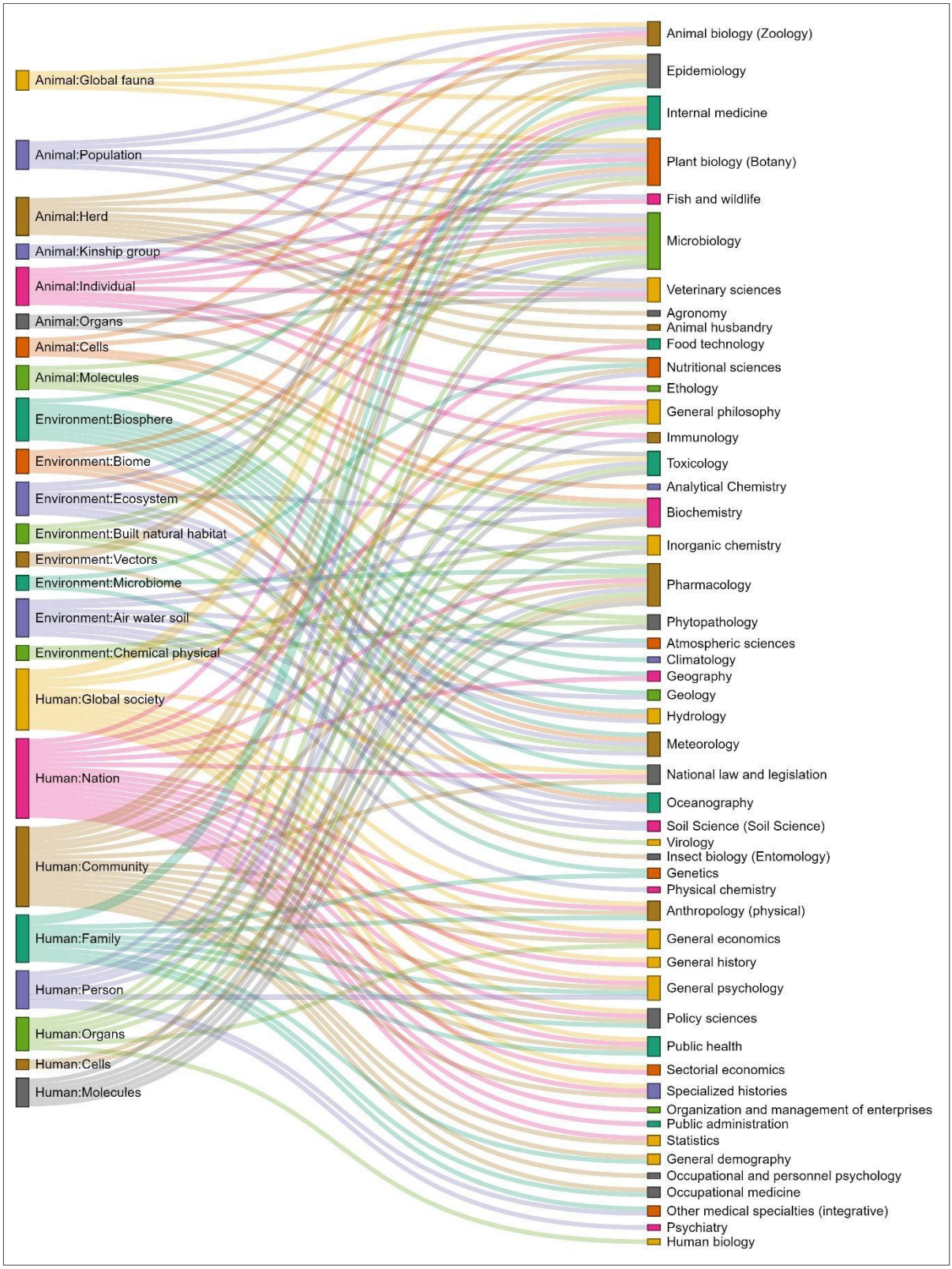


Fig. App. 10.3. Disciplines obtained after compiling the answers from all participants present at the workshop. The disciplines are linked to the scales proposed by Rabinowitz et al. (2018): animal (global fauna, population, herd, kinship group, individuals, organs, cells, molecules); environment (biosphere, biome, ecosystem, built natural habitat, vectors, microbiome, air-water-soil, chemical-physical); human (global society, nation, community, family, person, organs, cells, molecules).

1.3. Final reflections

The results obtained in the workshop indicate that a large number of disciplines could be useful to address the risks of coastal pathogens and related infectious diseases, under a broader One Health vision.

We can highlight three main issues. First, a need to integrate knowledge from many different disciplines. How to work on the intersection between disciplines might represent a key point to be addressed in future research, because a lot of research gaps exist in the interface between disciplines. Second, the variety of disciplines emerged show the need to work at multiple scales. Third, social sciences have emerged in many fields from anthropology, economics, demography, history, policy sciences, statistics, and philosophy, among others.

Appendix 2. System map

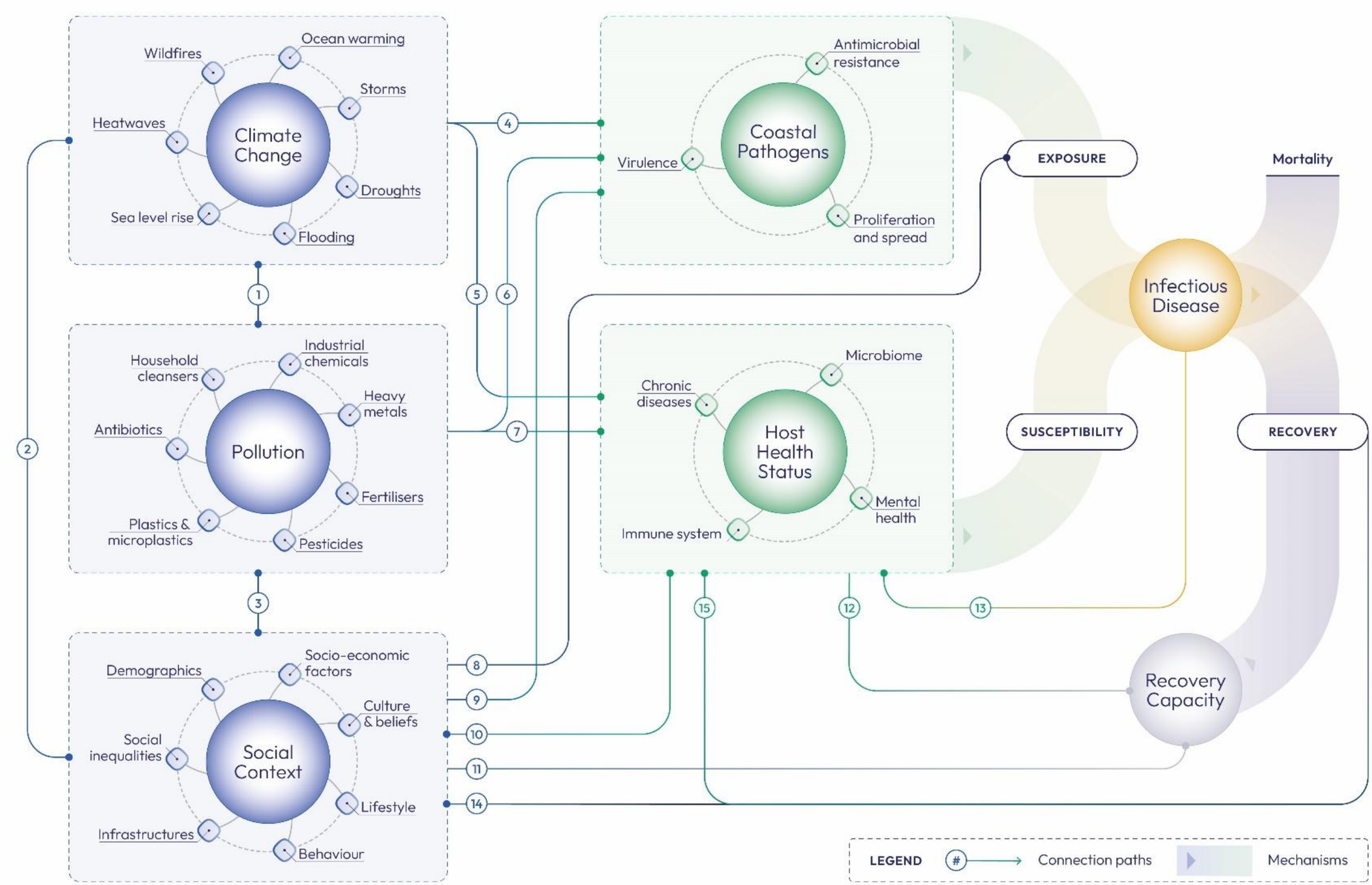


Fig. App. 10.4. System map: interactions among influencing factors and their impact on the risk of coastal pathogen infections. Each number represents a connection path between different influencing factors in the system

Glossary

Concept	Definition
Abiotic	refers to the non-living characteristics of a habitat or ecosystem that affect organisms' life processes.
Anatomy	is the branch of the science that studies the body structure of living organisms and their parts. It involves examining organs, tissues, cells, and their positioning.
Anthropogenic	refers to any process or phenomenon resulting from human activities or caused by human influence. It is commonly used to describe environmental changes such as human-made pollution.
Antibiotic resistance genes	are specific genes that encode proteins or enzymes that confer resistance to antibiotics in bacteria. These genes can be naturally present in bacterial populations or acquired through horizontal gene transfer, allowing bacteria to survive exposure to antibiotics that would otherwise inhibit or kill them.
Antibiotic-resistant bacteria	are strains of bacteria that have developed the ability to survive exposure to antibiotics, making these drugs less effective or ineffective in treating infections caused by these bacteria.
Antimicrobial resistance	occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobials. As a result of drug resistance, antibiotics and other antimicrobial medicines become ineffective and infections become difficult or impossible to treat.
Approach	is a perspective or strategy used to address a particular problem or issue.
Architectural imaginary	refers to how people visualise the built environment and includes the perception of the design of its structures and spaces.
Autoimmune disease	is the damage to a own’s organs due to an action of the immune system.
Autotroph	is an organism that uses carbon dioxide (CO2) as it principal carbon source.
Bacterial conjugation	is one of the horizontal gene transfer processes in which genetic material is transferred aided by a mobile genetic element from one bacterial cell (the donor) to another bacterial cell (the recipient). This transfer occurs through direct cell-to-cell contact, facilitated by a structure called the Type 4 Secretion System.
Bay	refers to an open, curving indentation made by the sea or a lake into a coastline.
Beach	is the unconsolidated material that covers a gently sloping zone, typically with a concave profile, extending landward from the low-water

	line to the place where there is a definite change in material or physiographic form (such as a cliff), or to the line of permanent vegetation (usually the effective limit of the highest storm waves); a shore of body of water, formed and washed by waves or tides, usually covered by sand or gravel, and lacking a bare rocky surface.
Biofilm	is a structured community of microorganisms, such as bacteria, that is attached to a surface and encased in a slimy, protective matrix of extracellular polymeric substances (EPS).
Biomedical approach	is a perspective on health that predominated until the end of the 20th century. It focuses on understanding disease primarily through biological mechanisms, such as genetics, physiology and biochemistry. It emphasises medical interventions (e.g. drugs and surgeries) to control and cure disease.
Biopsychosocial approach	is a perspective on health proposed by George Engel in 1977. It views health as the outcome of the interconnections between factors at different scales (e.g. biological, psychological and social factors).
Biotic	related to any living form.
Brackish waters	slightly salty water with a salinity between 0.5 ppt and 32 ppt.
Capsule	is a protective outer layer that surrounds the cell wall of certain bacteria. It is a well-defined, gelatinous structure composed of polysaccharides. The capsule is distinct from the cell wall and is not easily washed off, giving the bacterial cell an additional layer of protection.
Catchment	is (i) an area from which surface runoff is carried away by a single drainage system or (ii) the area of land bounded by watersheds draining into a river, basin or reservoir.
Cell-membrane	is a crucial component of all cells, serving as a selective barrier that separates the internal and external environments.
Cell-wall	is a structural layer surrounding the cell membrane of certain cells that provides support, shape, and protection. It is a characteristic feature of plant cells, fungi, bacteria, and some archaea.
Chlorophyll-α	is a green pigment, present in algae and higher plants, that absorbs light energy and thus plays a vital role in photosynthesis. Except in Cyanophyta (blue-green algae), chlorophyll is confined to chloroplasts.
Chloroplast	is an organelle in a cell containing photosynthetic pigment which transforms light energy into chemical energy.
Chronic disease	is a long-term illness that often requires ongoing medical attention or limits daily activity.
Coastal water	is (i) the water outside the low-water line or the outer limit of an estuary. (ii) Surface water on the landward side of a line, every point of which is at a distance of one nautical mile on the seaward side from the nearest point of the baseline from which the breadth of territorial

	waters is measured, extending where appropriate up to the outer limit of transitional waters.
Coastline	is the line that separates a land surface from an ocean or sea.
Cognitive	refers to cognition, which encompasses perception, thinking, reasoning and memory.
Comparative anatomy	refers to the branch of anatomy that compares different species. It helps to identify similarities and differences in the anatomical structures of organisms.
Conjugative plasmids	are a specific type of plasmid, a small, circular, double-stranded DNA molecule that is separate from the chromosomal DNA and is found in bacteria, archaea, and some eukaryotic organisms. They can transfer genetic material between bacterial cells by a process called conjugation. Plasmids in general, and conjugative plasmids in particular, are not essential for the survival of the host cell but often carry genes that can confer certain advantages, such as antibiotic resistance or the ability to metabolize specific nutrients.
Contaminants of emerging concern	refer to substances that are not traditionally monitored or regulated in the environment but have the potential to pose risks to human health, ecosystems, or both.
Copepod	is one of the most common herbivorous zooplankton.
Cyanobacteria	also called blue-green algae, comprise photosynthetic prokaryotic organisms similar to bacteria. They constitute the largest, most diverse, and most widely distributed group of photosynthetic prokaryotes.
Cytoplasm	is the semi-fluid substance that fills the interior of a cell, residing between the cell membrane and the cell nucleus in eukaryotic cells. It encompasses various organelles, cellular structures, and cytosol, a gel-like matrix composed of water, ions, enzymes, and other molecules.
Deoxyribonucleic acid	is a molecule that carries the genetic instructions used in the development, functioning, and reproduction of all known living organisms and many viruses.
Dissolved oxygen	refers to the amount of gaseous oxygen (O2) present in water expressed in terms either of its presence in the volume of water (milligrams of O2 per litre) or of its share in saturated water (percentage).
Dysbiosis	any change to the composition of resident commensal communities relative to the community found in healthy individuals.
Ecological imaginary	refers to how people imagine the interconnection between the natural environment and society and includes values related to biodiversity, ecosystem and other environmental issues.
Efflux pumps	are cellular transport proteins found in various organisms, including bacteria, that play a crucial role in pumping out toxic substances,

	drugs, or other unwanted molecules from the cell. These pumps are integral to the cell membrane and actively transport substances across the membrane, usually against their concentration gradient.
Empirical	refers to the knowledge based on direct observation, experience or experimentation.
Encephalitis	a serious illness caused by an infection that causes brain inflammation.
Environmental Health	refers to the branch of public health that is concerned with how human environments impact human health. It includes addressing issues related to air and water quality, food safety, hazardous substances, noise pollution, and other aspects of the physical environment.
Enzymes	are special proteins that act as biological catalysts, facilitating and speeding up chemical reactions within living organisms. They play crucial roles in various physiological processes, such as digestion, energy production, and cellular growth.
Epidemic	is the increased occurrence of a particular disease in a population or geographical area at a particular time. It refers to a rapid and widespread increase in the number of cases of a specific disease within a population.
Epistemology	is the theory or philosophy of knowledge. It is the branch of philosophy that studies the nature, methods, limitations, and validity of knowledge and belief.
Epizootic	is an outbreak of a disease in an animal population.
Erosion	is ate general process or the group of processes whereby the materials of Earth's crust are loosened, dissolved, or worn away and simultaneously moved from one place to another, by natural agencies, which include weathering, solution, corrosion, and transportation, but usually exclude mass wasting.
Estuary	is the area at the mouth of a river where it broadens into the sea, and where fresh and sea water intermingle to produce brackish water. The estuarine environment is very rich in wildlife, particularly aquatic, but it is very vulnerable to damage as a result of the actions of humans.
Eukaryotes	are unicellular or multicellular organisms whose cells have a nucleus and organelles (endoplasmic reticulum, Golgi apparatus, various plasters, mitochondria, etc.) delimited by membranes. Eukaryotes are, along with bacteria and archaea, one of the three groups of living organisms.
Eutrophication	is the excessive enrichment of waters with nutrients, and the associated adverse ecological effects.
Exposure	in epidemiology, exposure is the frequency and intensity at which an individual comes into contact with an infectious agent.
Faecal sources	refers to the origin of sources that may be contaminated by faeces, which typically come from humans or animals.

Flagella	is a whip-like appendage that protrudes from the surface of certain cells, providing motility. Flagella are found in a variety of organisms, including bacteria, archaea, and some eukaryotic cells, such as the tail of sperm cells.
Foodborne disease	is an illness caused by foods or drinks which have been contaminated by toxins or harmful microbes (e.g. bacteria and viruses).
Genome	is the entire amount of genetic material found in the cells of living organisms.
Germ cell	is a specialised cell that develops gametes, in fames is the egg and in males the sperm.
Harmful algal bloom	refers to types of microscopic algae that grow quickly in water, forming visible patches that may harm the health of the environment, plants, or animals. Harmful algal blooms (HABs) can deplete the oxygen and block the sunlight that other organisms need to live, and some algae release toxins that are dangerous to animals and humans.
Hazard	refers to the inherent capability of an agent or situation to have an adverse effect.
Health imaginary	refers to how people imagine health and illness, and their underlying causes, including the influence of social, political, and cultural values.
Hemochromatosis	is a genetic disease which causes an excessive absorption and storage of iron in the body.
Heterotroph	is an organism that requires an organic carbon source, also called an organotroph.
Heterotrophic	That which requires some nutrient components from exogenous sources. Heterotrophic bacteria cannot synthesize all of their metabolites and therefore require certain nutrients from other sources.
Holism	refers to an approach that highlights the interdependence and unity of the components of a system. It implies that comprehending any aspect of the system needs examining its connections to other parts and the system as a whole too.
Holobiont	is an individual entity and its microbial community which form a single ecological unit.
Horizontal gene transfer	is the process by which genetic material is transferred between different organisms that are not parent and offspring.
Humourism	was a medical practice that dominated Western medical thought from ancient Greece to the Renaissance. It was based on the belief that the human body is composed of four basic fluids or humours: blood (sanguine), phlegm (phlegmatic), black bile (melancholic) and yellow bile (choleric). The imbalance of these humours was considered to cause various diseases.

Imaginary dimension	refers to the set of cultural ideas and perceptions that constitute the manner people perceive and interpret the world.
Immunocompromised	refers to the situation in which the immune system is weakened.
Immunodeficient	refers to the absence of an adequate immune response.
Immunology	Is the study of the host's defence to a pathogen.
Immunosuppressed	refers to the quality of having weakened immune system.
Immunosuppressed	refers to the situation in which the immune system is inhibited.
Inclusions	refer to various non-membranous structures or particles within the cytoplasm of a cell. These structures are distinct from membrane-bound organelles and are often involved in storage, protection, or other specific functions.
Infectious disease	are illnesses caused by pathogens, including viruses, bacteria, fungi, or parasites. These diseases can spread from person to person through direct or indirect contact.
Inland water	refers to all standing or flowing water on the surface of the land, and all groundwater on the landward side of the baseline from which the breadth of territorial waters is measured.
Intersectional approach	is a framework that addresses social problems by recognising the multiple connections between different factors of discrimination, such as race, gender, social and economic class, etc.
Legacy pollutants	are compounds that were released decades ago but remain in the environment long after their introduction and at present have health and environmental effects.
Macrocosm	refers to the universe or the larger world, often used to describe the vastness of the cosmos or the entirety of existence on a grand scale.
Mangrove forest	is a type of forest that contains tree species that grow in tropical and subtropical estuaries. There are about 12 species though the black, red, and white are most common.
Manure	also known as livestock manure, is organic matter, mostly derived from animal faeces and urine, but normally also contains plant material (often straw), which has been used as bedding for animals and has absorbed the faeces and urine.
Marine water	is one of the main habitat types in the EUNIS habitats classification. Marine habitats are directly connected to the oceans, i.e. part of the continuous body of water which covers the greater part of the earth's surface and which surrounds its land masses. Marine waters may be fully saline, brackish or almost fresh. Marine habitats include those below the spring high tide limit (or below the mean water level in non-tidal waters) and enclosed coastal saline or brackish waters, without a permanent surface connection to the sea but either with intermittent surface or sub-surface connections (as in lagoons). Rock pools in the

	supralittoral zone are considered as enclaves of the marine zone. Includes marine littoral habitats which are subject to wet and dry periods on a tidal cycle including tidal saltmarshes; marine littoral habitats which are normally water-covered but intermittently exposed due to the action of wind or atmospheric pressure changes; freshly deposited marine strandlines characterised by marine invertebrates. Waterlogged littoral zones above the mean water level in non-tidal waters or above the spring high tide limit in tidal waters are included with marine habitats. Includes constructed marine saline habitats below water level as defined above (such as in marinas, harbours, etc.) which support a semi-natural community of both plants and animals. The marine water column includes bodies of ice.
Metabolism	is the conversion or breakdown of a substance from one form to another by a living organism.
Metabolite	refers to the substance resulting from the metabolism, the chemical transformation in an organism.
Miasma	was once believed to explain the disease, which was thought to be caused by bad smells. It was a widespread theory until the germ theory.
Microbiome	refers to the diverse community of microorganisms, including bacteria, viruses, fungi, and other microbes, as well as their genetic material and the particular environment they inhabit. In the context of human health, the term is often used to describe the microbial communities living in and on the human body, particularly in the gastrointestinal tract.
Microbiota	refers to the diverse and abundant community of microorganisms, including bacteria, archaea, fungi, viruses, and other microbes, that inhabit a particular environment or host organism. The term is often used in the context of the microbiota associated with the human body, where millions of microorganisms reside, primarily in the gastrointestinal tract but also on the skin, the respiratory tract, and other mucosal surfaces.
Microcosm	refers to a miniature, representative entity that represents the larger universe or world.
Microplastics	are small particles of plastic debris (<5 mm), resulting from the fragmentation of larger plastic items or intentionally manufactured for certain applications.
Mitochondria	is a membrane-bound cell organelle (mitochondrion, singular) that generates most of the chemical energy needed to power the cell's biochemical reactions.
Mobile genetic elements	are DNA sequences that can move or transpose from one location to another within the genome of one bacterium or among two different bacteria.
Mutation	is change (damage) in the DNA sequence, genes, or chromosomes of living organisms.

Mutations	are changes in the DNA sequence of an organism's genome. They can occur naturally as a result of errors during DNA replication or in response to environmental factors, and they are a fundamental aspect of biological evolution.
Nanoplastics	are very small particles of plastic debris (<1 μm), they are a subset of microplastics.
Natural antibiotics	are substances produced by living organisms that exhibit antimicrobial properties, inhibiting the growth or killing of bacteria, fungi, or other microorganisms. These compounds are often derived from plants, fungi, bacteria, or even animals. For example, penicillin.
Non-communicable disease	also known as a chronic disease, is a disease not transmitted from person to person, tends to be of long duration and is the result of a combination of genetic, physiological, environmental and behavioural factors.
Novel entities	are new substances or new forms of previously unknown substances or life forms that have been introduced into the environment by man and whose impact is unknown.
Ocean acidification	is the reduction in the pH of the ocean over an extended period, typically decades or longer, is caused primarily by the uptake of carbon dioxide from the atmosphere, but can also be caused by other chemical additions or subtractions from the ocean.
Ontology	is the branch of philosophy that studies what it means to exist.
Outbreak	in epidemiology disease outbreak is the occurrence of disease cases over normal expectancy. The spread of the disease may be localised within a specific area (e.g. a community, a village, a ship, or a closed institution) or the disease may spread to several countries. An outbreak may last a few days, several weeks, or several years.
Pandemic	is an outbreak of a disease that spreads over many regions of an area in a very short time or over almost an entire group of people, animals or plants.
Petri dish	is a shallow, circular, and transparent glass or plastic dish with a cover, commonly used in laboratories for culturing microorganisms such as bacteria or fungi.
pH	in expression of both acidity and alkalinity on a scale of 0 to 14, with 7 representing neutrality; numbers less than 7 indicate increasing acidity and numbers greater than 7 indicate increasing alkalinity.
Pharmaceuticals	often referred to as drugs or medicines, are substances used for the prevention, diagnosis, treatment, and relief of diseases and medical conditions in humans and animals. The pharmaceutical industry is involved in the research, development, production, and marketing of these therapeutic substances.
Phthalates	are a group of chemicals generally used as plasticisers.

Phylotype	in microbiology, a phylotype is a DNA sequence or group of sequences sharing more than an arbitrarily chosen level of similarity of a particular gene marker.
Phytoplankton	is an autotrophic organisms (algae, the equivalent of plants) that synthesise organic matter.
Placlitaxel	is a chemotherapy medication used to treat many cancers such as breast cancer and lung cancer.
Plague	is this deliverable it refers to a serious and highly contagious bacterial infection caused by *Yersinia pestis.* This bacterium was responsible for the Black Death in the 14th century, which had devastating consequences in Europe.
Planetary boundary framework	is a concept introduced in Earth system science to define and quantify the limits within which humanity can operate safely to avoid severe environmental degradation. It was first proposed by a group of scientists led by Johan Rockström and Will Steffen in 2009. The framework identifies key Earth system processes and sets boundaries for them to ensure a stable and resilient planet that can support human civilisation.
Plankton	are tiny, free-floating organisms of the ocean or other aquatic systems. They may be phytoplankton or zooplankton.
Political imaginary	is a way of transcending political reality, and thus challenging conformity. It can be used to visualise possible futures and to bring to life a real but distant past. It can be a consciously applied strategy or an unconscious way of processing desire.
Pollution	is the addition of any substance or any form of energy to the environment that can have negative effects on the environment, plants and wildlife, and often impacts human health and well-being.
Polyunsaturated fatty acids	are a subclass of fatty acids characterised by a single or double chain of carbon-carbon bonds.
Precautionary principle/approach	suggests that if an action has the potential to cause harm to the public or the environment, in the absence of scientific consensus, precaution, preventive measures and the need to avoid such actions are encouraged.
Prevalence	in epidemiology, indicates the percentage of a population suffering from a given disease.
Prokaryotes	are unicellular organisms in the domain of Bacteria and Archaea. Prokaryotes are characterised by their simple cell structure with a single circular DNA molecule, lack of membrane-bound organelles and smaller size compared to eukaryotic cells. Examples of prokaryotic microorganisms include bacteria such as *Escherichia coli*.
Protein	is a large molecule composed of one or more chains of amino acids in a specific order, formed according to genetic information.

Psychoanalytic framework	refers to the theoretical approach to a clinical method in psychology, psychoanalysis. It is based on the understanding of human behaviour, mental processes and personality.
Pyroaerobiology	is a recently introduced term which aims to understand the ecological and societal impacts of viable microbes (e.g. fungi and bacteria) transported by wildland fire smoke.
Real dimension	refers to the specific, material and palpable aspects which make up the world.
Recovery	in epidemiology, recovery is the elimination of infectious agents and the alleviation of symptoms.
Resilience	is the ability of a system, community or society exposed to hazards to resist, absorb, accommodate, adapt to, transform and recover from the effects of a hazard in a timely and efficient manner, including through the preservation and restoration of its essential basic structures and functions through risk management.
Ribosomes	are cellular structures responsible for protein synthesis in all living cells. They are composed of RNA and proteins, and they function as the cellular machinery that reads the genetic information encoded in messenger RNA (mRNA) and translates it into a specific sequence of amino acids to form proteins.
Rocky shore	is a coastal habitat characterised by rock formations, which are usually regularly exposed to the tides.
Runoff	is the precipitation that drains into a water body from the surface of the surrounding land.
Salinity	refers to the concentration of salts dissolved in salt water.
Saltmarsh	is a wetland flooded regularly by tidal, brackish water.
Salutogenesis	is a concept introduced by medical sociologist Aaron Antonovsky in the 1970s. Antonovsky developed this concept as an alternative approach to understanding health, focusing on the factors that promote and maintain health rather than those that cause diseases.
Scepticism	is a critical approach of doubt towards beliefs, propositions or dogmas.
Selection pressure	is the use of antibiotics in human healthcare, agriculture, and veterinary medicine creates a selection pressure that favours the survival and proliferation of bacteria with resistance traits. These resistant bacteria can then enter the environment through sewage, agricultural runoff, and other pathways.
Septicaemia	is characterised by the multiplication of microorganisms within the bloodstream.
Sewage water	is the water supply of a community after it has been fouled by various uses. From the standpoint of course, it may be a combination of the liquid or water-carried wastes from residences, business buildings, and

	institutions, together with those from industrial establishments, and with such groundwater, surface water, and stormwater as may be present.
Shallow water	refers to water of such a depth that surface waves are significantly affected by the bottom topography. It is common to consider shallow water as water with a depth of less than half the surface wavelength.
Smoke aerosol	refers to the solid particles and thousands of chemicals that are generated at high temperatures when a material combusts.
Social imaginary	is the social imaginary is not a set of ideas; rather, it is what enables, through making sense of, the practices of a society. Social imaginaries describe how human beings imagine living together in society and which expectations play a role.
Somatic cells	are the cells in the body other than sperm and egg cells (which are called germ cells). In humans, somatic cells are diploid, meaning they contain two sets of chromosomes, one inherited from each parent.
Sphalerite	(ZnS) is the main ore of zinc and is usually associated with galena and chalcopyrite.
Stigma	is a negative mark associated with a particular circumstance, quality or person.
Stream	is a general term for a body of flowing water. In hydrology, the term is generally applied to the water flowing in a natural channel as distinct from a canal.
Susceptibility	in epidemiology, is the propensity of an individual who has been exposed to an infectious agent to become infected.
Synergy	is the combined power of a group of elements working together. The resulting potency is greater than the potency achieved by each working separately.
Synthetic antibiotics	are chemically synthesised compounds created in laboratories to combat bacterial infections. Unlike natural antibiotics, which are derived from living organisms, synthetic antibiotics are designed and produced through chemical processes. These compounds are often developed to overcome specific challenges, including antibiotic resistance and the need for broader-spectrum activity. For example, sulphonamides.
System approach	is a method for understanding and addressing complex problems. It perceives a situation as a system composed of interconnected and interdependent elements. It is a valuable tool for addressing real-world problems involving multiple, interconnected factors.
Taboo	is a cultural conception that imposes limitations on certain behaviours or issues as unacceptable or morally questionable.
Technological imaginary	refers to how people visualise the technology and includes the expectations of technological innovation and progress.

Turbidity	refers to the hazy or cloudy condition of water due to the presence of suspended particles.
Ubiquitous	is something present, found or seeming to be found everywhere. It suggests that it is widespread, ubiquitous or prevalent in a wide range of places or situations.
Vector-borne diseases	are diseases transmitted by a living being, usually an arthropod vector, to a vertebrate host.
Virulence	refers to the degree or ability of a disease-causing organism (e.g. a bacterium, virus or parasite) to cause disease.
Virulence factors	are specific characteristics or traits possessed by pathogens (disease-causing microorganisms, such as bacteria or viruses) that enable them to cause disease and overcome the host's defences. These factors contribute to the pathogen's ability to infect, replicate within, and evade the immune system of the host organism.
Waterborne diseases	are those diseases that are transmitted by ingestion of contaminated water.
Xenobiotics	are chemical substances that are not produced by the metabolism of the organism, they have an external origin to the organism.
Zoonosis	is an infectious disease that occurs primarily in animals (wild and domestic) but can be transmitted to humans. Transmission can occur through direct contact with animals, their faeces or habitat, as well as through consumption of contaminated food and water.
Zooplankton	are the heterotrophic organisms of the planktonic community.

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