Environmental, human health and socioeconomic impacts of *Ostreopsis* spp. blooms in the NW Mediterranean

Elisa Berdalet[a], Anne-Sophie Pavaux[b], Rafael Abós-Herràndiz[c], Muriel Travers[d], Gildas Appéré[e], Magda Vila[a], Jérémy Thomas[d], Luc de Haro[f], Marta Estrada[a], Noemí Inmaculada Medina-Pérez[a,g], Laia Viure[a], Bengt Karlson[h], Rodolphe Lemée[b]

[a] Institute of Marine Sciences (ICM-CSIC), Passeig Marítim de la Barceloneta, 37-49, 08003 Barcelona, Catalonia, Spain

[b] Sorbonne Université - CNRS, Laboratoire d'Océanographie de Villefranche, UMR 7093, 181 Chemin du Lazaret, 06230 Villefranche-sur-mer, France

[c] Institut Català de la Salut, Departament de la Salut, Generalitat de Catalunya, Spain

[d] LEMNA, Institute of Economics and Management of Nantes, Nantes University, Chemin de la Censive du Tertre, BP 52231, 44322 NANTES Cedex 3 France

[e] GRANEM, Faculty of Law, Economics and Management, University of Angers, 13 allée François Mitterrand, BP 13633, 49036 Angers CEDEX 01 France

[f] Clinical Pharmacology and Poison Control Centre, APHM, Hôpital Sainte Marguerite, Marseille, France

[g] Department of Chemical Engineering and Analytical Chemistry, University of Barcelona, Avinguda Diagonal 645, 08028 Barcelona, Catalonia, Spain

[h] Swedish Meteorological and Hydrological Institute, Research and Development, Oceanography, Sven Källfelts gata 15, SE-426 71 Västra Frölunda, Sweden

[*] Corresponding author: berdalet@icm.csic.es (E. Berdalet)

Keywords: *Ostreopsis* blooms, human health, socioeconomy, ovatoxin, environmental impacts, management

Highlights:

- *Ostreopsis* blooms are addressed with a coupled natural - human systems perspective.
- Recurrent exposure to *Ostreopsis* blooms may have chronic effects on human health.
- Beach monitoring and surveillance in summer effectively prevent human health impacts.
- Confirmed alert thresholds are $3{\cdot}10^4$ cells L^{-1} water or $2{\cdot}10^5$ cells·g FW^{-1} macroalgae
- The occurrence of *Ostreopsis* blooms and their effects are poorly known by the general public.
- Potential economic impacts of increasing *Ostreopsis* blooms cannot be projected yet.

ABSTRACT

This paper summarizes the research conducted by the partners of the EU co-funded CoCliME project to ascertain the ecological, human health and economic impacts of *Ostreopsis* (mainly *O.* cf. *ovata*) blooms in the NW Mediterranean coasts of France, Monaco and Spain. This knowledge is necessary to design strategies to prevent, mitigate and, if necessary, adapt to the impacts of these events in the future and in other regions.

Ostreopsis proliferations in the Mediterranean have been related to massive mortalities of benthic organisms and to symptoms of respiratory and cutaneous irritation in humans. A six-year epidemiologic study in a *Ostreopsis* hot spot in Catalonia and the accumulated experience of the French Mediterranean National *Ostreopsis* Surveillance Network confirm the main effects of these blooms on human health in the NW Mediterranean. The impacts are associated to direct exposure to seawater with high *Ostreopsis* cell concentrations and to inhalation of aerosols containing unknown irritative chemicals produced under certain circumstances during the blooms. A series of mild acute symptoms, affecting the entire body as well as the ophthalmic, digestive, respiratory and dermatologic systems have been identified. A main remaining challenge is to ascertain the effects of the chronic exposure to toxic *Ostreopsis* blooms.

Still, the mechanisms involved in the deletereous effects of *Ostreopsis* blooms are poorly understood. Characterizing the chemical nature of the harmful compounds

synthesized by *Ostreopsis* as well as the role of the mucus by which cells attach to benthic surfaces, requires new technical approaches (e.g., metabolomics) and realistic and standardized ecotoxicology tests. It is also necessary to investigate how palytoxin analogues produced by *O.* cf. *ovata* could be transferred through the marine food webs, and to evaluate the real risk of seafood poisonings in the area. On the other hand, the implementation of beach monitoring and surveillance systems in the summer constitutes an effective strategy to prevent the impacts of *Ostreopsis* on human health.

In spite of the confirmed noxious effects, a survey of tourists and residents in Nice and Monaco to ascertain the socioeconomic costs of *Ostreopsis* blooms indicated that the occurrence of these events and their impacts are poorly known by the general public. In relationship with a plausible near future increase of *Ostreopsis* blooms in the NW Mediterranean coast, this survey showed that a substantial part of the population might continue to go to the beaches during *Ostreopsis* proliferations and thus could be exposed to health risks. In contrast, some people would not visit the affected areas, with the potential subsequent negative impacts on coastal recreational and touristic activities. However, at this stage, it is too early to accurately assess all the economic impacts that a potentially increasing frequency and biogeographic expansion of the events might cause in the future.

1. Introduction

"Toxic and harmful blooms cause negative impacts and economic losses in many parts of the world. ... Broadly speaking, there are four categories of deleterious effects, including risks to human health, loss of natural or cultured resources, impairment of tourism and recreational activities, and damages to non-commercial marine resources and wildlife (GEOHAB 2001)." This text from the Introduction of the GEOHAB program Science Plan applies in all senses to *Ostreopsis* blooms, which constitute a particular emerging challenge and paradigm of Harmful Algal Blooms (HABs).

Unicellular microalgae of the genus *Ostreopsis* grow in relatively shallow and well illuminated waters, mainly attached to benthic surfaces (macroalgae, corals, rocks, sands, ...). This dinoflagellate genus, initially reported in tropical areas has expanded its biogeographic distribution to temperate latitudes (see revision by Tester et al., 2020), especially in the Mediterranean coasts, which centre the study presented here. In this region, most harmful blooms are caused by *O.* cf. *ovata*, although *O.* cf. *siamensis* and *O. fattorussoi*, have also been identified (Penna et al., 2014; Tartaglione et al., 2016; Chomérat et al., 2019; 2020) in some beaches.

Ostreopsis can be defined as tychoplanktonic, having three different life stages (Figure 1): (i) benthic cells attached to living or inert substrates (Figure 1A, B, C), (ii) planktonic cells swimming in the water column (Figure 1D), and (iii) aggregated cells floating on the water surface (Figure 1E). Epiphytic or epibenthic cells attach to biotic or abiotic substrates by a self-produced mucilaginous matrix in which *Ostreopsis* cells aggregate (Honsell et al., 2013; Escalera et al., 2014). The benthic stage constitutes the reservoir or stock of *Ostreopsis* cells that determines the duration and maintenance of the blooms. Under certain combinations of biological processes and physical forcings, cells can detach from the substrate and become part of the plankton community or aggregate at the water surface, forming the so-called “sea-flowers", "fleurs d'eau" in French (Mangialajo et al., 2011; Pavaux et al., 2021). Planktonic cells and aggregates facilitate the dispersion of the bloom and the colonization of new sites. The three life stages have different roles in the interactions of *Ostreopsis* with the environment and on the impacts of its proliferations on humans and the marine ecosystem, as will be explained in this paper.

The main concern posed by *Ostreopsis* spp. blooms, is that some species synthesize toxins (e.g., Usami et al., 1995; Lenoir et al., 2004; Rossi et al., 2010) with a chemical structure very close to that of palytoxin (PLTX). PLTX was named after the tropical soft coral genus *Palythoa*, from which it was first isolated in 1971 (Moore and Scheuer, 1971). PLTX-contaminated seafood (fish and crustaceans) was probably the cause of fatalities in the tropics (e.g., Kodama et al., 1989; Onuma et al., 1999; Mahmud et al., 2000; see details and references in Deeds and Schwarz, 2010 and Tubaro et al., 2011) and some studies suggested that *Ostreopsis* was the biogenic origin of the toxins involved in the foodborne poisonings (e.g., Taniyama et al., 2003). However, as discussed by Tubaro et al. (2011) this link has not been clearly established yet. Details of the intracellular content of different PLTX analogues (ostreocins, mascarenotoxins and ovatoxins) produced by *Ostreopsis* species reported in the literature can be found in the revisions by Ciminiello et al. (2011) and Pavaux et al. (2020a) while new families of toxins are discovered due to continuous methodological progresses (Ternon et al., 2022).

In the Mediterranean coasts, different ovatoxins (OVTXs) and isobaric PLTX have been reported in mussels, sea urchins and omnivorous or herbivorous fish (Aligizaki et al., 2008; Amzil et al., 2012; Biré et al., 2013; 2015; see literature data in Table 3 of Pavaux et al., 2020a) at concentrations exceeding the safety alert threshold of 30 µg of PLTX-equivalent per kg of fresh flesh recommended by the European Food Safety Authority (EFSA, 2009). Luckily, no cases of seafood poisoning have been reported yet in the Mediterranean region.

However, in the last 20 years, blooms of *Ostreopsis* have become recurrent in certain beaches, and in some cases, they have been associated with mild acute respiratory illness and skin and mucosa irritation in humans (summarized in Table 2 of Pavaux et al., 2020a). PLTX-like compounds have been postulated as the toxins causing these problems although their direct implication has not yet been demonstrated. In any case, the potential health risks posed by *Ostreopsis* blooms stimulated the regular monitoring of these events in some areas, leading to occasional beach closures (Lemée et al., 2012; Funari et al., 2015). Some blooms have also been linked to massive benthic fauna mortalities (e.g., Sansoni et al., 2003; Vila et al., 2008; Shears and Ross, 2009). The overall risk posed by *Ostreopsis* blooms on human health and the environment is likely to impair socioeconomic activities on the Mediterranean coast.

The CoCliME project, *Co-development of Climate services for adaptation to changing Marine Ecosystems*, included the investigation of the past, present and future effects of *Ostreopsis* blooms on the environment, human health and the economy in Europe. This knowledge is necessary to design strategies to prevent, mitigate and, if necessary, adapt to the impacts of these events in the future. The NW Mediterranean coast is a densely populated area for which tourist and recreational use of the coast constitutes an important source of well-being. From a socioeconomic point of view, a relevant question is whether the *Ostreopsis* blooms have now or will have sufficiently significant health and socioeconomic effects to justify the implementation of specific new public policies.These policies would represent an additional financial and material burden for the society and therefore would compete with other public priorities requiring additional financial effort from taxpayers.

This paper summarizes the background and results of the research conducted by the CoCliME partners to ascertain the impacts of *Ostreopsis* blooms in the NW Mediterranean coasts of France, Monaco and Spain. The ecological impacts, poorly known and difficult to address, are only briefly reported here (see the recent review by Pavaux et al., 2020a, for more details). The effects of *Ostreopsis* blooms on human health will be presented at two different levels: a small-scale epidemiological study in a hot spot and a wider overview of the clinical perspective, considering the links with the dynamics of the blooms and the cell life stages. Finally, a first step in the complex investigation of the potential socioeconomic impacts of *Ostreopsis* proliferations in the future is described.

2. Materials & Methods

2.1. Background

2.1.1. Effects of* Ostreopsis *blooms on the environment.

The review by Pavaux et al. (2020a), conducted as part of the CoCliME project, provides a comprehensive picture on how *Ostreopsis* interacts with aquatic microorganisms, fauna and flora, in part depending on its cellular life stages (benthic, planktonic and aggregated at the water surface) shown in Figure 1. Pavaux et al. (2020a) details the interactions of *Ostreopsis* (mainly *O.* cf. *ovata*) with other marine organisms and the negative impacts of the exposure to the microalga. The main highlights of that review, a summary of the aspects focused on the Mediterranean Sea and some experimental research conducted under the CoCliME umbrella (Gémin, 2020; Pavaux et al., 2019, 2020b; Ternon et al., 2018) are briefly presented and discused here.

2.1.2. Effects on Human Health. Case study: Epidemiological studies on exposure to toxic aerosol in Sant Andreu de Llavaneres (Catalonia, NW Mediterranean coast of Spain); temporal link between the bloom and the human health impacts.

The first health problems associated to an *Ostreopsis* cf. *ovata* proliferation were reported in 2004 (Àlvarez et al., 2005; Vila et al., 2008) and affected 200 people inhabiting apartments in the shoreline of Sant Andreu de Llavaneres (NW Mediterranean, located about 40 km North of Barcelona, 41°33'07", 3°11'55"). Since then, the blooms have been recurrent as well as the impacts on humans exposed to the aerosols during these events. It was observed, that the health problems occurred for only a few days, when the *Ostreopsis* cell proliferation persisted for more than two months in the area. A parallel study of epidemiology and ecology conducted in 2013 (Vila et al., 2016) pointed to a complex combination of mechanisms involving meteorological and oceanic conditions, the physiology of *Ostreopsis* cells and the particular sensitivity of the affected people. A major open question was whether this pattern could be repeated or even get worse in the future, given the expansion of *Ostreopsis* in temperate coastal areas in the last 20 years (e.g., Tester et al., 2020). For this reason, similar studies were conducted from 2014 to 2018 in the same hot spot. The data of the 2013 study published in Vila et al., 2016 are included in the present paper, as part of the 6-year survey.

2.1.3. Effects on Human Health. The French Mediterranean National Ostreopsis Surveillance Network.

In the summer of 2006, following previous outbreaks of respiratory irritation in France between 2003 and 2005 (Appendix 1), the health authorities set up the French National *Ostreopsis* Surveillance Network (Kermarec et al., 2008), which is still operative. Its goal is to prevent human health problems by detecting and responding to *Ostreopsis* bloom events in recreational waters along the French Mediterranean coast. Here we describe the consolidated structure of this Network and the criteria for diagnosing the clinical symptoms associated with the different life cycle stages of the microalga. A brief history of how the clinical symptoms where untangled based on the experience of the Marseille Poison Control Centre is presented in Appendix 1.

2*.1.4. Socioeconomic effects.*

To carry out an overall socioeconomic appraisal of the effects of *Ostreopsis* blooms, it is necessary to evaluate the more or less visible economic losses (e.g., healthcare expenditures) associated with the health problems, and to ascertain the well-being costs inflicted to the affected people. It is also necessary to analyze the economic value linked to the different uses of the coastline that are impacted now by these blooms. In addition, since *Ostreopsis* blooms could be a more widespread human health problem in the future, a forecast analysis must be considered. Such a comprehensive economic assessment requires the complex evaluation of the loss of current and future economic value associated with a decrease in tourist activities, as well as the potentially noxious effects of *Ostreopsis* proliferations on non-commercial marine species and habitat biodiversity (essential for carbon storage and climate change mitigation, Mitra and Zaman 2015). Adams et al. (2018) propose a comprehensive literature review on the assessment of the economic consequences of HABs.

Following the methodology used by Morgan et al. (2010) to study the harmful effects of *Karenia brevis* blooms on marine-based activities in Florida based on observed behaviours, we implemented a partial and preliminary *ex ante* socioeconomic analysis focusing on current beachgoing behaviour for residents and tourists and its expected future variation (Figure 2). Beachgoing represents the key indicator at the core of the economic valuation of tangible and intangible effects due to *Ostreopsis* blooms. Tangible economic effects are those that have a visible impact on economic activity, or additional expenditures in the healthcare sector. Conversely, the intangible economic effects mean the loss of well-being of the human population affected by *Ostreopsis*:

these effects must be assessed by specific economic valuation methods, knowing that these populations can express a positive Willingness to Pay to avoid the effects of *Ostreopsis* blooms. If beach-goers keep going to the beach, they will be exposed to health risks which will result for some of them in more or less severe symptoms. Depending on how serious they are, the concerned users will have to seek medical care (meaning tangible costs) and will also experience a loss of well-being due to the pain, discomfort or stress (i.e., intangible costs) associated with the symptoms. As a result, they may reduce or stop beach-going, which will lead to other tangible and intangible economic losses. As a consequence, if these people stop going or go less often to the beach, they will suffer a loss of well-being (intangible costs) linked to a restriction of their recreational activities. If they are tourists, this negative experience could jeopardize how long they will stay in the area and their subsequent return, which could lower the number of future tourist visits (tangible costs). However, the importance of the effect mentioned above must be measured according to the priority they set on beach-going, among the reasons why tourists stay in the concerned city or region. Likewise, the decrease in beach-going could also go hand in hand with a decline in some additional commercial activities such as the bars, cafés or restaurants located near the beaches (tangible costs). It is therefore quite relevant to know exactly how heavily beach-going is impacted according to the population, be it tourist or resident and to determine the explanatory factors of these variations, especially with regard to the user groups most exposed to the risks associated with *Ostreopsis* blooms.

Before this, we wanted to ascertain if tourists and residents currently perceive the risks associated with *Ostreopsis* blooms, and whether these blooms represent an existing socioeconomic problem deserving the mobilization of public and private resources to avoid or reduce their consequences. Therefore, we explored the level of dissemination and credibility of scientific information about the human and environmental health effects of *Ostreopsis* blooms among tourists and residents. The knowledge would weigh on) the main tangible and intangible economic costs of *Ostreopsis* blooms on the recreational uses of beaches (Figure 2). For instance, health costs could be very low if, upstream, public measures or individual self-protection measures restricted access to the beaches or discouraged people from going. . Similarly, the net tangible cost in terms of loss of economic activity could be limited if the economic sector as a whole adapted by shifting to alternative activities less impacted by the *Ostreopsis* blooms (e.g., development of a form of tourism oriented to facilities such as museums or amusement parks).

2.2. Methodology

2.2.1. Effects on Human Health. Case study: Ecological and epidemiological studies on exposure to toxic aerosol in Sant Andreu de Llavaneres (Catalonia, NW Mediterranean coast of Spain)

Ecological study. *Ostreopsis* cf. *ovata* proliferates yearly in the shallow rocky beach heavily colonized by macroalgae from shoreline to at least 5-7 m depth. In front of this beach and along a 500 m longitudinal distance, a restaurant and several residences are located. During the six-year study period, the bloom was monitored as described in Vila et al. (2016). In front of the restaurant and the apartments, water and macroalgal samples were taken to estimate the *Ostreopsis* cf. *ovata* cell abundances in the plankton (cells L^{-1}) and in the benthos (cells per gram of macroalgae fresh weight $^{-1}$ - cells gFW^{-1}). Different biological, biochemical (toxins) and physical parameters were also measured and will be presented elsewhere. Samples were taken once or twice per week in July and August, twice per month in June, September and October, and monthly in November and December. Additional samples were collected when necessary in the fall. The data series for each year was organized by Julian days. To identify general trends in the six-year period and to smooth data variability, average Julian day cell concentrations were calculated first and subsequent 7-day moving averages were estimated.

Epidemiological study. The restaurant staff and the residents constituted the target populations invited to participate in the epidemiological surveys, which covered the entire period that *Ostreopsis* is found in that beach, that is, from June to December. In the restaurant, that opens from 10:00 am to 01:00 am, workers were exposed to marine aerosols during their 8 h worksheet time. The restaurant staff contributed to the study from 2013 to 2018. The residents of the apartments affected by the 2004 blooms (mentioned above) were incorporated into the epidemiological survey from 2015 to 2018; their exposure could occur over 24 h.

At the beggining of the summer season, daily self-administered questionnaires were distributed to the target populations, which were also regularlly contacted during the study. In 2013, the epidemiological questionnaire contained a list of 18 *Ostreopsis*-related symptoms (Supplementary Table 1 in Vila et al., 2016) similar to that in Tubaro et al. (2011). Other symptoms that became apparent in later years were incorporated in the questionnaire along the study, resulting on 27 *Ostreopsis*-related symptoms in 2018 (see 3.2.1. Results section).

In addition, the questionnaires recorded additional information about personal health background and asked whether people had required medical attention and treatment. All participants expressed their consent to contribute to the epidemiological surveillance following the ethical procedures of the Public Health Surveillance System from the Autonomous Government in Catalonia and the Spanish Research Council (CSIC).

2.2.2. Effects on Human Health. Epidemiological and clinical studies in France: French Mediterranean National* Ostreopsis *Surveillance Network

The French Mediterranean National *Ostreopsis* Surveillance Network operates on an active basis during the blooming period from June 15 to September 15. It includes a wide range of actors from the scientific, medical and public health (with all authorities levels, namely, town halls, departments, regions and nation) sectors. The French Mediterranean National *Ostreopsis* Surveillance Network integrates:

a) **Health surveillance** to detect suspected cases induced by exposure to *Ostreopsis* through direct contact with contaminated seawater or inhalation/contact with contaminated sea spray. Diagnosis and medical management of the poisoned patients are conducted by clinical toxicologists and experts on natural toxins of the Marseille Poison Control Centre (24/7 activity zone covering the whole French Mediterranean coast where blooms can occur).

b) **Environmental monitoring** of *Ostreopsis* by visual observation of recreational waters and by testing water samples on a routine and alert basis.

c) General Health Administration **Coordination** with other environmental and health surveillance agencies; publication of recommendations regarding *Ostreopsis* bloom control and management.

Alerts can be raised in two ways:

i) Through the Marseille Poison Control Centre after detecting at least two patients in the same locality with clinical symptoms (see below) compatible with exposure to *Ostreopsis* contaminated seawater.

ii) Through routine analyses detecting *Ostreopsis* levels above the threshold of $3 \cdot 10^4$ cells L^{-1} of seawater (no benthic samples are taken in the framework of the official French monitoring).

For both alert processes, the General Health Administration issues specific guidelines. When a proven hazard for the population is confirmed, a crisis team is formed by all network members to define adequate measures, which can include prohibiting access to contaminated beaches and/or consumption of shellfish and fish. Serial sampling and estimation of *Ostreopsis* cell concentrations in seawater by microscopy constitute the reference point, and protective measures are maintained until results confirm that the bloom is over.

2.2.3. Socioeconomic surveys in Nice and Monaco

An extensive face-to-face socioeconomic survey on the impact of *Ostreopsis* blooms on beach-going behaviour during the summer period was conducted between June 15 and August 15, 2019 in the city of Nice (France) and in the Principality of Monaco. Nice is located by the Mediterranean Sea in the south-east of France and is the fifth largest city in France (340,017 inhabitants, Insee 2017). The Principality of Monaco is located about 20 kilometers east of Nice with 38,350 inhabitants (IMSEE, 2020). These cities were selected because of the possible presence of *Ostreopsis* blooms on their coasts during the summer, their particular interest for the research on *Ostreopsis* (conducted also within the CoCliME project, e.g. Drouet et al., 2022) as well as their coverage by the RAMOGE Agreement (www.ramoge.org) dedicated to the prevention and fight against pollution of the Mediterranean marine environment. The survey encompassed residents of the two cities (selected using the quota sampling method, Moser, 1952; Moser and Stuart, 1953) and tourists visiting Nice. For Monaco, a preliminary literature review (Direction du Tourisme et des Congrès Monaco, 2010) had shown that beach attendance was not among the main reasons to visit it, which made the survey on tourists irrelevant. In order to avoid an on-site sampling that could lead to an over-frequentation bias, people were, as much as possible, interviewed in the two cities away from the beaches. Thus, a survey of how often beach-goers actually went to the beach was made possible as well as one of those who did not go to the beach during the summer. Tourists were also asked whether they had already visited Nice in the past and whether walking activities or beach-going were the main motivation for coming to Nice. Also, the sociodemographic profile of the interviewed people was collected.

The questionnaire included additional concise scientific information on the events and related symptoms (e.g., https://ramoge.org/wpcontent/uploads/2022/01/algue_ostreopsis_fr.pdf). Next, two hypothetical scenarios, based on realistic scientific assumptions developed in collaboration with biologists, were presented to the surveyed beachgoers only:

- Hypothetical scenario 1: Occurrence in a near future (summer 2019 for tourists; summer 2020 for residents) of *Ostreopsis* blooms causing moderate effects (i.e.,cold and cough) disappearing four hours after leaving the beach;
- Hypothetical scenario 2: Occurrence in a near future (summer 2019 for tourists; summer 2020 for residents) of *Ostreopsis* blooms causing more severe effects, including more symptoms (i.e., cold, cough, conjunctivitis, nausea, skin irritation, mild fever) that could last up to 48 hours after leaving the beach.

Consequently, throughout the questionaire, respondents were asked about:
i) their knowledge of toxic algae prior to the survey,
ii) their reactions towards the additional scientific information, including their perceived credibility of the scientific information, their perception of the potential negative socioeconomic consequences (tourists leaving the place, population panic), the severity of the various symptoms associated with *Ostreopsis*, and
iii) their reactions towards the hypothetical scenarios regarding future *Ostreopsis* blooms, including the degree of credibility attributed to the scenarios and their perception of a potential threat to their health which could possibly affected their future beach-going.

In order to explain the attitude of beach-goers to the additional scientific information about *Ostreopsis blooms* provided and their resulting risk perception, Probit type econometric models were used for each of the three sub-populations of respondents (residents of Nice and Monaco and Nice tourists). Probit models were also used in order to explain and predict the potential effects of a future growth of *Ostreopsis* blooms on beach-going . Among the explanatory variables, demographic and socioeconomic characteristics usually used in socioeconomic surveys (e.g., age, gender, education; e.g., Morgan et al., 2010) were also included. These characteristics are supposed to explain attitudes and recreational behaviours in the face of health risks related to *Ostreopsis*. For example, having children under 15 in a household can partly explain a stronger perception of symptom severity and a higher rate of stopping beachgoing. All the estimates in this paper take into account the heteroscedasticity of errors.

3. Results

3.1. Effects of **Ostreopsis** *blooms on the environment*

As a benthic dinoflagellate attached to biotic or abiotic surfaces by a sticky mucopolysaccharide matrix, *Ostreopsis* sp. can favour or inhibit the colonization of the substrate by other benthic microorganisms. The temporal monitoring of the microbenthic community during *Ostreopsis* blooms showed a succession of different microalgal taxa over time (Accoroni et al., 2016), including other dinoflagellates (*Coolia* spp., *Prorocentrum lima, Amphidinium* spp.), and also centric and pennate diatoms. This succession could be modulated by interactions among these species and *Ostreopsis*, involving allelopathic activity and competition for nutrients, surface substrate type and light. Also, particular bacterial assemblages (Bellés-Garulera et al., 2016; Vanucci et al., 2016) are shown to be associated with different phases of the *Ostreopsis* proliferation development, presumably due to the use of organics excreted by *Ostreopsis* and the whole microalgal carpet, possibly in combination with growth inhibition of some bacterial taxa. Documented effects of exposure of other microalgae to the presence of *Ostreopsis* include alteration of their growth (García-Portela et al., 2016), photosynthetic activity (Ternon et al., 2018), swimming speed (Yoo et al., 2015), cellular integrity (Pichierri et al., 2017), and adherence capability (García-Portela et al., 2016).

The nature of the chemical signals involved in *Ostreopsis* interactions with other marine organisms remains poorly understood (Pavaux et al., 2020a), although the first metabolomic studies are starting to shed light on this issue (Ternon et al., 2018; Gémin, 2020) and suggest the involvement of toxic compounds different from the known ovatoxins. Also, the critical role of the mucus is increasingly insinuated (Giussani et al., 2015; Ternon et al., 2018; Pavaux, 2020). This mucilaginous matrix could facilitate the retention of chemical compounds (including toxins), leading to increased *Ostreopsis* competitiveness with other microalgae and bacteria (Ternon et al., 2018). It could also constitute a defence against *Ostreopsis* predators by embedding them into this mucus, or by avoiding dilution of (toxic) chemicals in the environment and allowing their ingestion in high quantity by predators (Barone 2007; Giussani et al., 2015; Pavaux, 2020). In addition, the mucus could act as a deterrent agent against macroalgal grazers, thus resulting in a benefit for the benthic host.

If ingested, benthic and planktonic *Ostreopsis* and the floating aggregates enter into the food webs, and toxins can be potentially transferred to and bioaccumulated in upper trophic levels, posing a risk of seafood poisoning in humans. Indeed, high concentrations of *Ostreopsis*-derived toxins (PLTX analogues as ovatoxins) have been quantified in benthic macroorganisms, such as filter feeders, in herbivorous fish feeding on *Ostreopsis* sea-flowers and in carnivorous and omnivorous fauna (Amzil et al., 2012; Biré et al., 2013; 2015; Brissard et al., 2014; Gorbi et al., 2012; 2013; Milandri et al., 2010; Faimali et al., 2012; Pezzolesi et al., 2012; Giussani et al., 2016; see Table 3 of Pavaux et al., 2020a). Often, negative impacts on these vector organisms have not been apparent. As an example, experimental tests have proven that the benthic harpacticoid *Sarsamphiascus* cf. *propinquus*, which co-occurs with *Ostreopsis* cf. *ovata* in summer, is highly resistant to the presence of the microalga (Pavaux et al., 2019), suggesting some kind of acclimation or resistance mechanisms developed by the copepod. However, both *in situ* and experimental studies have suggested strong toxic effects on the reproduction of some organisms, leading to a clear decrease in the number of copepod nauplii of the epiphytic community accompanying *Ostreopsis* (Guidi-Guilvard et al., 2016) and in the fecundity and fertility ratios of *Sarsamphiascus* cf. *propinquus* (Pavaux et al., 2019). Impairments in reproduction ability and early-stage development have already been described for other marine organisms such as sea urchins (Neves et al., 2018; Miggliaccio et al., 2016). Mass mortalities of some macrofauna (mussels, sea urchins, cephalopods, cirripeds) have been documented in the Mediterranean concurrently to *Ostreopsis* blooms (as reviewed by Pavaux et al., 2020a). A combination of oxygen limitation, high temperatures and direct toxic effects from the exposure to the microalga appear the most plausible cause. The particular sensitivity of certain species, such as *Artemia franciscana,* when exposed to *Ostreopsis* cells, cell filtrates and toxin extracts, postulate them as relevant model organisms for ecotoxicological studies (Pavaux et al., 2020b). Indeed, the high sensitivity, the reproducibility and the low cost of the bioassay involving this model organism are major benefits in favour of its use for routine evaluation of the toxicity of *Ostreopsis* spp. in the field.

3.2. Effects on Human Health. Case study: Epidemiological studies on exposure to toxic aerosol in Sant Andreu de llavaneres (Catalonia, NW Mediterranean coast of Spain); the temporal link between the bloom and the human health impacts.

The number of questionnaires distributed and answered varied each year of the study (Table 1). In 2013 and 2014, 16 and 14 questionnaires were dispensed, respectively, and all were answered and returned (100 %). In 2017, the highest number of questionnaires (n = 118) were distributed; however, only 22 were answered (18.6 %). The people with *Ostreopsis*-related symptoms, identified based on the answered questionnaires, ranged from 5 to 22, with a prevalence rate oscillating from 35.7 % (in 2014) to 100 % (in 2017 and 2018).

Overall, a high variety of symptoms were reported in the six-year study (Table 2). In 2013 and 2014, when the cohorts only included the staff of the restaurant, seven clinical symptoms were registered. With the incorporation of the apartment residents from 2015 onwards the experienced symptoms increased up to 25. Three symptoms were noticed over the six-year period (Table 2): malaise, runny nose and sore eyes.

Headache and nose irritation were identified in five out of the six years. The rest of the symptoms had a highly variable presence and were reported between one and four years. Nausea and vomiting were never indicated.

The prevalence rate of the different symptoms (Table 2) was variable along the study period. As an example, and focusing on the most common health problems reported in all six years, the values varied between 3.1 % and 13.1 % for malaise, 2.6 % and 45.9 % for runny nose, and 2.3 % and 9.7 % for sore eyes. The numbers for headache and nose irritation were 0 % to 13.6 % and 0 % to 45.9 %, respectively. Interestingly, shortness of breath, reported by some residents, had a stable prevalence rate around 3 % from 2015 to 2018. The acute symptoms of workers and beach users usually went away, with or without minor medication, when people returned home and ended the exposure to marine aerosols. In the case of the apartment residents exposed the whole day to marine aerosols, the symptoms were relieved by closing windows and using air conditionning. In general, symptoms lasted for 3-4 days, rarely for up to 7 days. Only a few participants in the survey required occasional medical treatment, consisting on the administration of common use antihistaminic, analgesic and anti-inflammatory drugs.

The periods when people reported *Ostreopsis*-related symptoms exhibited a temporal pattern, with different intensity along the microalgal blooms and with certain interannual variability (Figure 3). Taking the benthic *Ostreopsis* cell concentrations as indicator of the physiological phase of each bloom (continuous line in Figure 3), symptoms (plotted with dashed lines and highlighted by arrows in Figure 3) started to be noticed at the beginning of the exponential phase of the bloom (in particular, at the end of June and the first week of July in 2015, 2017 and 2018), when cell abundances were increasing and approaching $2{\cdot}10^5$ cells·gFW^{-1}. The peak of health problems coincided with the early stationary phase (specially in the second half of July and the first week of August, in 2013, 2014, 2016 and 2017), when cell concentrations were estabilized and fluctuated around the mentioned values or even higher (up to $6.9\ 10^6$ cells·gFW^{-1}). Thereafter, when the blooms remained somehow in a stationary phase with relatively high cell abundances, less symptoms were reported. The described symptomatology pattern also applied when considering the dynamics of the *Ostreopsis* plankton cell concentrations in the water (dotted lines in Figure 3), although this parameter exhibits higher variability than the cell concentration in the benthos. The concentrations in the water increased up to ca. $3{\cdot}10^4$ cells·L^{-1} during the early exponential phase, and reached ca. $1{\cdot}10^5$ cells·L^{-1} in the stationary, with $1{\cdot}10^7$ cells·L^{-1} in some floating aggregates.

In terms of seasonality, *Ostreopsis*-related symptoms were noticed as early as the middle of June, around Julian day 160, when the bloom started early in the year, as was the case in 2017. Otherwise, July and August were the months when clinical symptoms were most often reported. A general picture, integrating the interannual variability, can be drawn from the moving average on the pooled six-year data (Figure 4). Overall, health problems tended to increase sharply approximately after Julian day 187, and the number of people with potential *Ostreopsis*-related symptoms reached a maximum around Julian day 195 (July 14th). Thereafter the symptoms might decrease sharply, although they could remain along August and September, depending on the duration of the annual bloom. In certain years (2013, 2014, 2015) when *Ostreopsis* was still present in the water in the fall, isolated cases of persons presenting some health problems occurred between the end of September and the end of October.

3.3. Effects on Human Health. Epidemiological and clinical studies in France: French Mediterranean National **Ostreopsis** *Surveillance Network*

During bloom periods, the high *Ostreopsis* cell densities embedded in the brownish mucus form a biofilm or "carpet" visible at naked eye covering benthic substrates (Figure 1A, B, C). This carpet makes a slippery ground to beach users. When high *Ostreopsis* cell numbers detach from the substrate and become part of the plankton and the floating aggregates at surface (Figure 1D, E), bathers in direct contact with *Ostreopsis* cells can experience skin or eye irritations. In addition, seawater retained in snorkel tubes and diving regulators (Pavaux and Lemée, pers. comm.) increases the exposure to the toxic compounds produced by this microalga. The acute clinical symptoms associated to the exposure of *Ostreopsis* in different life stages (benthic, plankton, floating aggregates described in the Introduction of this paper, Figure 1) and concentrations along the bloom are shown in Table 3. They have been identified from the experience of the Marseille Poison Control Centre attending people potentially exposed to *Ostreopsis* blooms as well as aquarists in contact with PLTX-producing corals (as described in Appendix 1). These symptoms agree with those of other reported cases in Italy, Spain, France, and Algeria (see Table 2 in Pavaux et al., 2020a).

3.4. Socioeconomic surveys in Nice and Monaco. Perception and reaction to current and future* Ostreopsis *blooms

3.4.1. Sampled populations. The selected sample was composed of 449 people: 161 residents of Nice (including 118 beachgoers, 73.3 %), 64 tourists in Nice (including 44 beach-goers, 68.8 %) and 224 residents of Monaco (including 176 beachgoers, 78.6 %). The sociodemographic structure of the people surveyed was similar for both residents of Monaco and Nice, with a lower percentage of men than women and a prevalence of people with a higher education being observed. It was also noticed that a majority of tourists going to the beach declared that they had already stayed in Nice in the past (72.7 %). Almost half (45.5 %) of them said that walking activities or beach-going were the first motivation for visiting Nice (see Supplementary Table 1).

3.4.2. Prior knowledge of people on *Ostreopsis* blooms and their health effects. Before the scientific information provided by the questionnaire, prior knowledge on *Ostreopsis* was low among the residents and tourists: only 17.8 % (80) of the respondents, with a significant difference at the 0.05 level of risk (Chi-squared test) between the Nice residents (24.8 %) and the other populations (i.e., Monaco residents - 13.8 % - and tourists of Nice - 14.1 % -), and with no significant difference between beachgoers (18.0 %) and non-beachgoers (17.1 %). For the few people who had heard of *Ostreopsis*, only a small proportion (24 respondents, 5.3 % of the total population surveyed) knew about the health risks associated with this microalga. The symptoms most cited by respondents were skin irritation (45.8 %), cough and respiratory tract damage (25.0 %), runny nose and sneezing (16.7 %) and eye irritation (16.7 %)

3.4.3. Beach-goers attitude towards additional information on *Ostreopsis* blooms and their resulting risk perception.

Most beachgoers (83.4 %) considered that the scientific information provided by the questionnaire was not overstated with a significant difference (at 0.05 level of risk) between people (tourists and residents) of Nice and residents of Monaco (Table 4). It is worth taking into account the fact that 22.2 % of the residents of Monaco considered that scientists overstate these risks. Moreover, 20.7 % of respondents stated that this scientific information could create an unnecessary panic and 53.3 % of respondents considered that it could scare away tourists.

Concerning the hypothetical future *Ostreopsis* scenarios, it was observed that they were credible for a majority of respondents (83.7 % for scenario 1, 81.7 % for scenario 2), with a substantial difference in the evaluation of whether these scenarios would represent a health threat (64.2 % for scenario 1 and 79.0 % for scenario 2). For a fairly large number of people (35.8 %), symptoms described in the first scenario do not really deter them, but this proportion falls (21.0 %) when the symptoms become more severe in scenario 2. Regarding specifically scenario 1, there were also significant differences at the 0.05 level of risk between tourists of Nice (50.0 %) and the residents of the two cities (39.0 % for Nice and 30.1 % for Monaco). When it comes to the perception of the severity of the symptoms associated with scenario 1 (i.e., sneezing / runny nose and cough), 56.2 % consider that these are not at all serious.

Regarding the perception of the severity of symptoms, there were no significant factors for residents of Monaco, while for residents of Nice, this perception was more acute among women, among people with a higher degree (i.e., above the baccalaureate) and among those with at least one child under 15 living in their household. Conversely for the tourists of Nice, having at least one child under 15 impacted on the perception negatively (Supplementary Tables 2, 3 and 4).

Regarding the judgments on the overall scientific information provided on the *Ostreopsis* blooms (including hypothetical scenarios), the probability that a resident of Monaco considers that scientists overstate the risks associated with *Ostreopsis* increases with age and decreases with a higher education degree, while for the Nice residents, there is no statistically significant explanation. For the tourists of Nice, this probability increases with a prior knowledge of the symptoms related to *Ostreopsis*. For the residents of Monaco, the probability that a respondent considers scenario 1 to be credible decreases for ages over 60. Likewise, for residents of Nice, age also significantly and negatively impacts the perceived credibility of the scenario concerning *Ostreopsis* blooms. In the case of the Nice tourists, age did not affect this probability, however, being a man impacted the perception of this credibility positively.

Regarding the consequences associated with the information provided on *Ostreopsis*, for the residents of Monaco, the probability to perceive scenario 1 as a threat to their health increased when the scenario was considered to be credible (hypothesis of exogeneity in the variable "Credibility" not rejected at 0.05 level of risk, p = 0.31). For the residents of Nice, this probability increased when the symptoms associated with *Ostreopsis* were perceived as quite severe or very severe (hypothesis of exogeneity in the variable "Severity" not rejected at 0.05 level of risk, p = 0.24). Conversely, for the tourists of Nice, there were no significant factors explaining the perception of a threat to health associated with scenario 1. Furthermore, for the residents of Monaco and Nice, the probability that scientific information was perceived as scaring tourists away increased when the person considered the scenario to be credible (hypothesis of exogeneity in the variable "Credibility" not rejected at 0.05 level of risk in the case of residents of Monaco, p = 0.70 and residents of Nice, p = 0.40). However, in the case of the residents of Nice, this perception decreased when respondents had at least one child under 15, while no statistically significant explanatory factor was observed for the tourists of Nice.

Finally, we observed that, for the residents of Monaco and for the tourists of Nice, the probability to perceive scientific information as likely to create unnecessary panic increased when people thought that scientists overstated the risks (hypothesis of exogeneity in this factor not rejected at 0.05 level of risk in the case of residents of Monaco, p = 0.95 and tourists of Nice, p=0.81). This probability decreased along with the perception of the severity of the symptoms in the case of the residents of Monaco and the residents of Nice (hypothesis of exogeneity in the variable "Severity" not rejected at 0.05 level of risk in the case of residents of Nice, p = 0.13). In addition, for the latter, the probability decreased with age and with having at least a child under 15 in the household.

3.4.4. Potential effects of a future development of blooms on beach-going.

Overall, a majority of residents will stop going to the beach and, in the case of Nice, this lower attendance is much stronger when the symptoms are more severe according to scenario 2 (Table 5). In Nice, in the case of scenario 1, the number of former beachgoers that will not go to the beach any more is significantly higher for residents (54.2 %) than for tourists (40.9 %). However, the difference between tourists and residents' behavior disappears in the case of scenario 2.

Furthermore, the fact that 44.1 % of people (17.3 % in the case of scenario 2) would not completely stop going to the beach indicates that, in the absence of suitable public measures (e.g., in terms of information on sites or even beach closures), future blooms could expose a substantial part of the residents and tourists to health risks. This exposure would ultimately cause tangible economic losses (e.g., healthcare expenditures) as well as intangible losses (e.g., suffering and stress of people with symptoms). At the same time, staying away from the beach for a majority of the population (respectively 55.9 % and 82.7 % for scenarios 1 and 2) would also produce tangible future economic losses (e.g., impacts on tourist activity) and intangible losses (e.g., loss of well-being due to the free leisure activity being made impossible in particular for the residents) in addition to the economic losses associated to healthcare. However, it should be highlighted that, in the case of Monaco (scenario 1), 52.3 % of people declaring that they would no longer go to the beach because of *Ostreopsis* said they would replace this free activity by market activities (e.g., going to swimming pool).

In order to highlight the determinants that may explain why people would stop beach-going under scenario 1 for the three populations studied, Probit type econometric models were implemented (Table 6). Whatever the population considered, the test shows that at 0.05 level of risk the hypothesis of exogeneity in explanatory variables is not rejected. The goodness of fit and the proportion of correct prediction of the three econometric models shows that the decision to stop beach-going is explained satisfactorily (Table 6).

It is important to notice that the perception of a threat to health significantly and positively explains the probability of stopping beach-going, whatever the population considered. For tourists of Nice, no sociodemographic variable can directly explain the decrease in attendance. Conversely, the two factors specific to tourists (i.e., previous stay in Nice and walking or going to the beach as the main reasons for the tourist stay) explain the probability of stopping going to the beach (positively for the former and negatively for the latter) (Table 6). In contrast, these two factors have no effect on the tourists' attitudes and reactions to the information on *Ostreopsis* (Supplementary Table 4).

In the case of the Nice and Monaco residents, some of the sociodemographic characteristics explain why they no longer go to the beach. Thus, the probability of not going increases with age and with having at least one child under 15. Conversely, this probability decreases when the person lives with his / her parents in the case of residents of Monaco and with being a man in the case of people residing in Nice. These results confirm that it is possible to identify groups that may be more or less exposed than others to the health risk due to *Ostreopsis*. We can also observe that the credibility of the scenario (for the residents of Nice) and the perception of how serious the symptoms are (for the residents of Monaco) makes stopping going to the beach a more likely option.

4. Discussion

4.1. Effects of *Ostreopsis* blooms on the environment

The effects of *Ostreopsis* blooms have been studied in different organisms, using different approaches, indicators and parameters to identify the potential damage. A general conclusion to be drawn is that these works are challenged by technical limitations that hinder the setup of ecologically realistic studies. Future steps to understand the interactions and impacts of *Ostreopsis* on other marine organisms include (i) clarification of the role of the mucus in these ecological interactions and impacts, (ii) investigation of the potential transfer of toxic compounds through the food web and (iii) elucidation of the variety of toxic compounds produced by *Ostreopsis* species and affecting other marine organisms. Technical improvements, specially concerning detection and identification of chemical compounds and standardization of ecotoxic tests, are required. Monitoring the effects of *Ostreopsis* blooms in the environment constitutes a major challenge as well.

4.2. Effects of *Ostreopsis* blooms on human health.

The two perspectives presented converge and complement offering a comprehensive vision of the impacts of *Ostreopsis* blooms on human health. The details of the small-scale case study conducted in Catalonia will be discussed first, and its results will then be integrated in the more general perspective provided by the French Mediterranean National *Ostreopsis* Surveillance Network.

For the first time, a six-year epidemiological survey was conducted simultaneously with the monitoring of recurrent, annual *Ostreopsis* cf. *ovata* blooms in a hot spot in the NW Mediterranean. During the study, the blooms exhibited a consistent temporal pattern, described earlier in the studied site and in the NW Mediterranean in general (Mangialajo et al., 2011; Vila et al., 2016). The period with health impacts covered mainly July and August, and coincided with the highest yearly abundances of *Ostreopsis* cf. *ovata* in the area. Overall, the results contribute to support the hypothesis that *Ostreopsis* blooms are associated to mild acute symptoms in humans exposed to marine aerosols, as suggested by previous studies (Ciminiello et al., 2006; Vila et al., 2016).

The analysis was conducted in an open human cohort directly exposed to marine aerosols for eight to 24 hours daily. Many of the individuals had already experienced *Ostreopsis*-related symptoms in previous years (Àlvarez et al., 2005; Vila et al., 2016). Along the six years, the participation in the epidemiological study in terms of number and percentage of questionnaires answered, was variable and, sometimes, even very low. This circumstance has been already described in applied epidemiology (Hartge and Cahill, 1998). In 2017 and 2018, the persons that answered the questionnaires reported *Ostreopsis*-related clinical symptoms; however, other people noticed some symptoms but did not return the questionnaires. For this reason, unfortunately, the self-administered questionnaires do not allow to determine the real prevalence rate per year.

In spite of these limitations, some trends concerning human symptoms associated to acute and repeated exposure to *Ostreopsis* blooms were confirmed. The dysfunctions affect the entire body as well as the otorhinolaryngic, ophthalmic, digestive, respiratory, dermal and cardiac systems. A total of 25 different symptoms potentially associated to *Ostreopsis* blooms were identified by survey participants. Many of them were also indicated in previous studies (Tubaro et al., 2011; Tichadou et al., 2010), and identified by the French Mediterranean National *Ostreopsis* Surveillance Network, but this work suggests that the *Ostreopsis*-related symptom profile may be broader in people recurrently exposed to the blooms of the microalga.

Five symptoms (malaise, headache, runny nose, nose irritation, sore eyes) were present in five or six of the years, and shortness of breath was consistently prevalent in the last four years of the study (2015 to 2018). Overall, these observations indicate that, despite the low prevalence of mild-moderate acute symptoms reported so far, the continuous exposure to *Ostreopsis* blooms can have some chronic health effects, as pointed out by the French Mediterranean National *Ostreopsis* Surveillance Network. Analogous observations has been noted concerning exposure to aerosolized brevetoxin during *Karenia brevis* outbreaks and to microcystins produced by cyanobacteria in freshwater lakes (Backer and Fleming, 2008). In general, there is a lack of information about chronic exposure and health effects related to harmful algal blooms, with most studies being concerned only with the acute symptomatology (Young et al., 2020). Future research should focus on this point. Furthermore, new studies should address the severity and interannual variability of the symptoms, which were not considered here.

During the 2013 *Ostreopsis* bloom (Vila et al., 2016), the health problem occurred mainly during a time window coinciding with the transition from the exponential to the stationary phase of the proliferation. The 2013-2018 data confirmed this trend. This finding suggests that the toxic substances responsible for the observed symptoms are produced under particular physiological conditions of the *Ostreopsis* cells.

From a management point of view, the six-year study stresses the need to monitor both the benthic and planktonic *Ostreopsis* cf. *ovata* populations, in order to appropriately alert for potential exposure and health effects. Establishing *Ostreopsis* abundance alert thresholds is not straightforward (Giussani et al., 2017). Former studies (Funari et al., 2015; Lemée et al., 2012; Mangialajo et al., 2017) suggested threshold alert values at $2{\cdot}10^5$ cells·g FW^{-1} of macroalgae and $3{\cdot}10^4$ cells·L^{-1}, in the benthos and the plankton, respectively, and were also considered by the French Mediterranean National *Ostreopsis* Surveillance Network (Table 3). The six-year study confirms that these approximate values could be taken as reference, although symptoms were noticed sometimes when cell concentrations were below these numbers.

The real problem during acute exposures is not qualitative but quantitative: while it is easy to treat one patient exposed to *Ostreopsis*, it is much more complex to take care of several hundred alarmed patients attending simultaneously and collapsing hospital or primary health care emergency facilities, which was often the case in Italy (Gallitelli et al., 2005; Brescianini et al., 2006) and Algeria (Illoul et al., 2012).

Repeated and chronic exposure may occur on people living or working near beaches or inlets where blooms develop during the summer season, conducting aquatic sports (swimming, surfing) in such areas or involved in seawater sample collection during *Ostreopsis* blooms and/or subsequent laboratory manipulation. In these last professional activities, efficient personal protection systems including hoods, gloves and masks (the same equipment is recommended to people exposed to marine aquaria with PLTX-producing soft corals) are recommended. Some patients repeatedly exposed and poorly protected have presented immune system problems (atopy, eczema, non-specific bronchial hyper-reactivity) with at least one case of respiratory impairment lasting for several years, after three seasons of contaminated seawater sampling (non-specific asthma evoking a reactive airways dysfunction syndrome; De Haro, unpublished). However, in the current state of knowledge it is difficult to assess the exact risks induced by chronic exposure to *Ostreopsis*.

In the Mediterranean, two differential pathologies can be erroneously attributed to exposure to *Ostreopsis* blooms. First, erythema and itching without respiratory symptoms may be due to the endemic cercarial dermatitis or swimmer's itch induced by the avian schistosome *Microbilharzia variglandis* (Horák et al., 2015), a common parasite of the Laridae family (gulls and sterns). The aquatic larvae of the bird parasite can penetrate human skin although they won't develop in humans. Second, dermatological signs accompanied by mucosal irritation (eyes, nose, and throat) during or after a sea bath can also be caused by exposure to blooms or presence of certain marine cyanobacteria (*Lyngbya*, *Schizothrix*, *Oscillatoria*, *Symploca*; Greillet et al., 2020), small pelagic molluscs with pointed shells (Gasteropoda, Thecosoma) or small cnidarians, which produce cytotoxins causing a clinical picture very similar to that presented by exposure to *Ostreopsis* blooms (De Haro, unpublished).

From a therapeutic point of view, exposure prevention and protection are key for protection against *Ostreopsis*-related health problems. Since beaches of the French coasts are closed during blooms and strictly supervised, poisoning of the general public is less frequent today. In addition, all professionally exposed workers should be protected with adapted devices. During a proven or suspected exposure, decontamination by a shower is always recommended. Experience in Europe and Algeria with several hundred cases (Illoul et al., 2012) shows that symptomatic treatment is effective for acute *Ostreopsis* poisonings: anti-inflammatory drugs and, if necessary, bronchodilators must be administered. The six-year epidemiology study also revealed that the reported acute symptoms usually disappeared when people decreased or stopped the inhalation of the marine aerosols; interestingly, air conditioning palliated the symptoms, as described in the case of *Karenia brevis* blooms (Fleming et al., 2011). However, we have no experience of the treatments that could be effective for the health problems induced by chronic *Ostreopsis* exposure.

More studies are required to improve our knowledge of the ultimate and direct involvement of the microalga in human health problems. Concurrent epidemiologic and ecologic studies along a whole year should be conducted. However, investigating the symptoms in humans outside the summer period is complex because the occupation of the site and beach activity are much lower and the effects of exposure to *Ostreopsis* can be misdiagnosed or confused with other seasonal diseases. This is the case when symptoms are reported in the fall, a typical flu period. The availability of specific biomarkers could help to clarify this question. Finally, it is necessary to explore whether symptoms similar to those caused by *Ostreopsis* occur when the microalga is not present, pointing out the responsibility of other organisms and/or abiotic conditions. In this context, it is necessary to determine the nature of the chemical compounds involved in the reported symptoms. Although PLTX analogues have been suggested and have shown respiratory effects in experiments with mice (Poli et al., 2018), they have been rarely found in the natural aerosol (Ciminiello et al., 2014). Complex interactions between biological processes and air-sea aerosol production dynamics seem to be involved in the aerosolization of *Ostreopsis*-produced toxins as recently observed using an aerosol producing incubation tank in the laboratory (Medina-Pérez et al., 2021). It is also possible that other biological compounds, fragments of cells and mucus could be at play (Casabianca et al., 2013). In association with an *Ostreopsis* bloom, involved ecological processes occurring within the benthic and planktonic food web (section 2) could also directly or indirectly affect humans. It is also unclear whether the chemicals affecting humans, which may be different from those with negative effects on marine organisms, remain intracellular or whether they are released to the water and/or retained by the mucus as well. As an example, in laboratory experiments, Giussani et al. (2015) reported PLTX-equivalent concentrations below detection limit in the dissolved fraction and less than 10 % in the mucus, with most toxin being intracellular. Concerning cells aggregated in sea-flowers at the surface water (Figure 1E), they provide an unpleasant aspect to the coast, and could be the major source of human respiratory intoxication on beach users and people working or living near *Ostreopsis* hot spots.

4.3. Socioeconomic consequences

The current and future socioeconomic consequences of *Ostreopsis* blooms depend first of all, on how much people, especially beach-goers, currently know about the risk and how they react to the new information they receive. Our results from the socioeconomic survey show that most people currently ignore the *Ostreopsis* issue and that a quite high proportion of beachgoers faced with new scientific information considers that scientists overstate these risks and even that the information could create an unnecessary panic and could scare away tourists. It was also observed that the attitude towards new scientific information and towards *Ostreopsis* health related risks differs according to sociodemographic and geographic characteristics.

Consequently, these results should be taken into account for future public communication strategies on health risks related to *Ostreopsis* blooms. For instance, due to a difference in risk perception, targeting various populations differently (e.g., tourists as opposed *to* residents) should be considered. Moreover, scientists and public authorities should be aware that a health risk communication based public policy, however much desirable it may be from a public health stand point could come up against a set of obstacles at the local level due to fear about its possible negative impact on the economy (e.g., on tourism activity).

Following the two hypothetical scenarios for *Ostreopsis* blooms in a near future, our results show that an increase in the associated health risks would entail various costs, depending first on how public authorities and beachgoers will react to the presence of these blooms and to the subsequent public rules set up about beach access. This is the very reason why, among other things, we have not yet assessed all these potential costs in monetary terms. In order to conduct such a valuation, the methodology would consist in distinguishing tangible from intangible costs in the valuation process. Tangible costs, such as costs of illness, could be calculated starting from the expected number of beachgoers suffering from symptoms due to *Ostreopsis* and using standard unit costs to treat these symptoms. For intangible costs, well-being losses (due to an expected decrease in access to the beaches and to an expected discomfort for those planning to keep going to the beach and for those affected by the symptoms) would have to be converted into money with specific economic valuation methods (e.g., Contingent Valuation Method, Choice Experiment Method) based on the Willingness to Pay concept.

5. General conclusions

The aim of this paper was to summarize the knowledge concerning the impacts of *Ostreopsis* (mainly *O*. cf. *ovata*) blooms on the ecosystems, human health and the economy in the Mediterranean coasts.

Although some studies have documented massive mortalities of benthic organisms concurrent to proliferations of *Ostreopsis* cf. *ovata* in the Mediterranean, understanding of the involved deleterious mechanisms is poor. Field studies ought to be conducted, but they are complex and challenging. Laboratory experiments can help to shed light on the issue, but require more realistic and standardized design. There is a clear need to homogenize experimental setups and ecotoxicological approaches, and to explore the species-specific sensitivity and responses to the presence of *Ostreopsis*. New methods, such as metabolomics, can help to clarify the chemical compounds involved in the interactions of the microalga with other marine organisms. While the role of the *Ostreopsis*-synthesized mucus seems very relevant, addressing its study is also difficult. It is also mandatory to investigate the factors determining the physiological state of and the dynamics of toxin production by *Ostreopsis* cells, the potential transfer of toxic compounds through the food web up to humans, and the actual risk of food poisoning due to ingestion of PLTX-contaminated seafood in the Mediterranean.

The public health studies conducted in the NE Mediterranean are instrumental in a better understanding of the effects of the direct and acute exposure to seawater containing *Ostreopsis* cells and of inhaled aerosolized compounds during its blooms. The two experiences presented here are complementary and consistent, and they prove the relationship between the *Ostreopsis* blooms and impacts on human health. Still, further multidisciplinary research is required to clarify the cause-effect links. Among others, appropriate human biological markers and tests with human culture tissues will help to characterize the health problems. A major conclusion is that addressing the effects of chronic exposure on human health is mandatory. This would require retrospective and prospective epidemiological studies with tests, face-to-face (or directed) interviews and preferably with larger human cohorts, stratified according to different levels of exposure to the ecological conditions.

Meanwhile, the implemented surveillance networks and strategies have proven efficient to prevent further impacts on human health and the potentially failing of the health care system. From a management point of view (Table 3), we suggest to monitor both the benthic and planktonic *Ostreopsis* cf. *ovata* populations, in order to appropriately alert to potential exposure and health effects. Threshold alert values at $2 \cdot 10^5$ cells·g FW^{-1} of macroalgae and $3 \cdot 10^4$ cells·L^{-1} in the water, respectively, as suggested in former studies seem to be appropriate, although symptoms can also be identified below these numbers.

Still, because the symptoms of acute exposure are mild and the chronic effects are unknown, the general public is poorly aware of the *Ostreopsis* blooms and its human health as well as socioeconomic risks associated, as revealed by the intensive survey conducted on residents and tourists in Nice and Monaco. As a consequence, blooms of *Ostreopsis* are not currently perceived as a risk or a real socioeconomic problem, thus making it premature to define adaptation strategies. That is the reason why, implementing a monitoring and public information system for the population seems to be a first priority. However, the effectiveness of such an approach, will depend on how the different population categories will react to this type of information, as revealed by the socioeconomic survey. In particular, the perceived severity of symptoms and the credibility granted to the scientific information and to the future risk scenarios varied significantly depending on the sociodemographic characteristics of the individuals. Therefore, the communication strategy on the risks associated with *Ostreopsis* blooms must be carefully designed, taking into account the target audiences, in particular the least receptive, as well as the alarm generated by the provided information on various economic activities (e.g., economic impact of lower tourist activity)). The socioeconomic survey clearly shows that the *Ostreopsis* blooms could become a major socioeconomic issue in the future. Indeed, these blooms may have a significant impact (even for moderate symptoms) on how often tourists and residents alike could consider going to the beach. All these consequences may lead therefore to future tangible (e.g. decrease in some market activities) and intangible (loss of wellbeing) economic effects.

Nowadays, understanding the complexity of the *Ostreopsis* bloom dynamics is therefore fundamental in order to anticipate these events in future climate change scenarios and in other areas. Furthermore, not only global warming but also the role of multiple anthropogenic forcings such as coastal habitats destruction, must be considered as drivers of the increase and expansion of *Ostreopsis* blooms in temperate coastal areas. *Ostreopsis* is the paradigm of the dependence of Human Health on Oceans Health, which requires to be approached by a holistic, One Health vision, as intended by the CoCliME project. This paper is an example of how the transdisciplinary collaboration between specialists in marine ecology, applied field epidemiology, and socioeconomy, can contribute to working out strategies to prevent and mitigate the impacts of *Ostreopsis* blooms in the Mediterranean and other regions (such as in the Bay of Biscay, North-East Atlantic, where harmful *Ostreopsis* spp. occurred in 2020 and 2021; Chomérat et al., 2022), as well as to designing potential adaptation tools. This particular approach also applies to other Harmful Algal Blooms.

6. Acknowledgements

This study was supported by the project CoCliME (a part of ERA4CS, an ERA-NET initiated by JPI Climate, and funded by EPA -Ireland-, ANR -France-, BMBF -Germany-, UEFISCDI -Romania-, RCN -Norway- and FORMAS -Sweden-, with co-funding by the European, Union; Grant 6904462), endorsed to the international programme of IOC UNESCO and SCOR GlobalHAB (www.globalhab.info). The epidemiology studies were also funded by the project OstreoRisk (CTM2014-53818-R) of the Spanish Government (MINECO). N.I. M.-P. was granted by the Agency for Management of University and Research Grants (Government of Catalonia) and the University of Barcelona with a PhD FI-SDUR fellowship. Special acknowledgements are addressed to the RAMOGE agreement (www.ramoge.org) for their support to conduct the face-to-face questionnaires in Monaco and to the Principality of Monaco for having authorized the survey in Monaco. Part of the studies concerning *Ostreopsis* impacts on ecosystems were realized in the framework of the ANR (French National Research Agency) project OCEAN 15 (*Ostreopsis* Chemical Ecology and Allelopathy Network). A.-S.P. and R.L. are members of French GDR

PHYCOTOX (Ifremer and CNRS). The ICM-CSIC is funded by the 'Severo Ochoa Centre of Excellence' accreditation of the Spanish "Ministerio de Ciencia, Innovación y Universidades", 2020-2023 (CEX2019-000928-S).

7. References

Accoroni, S., Romagnoli, T., Pichierri, S., Totti, C., 2016. Effects of the bloom of harmful benthic dinoflagellate *Ostreopsis* cf. *ovata* on the microphytobenthos community in the northern Adriatic Sea. Harmful Algae 55, 179–190. https://doi.org/10.1016/j.hal.2016.03.003

Adams, C. M., Larkin, S. L., Hoagland, P., Sancewich, B., 2018. Assessing the economic consequences of harmful algal blooms: a summary of existing literature, research methods, data, and information gaps. In: S. E. Shumway, J. M., Burkholder, S. L. Morton (Eds.). Harmful algal blooms: a compendium desk reference. John Wiley and Sons.

Aligizaki, K., Katikou, P., Nikolaidis, G., Panou, A., 2008. First episode of shellfish contamination by palytoxin.like compounds from *Ostreopsis* species (Aegean Sea, Greece). Toxicon 51, 418–427. https://doi.org/10.1016/j.toxicon.2007.10.016.

Àlvarez J., Pedrol A., Parrón I., Goxencia J., de Torres M., Manzanera M., Planas C., Cosculluela G., López A., Masó M., Vila M., Isalt R., 2005. Brote Epidémico de sintomatología irritativa en Sant Andreu de Llavaneres: ¿el origen está en el mar? In:

Proceedings of the XXIII Reunión de la Sociedad Española de Epidemiología, Las Palmas de Gran Canaria, Spain. Gaceta Sanitaria 19(Supl. 1), 3–139.

Amzil, Z., Sibat, M., Chomérat, N., Grossel, H., Marco-Miralles, F., Lemée, R., Nézan, E., Sechet, V., 2012. Ovatoxin-a and palytoxin accumulation in seafood in relation to *Ostreopsis* cf. *ovata* blooms on the French Mediterranean coast. Mar. Drugs 10, 477–496. https://doi.org/10.3390/md10020477

Backer, L.C., Fleming, L.E., 2008. Epidemiological tools for investigating the effects of oceans on public health. In: Walsh, P. (Ed.), Oceans and Human Health: Risks and Remedies From the Seas. Elsevier Publishers, Oxford, pp. 201–218.

Barone, R., 2007. Behavioural trait of *Ostreopsis ovata* (Dinophyceae) in Mediterranean rock pools: the spider's strategy. Harmful Algae News 33, 1–3.

Bellés-Garulera, J., Vila, M., Borrull, E., Riobó, P., Franco, J.M., Sala, M.M., 2016. Variability of planktonic and epiphytic vibrios in a coastal environment affected by *Ostreopsis* blooms. Sci. Mar. 80, 97–106. https://doi.org/10.3989/scimar.04405.01A

Biré, R., Trotereau, S., Lemée, R., Delpont, C., Chabot, B., Aumond, Y., Krys, S., 2013. Occurrence of palytoxins in marine organisms from different trophic levels of the French Mediterranean coast harvested in 2009. Harmful Algae 28, 10–22, https://doi.org/10.1016/j.hal.2013.04.007

Biré, R., Trotereau, S., Lemée, R., Oregioni, D., Delpont, C., Krys, S., Guérin, T., 2015. Hunt for palytoxins in a wide variety of marine organisms harvested in 2010 on the French Mediterranean coast. Mar. Drugs 13, 5425–5446. https://doi.org/10.3390/md13085425

Brescianini, C., Grillo, C., Melchiorre, N., Bertolotto, R., Ferrari, A., Vivaldi, B., Icardi, G., Gramaccioni, L., Funari, E., Scardala, S., 2006. *Ostreopsis ovata* algal blooms affecting human health in Genova, Italy, 2005 and 2006. Euro Surveill. 11(9), E060907. https://doi.org/10.2807/esw.11.36.03040-en

Brissard, C., Herrenknecht, C., Séchet, V., Hervé, F., Pisapia, F., Harcouet, J., Lémée, R., Chomérat, N., Hess, P., Amzil, Z., 2014. Complex toxin profile of French mediterranean *Ostreopsis* cf. *ovata* strains, seafood accumulation and ovatoxins prepurification. Mar. Drugs 12, 2851–2876. https://doi.org/10.3390/md12052851

Calon, T., Sinno-Tellier, S., de Haro, L., Bloch, J., 2019. Exposition à la palytoxine des personnes manipulant des coraux mous d’aquarium d’eau de mer : étude des cas rapportés au réseau des Centres Antipoison de 2000 à 2017. Toxicol. Anal. Clin. 31, 64–76. https://doi.org/10.1016/j.toxac.2018.11.003.

Casabianca, S., Casabianca, A., Riobó, P., Franco, J.M., Vila, M., Penna, A., 2013. Quantification of the toxic dinoflagellate *Ostreopsis* spp. by qPCR assay in marine aerosol. Environ. Sci. Technol. 47, 3788-3795. https://doi.org/10.1021/es305018s.

Chomérat, N., Bilien, G., Derrien, A., Henry, K., Ung, A., Viallon, J., Darius H.T., Gatti C.M.I., Roué, M., Hervé, F., Réveillon, D., Amzil, Z., Chinain, M., 2019. *Ostreopsis lenticularis* Y. Fukuyo (Dinophyceae, Gonyaulacales) from French Polynesia (South Pacific Ocean): A revisit of its morphology, molecular phylogeny and toxicity. Harmful Algae 84, 95–111. https://doi.org/10.1016/j.hal.2019.02.004

Chomérat, N., Bilien, G., Couté, A., Quod, J.P., 2020. Reinvestigation of *Ostreopsis mascarenensis* Quod (Dinophyceae, Gonyaulacales) from Réunion Island (SW Indian Ocean): molecular phylogeny and emended description. Phycologia 59*,* 140–153. https://doi.org/10.1080/00318884.2019.1710443

Chomérat, N., Antajan, E., Auby, I., Bilien, G., Carpentier, L., Casamajor, M.-N.d., Ganthy, F., Hervé, F., Labadie, M., Méteigner, C., Paradis, C., Perrière-Rumèbe, Snachez, F., Séchet, V., Amzil, Z. 2022. First Characterization of *Ostreopsis* cf. *ovata* (Dinophyceae) and Detection of Ovatoxins during a Multispecific and Toxic *Ostreopsis* Bloom on French Atlantic Coast. Mar. Drugs, 20, 461. https://doi.org/ 10.3390/md20070461

Ciminiello, P., Dell’Aversano, C., Fattoruso, E., Forino, M., Magno, G. S., Tartaglione, L., Grillo, C., Melchiorre, N., 2006. The Genoa 2005 Outbreak. Determination of putative palytoxin in Mediterranean *Ostreopsis ovata* by a new Liquid Chromatography tandem Mass Spectrometry Method. Anal. Chem. 78, 6153–6159. https://doi.org/10.1021/ac060250j.

Ciminiello, P., Dell’Aversano, C., Fattorusso, E., Forino, M., Grauso, L., Tartaglione, L., 2011. A 4-decade-long (and still ongoing) hunt for palytoxins chemical architecture. Toxicon 57, 362–367. https://doi.org/10.1016/j.toxicon.2010.09.005.

Ciminiello P., Dell'Aversano C., Dello Iacovo E., Fattorusso E., Forino M., Tartaglione L., 2014. First finding of O*streopsis* cf. *ovata* toxins in marine aerosols. Environ. Sci. Technol. 48, 3532–3540. https://doi.org/10.1021/es405617d

Deeds, J.R., Schwartz, M.D., 2010. Human risk associated with palytoxin exposure. Toxicon 56, 150–162. https://doi.org/10.1016/j.toxicon.2009.05.035

Direction du Tourisme et des Congrès (DTC) Monaco - CRT Côte d'Azur, 2010. « *Comportement et niveau de satisfaction des clientèles touristiques de la Principauté* » sur demande auprès du Comité Régional du Tourisme Côte d’Azur, France.

Drouet, K., Jauzein, C., Gasparini, S., Pavaux, A.-S., Berdalet, E., Marro, S., Davenet-Sbirrazuoli, V. Siano, R., Lemée, R. 2022. The benthic toxic dinoflagellate *Ostreopsis* cf. *ovata* in the NW Mediterranean Sea: Relationship between sea surface temperature and bloom phenology. Harmful Algae, 112, 102194, https://doi.org/10.1016/j.hal.2022.102184

EFSA Panel on Contaminants in the Food Chain (CONTAM), 2009. Scientific Opinion on marine biotoxins in shellfish – Palytoxin group. EFSA J. 7, 1393. https://doi.org/10.2903/j.efsa.2009.1393

Escalera, L., Benvenuto, G., Scalco, E., Zingone, A., Montresor, M., 2014. Ultrastructural Features of the Benthic Dinoflagellate *Ostreopsis* cf. *ovata* (Dinophyceae). Protist 165, 260–274. https://doi.org/10.1016/j.protis.2014.03.001

Faimali, M., Giussani, V., Piazza, V., Garaventa, F., Corrà, C., Asnaghi, V., Privitera, D., Gallus, L., Cattaneo-Vietti, R., Mangialajo, L., Chiantore, M., 2012. Toxic effects of harmful benthic dinoflagellate *Ostreopsis ovata* on invertebrate and vertebrate marine organisms. Mar. Environ. Res. 76, 97–107. https://doi.org/10.1016/j.marenvres.2011.09.010

Fleming L.E., Kirkpatrick B., Backer L.C., Walsh C.J., Nierenberg K., Clark J., Reich A., Hollenbeck J., Benson J., Cheng Y.S., Naar J., Pierce R., Bourdelais A.J., Abraham W.M., Kirkpatrick G., Zaias J., Wanner A., Mendes E., Shalat S., Hoagland P., Stephan W., Bean J., Watkins S., Clarke T., Byrne M., Baden D.G., 2011. Review of Florida Red Tide and Human Health Effects. Harmful Algae 20, 224–233. https://doi.org/10.1016/j.hal.2010.08.006.

Funari, E., Manganelli, M., Testai, E., 2015 *Ostreopsis* cf. *ovata* blooms in coastal water: Italian guidelines to assess and manage the risk associated to bathing waters and recreational activities. Harmful Algae 50, 45–56. https://doi.org/10.1016/j.hal.2015.10.008.

Gallitelli, M., Ungaro, N., Addante, L.M., Procacci, V., Silver, N.G., Sabbà, C., 2005. Respiratory illness as a reaction to tropical algal blooms occurring in a temperate climate. JAMA Lett. 239, 2595-2600. https://doi.org/10.1001/jama.293.21.2599-c.

García-Portela, M., Riobó, P., Franco, J.M., Bañuelos, R.M., Rodríguez, F., 2016. Genetic and toxinological characterization of North Atlantic strains of the dinoflagellate *Ostreopsis* and allelopathic interactions with toxic and non-toxic species from the genera *Prorocentrum, Coolia* and *Gambierdiscus*. Harmful Algae 60, 57–69. https://doi.org/10.1016/j.hal.2016.10.007

Gémin, M.-P., 2020. Effets *in situ* et *in vitro* des paramètres environnementaux sur l'abondance, le métabolome et le contenu toxinique d'*Ostreopsis* cf. *ovata* et purifications des ovatoxines. PhD Thesis, Université de Nantes, 244 pp.

GEOHAB, 2001. Global Ecology and Oceanography of Harmful Algal Blooms, Science Plan. P. Glibert and G. Pitcher (Eds). SCOR and IOC, Baltimore and Paris. 87 pp. http://hab.ioc-unesco.org/index.php?option=com_oe&task=viewDocumentRecord&docID=2947

Giussani, V., Sbrana, F., Asnaghi, V., Vassalli, M., Faimali, M., Casabianca, S., Penna, A., Ciminiello, P., Dell'Aversano, C., Tartaglione, L., Mazzeo, A., Chiantore, M., 2015. Active role of the mucilage in the toxicity mechanism of the harmful benthic dinoflagellate *Ostreopsis* cf. *ovata*. Harmful Algae 44, 46–53. https://doi.org/10.1016/j.hal.2015.02.006

Giussani, V., Costa, E., Pecorino, D., Berdalet, E., De Giampaulis, G., Gentile, M., Fuentes, V., Vila, M., Penna, A., Chiantore, M., Garaventa, F., Lavorano, S., Faimali, M., 2016. Effects of the harmful dinoflagellate *Ostreopsis* cf. *ovata* on different life cycle stages of the common moon jellyfish *Aurelia* sp. Harmful Algae 57, 49–58. https://doi.org/10.1016/j.hal.2016.05.005

Giussani, V., Asnaghi, V., Pedroncini, A., Chiantore, M., 2017. Management of harmful benthic dinoflagellates requires targeted sampling methods and alarm thresholds. Harmful Algae 68: 97-104. https://doi.org/10.1016/j.hal.2017.07.010.

Gorbi, S., Bocchetti, R., Binelli, A., Bacchiocchi, S., Orletti, R., Nanetti, L., Raffaelli, F., Vignini, A., Accoroni, S., Totti, C., Regoli, F., 2012. Biological effects of palytoxin-like compounds from *Ostreopsis* cf. *ovata*: A multibiomarkers approach with mussels *Mytilus galloprovincialis*. Chemosphere 89, 623–632. https://doi.org/10.1016/j.chemosphere.2012.05.064

Gorbi, S., Avio, G.C., Benedetti, M., Totti, C., Accoroni, S., Pichierri, S., Bacchiocchi, S., Orletti, R., Graziosi, T., Regoli, F., 2013. Effects of harmful dinoflagellate *Ostreopsis* cf. *ovata* exposure on immunological, histological and oxidative responses of mussels *Mytilus galloprovincialis*. Fish Shellfish Immunol. 35, 941–950. https://doi.org/10.1016/j.fsi.2013.07.003

Greillet, C., Labadie, M., Manel, J. de Haro, L., 2020. Etude des cas d’exposition aux cyanobactéries rapportés aux Centres antipoison entre le 01/01/2006 et le 31/12/2018. Toxicol. Anal. Clin. 32, 70–80.

Guidi-Guilvard, L. D., Gasparini, S., Lemée, R., 2012. The negative impact of *Ostreopsis* cf. *ovata* on phytal meiofauna from the coastal NW Mediterranean Cryptogamie Algologie 33, 121–128. https://doi.org/10.7872/crya.v33.iss2.2011.121.

Hartge, P., Cahill, J., 1998. Field Methods in Epidemiology. In: Rothman, K.J., Greenland, S. (Eds.), Modern epidemiology. Second edition. Lippincott Williams and Wilkins, pp. 163–180.

Honsell, G., Bonifacio, A., de Bortoli, M., Penna, A., Battocchi, C., Ciminiello, P., Dell’Aversano, C., Fattorusso, E., Sosa, S., Yasumoto, T., Tubaro, A., 2013. New insights on cytological and metabolic features of *Ostreopsis* cf. *ovata* Fukuyo (Dinophyceae): A multidisciplinary approach. PLoS ONE 8, e57291. https://doi.org/10.1371/journal.pone.0057291.

Horák, P., Mikes, L., Lichtenbergova, L., Skála, V., Soldánová, M., Brant S. V., 2015. Avian Schistomsomes and Outbreaks of Cercarian Dermatitis. Clin. Microbiol. Rev. 28(1), 165–190. https://doi.org/10.1128/CMR.00043-14.

Iddir-Ihaddaden, W., Ouled Abdellah, K., Merbout, G., Abtroun, R., Alamir, B., de Haro, L. 2009. Conséquences sanitaires d’efflorescences d’algues du genre *Ostreopsis* en

Algérie au cours de l’été 2009. Presse Méd. 42, 1281–1283. https://doi.org/10.1016/j.lpm.2012.10.020.

Illoul, H., Rodríguez, F., Vila, M., Adjas, N., Aït Younes, A., Bournissa, M., Koroghli, A., Marouf, N., Rabia, S., Ameur, F.L.K., 2012. The genus *Ostreopsis* along the Algerian coastal waters (SW Mediterranean Sea) associated with a human respiratory intoxication episode. Cryptogamie Algologie 33: 209–216. https://doi.org/10.7872/crya.v33.iss2.2011.209.

IMSEE, Institute Monegasque de la Statistique et des Études Économiques, 2020. https://www.imsee.mc

Insee, Institut national de la statistique et des études économiques, 2017. https://www.insee.fr/fr/accueil

Kermarec, F., Dor, F., Armengaud, A., Charlet, F., Kantin, R., Sauzade, D., Giannetti, S., de Haro, L. 2008. Les risques sanitaires liés à la présence d’*Ostreopsis ovata* dans les eaux de baignade ou d’activités nautiques. Environnement, Risques & Santé 7(5), 357–363.

Kodama, A.M., Hokama, Y., Yasumoto, T., Fukui,M., Manea, S.J., Sutherland,N., 1989. Clinical and laboratory findings implicating palytoxin as cause of ciguatera poisoning due to *Decapterus macrosoma* (mackerel). Toxicon 27, 1051–1053. https://doi.org/10.1016/0041-0101(89)90156-6.

Lemée, R., Mangialajo, L., Cohu, S., Amzil, Z., Blanfune, A., Chomerat, N., Ganzin, N., Gasparini, S., Grossel, H., Guidi-Guivard, L., Hoareau, L., Duff, F. le, Marro, S., Simon, N., Nezan, E., Pedrotti, M.-L., Sechet, V., Soliveres, O., Thibaut, T., 2012. Interactions between Scientists, Managers and Policy Makers in the Framework of the French MediOs Project on *Ostreopsis* (2008–2010). Cryptogamie Algologie 33, 137–142. https://doi.org/10.7872/crya.v33.iss2.2011.137

Lenoir, S., Ten-Hage, L., Turquet, J., Quod, J.-P., Bernard, C., Hennion, M.-C., 2004. First evidence of palytoxin analogues from an *Ostreopsis mascarenensis* (Dinophyceae) benthic bloom in Southwestern Indian Ocean. J. Phycol. 40, 1042–105. https://doi.org/10.1111/j.1529-8817.2004.04016.x.

Mahmud, Y., Arakawa, O., Noguchi, T., 2000. An epidemic survey on the freshwater puffer poisoning in Bangladesh. J. Nat. Toxins 9, 319–326.

Mangialajo, L., Ganzin, N., Accoroni, S., Asnaghi, V., Blanfuné, A., Cabrini, M., Cattaneo-Vietti, R., Chavanon, F., Chiantore, M.C., Cohu, S., Costa, E., Fornasaro, D., Grossel, H., Marco-Miralles, F., Masó, M., Reñé, A., Rossi, A.M., Sala, M.M., Thibaut, T., Totti, C., Vila, M., Lemée, R,. 2011. Trends in *Ostreopsis* proliferation along the Northern Mediterranean coasts. Toxicon 57, 408–420. https://doi.org/10.1016/j.toxicon.2010.11.019.

Medina-Pérez, N.-I., Dall'Osto, M., Decesari, S., Paglione, M., Moyano, E., Berdalet, E., 2020. Aerosol toxins emitted by harmful algal blooms susceptible to complex air-sea interactions. Environ. Sci. Technol. 55(1), 469–477. https://dx.doi.org/10.1021/acs.est.0c05795

Migliaccio, O., Castellano, I., Di Cioccio, D., Tedeschi, G., Negri, A., Cirino, P., Romano, G., Zingone, A., Palumbo, A., 2016. Subtle reproductive impairment through nitric oxide-mediated mechanisms in sea urchins from an area affected by harmful algal blooms. Sci. Rep. 6, 26086. https://doi.org/10.1038/srep26086.

Milandri, A., Ceredi, A., Riccardi, E., Gasperetti, L., Susini, F., Casotti, M., Faiman, L., Pigozzi, S., 2010. Impact of *Ostreopsis ovata* on marine benthic communities: accumulation of palytoxins in mussels, sea urchins and octopuses from Italy. In: Pagou, P., Hallegraeff, G. (Eds), Proceedings of the 14th International Conference on Harmful Algae. International Society for the Study of Harmful Algae and Intergovernmental Oceanographic Commission of UNESCO 2013. pp. 23–25.

Mitra, A., Zaman, S., 2015. Blue Carbon Reservoir of the Blue Planet. Springer Nature, Switzerland, 299 pp.

Morgan, K. L., Larkin, S. L., Adams, C. M. 2010. Red tides and participation in marine-based activities: estimating the response of Southwest Florida residents. Harmful Algae, 9, 333-341.

Moore, R. E., Scheuer, P. J. 1971. Palytoxin: a new marine toxin from a coelenterate. Science 172, 495–498. https://doi.org/10.1126/science.172.3982.495.

Moser, C. A. 1952. Quota sampling. Journal of the Royal Statistical Society. Series A (General), 115(3), 411-423.

Moser, C. A., Stuart, A. 1953. An experimental study of quota sampling. Journal of the Royal Statistical Society. Series A (General), 116(4), 349-405.

Neves, R. A., Contins, M., & Nascimento, S. M., 2018. Effects of the toxic benthic dinoflagellate *Ostreopsis* cf. *ovata* on fertilization and early development of the sea urchin *Lytechinus variegatus*. Mar. Environm. Res. 135, 11–17. https://doi.org/10.1016/j.marenvres.2018.01.014.

Onuma, Y., Satake, M., Ukena, T., Roux, J., Chanteau, S., Rasolofonirina, N., Ratsimaloto, M., Naoki, H., Yasumoto, T., 1999. Identification of putative palytoxin as the cause of clupeotoxism. Toxicon 37, 55–65. https://doi.org/10.1016/s0041-0101(98)00133-0.

Pavaux, A.-S., Rostan, J., Guidi-Guilvard, L., Marro, S., Ternon, E., Thomas, O. P., Lemée, R., Gasparini, S., 2019. Effects of the toxic dinoflagellate *Ostreopsis* cf. *ovata* on survival, feeding and reproduction of a phytal harpacticoid copepod. J. Exper. Mar. Biol. Ecol. 516, 103–113. https://doi.org/10.1016/j.jembe.2019.05.004.

Pavaux, A.-S., Berdalet, E., Lemée, R., 2020a. Chemical ecology of the benthic dinoflagellate genus *Ostreopsis*: review of Progress and Future Directions. Front. Mar. Sci. 7, 498. https://doi.org/10.3389/fmars.2020.00498.

Pavaux, A. S., Ternon, E., Dufour, L., Marro, S., Gémin, M. P., Thomas, O. P., and Lemée, R., 2020b. Efficient, fast and inexpensive bioassay to monitor benthic microalgae toxicity: Application to *Ostreopsis* species. Aquat. Toxicol., 223. https://doi.org/10.1016/j.aquatox.2020.105485

Pavaux, A.-S., Velasquez-Carjaval, D., Drouet, K., Lebrun, A., Hiroux, A., Marro, S., Christians, E., Castagnetti, S., Lemée, R., 2021. Daily variations of *Ostreopsis* cf. *ovata* abundances in NW Mediterranean Sea. Harmful Algae 110, 102144, https://doi.org/10.1016/j.hal.2021.102144

Penna, A., Battocchi, C., Capellacci, S., Fraga, S., Aligizaki, K., Lemée, R., Vernesi, C., 2014. Mitochondrial, but not rDNA, genes fail to discriminate dinoflagellate species in the genus *Ostreopsis*. Harmful Algae 40, 40–50. https://doi.org/10.1016/j.hal.2014.10.004.

Pezzolesi, L., Guerrini, F., Ciminiello, P., Dell'Aversano, C., Iacovo, E.D., Fattorusso, E., Forino, M., Tartaglione, L., Pistocchi, R., 2012. Influence of temperature and salinity on *Ostreopsis* cf. *ovata* growth and evaluation of toxin content through HR LC-MS and biological assays. Water Res. 46, 82–92. https://doi.org/10.1016/j.watres.2011.10.029

Pichierri, S., Accoroni, S., Pezzolesi, L., Guerrini, F., Romagnoli, T., Pistocchi, R., Totti, C., 2017. Allelopathic effects of diatom filtrates on the toxic benthic dinoflagellate *Ostreopsis* cf. *ovata*. Mar. Environ. Res. *131*, 116–122. https://doi.org/10.1016/j.marenvres.2017.09.016

Poli, M., Ruiz-Olvera, P., Nalca, A., Ruiz, S., Livingston, V., Frick, O., Dyer, D., Schellhase, C., Raymond, J., Kulis, D., Anderson, D., McGrath, S., Deeds, J., 2018. Toxicity and pathophysiology of palytoxin congeners after intraperitoneal and aerosol administration in rats. Toxicon 150, 235–250. https://doi.org/10.1016/j.toxicon.2018.06.067

Rossi, R., Castellano, V., Scalco, E., Serpe, L., Zingone, A., Soprano, V., 2010. New palytoxin-like molecules in Mediterranean *Ostreopsis* cf. *ovata* (dinoflagellates) and in Palythoa tuberculosa detected by liquid chromatography-electrospray ionization time-of-flight mass spectrometry. Toxicon 56, 1381–1387. https://doi.org/10.1016/j.toxicon.2010.08.003.

Sansoni, G., Borghini, B., Camici, G., Casotti, M., Righini, P., Rustighi, C., 2003. Fioriture algali di *Ostreopsis ovata* (Gonyaulacales: Dinophyceae): un problema emergente. Biol. Ambient. 17, 17–23.

Schmitt, C., de Haro, L., 2013. Clinical Marine Toxicology: A European perspective for clinical toxicologists and Poison Centers. Toxins (Basel) 5, 1343–1352. https://doi.org/10.3390/toxins5081343.

Schmitt, C., Torrents, R., Domangé, B., Glaizal, M., Simon, N., de Haro, L., 2018. Intoxication par palytoxines après manipulation de zoanthides d'aquarium : à propos de 3 cas survenus en France. Presse Méd. 47(2), 178–180. https://doi.org/10.1016/j.lpm.2017.11.004.

Shears, N.T., Ross, P.M., 2009. Blooms of benthic dinoflagellates of the genus *Ostreopsis*; an increasing and ecologically important phenomenon on temperate reefs in New Zealand and worldwide. Harmful Algae 8, 916–925. https://doi.org/10.1016/j.hal.2009.05.003

Taniyama, S., Arakawa, O., Terada, M., Nishio, S., Takatani, T., Mahmud, Y., Noguchi, T., 2003. *Ostreopsis* sp. a possible origin of palytoxin (PTX) in parrotfish *Scarus ovifrons*. Toxicon 42, 29–33. https://doi.org/10.1016/s0041-0101(03)00097-7.

Tartaglione, L., Mazzeo, A., Dell'Aversano, C., Forino, M., Giussani, V., Capellacci, S., Penna, A., Asnaghi, V., Faimali, M., Chiantore, M., Yasumoto, T., Ciminiello, P., 2016. Chemical, molecular, and eco-toxicological investigation of *Ostreopsis* sp. from Cyprus Island: structural insights into four new ovatoxins by LC-HRMS/MS. Anal. Bioanal. Chem. 408, 915–32. https://doi.org/10.1007/s00216-015-9183-3.

Ternon, E., Pavaux, A.-S., Marro, S., Thomas, O.P., Lemée, R., 2018. Allelopathic interactions between the benthic toxic dinoflagellate *Ostreopsis* cf. *ovata* and a co-occurring diatom. Harmful Algae 75, 35–44. https://doi.org/10.1016/j.hal.2018.04.003.

Ternon, E., Glukhov, E., Trytten, E., Lemée, R., Gerwick,W.H. 2022. On the Hunt for New Toxin Families Produced by a Mediterranean Strain of the Benthic Dinoflagellate *Ostreopsis* cf. *ovata*. Toxins 14, 234. https://doi.org/10.3390/toxins14040234

Tester, P.A., Litaker, W., Berdalet, E., 2020. Climate Change and Benthic Harmful Algae. Harmful Algae 91, 101655. https://doi.org/10.1016/j.hal.2019.101655.

Tichadou, L., Glaizal, M., Armengaud, A., Grossel, H., Lemée, R., Kantin, R., Lasalle, J.L., Drouet, G., Rambaud, L., Malfait, P., de Haro, L., 2010. Health impact of unicellular algae of the *Ostreopsis* genus blooms in the Mediterranean Sea: experience of the French Mediterranean Coast Surveillance Network from 2006 to 2009. Clin. Toxicol. 48, 839–844. http://dx.doi.org/10.3109/15563650.2010.513687

Tubaro, A., Durando, P., Del Favero, G., Ansaldi, F., Icardi, G., Deeds, J.R., Sosa, S., 2011. Case definitions for human poisonings postulated to palytoxins exposure. Toxicon 57, 478–495. https://doi.org/10.1016/j.toxicon.2011.01.005

Usami, M., Satake, M., Ishida, S., Inoue, A., Kan, Y., Yasumoto, T., 1995. Palytoxin analogs from the dinoflagellate *Ostreopsis siamensis*. J. Am. Chem. Soc. 117, 5389–5390. https://doi.org/10.1021/ja00124a034.

Vanucci, S., Guidi, F., Pistocchi, R., Long, R.A., 2016. Phylogenetic structure of bacterial assemblages co-occurring with *Ostreopsis* cf. *ovata* bloom. Harmful Algae 55, 259–271. https://doi.org/10.1016/j.hal.2016.04.003.

Vila, M., Masó, M., Sampedro, N., Illoul, H., Arin, L., Garcés, E., Giacobbe, M. G., Alvarez, J., Camp, J. 2008. The genus *Ostreopsis* in recreational waters of the Catalan Coast and Balearic Islands (NW Mediterranean Sea): is this the origin of human respiratory difficulties? In: Moestrup Ø. et al. (eds), Proceedings of the 12th International Conference on Harmful Algae, Copenhagen, Denmark, 4–8 September 2006. ISSHA and IOC of UNESCO, pp. 334–336.

Vila, M., Abós-Herràndiz, R., Isern-Fontanet, J., Àlvarez, J., Berdalet, E., 2016. Establishing the link between *Ostreopsis* cf. *ovata* blooms and human health impacts using ecology and epidemiology. Sci. Mar. 80, 107-115. https://doi.org/10.3989/scimar.04395.08A

Yoo, Y.D., Jeong, H.J., Lee, S.Y., Yoon, E.Y., Kang, N.S., Lim, A.S., Lee, K.H., Jang, S.H., Park, J.Y., Kim, H.S., 2015. Feeding by heterotrophic protists on the toxic dinoflagellate *Ostreopsis* cf. *ovata*. Harmful Algae 49, 1–9. https://doi.org/10.1016/j.hal.2015.08.001

Young, N., Sharpe, R. A., Barciela, R., Nichols G., Davidson, K., Berdalet, E., Fleming, L. E., 2020. Marine harmful algal blooms and human health: A systematic scoping review. Harmful Algae 98: 101901, https://doi.org/10.1016/j.hal.2020.101901

8. Figure Legends

Figure 1. Different images of an *Ostreopsis* cf. *ovata* roliferation. Benthic cells form the brownish mucilaginous carpet covering pebbles (A) and macroalgae (B, C). Detached from the bottom, high planktonic cell abundances are visible in the water column (D) and aggregates are also found floating at the sea surface (E) forming “sea-flowers” or "fleurs d'eau" in French. A, B, C and D pictures from Rochambeau, Villefranche-sur-mer, France; E photo taken in Sant Andreu de Llavaneres, Catalonia, Spain.

Figure 2. Conceptual approach to initiate the evaluation of the main tangible and intangible socioeconomic impacts of *Ostreopsis* blooms. Source: from authors.

Figure 3. Temporal dynamics (from June 1st, Julian day 150, to the end of December, Julian day 360) of the monitored *Ostreopsis* cf. *ovata* blooms and the number of people reporting *Ostreopsis*-related symptoms in each studied year (2013 to 2018) in Sant Andreu de Llavaneres. Epidemiological data are represented by dashed lines and highlighted by arrows, with units (0-20) in the first left Y-axis. *O.* cf. *ovata* cell concentrations in the benthos (continuous line, second left Y-axis) and in the plankton (dotted lines, right Y-axis) are presented in logarithmic scale. The two horizontal lines indicate alert thresholds for cell abundance, respectively, $2·10^5$ cells gFW^{-1} of macroalgae (continuous line) and $3·10^4$ cells L^{-1} of water (dotted line) used in some management procedures (see Discussion).

Figure 4. Temporal variation of the number of people (dotted line, left Y-axis) reporting *Ostreopsis*-related symptoms and the *Ostreopsis* cf. *ovata* cell concentration (continuous line, right Y-axis) in the benthos (upper graph) and in the plankton (lower graph) in Sant Andreu de Llavaneres. The plotted data correspond to the mobile average (every 7 days) of the epidemiologic and *Ostreopsis* abundance data obtained for each Julian day along the 6-year study. In each graph, dashed horizontal lines indicate cell abundance alert thresholds, respectively, $2 \cdot 10^5$ cells·g FW^{-1} of macroalgae and $3 \cdot 10^4$ cells·L^{-1} of water, used in some management procedures (see Discussion).

9. Declaration of Competing Interest and Authors contributions

All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. All authors contributed to the writing and approved the final version. In particular, R.L. and A.-S.P. were in charge of the environment impacts section; E.B., R.A.-H., N.I.M.-P., M.V. and L.V. conducted the environmental and epidemiology studies in Catalonia; L.d.H. and R.L. coordinated the human health studies in France; M.T., G.A. and J.T. conducted the socioeconomic studies; E.B., B.K. and R.L. coordinated the overall study within the CoCliME project.

Figure 1.

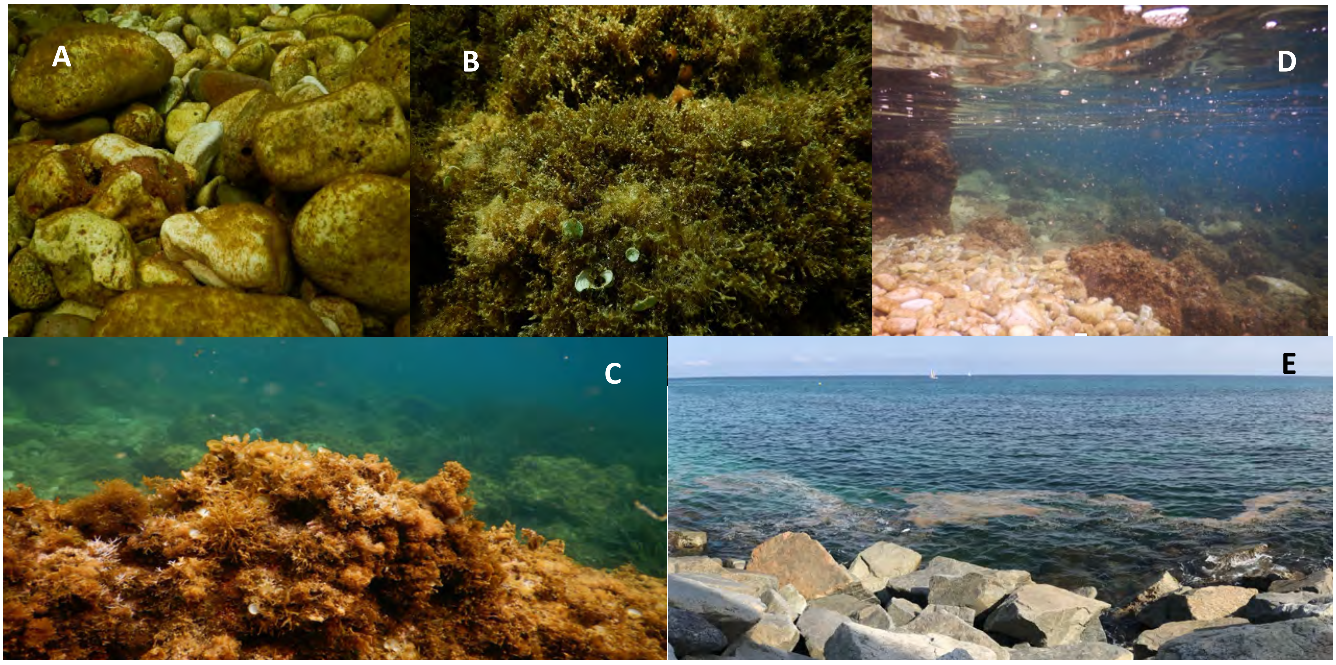


Figure 2.

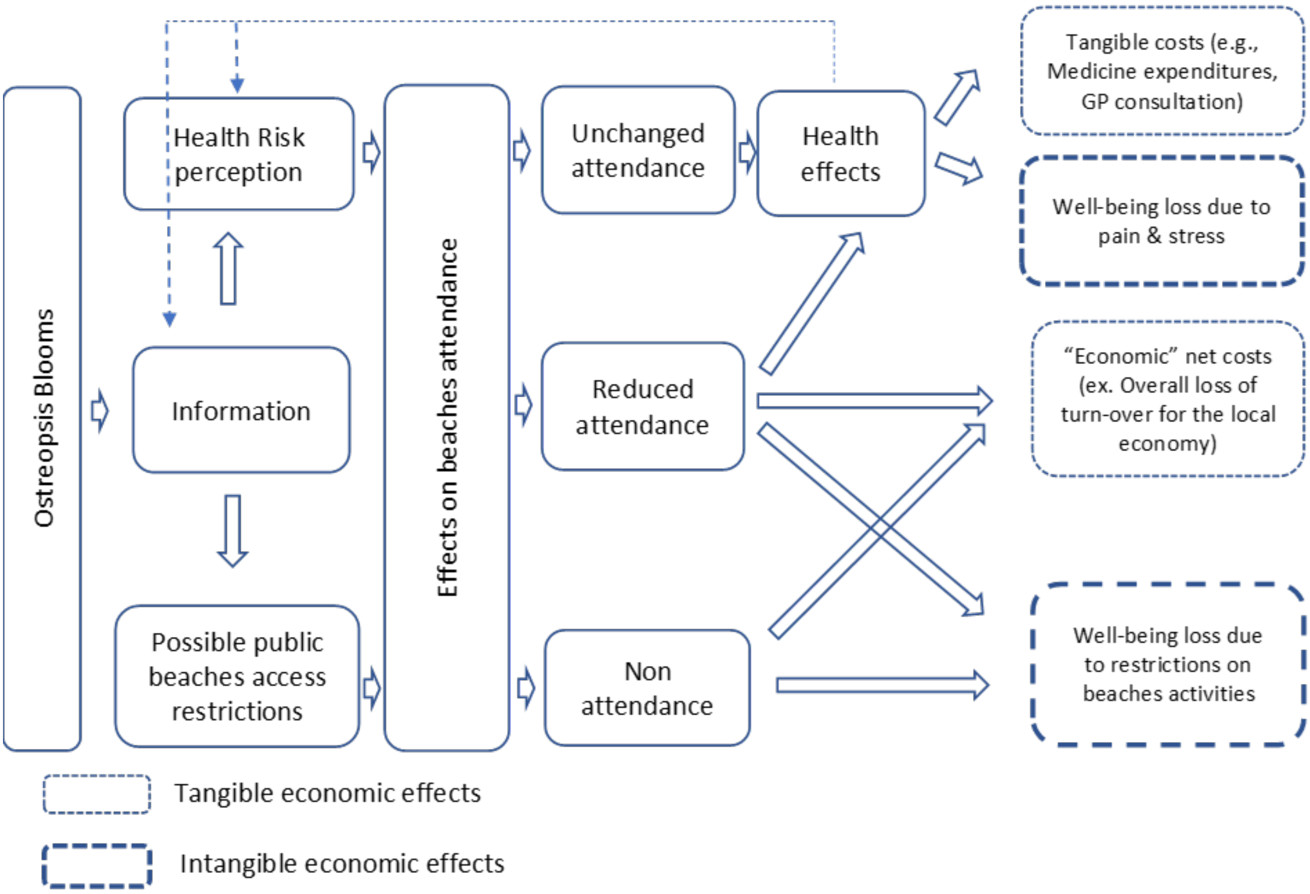

Ostreopsis Blooms
Health Risk perception
Information
Possible public beaches access restrictions
Effects on beaches attendance
Unchanged attendance
Reduced attendance
Non attendance
Health effects
Tangible costs (e.g., Medicine expenditures, GP consultation)
Well-being loss due to pain & stress
"Economic" net costs (ex. Overall loss of turn-over for the local economy)
Well-being loss due to restrictions on beaches activities
Tangible economic effects
Intangible economic effects

Figure 3.

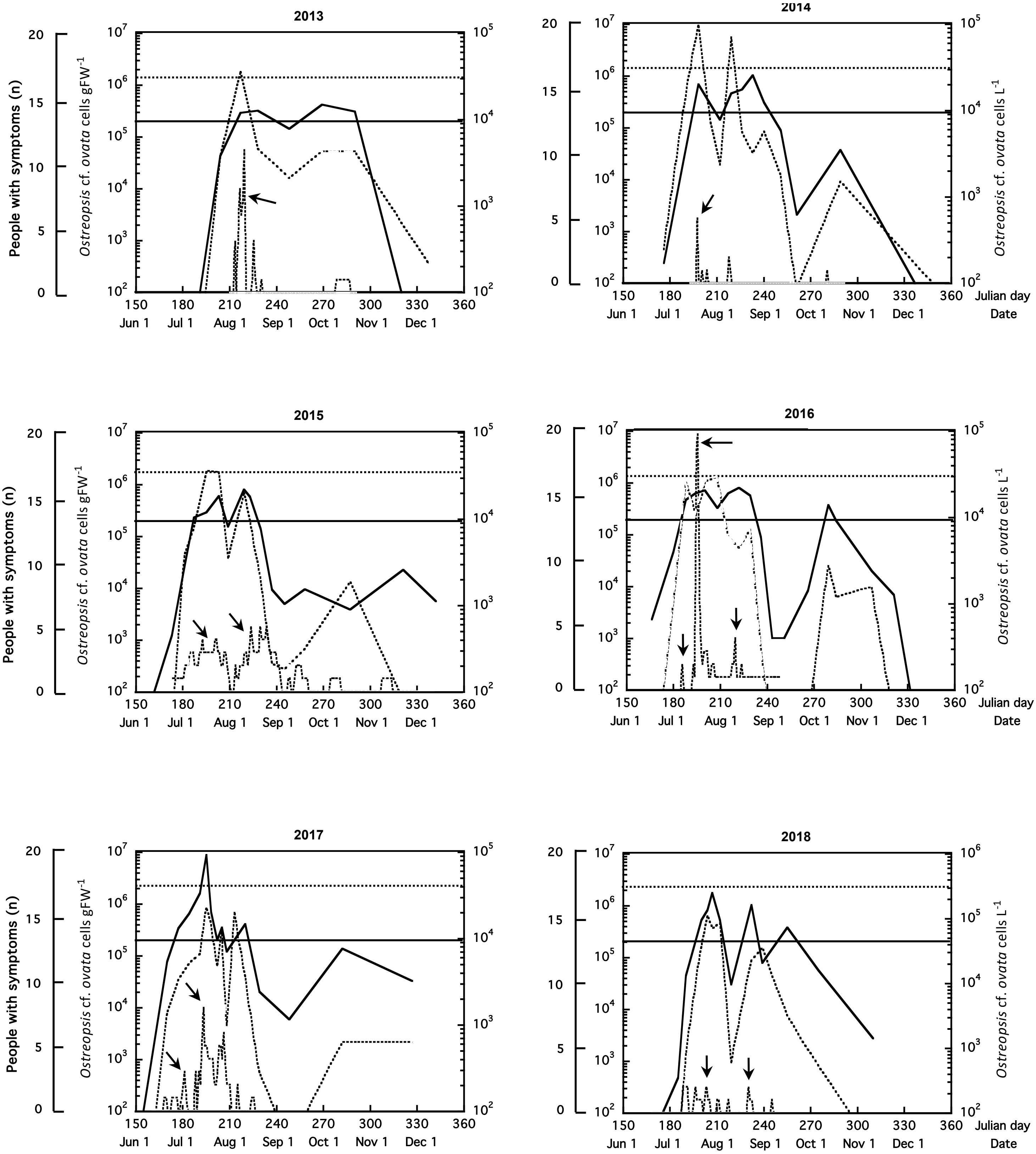
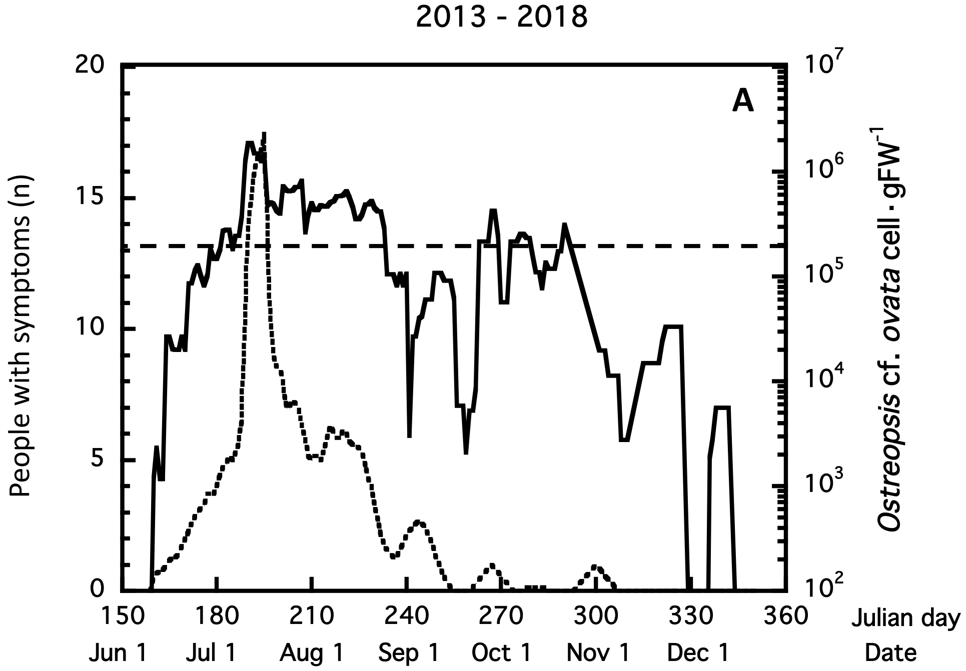

2013
2014
2015
2016
2017
2018
People with symptoms (n)
Ostreopsis cf. ovata cells gFW-1
Ostreopsis cf. ovata cells L-1
Julian day
Date
150
180
210
240
270
300
330
360
Jun 1
Jul 1
Aug 1
Sep 1
Oct 1
Nov 1
Dec 1

Figure 4


2013 - 2018
A
People with symptoms (n)
Ostreopsis cf. ovata cell · gFW-1
20
15
10
5
0
10^7
10^6
10^5
10^4
10^3
10^2
150
180
210
240
270
300
330
360
Julian day
Jun 1
Jul 1
Aug 1
Sep 1
Oct 1
Nov 1
Dec 1
Date

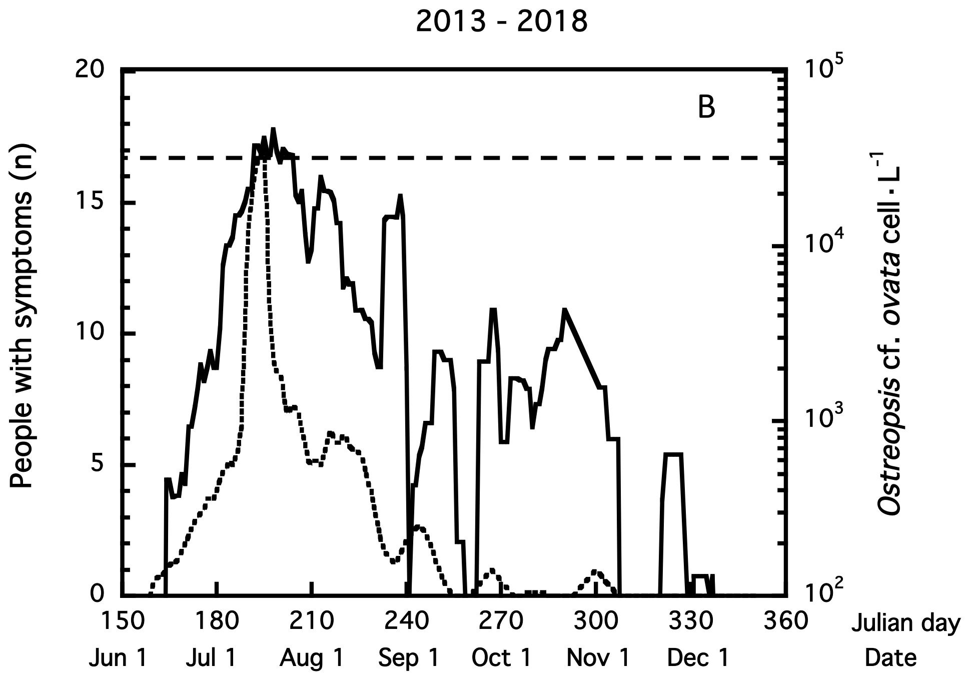

2013 - 2018
B
People with symptoms (n)
Ostreopsis cf. ovata cell · L-1
20
15
10
5
0
10^5
10^4
10^3
10^2
150
180
210
240
270
300
330
360
Julian day
Jun 1
Jul 1
Aug 1
Sep 1
Oct 1
Nov 1
Dec 1
Date

Table 1. Basic information concerning the distributed questionnaires per year. The prevalence rate (%) is defined as the percentage of people that presented symptoms in the answered questionnaires.

Year	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Questionnaires distributed (n)	16	14	68	68	118	43
Questionnaires answered (n)	16	14	29	28	22	5
Questionnaires answered (%)	100	100	42.6	41.2	18.6	11.6
People with symptoms (n)	13	5	13	21	22	5
Prevalence rate (%)	81.3	35.7	44.8	75	100	100

Table 2. Prevalence rate (in %) of the different symptoms registered in questionnaires every year. Symptoms are listed alphabetically within the corresponding human organ system. Empty cells indicate that the particular health problem was not reported.

Organ system	Symptoms	2013	2014	2015	2016	2017	2018
General	Chill				1.6	3.7	1.3
	Fever			3.1	1.1		
	Headache		13.1	13.6	8.8	9.6	3.5
	Leg cramps			0.2		7.1	3.1
	Malaise	5.9	13.1	8.7	8.0	4.2	3.1
	Muscular pain			7.5	1.9	9.0	5.3
	Somnolence					0.4	2.6
	Tiredness				0.8	1.5	4.4
Otorhinolaryngologic	Loss of voice				1.1		3.1
	Nose irritation	45.9	39.5	0.3	7.4		1.3
	Runny nose	45.9	2.6	13.7	16.1	10.7	17.2
	Sneezes		21.1		4.5		11.9
	Sore throat			9.0	8.3	10.1	4.4
Ophthalmologic	Sore eyes	2.3	5.3	8.1	9.7	7.4	2.6
	Weeping eyes			12.6	8.2	7.6	2.6
Digestive	Diarrhoea					1.0	
	Metallic taste			3.6	2.7	7.4	9.3
	Nausea						
	Vomiting						
Respiratory	Cough			13.0	13.2	11.4	7.5
	Hoarseness			1.0	1.1	0.9	
	Mucus in the throat		5.3		0.5		11.5

	Shortness of breath	3.8	3.4	3.6	3.1
	Wheezing		1.1		2.2
Dermatologic	Itching skin		0.5	0.9	
	Red skin (rash)	0.1			
Cardiac	Irregular	1.7		3.5	

Table 3. Acute symptoms related to exposure to *Ostreopsis* along the bloom and relationship with the life stage of the cells, based on the experience of the French Mediterranean National *Ostreopsis* Surveillance Network. Reference cell abundances in the benthos (B), plankton (P) and floating aggregates (A), based on the experience in France, Italy (Funari et al., 2015) and the data presented in the 6-year epidemiology-ecology study in Catalonia (section 3.2.1); values in brackets are maximum numbers shown in Figure 3.

Stage	***Ostreopsis* abundance**	***Ostreopsis* bloom / life stage**	**ACUTE SYMPTOMS**
1	B: $2{\cdot}10^4$ - $2{\cdot}10^5$ cells·gFW^{-1} P: < $3{\cdot}10^4$ cells·L^{-1}	Pre-bloom conditions, early exponential phase. Large cell concentrations mostly in the benthic stage.	Skin irritations only after direct contact with the benthic substrate (macrophyte, rocks).
2	B: $2{\cdot}10^5$ to ≥ $5{\cdot}10^5$ (6.9 10^6) cells·gFW^{-1} P: ≥ $3{\cdot}10^4$ ($1{\cdot}10^5$) cells·L^{-1}	Bloom conditions, exponential and early stationary phase. Well established benthic as well as planktonic populations.	Cutaneous signs become more important, including mucosal symptoms: eye irritation from conjunctivitis to keratitis, rhinorrhoea, bronchorrhoea with dyspnoea and cough; characteristic sign of metallic taste.
3	A: >$1{\cdot}10^6$ ($1{\cdot}10^7$) cells·L^{-1}	Stationary bloom conditions. Well established benthic as well as planktonic populations. Floating aggregates containing high cell concentrations found at the sea surface, especially under windy conditions.	More severe general signs even without direct contact with seawater, mainly by inhalation of contaminated aerosols and in people without a previous respiratory history (i.e., walkers, residents). Irritation symptoms as in stage 2: fever, myalgia, arthralgia, digestive symptoms, bronchospasm with asthma attack. Most serious cases reported in high-risk populations (children or elderly people with asthma or respiratory deficiency) or under special circumstances (e.g., divers exposed to contaminated droplets condensed in the air tanks regulator).

Table 4. Attitude and reactions (in %) towards obtaining additional information on *Ostreopsis* blooms. Source: from authors.

	Monaco resident	Nice resident	Nice tourist	Total
Not overstated scientific information	77.8	88.1	93.2	83.4
Unnecessary panic	23.9	19.5	11.4	20.7
Scare away tourists	50.0	56.8	56.8	53.3
Credibility of scenario 1	85.2	85.6	72.7	83.7
Credibility of scenario 2	83.5	80.5	77.3	81.7
Threat to the health (scenario 1)	69.9	61.0	50.0	64.2
Threat to the health (scenario 2)	79.0	79.7	77.3	79.0
Severity of the symptoms	46.0	42.4	38.6	43.8

Table 5. Potential attendance to the beach (in %) in the two future scenarios described in section 2.3. Source: from authors.

	Scenario 1			**Scenario 2**		
	No more attendance	**Reduced attendance**	**Unchanged attendance**	**No more attendance**	**Reduced attendance**	**Unchanged attendance**
Monaco resident	60.8	16.5	22.7	-	-	-
Nice resident	54.2	27.1	18.7	83.1	11.0	5.9
Nice tourist	40.9	29.5	29.5	81.8	13.6	4.6
Overall	55.9	21.9	22.2	82.7	5.6	11.7

Table 6. Highlighted determinants of stopping beach-going (scenario 1). Source: from authors.

	Monaco resident	Nice resident	Nice tourist
Constant term	-1.280*** (0.490)	-1.997*** (0.634)	-1.467* (0.768)
Age (years)	0.015** (0.007)	0.022** (0.009)	
With people under 15 in the household (1 if yes, 0 if no)	0.877*** (0.251)	0.709*** (0.271)	---
Gender (1 if male, 0 if female)	---	-0.611** (0.260)	---
Living with his /her parents during the survey (1 if yes, 0 if not)	-1.052** (0.427)	---	---
With a higher education degree (1 if post baccalaureate degree, 0 otherwise)	---	---	---
Prior knowledge of *Ostreopsis* (1 if knowledge of the symptoms related to the blooms of *Ostreopsis*, 0 if no)	---	---	---
Overstated information (1 if yes, 0 if no)	---	---	---
Severity of symptoms (1 if the symptoms associated with *Ostreopsis* are considered quite severe or severe, 0 otherwise)	0.373* (0.218)	---	---
Credibility of scenario 1 (1 if yes, 0 if no)	---	0.755** (0.379)	---
Threat to health (1 if yes, 0 if no)	0.744*** (0.241)	0.972*** (0.266)	0.847* (0.444)
Previous tourist stay in Nice (1 if yes, 0 if no)	----	----	1.472** (0.644)

Walking or beach-going is the main reason for the tourist stay (1 if yes, 0 if not)	----	----	-0.805* (0.433)
Pseudo R²	0.22	0.18	0.26
Correctly classified	77.3 %	70.3 %	70.5 %
Number of observations	176	118	44

Note: Each number (e.g., 0.015) corresponds to the estimated coefficient of the variable used to explain the probability of stopping beach-going. The standard errors of the estimated coefficient are indicated in brackets.
***, **, * indicates significance at 0.01, 0.05 and 0.1 level of risk; --- : indicates not significance at the 10 % level of risk.

APPENDIX 1

Deciphering the clinical and epidemiological symptoms associated to exposure to *Ostreopsis* blooms in the case study in Catalonia and in the Mediterranean French coast.

At the beginning of the 21st century, the international experience about the effects of *Ostreopsis* blooms on human health was very limited and confusing. The taxon had been linked to severe foodborne poisonings in the tropics, because some *Ostreopsis* species were found to produce PLTX analogues; however, no *Ostreopsis* blooms had been reported in these tropical areas. The PLTX contaminated seafood consisted on either particular pelagic fish species (that feed on plankton) or crustaceans and benthic fish species living in coral reefs (see e.g., review by Tubaro et al., 2011), pointing to both a planktonic and a benthic source of the toxin. The clinical picture of the foodborne poisonings in the tropics started by a metallic taste, followed by discomfort accompanied by digestive symptoms, and very quickly the appearance of neurological and especially cardiovascular problems sometimes threatening the vital prognosis. Still, the toxicity of PLTX and analogues in humans was poorly known, and no PLTX-analogues analyses were conducted at that time.

In Europe, the first health problems attributed to exposure to *Ostreopsis* toxins consisted on respiratory and cutaneous irritations and, fortunately, did not resemble these dramatic tropical case reports following seafood ingestion. However, during the first episodes of *Ostreopsis* proliferations in Europe, clinical toxicologists who cooperated with the emergency workers on the front lines had no experience of the potential clinical features that could be induced by these events. There was no model or equivalent pathology to rely on from a clinical point of view. The first isolated and confirmed cases of respiratory symptoms in people exposed to sea spray were reported in 2003 in Italy (Gallitelli et al.,

2005) with suspected human cases since 1998 in Tuscany (Sansoni et al., 2003) and in 2004 in Spain (Vila et al., 2008). In 2005, the Italian city of Genoa in Liguria, neighbouring the French Riviera, was concerned by respiratory problems observed in approximately 200 people who inhaled contaminated sea spray in one single day (Brescianini et al., 2006), with many patients treated in the local hospital emergency units.

On August 4th-10th, 2004, an epidemic outbreak of upper respiratory irritation symptoms occurred in Sant Andreu de Llavaneres (Catalonia, Spain, NW Mediterranean; Àlvarez et al., 2005; Vila et al., 2008). About 200 people inhabiting the apartments in the shoreline were affected. The main reported symptoms and the corresponding prevalence rates were runny nose (74.2 %), nose irritation (66.1 %), sore throat (62.9 %), cough (59.7 %), expectoration (51.6 %), sore eyes (41.4 %) and headache (40.3 %). Exposure to anthropogenic toxic chemicals (e.g., pesticides, fertilizers, industry products, ship spills, ...) was discarded. Seawater analyses detected the presence of *Ostreopsis* spp. at concentrations of ca. $2.3 \cdot 10^4$ cells$\cdot L^{-1}$ within the outbreak period. This event, similar to those reported in Italy (Gallitelli et al., 2005; Brescianini et al., 2006), was also attributed to the *Ostreopsis* presence in the water in relatively high concentrations as the most plausible cause of the respiratory signs.

The first poisonings in France occurred in 2006. In the Frioul Island (Marseille), four divers with no previous relevant medical history, experienced mucosal irritation, breathing difficulties and systemic symptoms (fever, headache, diarrhoea and asthenia) after exploring a beach closed to the public during an important *Ostreopsis* bloom (cell densities of $2.5 \cdot 10^4$ - $90 \cdot 10^4$ cells L^{-1}; Tichadou et al., 2010).

Concurrently to these irritative symptomatology, a completely new phenomenon appeared into the scene: the tropical reef tanks (Schmitt and De Haro, 2013). This was a new aquarist practice of maintaining, in private home aquariums, small artificial reefs containing soft corals (*Palythoa, Protopalythoa*, *Zoanthus*). These three genera, as well as other related taxa, are known to contain high quantities of PLTX in their tissues. Soft corals are sometimes intentionally introduced into aquariums, but more often they are invaders that have been brought inadvertently in the form of larvae attached to another invertebrate or to a mineral substrate. The aquarist who then wants to get rid of intruders must be very careful. If the tissues of these soft corals are damaged, they release large amounts of PLTX, not only into the water but also into the atmosphere, due to the contamination of micro-droplets formed by the aeration system of the tank. Then, humans in the same room can present skin injuries (from simple irritation to bullous and necrotic lesions), metallic taste in the mouth, mucosa irritation with rhinorrhoea, conjunctivitis (or even keratitis due to direct contact with the water), respiratory distress, fever, myalgia, and digestive symptoms. Several cases of ocular sequelae with definitive decline in visual acuity and / or post corneal ulcer opacifications have been reported (Schmitt et al., 2018; Calon et al., 2019). These clinical features were somehow similar to those reported during *Ostreopsis* blooms.

European clinical toxicologists were thus confronted with human exposures to marine toxins causing cutaneous and respiratory symptoms: i) amateur or professional aquarists exposed to large amounts of PLTX contained in soft corals, and ii) swimmers, divers or waterside walkers and residents exposed during *Ostreopsis* proliferations to probably similar toxins. The data accumulated from the aquarists experiences and from many *Ostreopsis* blooms in the Mediterranean coasts (see Table 2 in Pavaux et al., 2020a) that have generated several hundred cases in Italy, Spain, France and Algeria (Illoul et al., 2012; Iddir-Ihaddaden et al., 2013; where the Marseille Poison Control Centre is involved), allowed to draw a clinical picture of acute *Ostreopsis* poisoning. This picture depends on the *Ostreopsis* bloom phase at the time of contact and is presented in Table 3 of this paper).

The existence of a plausible biological link between the proliferations of this toxic dinoflagellate and health impacts was supported by the first prospective epidemiological follow-up conducted simultaneously with the monitoring of the microalgal dynamics (Vila et al., 2016). In 2013, 81 % of the followed human cohort, composed by the staff of a restaurant in front of the hot spot, experienced at least one *Ostreopsis*-related symptom (eye irritation, nose irritation, runny nose or malaise). Since that study, epidemiology surveys in the same population in parallel to ecological studies continued to be conducted in the hot spot, and are presented in this study (sections 2.1.2, 2.2.1, 3.2, 4.2).

SUPPLEMENTARY INFORMATION

Supplementary Table 1. Sociodemographic characteristics of the interviewed people. Source: from authors.

	Monaco residents			**Nice residents**			**Nice tourists**		
	Non beachgoers	**Beachgoers**	**Total**	**Non beachgoers**	**Beachgoers**	**Total**	**Non beachgoers**	**Beachgoers**	**Total**
Age (average)	64.2	44.6	48.8	62.1	42.4	47.6	52.3	40.3	44.4
With people under 15 in the household (%)	27.1	40.3	37.5	11.6	38.1	31.1	45.0	43.2	43.8
Gender (% of males)	31.3	44.3	41.5	41.9	51.7	49.1	60.0	50.0	53.1
Living with his / her parents during the survey (%)	0.0	13.1	10.3	0.0	9.3	6.8	0.0	9.1	6.3
With a higher education degree (%)	29.2	60.2	53.6	41.9	67.8	60.9	55.0	86.4	76.6
Tourist who has already stayed in the city of Nice (%)							85.0	72.7	76.6
Tourist whose main reason for staying is to walk or go to the beach (%)							35.0	45.5	42.2

Supplementary Table 2. Econometric estimations for the residents of the Monaco Principality. Source: from authors.

	Prior knowledge of *Ostreopsis*	Overstated information	Tourists leaving the place	Panic	Severity	Credibility	Threat
Constant term	---	-1.222*** (0.335)	-0.396 (0.254)	-0.702*** (0.150)	---	1.198*** (0.144)	-0.097 (0.247
Age	---	0.017*** (0.006)	---	---	---		---
Over 60 years old						-0.489** (0.249)	
With people under 15 in the household	---	---	---	---	---	---	---
Gender (Male)	---	---	---	---	---	---	---
Living with his /her parents during the survey	---	---	---	---	---	---	---
With a higher education degree	---	-0.603*** (0.221)	---	---	---	---	---
Prior knowledge of *Ostreopsis*		---	---	---	---	---	---
Overstated information			---	0.596** (0.242)	---	---	---
Severity		---	---	-0.373* (0.216)		---	---
Credibility		---	0.463* (0.274)	---	---		0.740*** (0.271)
Threat		---	---	---	---	---	

Pseudo R^2	---	0.096	0.012	0.044	---	0.026	0.035
Correctly classified	---	79.0 %	54.6 %	76.1 %	---	85.2 %	71.0 %
Number of observations	176	176	176	176	176	176	176

Note: Each number (e.g., 0.017) corresponds to the estimated coefficient of the variable (in row) used to explain the probability of observing the phenomenon studied (in column). The standard errors of the estimated coefficient are indicated in brackets.
***, **,* indicates significance at 0.01, 0.05 and 0.1 level of risk respectively. ; --- : indicates no significance at the 0.1 level of risk.

Supplementary Table 3. Econometric estimations for the residents of Nice. Source: from authors.

	Prior knowledge of *Ostreopsis*	**Overstated information**	**Tourists leaving the place**	**Panic**	**Severity**	**Credibility**	**Threat**
Constant term	-1.811*** (0.316)	---	-0.521 (0.343)	0.262 (0.408)	-0.457* (0.246)	2.174*** (0.485)	0.074 (0.152)
Age	---	---	---	-0.015* (0.008)	---	-0.024** (0.010)	---
Over 60 years old							
With people under 15 in the household	---	---	-0.633*** (0.244)	-0.838** (0.350)	0.501** (0.255)	---	---
Gender (Male)	0.690* (0.376)	---	---	---	-0.569** (0.244)	---	---
Living with his /her parents during the survey	---	---	---	---	---	---	---
With a higher education degree	---	---	---	---	0.506* (0.270)	---	---
Prior knowledge of *Ostreopsis*		---	---	---	---	---	---
Overstated information			---	---	---	---	---
Severity		---	---	-0.806** (0.325)		---	0.509** (0.243)
Credibility		---	1.087*** (0.349)	---	---		---
Threat		---	---	---	---	---	

Pseudo R^2	0.055	---	0.097	0.146	0.086	0.074	0.028
Correctly classified	91.5 %	---	64.4 %	79.7 %	66.1 %	85.6 %	61.0 %
Number of observations	118	118	118	118	118	118	118

Each number (e.g., 0.690) corresponds to the estimated coefficient of the variable (in row) used to explain the probability of observing the phenomenon studied (in column). The standard errors of the estimated coefficient are indicated in brackets. ***, **,* indicates significance at 0.01, 0.05 and 0.1 level of risk respectively. ; --- : indicates no significance at the 0.1 level of risk.

Supplementary Table 4. Econometric estimations for the tourists of Nice. Source: from authors.

	Prior knowledge of *Ostreopsis*	Overstated information	Tourists leaving the place	Panic	Severity	Credibility	Threat
Constant term	---	-1.668*** (0.335)	---	-1.453*** (0.296)	0.151 (0.255)	0.230 (0.273)	---
Age	---	---	---	---	---	---	---
Over 60 years old							
With people under 15 in the household	---	--	--	--	-1.154*** (0.444)	--	--
Gender (Male)	--	--	--	--	--	0.867** (0.435)	--
Living with his /her parents during the survey	---	---	---	---	---	---	---
With a higher education degree	---	---	---	---	---	---	---
Prior knowledge of *Ostreopsis*		1.668* (0.957)	---	---	--	--	---
Overstated information			---	1.883** (0.813)	---	---	---
Severity		---	---	---		---	---
Credibility		---	---	---	---		---
Threat		---	---	---	---	---	
Previous tourist stay in Nice	---	---	---	---	---	---	---

Walking or beach-going is the main reason for the tourist stay	---	---	---	---	---	---	---
Pseudo R^2	---	0.14	---	0.19	0.13	0.08	---
Correctly classified	---	93.2 %	---	90.9 %	68.2 %	72.7 %	---
Number of observations	44	44	44	44	44	44	44

Each number (e.g., 1.668) corresponds to the estimated coefficient of the variable (in row) used to explain the probability of observing the phenomenon studied (in column). The standard errors of the estimated coefficient are indicated in brackets. ***, **,* indicates significance at 0.01, 0.05 and 0.1 level of risk respectively. ; --- : indicates no significance at the 0.1 level of risk.