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Mortality of marine mussels *Mytilus edulis* and *M. galloprovincialis*: systematic literature review of risk factors and recommendations for future research

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Abstract :

The aim of this study was to summarise the literature reporting the risk factors for mortality in the mussel species Mytilus edulis and Mytilus galloprovincialis in order to identify potential science-based solutions to prevent or mitigate mussel mortality outbreaks. We followed the PRISMA methodology: Preferred Reporting Items for Systematic Reviews and Meta-Analyses. The studied corpus of 91 publications (114 studies) was highly heterogeneous with respect to the methodological approaches used to define or estimate mussel mortality and the related putative risk factors. Results showed that the mortality risk of both mussel species M. edulis and M. galloprovincialis varied across the seasons, increased with an elevated seawater temperature above a thermal threshold of 20 and 24°C, respectively, decreased by

protecting mussels from predation, and was associated with the presence of pathogens in M. edulis. For M. galloprovincialis, using mussel spat from the same area where the farming is carried out and farming them together with another mussel species appears to reduce the mortality risk. However, for M. edulis, this could be achieved by using pure crosses and in particular mussel spat having a selected genotype. For wild bed conservation, sand accumulation and anthropogenic sedimentation should be minimised. Our analysis showed that current approaches to this research topic are limited and are unlikely to yield actionable evidence to identify mussel mortality prevention or mitigation strategies. Therefore, recommendations are offered to increase the ability of future eco-epidemiological research to identify multiple exposures associated with mussel mortality, underpinned by standardised efforts and cooperative initiatives.

Keywords : eco-epidemiology, environment, husbandry practices, mussel health, pathogens

1. Introduction

Over the last decade, massive mortalities have been reported on a recurrent basis in different marine bivalve species along the French coastline: spat of the Pacific oyster (*Crassostrea gigas)* (Miossec *et al*., 2009), wedge clam (*Donax trunculus)* (Garcia *et al*., 2018), marketable-size Pacific oysters (Garcia *et al*., 2014), cockles (*Cerastoderma edule*) (Garcia *et al*., 2019), and mussels (*Mytilus* sp.) (Garcia et al., 2015 ; Lupo & Prou, 2016). The aetiology of these mortalities is often unknown and the current consensus within the scientific community is that their origins are multifactorial. These mass mortalities may reflect a marine disturbance, and thus, damaged health of the marine coastal ecosystem (Sherman, 2000). Additionally, these recurrent mortalities cause an imbalance in the entire coastal socio-ecosystem, and stakeholders need to adapt permanently to ensure the sustainability of their socio-economic activities (Guillotreau *et al*., 2017). Representative bodies of the shellfish industry often alert the government authorities about these sustainability concerns, asking either for research to be conducted to explain these mass mortality events and to mitigate the outbreaks, or for financial compensation to mitigate their effects on socio-economic activities. For example, during the massive mortality events that occurred in mussels along the Atlantic coastline of France in 2014, several regional-scale studies were rapidly launched by various research groups (Bernard & Allain, 2016 ; SMIDAP, 2016 ; Travers et al., 2016).

After almost a decade of research on shellfish mortalities, the French Ministry in charge of Agriculture decided to coordinate research efforts at the national level by establishing a research programme, and in 2016 set up a national expert panel (called the Scientific and Technical Council, STC) to supervise this project, which consisted of the co-authors of this manuscript. The STC panel brought together all the scientific and technical bodies and institutions in France that have expertise in key related areas, including laboratory diagnostic

analyses, shellfish farming and fishery practices, the chemistry of coastal and marine environments, economics, ecotoxicology, epidemiology, genetics, hydrodynamic modelling, shellfish pathology, shellfish physiology, and ecosystem quality. The formulated objective of the research programme was "*to understand the interactions between the physicochemical conditions (abiotic factors) and the biotic factors in the environment, and the infectious status, as well as the impact of these interactions on the mortalities of the farmed and wild shellfish. […] The programme should explore how contaminants from the terrestrial and marine environments, currents and sediment fluxes, and physicochemical changes in seawater, contribute, as a function of the presence of pathogens, to influence the level of survival of Pacific oysters, mussels and other shellfish species affected by unexplained massive mortality events, at different physiological stages, and taking into account farming or fishing practices and genetics, if necessary*" (Anon, 2016). The first step was to review the knowledge related to the risk factors for shellfish mortalities in order to identify potential solutions to limit the impact of mortality events. If required, a second step would be to conduct a large eco-epidemiological study at the national level. As massive mortalities in marine mussels were reported at that time (Garcia *et al.*, 2015 ; Lupo & Prou, 2016), the STC chose to carry out a literature review on these species. The STC panel started its activities in November 2016 and submitted its final report in January 2019.

The objective of this study was to summarise the current literature reporting the risk factors for mortality in the mussel species exploited in France, *Mytilus edulis* and *Mytilus galloprovincialis*, in order to identify potential solutions to prevent or mitigate mussel mortality outbreaks, using the systematic review methodology. A systematic review is an overview of existing evidence relevant to a clearly formulated and specific question, which uses pre-specified standardised methods to identify and critically appraise relevant research,

and to collect, report and analyse data from the studies that are included in the review (Moher *et al.*, 2009). Methodological rigour, transparency and reproducibility are the fundamental principles underyling a systematic review. This method follows a series of steps to reduce bias in the selection and inclusion of the studies that address the review question, and to objectively summarise the quantity and the quality of evidence. Systematic reviews can be helpful when there is a large amount of evidence because they can guide funding decisions for future research and reduce unnecessary duplication of research. If the evidence is scarce, systematic reviews can be particularly helpful to formally identify knowledge gaps and to identify evidence not previously known to exist. If the research findings identified are of poor quality, then this method will document the limitations and weaknesses of the existing evidence and make informed proposals for the design of future research (European Food Safety Agency, 2010). Thus, as part of the review process, this study also aimed to identify gaps in knowledge on mussel mortality risk factors, and to formulate recommendations to help target future research.

2. Methods

2.1. Scope of the study and research question

This review was conducted following a protocol developed *a priori* to minimise the subjective decisions that could be made during the review process, and was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher *et al.*, 2009).

Based on the terms of reference formulated by the French Ministry in charge of Agriculture (Anon, 2016), this review covers risk factors for marine mussel mortalities, with the following question: “What are the risk factors for mussel mortality included in the topics of animal characteristics, farming or fishery practices, seawater characteristics, contaminants from the terrestrial and marine environments, pathogens, climate characteristics, and geographic characteristics of the farming/fishing site?”. Thus, the specific research question was defined including the key elements for review of risk factors, using the PECO format:

- *Population of interest (P)*: mussel species exploited for human consumption in France, i.e. *Mytilus edulis* and *M. galloprovincialis*;
- *Exposure (E)*: any exposure to factors pertaining to the following seven topics: animal characteristics, farming or fishery practices, seawater characteristics, contaminants from the terrestrial and marine environments, pathogens, climate characteristics, and geographic characteristics of the farming/fishing site;
- *Comparator (C)*: only explanatory studies employing some form of comparison or control group against which the exposure can be compared, were included;
- *Outcome of interest (O)*: mortality.

2.2. Literature search strategy

An exhaustive literature search, including electronic and manual searching, was performed. To ensure completeness of the search, key PECO elements were combined in a search algorithm using Boolean operators. Search equations were adapted to the different databases explored (Appendix I).

Searches were carried out in the following online bibliographic databases: Web of Science, Scopus, Aquatic Sciences and Fisheries Abstracts, CAS Abstracts, Pascal and Francis, and Environmental Sciences and Pollution Management, on 03 May 2017; the search was updated on 05 April 2018, and 13 November 2018. Manual searches were also performed in available online databases and proceedings of the following conferences: Society for Veterinary Epidemiology and Preventive Medicine (SVEPM), International Symposia on Veterinary Epidemiology and Economics (ISVEE), National Shellfisheries Association (NSA), World Aquaculture Society (WAS), European Aquaculture Society (EAS), European Association of Fish Pathologists (EAFP), Annual meeting of the European Union Reference Laboratories for mollusc diseases, International Symposium on the Advances in Marine Mussel Research (AMMR), Annual council of the French Shellfish Industry, and Annual Ifremer meeting of Surveillance and Reference for mollusc diseases. To identify grey literature (i.e. unpublished studies) focused on risk factors for mussel mortalities, regional and national representative bodies for shellfish farmers and those for fishermen, regional technical institutes, and private consulting engineers were contacted and data were requested in February 2017; the search was updated in November 2018. These bodies belonged to the SCT panel or to their networks. Manual searching of the reference lists in all of the citations that met the eligibility criteria (see below) was conducted as the review progressed.

A unique code was attributed to each captured citation. Citations captured by the search on the online bibliographic databases were saved in .ris format. All the identified citations were

gathered in a single electronic database. Duplicate citations were removed by electronic and manual scanning. The final unit of this work was no longer the citation but the study, identified by a unique study code derived from the citation code.

2.3. Study selection: inclusion and exclusion criteria

Inclusion and exclusion criteria were built using the key PECO elements. Both laboratory and observational studies were included. The following additional exclusion criteria were applied: citations published in languages other than English or French, or before 2006 (to account for progress in the techniques used for pathogen or chemical detection), or concerning mussel larvae (i.e. before their fixation on a collector), or concerning human foodborne pathogens (e.g. *Vibrio parahaemolyticus*), or purely descriptive or case report studies. Only original research studies were included; review articles were excluded.

2.4. Review process

The purpose of relevance screening in the systematic review methodology is to rapidly remove citations not relevant to the review, as the literature search process should be highly sensitive, with low specificity. This first step was based on title and abstract screening of the identified citations. Citations excluded at this stage were not assessed further. The study selection was conducted unmasked, i.e. the reviewers had access to the authors' names. Screening of the whole corpus was conducted by a single reviewer, with a second independently examining the first reviewer's work for a random sample of the identified citations, with 30 citations per member of the STC (N = 13). The second step was based on the full text examination of the citation. Citations excluded at this stage were documented for the reason behind their exclusion in a dedicated table (Appendix II). The full text screening

was conducted by a single reviewer, with a second validating the first reviewer's work for two citations per member of the STC (N = 11).

When disagreements on study selection occurred, the reviewers discussed and sought consensus. At each step, the kappa coefficient was calculated to evaluate the agreement between the inclusion/exclusion decisions of the first reviewer and the STC, using the interpretation of (Landis & Koch, 1977), where values <0 indicate no agreement, values 0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-80.80 substantial, and 0.81-1 almost perfect agreement.

2.5. Study methodological quality and field transposition assessment

For each included study, we built a quality score based on key features of the study design, to assess the appropriateness of the methodological aspects to identify a risk factor. Three levels (low, moderate or high) were assigned to this methodological quality score, based on a combination of key study design features for observational and experimental studies. For observational studies, criteria were the random selection of epidemiological units and the strength of proof of causal association provided by the study design. A moderate strength of proof was attributed to transversal and single cohort studies, whereas a high strength of proof was attributed to exposed/non-exposed cohort and case-control studies. For experimental studies, criteria were the use of a control during the experiment or a design of experiments (when several risk factors were investigated), and the number of replicates of the experiment. At least three replicates were considered as strength to assess the variations in experiment outcomes.

For laboratory studies, an additional criterion was built to evaluate the relevance of the results to "real-world" conditions. Two levels (low or satisfactory) were assigned to this field transposition score, based on the environmental relevance of the physical parameters of the seawater and of the tested chemical concentrations, and the route of exposure to the pathogens, and by excluding intramuscular injection that forced the natural barriers of the mussels. To assess the environmental relevance of the physical parameters of the seawater, we used the ocean monitoring indicators collected by the EU Copernicus Marine Service Information (EU Copernicus Marine Service Information, 2019) for the 1993–2017 period for seawater temperature and salinity, and 2001–2016 period for seawater pH. To assess the environmental relevance of the chemical concentrations, we used the chronic predicted no-effect concentration (PNEC) in marine waters, which is the concentration of a substance in any environment below which adverse effects will most likely not occur during long-term exposure (INERIS, 2019). Results of studies using chemical concentrations greater than 250 times the PNEC were considered as not relevant to the "real-world" conditions, except when the studies mimicked a field pollution event. In addition, studies using the stress on stress (SOS) test, i.e. survival in air test, to identify the negative effects of chemicals were excluded.

Scoring for methodological quality and field transposition assessment was conducted by one reviewer. The studies with low quality scores or low field transposition scores were excluded from the review (Appendix II).

2.6. Data extraction from the included studies

Data were extracted and collated in a Microsoft© Excel spreadsheet. Two templates, for either laboratory or observational studies, were developed *a priori* to standardise the extraction of information from the selected studies as far as possible. The unit was no longer the citation

but the study. The templates were further reviewed and enriched by all co-authors and pilot tested before use. Some fields were standardised, using drop-down lists, and others were left open because the related information was considered difficult to predict. Table 1 lists all extracted data, if available, from the selected corpus.

For each putative risk factor, the effect of exposure on mussel mortality risk was extracted and categorized as increasing, decreasing or no effect. Absence of effect referred to comparisons between controls and treatment/cases that were statistically non-different. Seven topics concerning mortality risk factors were defined based on a consensus among the STC members: pathogens, mussel characteristics, seawater characteristics, characteristics of the farming or fishing site, farming or harvesting practices, pollutants from the terrestrial and marine environments, and climate characteristics.

Data extraction was conducted by a single reviewer and was checked by a second reviewer for two citations per member of the STC.

2.7. Data analyses

Summary distributions of extracted characteristics were examined by mussel species and study conditions (i.e. observational or experimental). A qualitative analysis of open fields was conducted *a posteriori*, to build categorical variables having different response modalities. Each categorical variable was then described in terms of numbers and frequency of its modalities. These were used to write a narrative synthesis of the results, summarising information on the characteristics of the included studies, such as study conditions and design, and the outcome and exposure effect measures used.

Multiple correspondence analysis (MCA) was used to identify groups of studies with similar profiles regarding the extracted characteristics (i.e. categorical variables) and the associations between studies and characteristics (Greenacre, 1984). This method is used to detect and represent underlying structures in a dataset, by representing data as points in a low-dimensional Euclidean space. It produces graphs on which the studies are represented by points which tend to group together if the studies are similar; differences, on the contrary, tend to produce distance. Fourteen active variables were used for the MCA: year of publication, mussel species, study conditions, geographical location, mussel population type, quality score, the seven themes of mortality risk factors, and interaction considerations between risk factors. When the frequency of studies in a variable category was <10%, this category was grouped with another category, if relevant. The contributions of the variables to each factorial axis and the plots of the MCA were used to interpret each factorial axis.

The descriptive analysis was conducted by using R software, version 3.6.1 (R Core Team, 2019). Study screening based on the title and abstract was conducted using the Metagear package (Lajeunesse, 2016). MCA was carried out using the FactoMineR (Lê *et al.*, 2008) and Factoextra (Kassambra & Mundt, 2017) packages. Plots were built using the ggplot2 package (Wickham, 2016).

3. Results

3.1. Literature search and selection

The initial search identified 5,450 citations in the electronic databases, and through manual searching in the conferences and referrals from the SCT, published between 2006 and 2018. After removal of duplicates, 3,715 remained for further screening. Screening the titles and abstracts excluded another 3,526 citations, leaving 189 citations for a full text review. Subsequently, an additional 92 citations were excluded. We included 19 articles by scanning the reference lists of included citations. These 116 citations contained reports on 152 studies that were critically appraised individually. Assessment of the methodological quality and field transposition excluded an additional 12 and 26 studies, respectively. Appendix II lists the studies that were rejected on full-text screening, methodological quality and field transposition assessments, together with the reasons for exclusion. Finally, a total of 91 citations met the eligibility criteria for inclusion in the systematic review. They reported on 114 studies, listed in Appendix III. Figure 1 shows the selection process workflow.

Agreement between reviewers was substantial at the abstract and title screening level (Kappa coefficient = 0.66, CI95% [0.58 - 0.75] calculated on 9.9% (366/3,715) of the identified citations), and almost perfect at the full-text screening level (Kappa coefficient = 0.92, CI95% [0.78 - 1] on 14.3% (27/189) of the citations).

3.2. Description of the included studies

Among the 91 included citations, 82 were scientific journal articles, 6 unpublished study reports, 2 Ph.D. thesis reports, and 1 conference proceedings. Among the 114 included studies, almost half of the studies about *M. edulis* (44%; 29/66) were conducted after 2015, whereas the annual number of studies on *M. galloprovincialis* varied regularly over the last

decade (Figure 2). Almost one quarter of the studies about *M. edulis* were conducted in France, and about one third in North America (Figure 3a). For *M. galloprovincialis*, almost half of the studies were conducted in Southern Europe (particularly in Spain) and in South Africa (Figure 3b). Overall, the included studies aimed to understand mussel production losses (45%; 52/114), mussel species distribution and habitat segregation (21%; 24/114), or they used mussels as bioindicators to assess environment quality or climate change effects (33%; 38/114).

Table 2 describes the main characteristics of the corpus. The species *M. edulis* was mainly studied under observation conditions (58%; 38/66 studies), whereas *M. galloprovincialis* was equally studied under either experimental or observation conditions (48%; 23/48 and 52%; 25/48 studies, respectively). For the two species, the studied populations were mainly farmed mussels or mussels from wild beds. The age class of the studied mussel populations was not reported for two thirds of the studies, as most of them rather described mussel size, especially for *M. galloprovincialis*. Only 34% of the studies showed a high methodological quality score to identify a risk factor. The vast majority of observation studies did not select the mussels at random (48/63), and used a study design with a low strength of proof to identify a risk factor (47/63). One quarter (13/51) of the laboratory studies did not use a control, and half of them (26/51) did not reproduce the experiment in triplicate.

The first two factorial axes, which explained the larger amount of variance of all the 14 variables used to run the MCA, were used to interpret the pattern of relationships of the descriptive characteristics of the studies. They represented 28.0% of the total inertia (i.e. total variance of all variables included in the analysis), with 15.5% and 12.5% of variance explained, respectively. The 114 studies could be differentiated based on the modalities of all the variables used to run the MCA, except the geographical location, when the ellipses of the

variable modalities were distinct (Figure 4). This figure also shows that the studies could be divided into two main groups. On the left quadrants, a first group gathered studies conducted on *M. edulis* in observational conditions, with a satisfactory methodological score, and investigating mortality risk factors pertaining to animal characteristics, and characteristics of the site and farming or harvesting practices. On the right quadrants, the second group gathered studies conducted on *M. galloprovincialis* in laboratory conditions in the Black Sea or the Mediterranean, exploring the effects of seawater characteristics and pollutants on the mussel mortality risk. The absolute contributions of the variables and their modalities are reported in Appendix IV.

3.3. Definition and estimation of mussel mortality

Even though all the 114 studies dealt with mussel mortality, a broad variation in terms of methodological approaches to define or estimate this outcome was found (Table 2). In laboratory studies, experimental mussel mortality was defined at the animal level as a binary outcome, the mussel being dead or alive. Half of the studies did not define criteria to assess the death of a mussel, and the other half used varying criteria. In the vast majority of observational studies, mortality was quantified at the mussel population level and expressed as a proportion, using a number of dead mussels as the numerator, and a total number of mussels as a denominator. For most of the studies in both mussel species (59/63), this proportion was a final prevalence or a cumulative prevalence, monitored throughout the study. No studies used mortality incidence as an outcome. To estimate the mortality proportion, most of the studies (52/63) used counts, but counting methods varied greatly among the studies. Almost three quarters of the studies measured mussel mortality regularly throughout the study course. Mussel mortality was mainly reported on a monthly basis in observational conditions, and on a daily basis in laboratory conditions.

3.4. Association measures between mortality and risk factors

Studies used various statistical associations between the outcome of interest (mussel mortality) and the exposures of interest (e.g. factor modalities, treatments, concentrations) (Table 3). For qualitative factors of interest, comparison of mortality means, medians or proportions were used, whereas for quantitative factors of interest (e.g. chemical compound concentrations), several types of correlations were used. Laboratory studies, in particular those investigating the impact of pollutants, used substance concentrations causing 50% mortality (LC_{50}) within a fixed period of time (24 or 96 hours), or time leading to 50% mortality (LT_{50}).

3.5. Risk factors for mussel mortality

In total, 102 putative risk factors were examined in the 114 studies, with 62 factors for *M. galloprovincialis* (Table 4) and 67 factors for *M. edulis* (Table 5), pertaining to seven topics: pathogens, mussel characteristics, seawater characteristics, characteristics of the farming or fishing site, farming or harvesting practices, contaminants from the terrestrial and marine environments, and climate characteristics. The key results of the studies included in the following narrative review are provided in Appendix III.

3.5.1. Factors related to pathogens

The effect of pathogens on the mortality risk was studied equally in *M. edulis* (11 factors by 8 studies, Table 5) and in *M. galloprovincialis* (9 factors by 8 studies, Table 4).

In *M. edulis*, horizontal transmission of a putative causal agent of mortality was reproduced in laboratory conditions between two wild mussels stocks sampled after mortality events

(Benabdelmouna *et al*., 2018). An additional experimental reproduction of this phenomenon was reported between wild mussels sampled after mortality events and sentinel hatchery produced mussels (Pépin *et al*., 2017). However, in both studies, pathogen identification was not successful.

Across the investigated pathogens in both mussel species, evidence of absence was consistently reported for Ostreid herpesvirus OsHV-1 (Benabdelmouna *et al.*, 2018) and the OIE listed parasite *Marteilia refringens* (Bernard et al., 2018b ; Benabdelmouna *et al.*, 2018). However, results reported for bacteria were not straightforward. In both mussel species, no effect of the overall bacteriological profile of the mussels was shown on the mortality risk (Bernard *et al.*, 2018b). In *M. edulis*, the bacterium *Vibrio aestuarianus* was not detected in moribund mussel tissues (Benabdelmouna *et al.*, 2018), whereas a possible association with mortality risk was suspected for anaerobic bacteria (Babarro & De Zwaan, 2008), opportunistic heterotrophic bacteria present in the seawater (Eggermont *et al*., 2014), or bacteria belonging to the genus *Photobacterium* (Eggermont *et al*., 2017). Bacteria belonging to the *Splendidus* clade of the genus *Vibrio* were inconsistently detected in moribund mussel tissues or haemolymph, challenging their role in mortality risk (Benabdelmouna *et al.*, 2018 ; Eggermont *et al.*, 2017). In *M. galloprovincialis*, conflicting results were reported regarding the effect of the presence of bacteria *Vibrio aestuarianus* or *Vibrio* belonging to the *Splendidus* clade on the mortality risk, even when mussels were exposed to high concentrations of bacteria in the seawater (10^{10} CFU.mL^{-1}) (Romero *et al*., 2014). To induce mussel mortality, additional exposures to an elevated temperature of the seawater (25°C), and to 8 hours emersion to reproduce hypoxia stress were needed.

Algae effects were also investigated. Lethal effects of toxic dinoflagellate algae were reported in *M. galloprovincialis* with *Ostreopsis* cf *ovata* (Carella *et al*., 2015) and in *M. edulis* with *Karlodinium armiger* (Binzer *et al*., 2018). On sheltered rocky shores, the presence of epibiotic algae on the shell was reported to increase the mortality risk in both mussel species (O'Connor, 2010). In *M. galloprovincialis*, conflicting results were reported concerning the effect of parasitic phototrophic shell-degrading endoliths, showing a protective effect against heat stress mortality by decreasing their body temperature (Zardi *et al*., 2016), or a sub-lethal effect because of induced shell weakening (Marquet *et al*., 2013) or of energy trade-off between shell repair and other physiological constraints (Nicastro *et al*., 2018).

3.5.2. Factors related to mussel characteristics

The effect of mussel characteristics on the mortality risk was more commonly studied in *M. edulis* (15 factors by 22 studies, Table 5) than in *M. galloprovincialis* (4 factors by 7 studies, Table 4).

Among these factors, genetic characteristics were the main factors investigated, in particular species and genotype. The mortality risk of *M. edulis* did not differ from that of *M. trossulus* in field conditions (Lowen, 2008 ; Penney et al., 2006), whereas it was lower in a laboratory study reproducing coastal and estuarine conditions (Gardner & Thompson, 2001). In the field, the mortality risk of *M. galloprovincialis* did not differ from that of *M. trossulus* (Shields *et al*., 2008), whereas a lower mortality risk was observed in two laboratory studies where animals were exposed to either air or seawater thermal stress (Dowd & Somero, 2013 ; Schneider, 2008). In *M. galloprovincialis*, the effect of the genotype on the mortality risk depended on the species crossed. On the one hand, the mortality risk of mussels having a hybrid genotype of *M. galloprovincialis* and *M. trossulus* showed no difference when

compared to pure native *M. trossulus* and to pure introduced *M. galloprovincialis* (Shields *et al.*, 2008). On the other hand, hybrids of *M. galloprovincialis* and *M. edulis* showed a higher mortality risk than the populations from pure crosses (Fuentes *et al*., 2002). Hybrids of *M. edulis* and *M. trossulus* also showed a higher mortality risk than the pure populations (Lowen, 2008). In *M. edulis*, a selected intraspecific genotype showed inconsistent effects on mortality risk, perhaps depending on the number of selected generations. In fact, the first selected generation, i.e. the survivor mussels of a preceding mortality event, still presented an increased mortality risk in subsequent years (Myrand & Gaudreault, 1995), whereas two studies reported a lower mortality risk for spat descending from parents that had survived a previous mortality event, compared to spat with a non-selected genotype (Pépin *et al.*, 2017 ; Pépin et al., 2018). A low degree of multiple-locus heterozygosity was associated with an increased risk of mortality in *M. edulis* (Tremblay *et al*., 1998). A high percentage of genomic abnormalities in haemocytes was found to be associated with an increased mortality risk in *M. galloprovincialis* (Benabdelmouna & Ledu, 2016)), although inconsistent association was reported in *M. edulis* (Benandelmouna and Ledu, 2016 ; Pépin *et al.*, 2017 ; Pépin et al., 2018).

Physiological characteristics were also explored, mainly in *M. edulis*. The effect of mussel size on the mortality risk was the most commonly investigated factor. Although no effect was observed in the two studies on *M. galloprovincialis* (Lok et al., 2007 ; O'Connor, 2010), inconsistent results were reported for the effect of this trait on the mortality risk of *M. edulis*. Discrepancies may be explained by different study conditions: mussel size was sometimes studied in combination with hypoxic conditions (Altieri & Witman, 2006), in the context of new socking material to protect mussels from predation (Dionne *et al*., 2006), or in the context of exploration of massive mortalities of wild beds (Tsuchiya, 1983) or cultivated

mussels (Tremblay *et al.*, 1998). A study also explored the effect of the initial seed size, showing that small seed had a higher mortality risk than larger seed (Lauzon-Guay *et al.*, 2005). These types of differences in study conditions prevented any direct comparison or synthesis of the results. Individual traits related to a poor condition were also investigated in *M. edulis* to a lesser extent. A low condition index (Hiebenthal *et al.*, 2013), low energy reserves due to depleted reserves after spawning (Myrand *et al*., 2000), and high bio-energetic needs for maintenance metabolism (Tremblay *et al.*, 1998) were reported to be associated with an increased mortality risk in *M. edulis*. This is further supported by reported synchronous timing between mortality and gametogenesis (Pépin *et al.*, 2017), when the mussels use high bio-energetic resources for reproduction.

3.5.3. Factors related to seawater characteristics

The effect of seawater characteristics on the mortality risk was more often studied in *M. edulis* (8 factors by 17 studies, Table 5) than in *M. galloprovincialis* (5 factors by 9 studies, Table 4).

In *M. galloprovincialis*, these factors were exclusively studied under laboratory conditions. As the only study showing no effect of the seawater temperature (Gestoso *et al*., 2016) tested a maximum temperature of 21°C, the mortality risk seemed to increase above a value of this factor of ≈ 24°C (Anestis et al., 2007 ; Dowd & Somero, 2013 ; Gazeau et al., 2018). In *M. edulis*, the mortality risk was associated with a thermal threshold of ≈ 20°C (Incze et al., 1980 ; Jones et al., 2010 ; Hiebenthal *et al.*, 2013 ; Cottrell et al., 2016 ; Hutchison et al., 2016 ; Clements et al., 2018 ; Lenz et al., 2018 ; Wang et al., 2018 ; Bernard et al., 2018a). The two studies showing no association between an elevated temperature and mussel mortality risk explored the effect of this factor in combination with other simultaneous exposures: to

zinc or cadmium (Ali & Taylor, 2010) or to a decreased pH and decreased oxygen concentration in water (Stevens & Gobler, 2018). The interactions with other stressors may have compensated the effect of the elevated seawater temperature on the mortality risk. Moreover, Ali and Taylor (2010) used lower values of the seawater temperature than the other studies (6°C and 12°C). Exposure to a cold temperature of 4°C also increased the mortality risk of *M. edulis* (Wang *et al.*, 2018). Opposite results were reported for the effect of an increasing number of thermal stresses on the mortality risk of *M. edulis* (Jones et al., 2009 ; Lenz *et al.*, 2018), whereas no effect was observed in *M. galloprovincialis* (Lenz *et al.*, 2018).

In both mussel species, an increased mortality risk was reported with low salinity values (20 and 28 practical salinity units, psu) in laboratory conditions (Hamer et al., 2008 ; Ali & Taylor, 2010), which may sometimes be observed in field conditions in a wide desalination context.

Among seawater characteristics, the effect of acidification of seawater showed conflicting results in both mussel species, probably because of the broad variation in laboratory conditions (levels of pH tested, exposure duration, or acute vs. gradual exposure). Low levels of seawater pH increased the mortality risk of *M. edulis* (Sun et al., 2016 ; Stevens & Gobler, 2018), whereas one study reported no effect of elevated CO_2 concentrations (Clements *et al.*, 2018). However, no effect was observed when this factor was combined with a low level of dissolved oxygen or with an elevated temperature, suggesting antagonist interactions between these stressors (Stevens & Gobler, 2018). In *M. galloprovincialis*, extended exposure (6 months) of mussels to a low level of pH was associated with an increased mortality risk, whereas shorter exposure (3 months) did not show any effect (Bressan *et al*., 2014). Acute exposure to acidification was associated with an increased mortality risk (Gestoso *et al.*,

2016), whereas gradual acclimation to similar lowered pH over a few weeks did not show any effect (Gazeau *et al.*, 2018).

Low levels of dissolved oxygen in seawater did not show any effect on the mortality risk of *M. edulis* (Stevens & Gobler, 2018). In *M. galloprovincialis*, hypoxia-induced stress, reproduced in laboratory conditions using an 8-hour emersion treatment, increased the risk of mortality when mussels were also simultaneously exposed to pathogens and to an elevated seawater temperature of 25°C (Romero *et al.*, 2014).

Concerning seawater characteristics, the effect of food availability (quantity and quality) was also explored in *M. edulis*. A rapid decrease in the quantity of phytoplankton preceded mortality onset (Incze *et al.*, 1980), leading the authors to suggest that the mortalities may be triggered by reduced ration and starvation. A decline in indicators of phytoplankton species richness (Shannon index and total abundance) was also reported before mussel mortality onset (Travers *et al.*, 2016).

3.5.4. Factors related to characteristics of the farming or fishing site

The effect of characteristics of the farming or fishing site on the mortality risk was more commonly studied in *M. edulis* (10 factors by 25 studies, Table 5) than in *M. galloprovincialis* (8 factors by 14 studies, Table 4).

In both mussel species, broad spatial variation in the mortality risk between different farming or fishing sites was reported in several studies (Fuentes et al., 1994 ; Penney *et al.*, 2006 ; Bownes & McQuaid, 2010 ; Gardner, 2013 ; Travers *et al.*, 2016 ; Glize et al., 2017 ; Moschino et al., 2017 ; Pépin *et al.*, 2017 ; Bernard *et al.*, 2018b ; Glize & Gourmelen, 2018

; Pépin *et al.*, 2018), whereas other studies did not observe a mortality risk variation across locations (Fuentes et al., 1992 ; Myrand & Gaudreault, 1995 ; Stirling & Okumus, 1994 ; Lauzon-Guay *et al.*, 2005 ; Mallet et al., 1987 ; Mallet et al., 1990). However, except in one study which explored mussel position on the shore (Bownes & McQuaid, 2010), the characteristics of the geographical sites potentially explaining this variation were never detailed.

Some site characteristics have been studied, specifically to understand species invasion or habitat segregation of several mussel species. In *M. galloprovincialis*, characteristics of mussel wild beds have been explored to evaluate the effects of hydrodynamic stress and sand stress, by comparing bay and open coast habitats. An increased mortality risk was reported in open coast conditions (Nicastro et al., 2008 ; Nicastro et al., 2010) and when the shore was exposed to waves (O'Connor, 2010). No effect of the position of mussels in the bed, either at the edge or in the centre, was observed (Nicastro *et al.*, 2008). Wave height was found to be a risk factor of mortality in a bay habitat (Nicastro *et al.*, 2010 ; Zardi et al., 2008), whereas it had no effect in open coast conditions (Nicastro *et al.*, 2010). Sand accumulation on mussel beds, either because of sand burial or suspended sand in the seawater, was associated with an increased mortality risk in two studies (Zardi et al., 2006 ; Nicastro *et al.*, 2010). However, one study showed no effect of this factor (Zardi *et al.*, 2008). In *M. edulis*, sediment parameters were investigated in particular. Mortality increased with increasing duration of burial (Hutchison *et al.*, 2016 ; Cottrell *et al.*, 2016), but conflicting results were reported for the effect of the depth of burial (Hutchison *et al.*, 2016). Fine sediment fractions (Hutchison *et al.*, 2016 ; Cottrell *et al.*, 2016) and high concentrations of organic matter in the sediment (Cottrell *et al.*, 2016) were associated with an increased mortality risk.

Emersion stress has also been explored in various studies. No effect of the mussel bed position on the shore was reported for *M. galloprovincialis* (Bownes & McQuaid, 2010 ; Marquet *et al.*, 2013), whereas mortality risk increased in *M. edulis* on higher tidal height in the context of snail predator activity (Petraitis, 1998) or of heat wave exposure (Tsuchiya, 1983).

The presence of predators on the farming or fishing site was studied either to explain mussel mortalities (for example crabs (Brousscau et al., 2014 ; Christensen et al., 2012) and diving ducks (Dionne *et al.*, 2006) for *M. edulis*; flatworm (Gammoudi *et al*., 2017), and benthic and pelagic predators (Plass-Johnson *et al.*, 2010) for *M. galloprovincialis*) or to understand the absence of mussels at a certain level of rocky shore, e.g. hypothetically due to the activity of the snail *Nucella lapillus* (Petraitis, 1998).

The mortality risk due to predation was reduced in reefs with small inter-structural spaces (Bertolini *et al*., 2018). One study showed that the presence of the Pacific oyster (*Crassostrea gigas*) deterred predator attacks from mussels and reduced their mortality risk (Waser *et al*., 2015).

3.5.5. Factors related to farming or harvesting practices

The effect of farming or harvesting practices on the mortality risk was more closely studied in *M. edulis* (15 factors by 22 studies, Table 5) than in *M. galloprovincialis* (8 factors by 13 studies, Table 4).

Concerning farming practices, the geographical origin of the seed was mainly investigated. Several studies reported an effect of this factor on the mortality risk of *M. edulis* (Myrand & Gaudreault, 1995 ; Mallet *et al.*, 1987 ; Mallet *et al.*, 1990 ; Bernard *et al.*, 2018a), whereas

other studies showed no effect (Glize *et al.*, 2017 ; SMIDAP, 2016-2017 ; Glize & Gourmelen, 2018). In particular, the effect of seed translocation on the mortality risk was explored. This farming practice, widely spread across the world in aquaculture, consists in transplanting mussel spat to areas with favourable conditions for growth (Aypa, 1990). In *M. edulis*, most of the studies reported no effect of this practice on the mortality risk (Penney *et al.*, 2006 ; Myrand & Gaudreault, 1995 ; Mallet *et al.*, 1987 ; Fuentes *et al.*, 2002 ; Mallet *et al.*, 1990 ; Glize *et al.*, 2017 ; SMIDAP, 2016) although one study reported reduced mortality in mussel spat collected on-site compared to translocated spat (SMIDAP, 2016-2017). In *M. galloprovincialis*, almost all the studies reported translocated spat having a higher mortality risk than local spat (Ramon et al., 2007 ; Gardner, 2013 ; Fuentes *et al.*, 1992 ; Ajjabi et al., 2018 ; Fuentes *et al.*, 1994 ; Kovacic et al., 2017 ; Bernard *et al.*, 2018a). Only one study, conducted in the context of understanding the spatial distribution of native, introduced and hybrid *Mytilus* sp. (Shields *et al.*, 2008), observed a different result. The authors suggested that translocation to a site with cooler water temperatures decreased the mortality risk by reducing thermal stress.

A protective effect of a thermal challenge, either using elevated water temperature or air exposure before their deployment to the farming sites, was reported on *M. edulis* spat (LeBlanc *et al*., 2008). The authors suggested a selective effect of this treatment by selecting mussels with higher levels of heterozygosity, providing them more physiological flexibility.

The effect of the initial farming density on the mortality risk of *M. edulis* was controversial, with one study reporting no short-term effect (3 months), but a long-term effect (10 months) (Lauzon-Guay *et al.*, 2005). Interestingly, another study reported no effect of this factor after 15 months (Lowen, 2008).

Regarding other farming practices, the effect of different suspended farming structures on the mussel mortality risk was investigated. In *M. edulis*, no effect of the depth of the lantern nets in a suspended raft was reported (Karayucel & Karayucel, 2000), whereas mussel mortality risk was higher in suspended mesh plastic cages maintained deeper in the open sea (14 m depth) than in the lagoon (4 m depth) (Myrand *et al.*, 2000). Conflicting results about the effect of the position of the mussels within a suspended raft on their mortality risk were reported, with studies showing no effect of this factor for both species (Karayucel & Karayucel, 2000 ; Fuentes *et al.*, 1992) or a higher mortality risk in the fore-part than the aft-part of the suspended raft in *M. galloprovincialis* (Fuentes *et al.*, 1994).

A few studies focused on the effects of certain commercial husbandry practices regarding mussel transportation to the market. In *M. galloprovincialis*, no effect of the stocking density during re-immersion into seawater after harvesting and grading and before transport was reported (Theodorou *et al*., 2017). Re-immersion beyond 11 days increased the mortality risk (Theodorou *et al.*, 2017). In *M. edulis*, re-immersion before transport did not have a significant effect on the mussel mortality risk, whether they were stored with ice or at a chilled ambient temperature of 5°C during transport, at any stage of the supply chain (pre-transportation or post-transportation) (Barrento & Powell, 2016). Mussels being re-immersed before transport and stored on ice showed reduced mortalities compared to mussels being not re-immersed before transport and stored at ambient temperature (Barrento & Powell, 2016).

All aspects of mussel culture are impacted by tunicate fouling and the effect of anti-biofouling chemical treatments to mitigate their consequences on the mussel mortality risk was also studied. Results showed that the potassium monopersulphonate triple salt based disinfectant

(Virkon® Aquatic) has no significant effect on mussel mortality until three weeks post-treatment (Paetzold & Davidson, 2011). Vinegar, brime or lime could also be applied either before transportation, followed or not by a seawater rinse, or after transportation without provoking an increased mussel mortality risk (Vickerson, 2009).

When predation was the acknowledged mortality cause in *M. edulis*, some studies tested solutions to limit its impact on mussel production, e.g. use of mussels collected in suspended culture versus mussels collected from natural bottom mussel beds for bottom culture production, despite the presence of crabs (Christensen *et al.*, 2012), or protective socking material to protect mussels from diving ducks (Dionne *et al.*, 2006).

Farming mixed mussel species, i.e. *M. edulis* and *M. trossulus* (Lowen, 2008) or *M. galloprovincialis* and *Xenostrobus securis* (Gestoso *et al.*, 2016 ; Olabarrial et al., 2016) was found to lower the mortality risk. Integrated multi-trophic aquaculture (IMTA) showed a lower mortality risk for *M. galloprovincialis* when mussels were cultivated with algae (Ajjabi *et al.*, 2018), but did not show any effect when mussels were farmed with fishes (Gvozdenovic *et al*., 2017).

On wild beds, the intensive human trampling during harvesting of *M. galloprovincialis* increased mussel mortality, particularly when mussels were infested with parasitic endoliths (Nicastro *et al.*, 2018).

3.5.6. Factors related to contaminants from the terrestrial and marine environments

The effect of terrestrial or marine pollutants on the mortality risk was studied more frequently in *M. galloprovincialis* (24 factors by 7 studies, Table 4) than in *M. edulis* (4 factors by 3 studies, Table 5).

All chemical compounds tested in laboratory conditions showed a lethal effect on mussels (*M. edulis*: (Suni et al., 2007 ; Akaishi et al., 2007 ; Ali & Taylor, 2010); *M. galloprovincialis*: (Danellakis et al., 2011 ; Li et al., 2018 ; Oliveira et al., 2017 ; Rosen & Lotufo, 2007 ; Tsarpali et al., 2015 ; Tsarpali & Dailianis, 2012), except for two explosive compounds in *M. galloprovincialis* (Rosen & Lotufo, 2007). Most of these studies mimicked pollution events. Only one study investigated the effect of several chemical compounds on the mortality risk of *M. galloprovincialis* in field conditions, in Italy (Moschino *et al*., 2016). This may be explained because it is easier to control these parameters in laboratory conditions. Results showed that concentrations in mussel soft tissues of aluminium, iron, lead and polycyclic aromatic hydrocarbons (PAHs) were correlated with the mussel mortality rate. The other 11 metals and micro-organic pollutants detected in mussel samples showed no association with mussel mortality (Moschino *et al.*, 2016).

3.5.7. Factors related to climate characteristics

The effect of climate characteristics on the mortality risk was studied equally in both mussel species (4 factors by 8 studies, Tables 4 and 5).

In both mussel species, wide seasonal variations in the mortality risk were reported in several studies (Myrand *et al.*, 2000 ; Nicastro *et al.*, 2008 ; Nicastro *et al.*, 2010 ; Bernard *et al.*, 2018a) except for one (Mallet *et al.*, 1987). Risky seasons varied across the hemispheres and

were not necessarily the warmest ones, particularly in South Africa where mortality peaks were reported during winter (Nicastro *et al.*, 2010).

Aerial temperature was the main seasonal factor investigated, often in the context of stress responses and exploration of physiological capacities to explain species invasion or habitat segregation of several mussel species. In *M. edulis*, the mortality risk increased with increasing air temperature in the context of heatwave exposure (Tsuchiya, 1983), rising high summer temperatures (Jones *et al.*, 2010) or in laboratory conditions (Jones *et al.*, 2009). Only one study showed no effect of elevated air temperatures on the mussel mortality risk (Travers *et al.*, 2016), but the seasonal temperature variation reported was much less contrasted than in the other studies. In *M. galloprovincialis*, heatwave exposure above 27°C was also reported to be associated with an increased mortality risk (Olabarrial *et al.*, 2016). Conflicting results were reported for the effect of an increased number of aerial thermal stresses, with studies showing an increased mortality risk in *M. edulis* (Jones *et al.*, 2009 ; Jones *et al.*, 2010), a decreased mortality risk when the mussels had previously been exposed to chronic chemical contamination (Peden *et al*., 2018), or no effect in *M. galloprovincialis* (Dowd & Somero, 2013). In *M. galloprovincialis*, the thermal range between air and water temperature exposures showed inconsistent effects on the mortality risk between the laboratory studies (Anestis et al., 2010 ; Dowd & Somero, 2013 ; Schneider, 2008), probably because of the heterogeneity of the ranges investigated, varying from 2°C to 20°C.

3.5.8. Interactions between factors

Among the 114 studies, only one quarter (28/114; 25%) investigated the effect of interactions between exposure factors on the mussel mortality risk. This represented 30% of the studies (20/66) on *M. edulis*, and 17% of the corpus (8/48) on *M. galloprovincialis*. In both species,

these studies were conducted to the same extent in observation or in laboratory conditions. Almost two thirds of these studies (17/28) explored the combined effect of three factors, while another third (11/28) investigated interactions between two factors. In *M. galloprovincialis,* the most frequently studied interactions fell under site characteristics, while in *M. edulis,* interactions were explored for exposures pertaining mainly to mussel and site characteristics, and husbandry or fishery practices (Figure 5).

Synergistic effects, i.e. a combined effect greater than the sum of the individual effects of the exposure factors, were reported on mussel mortality risk. In *M. galloprovincialis*, a synergistic effect was reported between exposure of mussels to high concentrations of bacteria *Vibrio aestuarianus* or *Vibrio* belonging to the *Splendidus* clade in seawater, an elevated seawater temperature (25°C), and to 8-h emersion to mimic hypoxia-induced stress (Romero *et al.*, 2014). Trampling and endolith-infestation were reported to act together to increase the mortality risk in large *M. galloprovincialis* mussels (Nicastro *et al.*, 2018). In *M. edulis*, a synergistic joint-effect was observed with exposure to heavy metals (cadmium or zinc) in combination with low salinity and high temperature of seawater (Ali & Taylor, 2010). In this species, the negative impact of enrichment of sediment with organic matter on mussel mortality was exacerbated in conditions of burial in fine sediments (Cottrell *et al.*, 2016).

Antagonistic effects, i.e. combined effects lower than the sum of the individual effects of the exposure factors, were also reported, particularly among seawater characteristics. In *M. edulis*, antagonistic effects were observed between low levels of pH and dissolved oxygen (Stevens & Gobler, 2018), low levels of pH, low levels of dissolved oxygen and elevated seawater temperature (Stevens & Gobler, 2018), and between elevated seawater temperature and elevated seawater CO_2 concentrations (Clements *et al.*, 2018). In *M. galloprovincialis*,

such antagonistic effects were reported between a lowered pH and an elevated seawater temperature (Gazeau *et al.*, 2018).

Other non-specific interactions were reported, with exposure factors modulating the individual effect on the mussel mortality risk of another factor, without a straightforward overall interpretation when multiple factor interactions were reported. In both mussel species, interactions were reported between the presence of algal epibionts and the wave exposure of the shore, showing a negative effect of epibiotic algae on mussel survival on sheltered shores (O'Connor, 2010). In *M. galloprovincialis*, a decreased effect of a lowered pH of the seawater was reported on the mortality risk when animals were clumped with mussels of another species *Xenostrobus securis* (Gestoso *et al.*, 2016). Another study showed a negative effect of decreased seawater salinity on the mussel mortality risk, only if associated with an elevated temperature (Hamer *et al.*, 2008). In the context of the understanding of the success of *M. galloprovincialis* as an invasive species in South Africa, interactions were reported between the location, site or zone on the mussel mortality risk (Bownes & McQuaid, 2010 ; Marquet *et al.*, 2013). In *M. edulis*, three studies explored solutions to limit the impact of predation on mussel production or populations, and found statistically significant interactions between mussel size and either farming material by showing that protective socking material was more efficient in large mussels against diving ducks (Dionne *et al.*, 2006), characteristics of the site by reporting that clumped habitats were more protective for small mussels against crab or starfish (Bertolini *et al.*, 2018), or the presence of oysters *Crassostrea gigas* by showing that this presence significantly reduced the mortality of small sized mussels, but the effect varied according to crab size (Waser *et al.*, 2015). Another study reported the effect of hypoxia-induced stress on mussel mortality to be size-specific, with larger mussels having an increased mortality risk under hypoxia conditions than smaller ones (Altieri & Witman, 2006). Gradual

acclimation of the mussels to warmer temperatures modulated the effect on *M. edulis* mortality of the combined exposure of mussels to chronic chemical contamination and acute heat stress (Peden *et al.*, 2018). The effect of the initial farming density on the mortality risk was modulated by mussel size, with mortality of small seed generally increasing with increasing initial density, while mortality of large seed was not affected by initial farming density (Lauzon-Guay *et al.*, 2005). Interactions between the geographical origin of the spat and mussel age were reported on the *M. edulis* mortality risk (Mallet *et al.*, 1990). Along the supply chain, interactions between non-depuration treatment before transport and ambient temperature treatment during transport were reported concerning the mortality risk of *M. edulis* mussels at the post-rewatering stage (Barrento & Powell, 2016).

Non-significant interactions were also observed, for example between duration of burial and the sediment fraction size, or between the duration of burial and the temperature of the seawater concerning the mortality risk of *M. edulis* (Hutchison *et al.*, 2016), in the context of sudden deposited sediment on the mussel bed.

Conflicting results were reported about the interaction effect of mussel stock origin (i.e. genotype) and site on the mortality risk of *M. edulis*, with some studies reporting a significant interaction (Penney *et al.*, 2006 ; Mallet *et al.*, 1987 ; Fuentes *et al.*, 1992), and one study reporting no interaction (Myrand & Gaudreault, 1995).

4. Discussion

The aim of this systematic review was to summarize the findings from the literature that report risk factors for mortality of marine mussels *M. edulis* and *M. galloprovincialis*. The motivation for this study was to provide science-based information to inform actionable solutions to mitigate, or even prevent, mussel mortalities.

4.1. Literature heterogeneity

The literature reviewed was highly heterogeneous. Across the corpus, there was considerable variability among studies with respect to methodological approaches used to define or estimate mussel mortality, and to define putative mortality risk factors and exposure metrics.

Although a systematic review question should be focused and explicit (European Food Safety Agency, 2010), the present review question was broad in scope due to the wide range of risk factors to be considered, as requested by the French Ministry in charge of Agriculture (Anon, 2016). Members of the Scientific and Technical Council (STC) were not aware of large volumes of literature on studies formally designed to identify risk factors of mussel mortality pertaining to different topics. The literature search strategy was thus chosen to be highly sensitive and not too specific to ensure that it captured most information regarding the factors associated with mussel mortality, even though this was not the main objective of the studies. Only 2.4% of the identified unique citations were ultimately selected as relevant. In fact, less than half of the included studies aimed to understand mussel production losses and were thus likely to identify potential risk factor that could be used to inform actionable solutions to mitigate or prevent mussel mortalities. The included studies were roughly concerned either with understanding mussel species distribution and habitat segregation, or used mussels as bioindicators to assess environment quality or climate change effects. Although these

concerns are not completely separate, one does not replace the other and results cannot systematically be extrapolated to mussel mortality risk. Additionally, within the selected corpus, there were only a few studies with a high level of methodological quality in the STC assessment. Importantly, none of the identified studies applied the full set of known standards of epidemiological research (Martin *et al*., 1987), and none explored the effect of several risk factors pertaining to different topics and their interactions on mussel mortality in field conditions. The final corpus, made of 91 publications corresponding to 114 studies and belonging to many different research disciplines, integrated the diverse streams of evidence, observational studies and experimental information. These studies were conducted in experimental or observational conditions, and required different standards, norms and constraints to report mortality and to characterise exposures. Designs and end-points were thus diverse and were subject to research objectives.

Another cause of heterogeneity between the results of the studies was the mussel species considered. This was expected because geographical range, ecology, physiology or functional traits differ between *M. edulis* and *M. galloprovincialis*. Multiple correspondence analysis showed a split of the corpus in two groups based on mussel species in particular. Thus, the results of the present review were separated by mussel species.

As a consequence, knowledge was too heterogeneous to be summarised in a quantitative manner; notably aggregating these heterogeneous results into a meta-analysis was not possible. Therefore, the review results were interpreted and discussed narratively.

4.2. Risk factor identification and ranking

In this systematic review, more than 100 factors related to mussel mortality were identified, which highlights the diversity of variables that researchers considered as potential risks or protective factors in mussel mortality. However, it is interesting to note that although some factors coincided between studies, these were not repeated in a large number of studies. As detailed above, the small number of studies and the diversity of the definitions and exposure metrics captured for a given risk factor prevented any meta-analysis and quantification of effects on the mussel mortality risk. Therefore, comparisons of the strengths of association between mussel mortality and factors, and the subsequent ranking of risk factors were not possible. Moreover, the number of studies was artificially increased for some factors, when the same research group published several papers, or several studies in the same paper on the same subject. This publication bias limited the relevance of an evidence interpretation strictly on a quantitative basis, i.e. the number of studies, and thus prevented the use of the vote counting method (Allen, 2017) for establishing a ranking of the risk factors.

Even when looking at the studies that explored one particular factor, there was not often consistent evidence of an overall qualitative effect on the mussel mortality risk. Nevertheless, this systematic review highlighted that the mortality risk of both mussel species *M. edulis* and *M. galloprovincialis* varied across the seasons. It furthermore acknowledged the negative impact of an increased seawater temperature with a thermal threshold of 20°C and 24°C, respectively. The mortality risk of *M. edulis* could also be associated with pathogens. However, these risk factors relate to the impacts of global changes in ocean and coastal ecosystems (Burge et al., 2014 ; IPCC (Intergovernmental Panel on Climate Change), 2019) and cannot be changed. Therefore, although this systematic review was comprehensive, it offered limited evidence to define actionable control or mitigation strategies of mussel mortality either for policy-making, mussel industry, or wild bed conservation. For *M.*

galloprovincialis, the preventive husbandry practices would be using mussel spat from the same area where the farming is carried out, protecting mussels from predation, or farming together with another mussel species, if possible. For *M. edulis*, they would be protecting mussels from predation, using pure crosses and particulary mussel spat having a selected genotype, i.e. parents that survived a previous mortality event, whether the selection was natural or anthropic. For wild bed conservation of both mussel species, the impacts of marine anthropic factors, e.g. the activities of the marine aggregate extraction industry (Barrio Frojan *et al*., 2008), marine renewable energy technology (Miller *et al*., 2013) or dredging to maintain access to harbours, should be evaluated *ex ante* before their implementation, to minimise anthropogenic sedimentation or sand accumulation on wild beds.

4.3. Review limitations

Although the systematic review is an unbiased approach, the present study is subject to a few limitations that are mainly explained by the trade-off between limited resources and risk of error.

Only one reviewer read the full content and conducted the data extraction from the corpus considered in this systematic review, ensuring homogeneous data analysis across the whole corpus. However, to limit the risk of errors in data extraction, pilot-tests and standardised extraction forms were used. In addition, the STC implemented collective study selection based on the title and abstract screening and data extraction verification based on random samples of the studies, respectively 9.9% and 14.3% of the corpus. The agreement between the reviewers was substantial at the abstract and title screening level and almost complete at the data extraction stage, showing that selection or measurement bias were unlikely to have affected the review results.

The language restriction applied (French and English), due to the lack of resources to translate other languages, biased the study selection towards English and French speaking countries. It is possible that knowledge from some regions of the world has been under-represented, specifically data from Spain which is the main European producer of mussels (FAO, 2019).

This review included some subjective interpretation as risk factors were rarely the main focus of the included studies. Effectively, translation of concepts across studies was subject to reviewer interpretation. We are therefore confident that our interpretation accurately reflects the data, although we agree that other interpretations are possible and may be equally valid.

Because this review covered a wide range of risk factors, the findings are at a high level of aggregation; a focus on more specific exposure topics would have allowed for more in-depth evaluation.

5. Research gaps and future directions

This literature review revealed significant gaps in knowledge of marine mussel risk factors, which led the STC to develop recommendations for future research to be undertaken on mussel mortality determinants.

5.1. Develop standardised methodologies to estimate mortality in the field

The first recommendation involves the development of standardised methodologies to estimate mussel mortality in the field, which use shared epidemiological indicators. This literature review showed high heterogeneity to define and estimate mortality in mussels, which is not solely explained by the different standards required by the numerous research disciplines. In particular, technical constraints that challenge mortality estimation in mussel populations, notably in farming conditions, have so far precluded the standardised estimation of mortality. Similarly, the large population sizes and the difficulties in gaining access to the animals prevent robust estimation of epidemiological indicators, since accurately measuring the numbers of dead animals (numerator) and the total population size (denominator) is challenging (Peeler & Taylor, 2011 ; Lupo et al., 2012). In addition, mortality is rarely homogeneously distributed in such large populations, which prevents simple application of representative sampling. Thus, and unfortunately, it seems that regardless of the innovative tools that could be developed, accurately counting dead and live mussels to calculate a mortality proportion would still be an issue. A shift in the paradigm to estimate mussel mortality is thus needed, and scaling of the concept may be a possible solution.

Marine bivalves share many epidemiological challenges with honey bees. In the context of the French surveillance programme of massive bee mortality, bee mortality is defined at the apiary level using a two-step approach over a 15-day period (Anon, 2018). A bee operation

owned or managed by one beekeeper is made of several apiaries, which consist of several bee colonies located in the same area, themselves made up of a group of individual bees. The first step consists in assessing a bee colony as "dead" if more than one litre of dead bees is observed in front of the hive or if the colony is depopulated. The second step involves considering the apiary to be "dead" if more than 20% of its forming colonies are dead. For medium apiaries (from 6 to 10 colonies), it is considered dead if two dead colonies are observed. For small apiaries (from 2 to 5 colonies), it is considered dead if one dead colony is reported (Anon, 2018). Therefore, to obtain an accurate estimation of mortality at the population level, based on the observed mortality on the sampled colonies, calculation of the mortality proportions is related to the size of the apiaries. Honeybee colony mortality is a weighted average, by apiary size, of the colony mortality proportion of each apiary (Chauzat *et al*., 2016). The STC believes that the marine mussel community should consider this type of approach of (1) assessing mortality at a farming unit level, instead of the accurate individual animal scale, and (2) combining qualitative and quantitative criteria within a defined time period (e.g. a tide cycle). It is considered that a mussel farm owned by one mussel farmer is made of several farming places, e.g. leasing grounds, which consist of several farming structures i.e. "bouchot" for *M. edulis* or raft for *M. galloprovincialis*, themselves made of a group of individual mussels. Thus, a multistage sampling plan may be adapted to estimate mortality at each unit of interest by accounting for the unit hierarchy. At each unit level, thresholds to assess whether the unit is affected by mussel mortality (i.e. "dead") could be defined by using standardised semi-quantitative criteria.

5.2. Use study designs that can address multiple interactions between risk factors

The second recommendation concerns the application of study designs adequately addressing the identification of many interacting mussel mortality risk factors pertaining to different

topics, since the methodological quality assessment revealed frequent weaknesses in the reviewed corpus. More data are required on the combined effects of multiple risk factors. For this approach to succeed, there is a need for concomitant collection, i.e. at the same time and in the same place, of data on multiple exposures of different types. The essential concept should be to compare the exposure profiles of dead versus healthy mussel populations, and over time, to provide valuable clues about the risk factors of mortality. A preliminary approach would be the development of eco-epidemiological studies, which aim to analyse determinants and outcomes at different levels of organisation of the studied system, from the molecular to the social (Susser & Susser, 1996). These should necessarily be integrative and multidisciplinary to cover all the different risk factor topics. Guidelines to design and report epidemiological studies (STROBE-Vet) should be used (Sargeant *et al*., 2016). A second approach would be the development of mesocosm experiments, which are used to simulate complex exposure dynamics under realistic field conditions (Culp *et al*., 2017). Mesocosms are a hybrid of field and laboratory conditions; their advantages include increased control and replication compared to field studies and more realistic conditions than laboratory experiments. Currently, these approaches are used to study the effects of contaminants in the marine ecosystem (Alexander *et al*., 2016). Once this screening step of potential risk factors is achieved, targeted experimental approaches could be developed further to assess their causality while controlling the other factors.

5.3. Integrate the concept of exposome

The third recommendation includes the integration of the concept of exposome, i.e. every exposure to which an individual is subjected from conception to death (Wild, 2005), in future investigations undertaken on multiple exposure-mortality associations in mussels. This literature review showed that only one third of the studies had explored the combined effects

of multiple factors on the mussel mortality risk, and when they had, the effect of no more than three factors was investigated. The exposome is assessed at the individual level by characterising the specific signatures (or profiles) of the effects of previous exposures based on "omics" technologies (Wild, 2012). The exposome complements the genome by providing a comprehensive description of the lifelong exposure history of an individual. On the one hand, the recent use of tissue and molecular biomarkers in mussels *M. galloprovincialis* has enabled us to distinguish coastal sites according to their pollution level (Carella et al., 2018 ; Matozzo et al., 2018). On the other, the application of "omics" approaches has significantly improved knowledge about the interactions between the Ostreid herpesvirus OsHV-1 and the Pacific oyster *Crassostrea gigas* (Nguyen et al., 2018). Further application of "omics" technologies should be encouraged to develop and validate sets of biomarkers relevant to multiple exposures in the context of mussel mortality events. However, exposure biomarker approaches should be coupled with refined questionnaire-based approaches to collect husbandry practices and the life history of the mussel population under study, and environmental monitoring at different temporal and geographical scales.

5.4. Develop tools to assess multi-exposure of mussels on a routine basis

The fourth recommendation draws attention to the need for tools for mussel exposure assessment. In particular, there is a need to develop screening tools that capture multiple pathogens and pollutants on a routine basis. Effectively, in the literature reviewed, these risk factor topics were often explored using targeted approaches and only a few pathogens or pollutants were simultaneously investigated. Generic methods such as histopathology allow for detection of multiple infections and emerging diseases, but their slowness and low sensitivity for detection of small protistan, viral or bacterial pathogens are not suitable for extensive routine use. Rapid tools such as multiplex DNA-based polymerase chain reaction

(PCR) and DNA microarray-based assays have low detection limits but require that the specific target pathogens have been identified, which is not appropriate in mortality exploration without prior knowledge of the causative pathogen. Development of microbial metagenomics should be encouraged because such approaches allow simultaneous identification of a large number of pathogen genomes (abundance and diversity) from the same sample at the same time, without prior knowledge of their genomic sequences (Gilbert & Dupont, 2011). This type of overall approach has the ability to identify coinfections within the host (Yang *et al.*, 2011) and is also applicable to environmental samples (Munang'andu, 2016). The development of high-throughput sequencing (HTS) technologies and bioinformatics tools for nucleic acid sequence assembly and annotation has made it possible to use these approaches in a cost-effective manner, and thus, at a large scale. Although microbial metagenomics is still underused in aquaculture (Martinez-Porchas & Vargas-Albores, 2017), studying mussel mortalities through the metagenomics perspective should be favoured to help understand the involvement of pathogens in mortality outbreaks by comparing the microbial profiles of animals and seawater in sites in which mortality occurs vs. sites with a non-mortality context, or before vs. during the course of mortality events. To go further, as positive results provided by DNA-based methodology are not clearly indicative of actual infection, metatranscriptomics approaches should be preferentially developed, in agreement with the exposome concept detailed above, to identify only active pathogens in a replication state. This would facilitate the biological interpretation of the results and discard environmental DNA or traces that are not relevant to the mortality occurrence. First milestones in that direction have been laid by combining microbiome characterization (16S rRNA HTS) and host-gene expression profiles (RNA-seq) to decipher the factors underlying mass mortality in the stripped venus clam, *Chamelea gallina*, which suggested potential chemical pollutant-pathogen interactions (Milan et al. 2019).

Similarly, further work is needed on long-term monitoring of multiple relevant pollutants in marine environments. Data are required to assess the effects of long-term and low-level exposure to multiple contaminants on the mortality risk of mussels. However, progress in *in situ* sensor technologies is still needed to enable cost-effective and continuous monitoring of contaminants in seawater (Justino *et al*., 2015). In particular, passive sampling technologies (Schintu *et al*., 2014) that capture a wide range of environmental pollutants, should enable us to assess the effects of multiple exposures (i.e. a cocktail effect) and of chronic exposure to contaminants on the mortality risk of mussels.

In addition to these previous recommendations, the STC highlights the need to cautiously define the epidemiological units and their appropriate related exposures, as the hierarchical organisation of the system under study should be considered. Future investigators should be warned against the ecological fallacy, i.e. inferring causation at the individual level from population level comparisons, as well as the atomistic fallacy, i.e. inferring causation at the population level from individual level comparisons (Schwartz, 1994 ; Susser, 1973).

5.5. Assess the impact of husbandry and fishery practices on the mortality risk

The fifth recommendation pertains to the need for assessment of the impact of husbandry and fishery practices on mussel mortality risk. Although one third of the corpus reviewed investigated the effect of husbandry practices on mussel mortality, these were always controlled field trial studies, i.e. studies in which the investigator controls the allocation of the mussels to the study groups, with or without application of the practice under study. Future research should include long-term monitoring of mussel populations and the multiple exposures, and importantly practices occurring in usual farming or harvesting conditions.

Observation studies of this kind would involve engaging mussel farmers and fishermen in the study.

5.6. Co-construct studies with stakeholders

The last recommendation is the need for co-construction of future large-scale prospective studies on mussel mortality risk factors with stakeholders, specifically mussel farmers and fishermen, to guarantee sustainability and utility of the results. Stakeholders should be engaged as early as possible and throughout the process, in as many of the following phases as possible: knowledge provision, data collection and integration, interpretation of results, and development of mitigating solutions (Reed, 2008).

Addressing the STC recommendations implies the need for interdisciplinary research. Conducting large-scale eco-epidemiological analyses of multiple exposures associated with mussel mortality, including the different organisation levels of the system under study, would require increased collaboration between epidemiologists, biostatisticians, and experts in bioinformatics and biotechnologies, as well as laboratory, environmental and social scientists. Processing and analysing large datasets generated and collected at different scales would also require adapted capabilities for the management and analysis of large data flows. The STC panel, by gathering scientists from different research disciplines, the shellfish industry, and government authorities, represents a first step in this interdisciplinary process. This configuration made it possible to build over-arching recommendations that highlight multidisciplinary research needs.

The STC also recognised that, although assessing all risk factors of mussel mortality within a large- scale survey would be ideal, it is not realistically achievable at this time. By their

nature, prospective cohort studies take time as well as funding. The cost of equipment and technologies needed may be high, and therefore their application to population-based studies may also be costly. This type of project would require an enormous effort for general coordination, for the supervision of the participating mussel farmers and fishermen, and for the maintenance of a central database. These recommendations also involve a significant financial contribution and may not always be immediately feasible as innovative tools and developments are needed, e.g. for improved measurement of multiple exposures at different time points of the production cycle of mussels. Thus, given the very high costs of such studies and the complexity of putative risk factors in mussel mortality, even a partial understanding of a sub-set of exposures could provide substantial advances in understanding mussel mortality determinants. There could be further efforts to coordinate a major national prospective cohort study, supported by coordinated national investment with regional funders, able to target their contribution to exposures of regional priority. Data generated should be shared in a common and publicly available database among stakeholders, to facilitate cooperation. Overall, standardising the efforts and developing cooperative initiatives would facilitate comparisons between studies to increase the robustness of data if meta-analyses are required.

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Table 1. Characteristics extracted from the studies included in the systematic review of the risk factors for mussel mortality

Characteristics	Standardised modalities
All studies	
Authors' names	Open field
Title	Open field
Journal name and volume	Open fields
Year of publication	Open field
Type of document	Journal, conference paper/abstract, report, thesis
Mussel species†	*Mytilus edulis, Mytilus galloprovincialis*
Country and region	Open field
Study conditions	Laboratory, observational
Population type†	Farmed, wild, hatchery, other
Mussel age class †	Juveniles, adults
Mussel size	Open field
Epidemiological unit	Individual, group
Frequency of mortality estimation	Open field
Risk factor topic†	Animal characteristics, site characteristics, climate characteristics, seawater characteristics, contaminants, pathogens, farming/fishery practices
Risk factor(s) studied	Open field
Interactions addressed	Yes, no
Methodological quality score	Poor, moderate, satisfactory
Field transposition score	Poor, satisfactory
Measure of association between the mortality and the exposure of interest	Open field
Effect of exposure to the factor on the mortality risk	Increasing, decreasing, no effect

† Several choices were possible

Observational studies	
Study design	Cross sectional, case-control, exposed/non exposed cohorts, single prospective cohort
Random sampling	Yes, no
Mortality estimation	Open field
Mortality counting method	Open field
Laboratory studies	
Control presence	Yes, no
Triplicate of the trial	Yes, no
Mortality definition criteria	Open field

Table 2. Characteristics and numbers of included studies investigating risk factors of marine mussel mortality (N = 114)

Characteristics	***M. edulis***		***M. galloprovincialis***	
	Number of observational studies (N = 38)	**Number of experimental studies** (N = 28)	**Number of observational studies** (N = 25)	**Number of experimental studies** (N = 23)
Geographic focus				
North Sea	3	10	0	1
Black Sea / Mediterranean	0	0	8	11
Atlantic Ocean				
Pacific Ocean	31	16	15	9
	4	2	2	2
Population type[*]				
Farmed	22	7	10	12
Wild	11	20	15	11
Hatchery	6	1	1	0
Not reported	0	1	0	0
Mussel age class [†]				
Juveniles	6	3	2	2
Adults	5	10	2	10
Not reported	28	15	21	11
Mussel size				
<20 mm	4	5	7	2
20-30 mm	6	5	5	4
30-40 mm	5	6	8	4
40-50 mm	4	4	5	3
50-60 mm	3	7	7	8
60-70 mm	2	1	4	1
>70 mm	1	0	4	2
Not reported	22	10	10	1
Epidemiological unit				
Individual	0	4	1	0
Group	38	24	24	23
Study design				

[*] Several population types could be examined in a single study; thus, the sum of studies per population type could be greater than the total number of studies

[†] Several age classes could be examined in a single study; thus, the sum of studies per age class can be greater than the total number of studies.

Cross-sectional	2		2	
Case-control	0		0	
Exposed/non exposed cohorts	10		6	
Single prospective cohort	26		17	
Strength of proof of causal association provided by the study design				
Low	28		19	
High	10		6	
Random sampling				
Yes	7		8	
No	31		17	
Control presence				
Yes		19		19
No		9		4
Triplicate of the trial				
Yes		15		10
No		13		13
Quality score				
Moderate	24	20	16	15
High	14	8	9	8
Mortality definition criteria[‡]				
Failure to close the valves in response to external stimuli		10		9
Widely open valves		7		7
Not defined		18		14
Mortality estimation methods				
Counting	34		18	
Analysis of digital pictures of quadrats	0		2	
Drop-in density of live mussel	1		0	
Not reported	3		5	
Mortality counting methods				
Dead and live mussels	6		2	
Remaining live mussels	7		4	
Dead mussels	1		3	
Freshly dead mussels	0		1	
Empty shells	3		1	

[‡] Several criteria could be used in a single study; thus, the sum of studies per criterion can be greater than the total number of studies.

Not reported	17		7	
Mortality statistics				
Final prevalence	14		12	
Cumulative prevalence	21		12	
Instantaneous proportion	2		0	
Half-stock index	1		1	
Frequency of mortality estimation[§]				
Daily	2	9	2	10
Weekly	3	3	1	3
Bi-monthly	5	1	0	0
Monthly	15	2	11	3
Quarterly	5	0	5	0
Bi-annually	1	0	0	0
Annually	1	0	0	0
At the end of the study	9	5	6	6
Not reported	3	12	1	3
Risk factor topics[**]				
Pathogens	2	6	5	3
Animal characteristics	17	3	5	2
Seawater characteristics	4	11	0	9
Site characteristics	18	7	13	1
Farming or fishery practices	21	2	10	3
Contaminants	0	3	1	6
Climate characteristics	6	2	3	5

[§] Mussel mortality could be measured at several frequencies in a single study; thus, the sum of studies per frequency can be greater than the total number of studies.

[**] Several risk factor topics could be investigated in a single study; thus, the sum of studies per topic can be greater than the total number of studies.

Table 3. Association measures between mussel mortality and factors of interest (N = 114 studies)

Association measure	**Nb. of studies**	
	Mytilus edulis (66)	***Mytilus galloprovincialis*** (48)
Comparison of mortality means	20	15
Comparison of mortality proportions	34	20
Comparison of survival curves	7	3
Median survival	1	0
Correlation	2	4
Concentration leading to 50% mortality	2	5
Time leading to 50% mortality	0	1

Table 4. Factors studied in *M. galloprovincialis* and reported effect on the mortality risk (23 experimental studies, 25 observation studies). Experimental studies are highlighted in grey; studies accounting for interactions between factors are in bold; in the last column, NR stands for non-relevant.

Studied factors	**Nb. studies**	**Effect on mortality risk**			**Consistency of study results**
		Increase	**Decrease**	**No effect**	
Pathogens	**8**				
Non-identified infectious agent	1	Benaldelmouna *et al*. (2018)			NR
Bacteriological profile	1			Bernard *et al*. (2018b)	NR
Bacteria *Vibrio aestuarianus*	3	**Romero *et al*. (2014)**[1]		Benaldelmouna *et al*. (2018); **Romero *et al*. (2014)**[2]	No
Bacteria *Vibrio Splendidus* clade	3	**Romero *et al*. (2014)**[1]		Benaldelmouna *et al*. (2018); **Romero *et al*. (2014)**[2]	No

[1] Infection by exposure to contaminated seawater with 10^{10} CFU/mL, with seawater temperature at 25°C and in emersion for 8 hours (to simulate hypoxia conditions)
[2] Infection by exposure to contaminated seawater with 10^{10} CFU/mL, with seawater temperature at 15°C or at 25°C

Ostreid herpesvirus OsVH-1	1			Benaldelmouna *et al*. (2018)	NR
Parasite *Marteilia refringens*	1			Benaldelmouna *et al*. (2018)	NR
Toxic algae dinoflagellate *Ostreopsis* cf *ovata*	1	Carella *et al*. (2015)[3]			NR
Presence of epibiotic algae on the shell	2	**O'Connor (2010)[4]**		**O'Connor (2010)[5]**	No
Endolithic infestation	3	Marquet *et al*. (2013); **Nicastro *et al*. (2018)[6]**	**Zardi *et al*. (2016)[7]**		No
Animal characteristics	**7**				
Species vs. *M. trossulus*	3		Dowd and Somero (2013); Schneider (2008)	Shields *et al.* (2008)	No
Intraspecific vs. interspecific genotype	2		Fuentes *et al*. (2002)[8]	Shields *et al.* (2008)[9]	No

[3] Dose effect
[4] In sheltered rocky shores
[5] In shores exposed to waves
[6] Mortality due to trampling (anthropogenic stressor) in the context of recreational or harvesting use of wild beds
[7] Mortality due to a heat wave

High frequency of individuals having more than 10% cytogenetic abnormalities in haemocytes in the population	1	Benabdelmouna and Ledu (2016)		NR
Small size	2		Lok *et al*. (2007); **O'Connor (2010)**[10]	Yes
Seawater characteristics	**9**			
Elevated temperature	4	Anestis *et al*. (2007)[11]; Dowd and Somero (2013)[12]; Gazeau *et al*. (2018)[13]	Gestoso *et al*. (2016)[14]	No
Increased number of thermal stresses	1		Lenz *et al*. (2018)[15]	NR
Decreased salinity	2	**Hamer *et al*. (2008)**[16]	**Hamer *et al*. (2008)**[17]	NR

[8] Different genotypes of *M. galloprovincialis* vs. different hybrid genotypes of *M. edulis* and *M. galloprovincialis*
[9] Native genotype of *M. trossulus* vs. introgressed vs. introduced genotype of *M. galloprovincialis*
[10] Mortality due to epibiotic algae on the shell
[11] Thermal threshold at 24°C; elevation from 18°C to 30°C by 0.1°C increase per minute (thus in 2 hours in total)
[12] Seawater from 13°C to 33°CC
[13] Thermal threshold 25°C; variations from 15.7°C to 27.8°C and elevation of 1°C per week for 3 weeks
[14] Seawater at 21°C vs. 16°C
[15] Seawater from 19°C to 29°C, two thermal stresses separated by 14 day-long recovery phases
[16] Salinity below 28 psu, with seawater temperature at 27°C
[17] Salinity below 28 psu, with seawater temperature at 13°C

Decreased pH/Acidification	4	Bressan *et al*. (2014)[18]; **Gestoso *et al*. (2016)**[19]	**Gazeau *et al*. (2018)**[20] ; Bressan *et al*. (2014)[21]	No
Decreased dissolved oxygen/Hypoxia	2	**Romero *et al*. (2014)**[22]	**Romero *et al*. (2014)**[23]	No
Characteristics of the farming / fishing site	**14**			
General effect	5	Bownes and McQuaid (2010); Fuentes *et al*. (1994); Gardner (2013); Moschino *et al*. (2017)	Fuentes *et al*. (1992)	No
Coast vs. bay	2	Nicastro *et al*. (2008); Nicastro *et al*. (2010)		
Sand burial or accumulation	4	Nicastro *et al*. (2010); Zardi *et al*. (2006);	Zardi *et al*. (2008)	No

[18] Constant pH of 7.4 for 6 months
[19] When mussels *M. galloprovincialis* are mixed with mussels *Xenostrobus securis*
[20] Gradual decrease of 0.3 pH units (from 8.01 to 7.98); decrease of 0.1 unit per week for 3 weeks then maintenance for 10 months; irrespective of the seawater temperature between 12-25°C
[21] Constant pH of 7.4 for 3 months
[22] With seawater temperature at 25°C
[23] With seawater temperature at 15°C

		Zardi *et al*. (2006)			
Wave exposure	2	**O'Connor (2010)**[4]		**O'Connor (2010)**[5]	No
Wave height	3	Zardi *et al*. (2008); **Nicastro *et al*. (2010)**[24]		**Nicastro *et al*. (2010)**[25]	No
High position on the shore	2			Bownes and McQuaid (2010); Marquet *et al*. (2013)[26]	Yes
Border vs. central position in the bed	1			Nicastro *et al*. (2008)	NR
Predation	2	Gammoudi *et al*. (2017)[27]; Plass-Johnson *et al*. (2010)			Yes
Farming / harvesting practices	**13**				
Geographic origin of the spat: local. vs transplanted	7	Shields *et al*. (2008)	Bernard *et al*. (2018a); Fuentes *et al*. (1992);		No

[24] Bay habitat
[25] Coast habitat
[26] Mortality due to endolith infestation
[27] Mortality due to predation by the polyclad flatworm *Imogine mediterranea*

			Fuentes *et al*. (1994); Gardner (2013) ; Kovacic *et al*. (2017); Ramon *et al*. (2007)		
Position inside the farming structure	2		Fuentes *et al*. (1994)	Fuentes *et al*. (1992)	No
Mixed mussel species	2		**Gestoso *et al*. (2016)**[28]; Olabarrial *et al*. (2016)[28]		Yes
Polyculture (fish)	1	Gvozdenovic *et al*. (2017)			NR
Polyculture (algae *Gracilaria verrucosa*)	1		Ajjabi *et al*. (2018)		NR
Re-immersion duration of the mussels before sale > 11 days	1	Theodorou *et al*. (2017)			NR
Stocking density during immersion before transport for sale (kg/bag)	1			Theodorou *et al*. (2017)	NR
Increasing intensity of human trampling during bed harvesting	1	Nicastro *et al*. (2018)			NR

[28] With *Xenostrobus securis*, invasive species in Galicia, Spain

Contaminants from the terrestrial and marine environments	**7**			
Total metals (As, Cd, Cr, Cu, Hg, Ni, V, Pb, Zn, Al, Fe)	1	Moschino *et al*. (2016)[29]		NR
Al	1	Moschino *et al*. (2016)[29]		NR
As	1		Moschino *et al*. (2016)[29]	NR
Cd	1		Moschino *et al*. (2016)[29]	NR
Cr	1		Moschino *et al*. (2016)[29]	NR
Cu	1		Moschino *et al*. (2016)[29]	NR
Fe	1	Moschino *et al*. (2016)[29]		NR
Hg	1		Moschino *et al*. (2016)[29]	NR
Ni	1		Moschino *et al*. (2016)[29]	NR
Pb	1	Moschino *et al*. (2016)[29]		NR
V	1		Moschino *et al*. (2016)[29]	NR
Zn	1		Moschino *et al*. (2016)[29]	NR
Polycyclic aromatic hydrocarbons (PAHs)	1	Moschino *et al*. (2016)[29]		NR
Polychlorinated biphenyls (PCBs)	1		Moschino *et al*. (2016)[29]	NR
Carbamazepine (antiepileptic pharmaceutical drug)	1	Oliveira *et al*. (2017)		NR
Phthalates (plasticisers)	1		Moschino *et al*. (2016)[29]	NR

[29] In mussel tissues

Alkylphenols (detergents, fuel and oil additives, resins)	1		Moschino *et al*. (2016)[29]	NR
Zinc oxide nanoparticles (ZnO)	1	Li *et al*. (2018)		NR
2,4,6-trinitrotoluene (TNT, explosive compound)	1	Rosen and Lotufo (2007)		NR
Hexahydro-1,3,5,-triazine (RDX, explosive compound)	1		Rosen and Lotufo (2007)	NR
Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX, explosive compound)	1		Rosen and Lotufo (2007)	NR
Imidazolium ionic liquids (1-butyl-3-methylimidazolium and 1-methyl-3-octylimidazolium tetrafluoroborate), alternative to conventional organic solvents	1	Tsarpali *et al*. (2015)		NR
Olive mill wastewater (by-product of olive oil production)	1	Danellakis *et al*. (2011)		NR
Landfill leachate	1	Tsarpali *et al*. (2012)		NR
Climate characteristics	**8**			
Season	3	Bernard *et al*. (2018a)[30]; Nicastro *et al*. (2008)[31];		Yes

[30] In France, spring (March-May) vs. other seasons
[31] In South Africa, end of summer (February) vs. other seasons

		Nicastro *et al*. (2010)[32]			
Elevated air temperature	1	Olabarrial *et al*. (2016)			NR
Air vs. seawater thermal range	4	Anestis *et al*. (2010)[33]; Dowd and Somero (2013)[34]	Schneider (2008)[35]	Schneider (2008)[36]	No
Increased number of aerial thermal stresses	1			Dowd and Somero (2013)[37]	NR

[32] In South Africa, **on the coast**: mortality peaks at the end of summer (February) and in winter-spring (June-October) / **in the bay**: mortality peaks in summer (February) and in winter (June)
[33] Seawater at 18°C or 26°C and air at 32°C
[34] Seawater at 13°C and air at 33°C
[35] Seawater at 12°C and air from 20 to 30°C
[36] Seawater at 18°C and air from 20 to 30°C
[37] 33°C, three times

Table 5. Factors studied in *M. edulis* and reported effect on the mortality risk (28 experimental studies, 38 observation studies). Experimental studies are highlighted in grey; studies accounting for interactions between factors are in bold; in the last column, NR stands for non-relevant.

Studied factors	**Nb. studies**	**Effect on mortality risk**			**Consistency of study results**
		Increase	**Decrease**	**No effect**	
Pathogens	**8**				
Non-identified infectious agent	2	Benabdelmouna *et al*. (2018) ; Pépin *et al.* (2017)			Yes
Bacteriological profile	1			Bernard *et al*. (2018b)	NR
Anaerobic bacteria	1	Barbarro and De Zwaan (2008)			NR
Opportunistic heterotrophic bacteria	1	Eggermont *et al*. (2014)			NR
Bacteria *Vibrio aestuarianus*	1			Benabdelmouna *et al*. (2018)	NR
Bacteria *Vibrio Splendidus* clade	2	Eggermont *et al*. (2017)		Benabdelmouna *et al*. (2018)	No

Bacteria *Photobacterium*	1	Eggermont *et al*. (2017)			NR
Ostreid herpesvirus OsVH-1	1			Benabdelmouna *et al*. (2018)	NR
Parasite *Marteilia refringens*	2			Benabdelmouna *et al*. (2018); Bernard *et al*. (2018b)	Yes
Toxic algae *Karlodinium armiger*	1	Binzer *et al*. (2018)			NR
Presence of epibiotic algae on the shell	2	**O'Connor (2010)**[1]		**O'Connor (2010)**[2]	No
Animal characteristics	**22**				
Species vs. *M. trossulus*	3		Gardner and Thompson (2001)	Penney *et al*. (2006) ; Lowen (2008)	No
Interspecific genotype	2	Fuentes *et al*. (2002)[3]; Lowen (2008)[4]			Yes

[1] In sheltered rocky shores
[2] In shores exposed to waves

Intraspecific genotype	3		Pépin *et al*. (2017)[5]; Pépin *et al*. (2017)[5]	Myrand and Gaudreault (1995)	No
Low degree of multiple-locus heterozygosity	1	Tremblay *et al*. (1998)			NR
High frequency of individuals having more than 10% cytogenetic abnormalities in haemocytes in the population	4	Benabdelmouna and Ledu (2016); Pépin *et al*. (2017); Pépin *et al*. (2018)		Pépin *et al*. (2017)	No
Neoplastic process in the haemocytes	2	Pépin *et al*. (2018)		Bernard *et al*. (2018b)	No
Small size	7	**Altieri and Witman (2006)**[6]; **Dionne *et al.* (2006)**[7]; Lauzon-Gay *et al*. (2005); Lauzon-Gay *et al*. (2005)		**O'Connor (2010)**[8]; Tremblay *et al*. (1998); Tsuchiya (1983)	No
Low growth rate	2	**Altieri and Witman**			Yes

[3] Different hybrid genotypes between *M. edulis* and *M. galloprovincialis* vs. pure crosses of *M. galloprovincialis*
[4] Hybrid genotypes between *M. edulis* and *M. trossulus* vs. pure crosses of *M. edulis* vs. pure crosses of *M. trossulus*
[5] Selected (i.e. which parents survived a previous mortality event) vs. non-selected genotype
[6] Under hypoxia conditions
[7] Mortality due to predation by diving ducks
[8] Mortality due to epibiotic algae on the shell

		(2006)[6]; Hiebental *et al*. (2013)			
Low condition index	1	Hiebental *et al*. (2013)			NR
Age (juveniles vs. adults)	1		Mallet *et al*. (1990)		NR
Low energetic resources / high energetic needs for maintenance	2	Myrand *et al*. (2000); Tremblay *et al*. (1998)			Yes
End of spawning period	1	Myrand *et al*. (2000)			NR
Spawning period	1	Pépin *et al*. (2017)			NR
Lipofuscin accumulation	1	Hiebental *et al*. (2013)			NR
Shell resistance	1			Hiebental *et al*. (2013)	NR
Seawater characteristics	**17**				
Elevated temperature	12	Bernard *et al*. (2018a)[9] Clements *et al*. (2018)[10]; Cottrell *et al*. (2016)[11];		**Ali and Taylor (2010)**[17]; **Stevens and Gobler (2018)**[18]	No

[9] Over 19-20°C

		Hiebenthal *et al*. (2013)[12]; **Hutchison et al. (2016)[13]**; **Incze *et al.* (1980)[14]**; Jones *et al*. (2009); Jones *et al*. (2010); Lenz *et al*. (2018)[15]; Wang *et al*. (2018)[16]			
Increased number of thermal stresses	2	Jones *et al*. (2009)	Lenz *et al.* (2018)		No
Decreased temperature	1	Wang *et al*. (2018)[19]			NR
Decreased salinity	1	**Ali and Taylor (2010)**[20]			NR
Decreased pH/Acidification	4	**Stevens and Gobler (2018)**[21];		Clements *et al*. (2018); **Stevens and Gobler**	No

[10] 22°C vs. 16°C
[11] 20°C vs. 15°C
[17] 6°C or 12°C; mortality due to zinc (Zn) or cadmium (Cd) exposure; with a low salinity of 20 psu
[18] 20°C vs. 26°C
[12] Over 20-25°C
[13] From 8°C to 20°C; with several burial depths
[14] Thermal threshold at 20°C, with a rapid decline of total chlorophyll concentration
[15] From 15°C to 28°C, two thermal stresses separated by 14 day-long recovery phases
[16] 35°C
[19] 4°C
[20] 20 psu; mortality due to zinc (Zn) or cadmium (Cd) exposure
[21] pH = 7.2 vs. 9.7

		Sun *et al.* (2016)[22]	**(2018)**[21]	
Variations of dissolved oxygen concentration	2		**Stevens and Gobler (2018)**[23]; **Stevens and Gobler (2018)**[23]	Yes
Low quantity of food	1	Incze *et al.* (1980)[24]		NR
Low phytoplankton diversity index	1	Travers *et al.* (2016)		NR
Characteristics of the farming / fishing site	**25**			
General effect	10	Bernard *et al.* (2018a); Glize *et al.* (2017); Glize and Gourmelen (2018); Penney *et al.* (2006); Pépin *et al.* (2017)	Lauzon-Gay *et al.* (2005); Mallet et al. (1987); Mallet *et al.* (1990); Myrand and Gaudreault (1995); Stirling and Okumus (1994)	No
Increased burial sediment depth	2	Hutchison *et al.* (2016)	Hutchison *et al.* (2016)	No

[22] pH = 6.5
[23] 2.0 mg/L vs. 8.0 mg/L during 4 weeks
[24] Rapid decline of total chlorophyll concentration

Increased burial sediment duration	3	Cottrell *et al*. (2016); Hutchison *et al*. (2016); Hutchison *et al*. (2016);			Yes
Fine burial sediment fraction (<0.3 mm)	2	Cottrell *et al*. (2016); Hutchison *et al*. (2016)			Yes
High concentration (1%) of organic matter in burial fine sediment	1	Cottrell *et al*. (2016)			NR
Wave exposure	2	**O'Connor (2010)**[1]		**O'Connor (2010)**[2]	No
Spatially complex habitat (with small inter-structural spaces)	2		**Bertolini *et al.* (2018)**[25]	**Bertolini *et al.* (2018)**[26]	No
High position on the shore	2	Petraitis (1998)[27]; Tsuchiya (1987)			Yes
Predation	10	Bertolini *et al*. (2018)[25]; Bertolini *et al*. (2018)[26]; Brousscau *et al*.		Altieri and Witman (2006)[6]	No

[25] Mortality due to predation by the shore crab *Carcinus maenas*
[26] Mortality due to predation by the starfish *Asterias rubens*
[27] Mortality due to the predatory snail *Nucella lapillus*

		(2014)[28]; Brousscau *et al*. (2014)[28]; Christensen et al. (2012); Christensen et al. (2012); Dionne *et al*. (2006)[7]; Petraitis (1998)[27]; Waser *et al*. (2015)[25]			
Presence of the oyster *Crassostrea gigas*	1		**Waser *et al*. (2015)**[25]		NR
Farming / harvesting practices	**22**				
Geographic origin of the spat	7	Bernard *et al*. (2018a); Myrand and Gaudreault (1995); Mallet *et al.* (1987); Mallet *et al.* (1990)		Glize *et al*. (2017); Glize and Gourmelon (2018); SMIDAP (2016-2017)	No
Geographic origin of the spat: local. vs transplanted	7	SMIDAP (2016-2017)[29]		Glize *et al*. (2017)[29]; Penney *et al.* (2006); Mallet *et al*. (1987);	No

[28] Mortality due to predation by the Asian shore crab *Hemigrapsus sanguineus*
[29] Local origin with mortality events vs. transplanted origin without mortality events, France

				Mallet *et al*. (1990); Myrand and Gaudreault (1995) ; SMIDAP (2016)[29]; Stirling and Okumus (1994)	
Origin of the spat: use of mussels collected in suspended culture vs. mussels collected from natural bottom beds (for bottom culture production)	2		**Christensen *et al.* (2012)[25]**	**Christensen *et al.* (2012)**[25]	No
Depth of the farming structure: deep vs shallow	2		Myrand *et al*. (2000)[30]	Karayucel and Karayucel (2000)[31]	NR
Position inside the farming structure	1			Karayucel and Karayucel (2000)[32]	NR
High farming density	3	**Lauzon-Gay *et al.* (2005)**[33]		Lauzon-Gay *et al*. (2005); Lowen (2008)[34]	No

[30] Suspended cages at 16 m (open water) vs. 6 m depth (lagoon)
[31] Lantern nets at 6 m vs. 2 m depth
[32] Inflow or outflow of the raft
[33] 273 mussels/30 cm section of a sock, small sized mussels
[34] 30 mussels per cage (15 *M. edulis* and 15 *M. trossulus)*

Protective socking material	1	**Dionne et al. (2006)[7]**		NR
Thermal assay of spat (<10 mm) before field deployment	1	LeBlanc *et al*. (2008)[35]		NR
48H pre-transportation depuration vs. no depuration of the mussels,	1		Barrento and Powell (2016)[36]	NR
48H depuration pre-transportation vs. no depuration of the mussels, either with ice storage or at ambient temperature during transport	1		**Barrento and Powell (2016)**	NR
48H pre-transportation depuration + ice storage during transport vs. no depuration pre-transportation + storage at ambient temperature during transport	1	**Barrento and Powell (2016)[37]**		NR
Mixed mussel species	1	Lowen (2008)[38]		NR

[35] Elevated seawater temperature
[36] Mortality before transport
[37] Mortality during re-watering, after transport
[38] With *M. trossulus*

Anti-biofouling treatment with potassium monopersulfphonate triple salt	1		Paetzold and Davidson (2001)	NR
24H pre-transportation anti-biofouling treatment (vinegar, brine or lime), with or without seawater rinsing	1		Vickerson (2009)	NR
After transportation anti-biofouling treatment (vinegar, brine or lime)	1		Vickerson (2009)	NR
Contaminants from the terrestrial and marine environments	**3**			
Cd	1	**Ali and Taylor (2010)**[20]		NR
Zn	1	**Ali and Taylor (2010)**[20]		NR
Untreated municipal sewage	1	Akaishi *et al.* (2007)		NR
Diesel oil	1	Suni *et al.* (2007)		NR
Climate characteristics	**8**			

Season	3	Bernard *et al*. (2018a)[39]; Myrand *et al*. (2000)[40]		Mallet *et al.* (1987)	No
Elevated air temperature	4	Jones *et al*. (2009); Jones *et al*. (2010); Tsuchiya (1987)		Travers *et al.* (2016)	No
Increased number of thermal stresses	3	Jones *et al*. (2009); Jones *et al*. (2010)	**Peden *et al*. (2018)[41]**		No
Pluviometry	1			Travers *et al.* (2016)	NR

[39] France, spring (April-June) vs. other seasons
[40] Canada, summer (June-September) vs. other seasons
[41] From 20°C to 35°C; mussels collected from a heavily polluted area

Figure 1. PRISMA workflow diagram representing the study selection process.

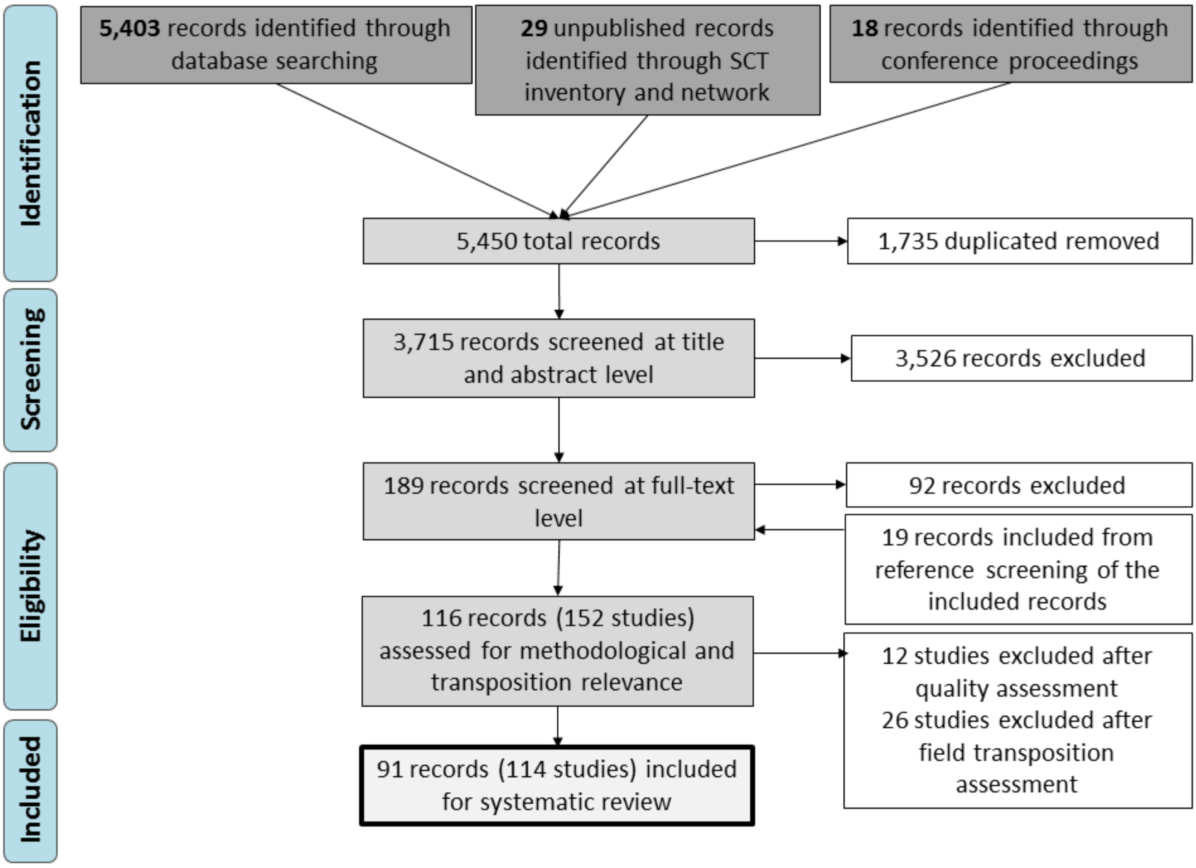


Figure 2. Yearly distribution of the number of studies on risk factors for mussel mortalities from 1980 to 2018, per mussel species (N = 114). The dotted black line separates included studies using the initial temporal inclusion criteria (i.e. published after 2006) from additional older studies.

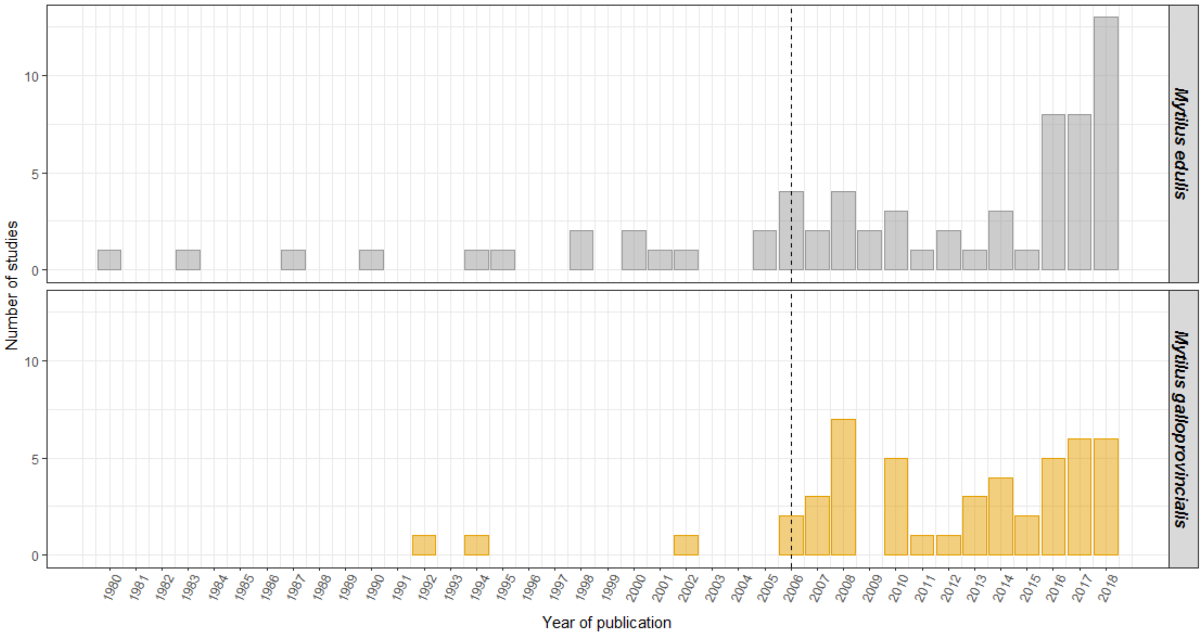
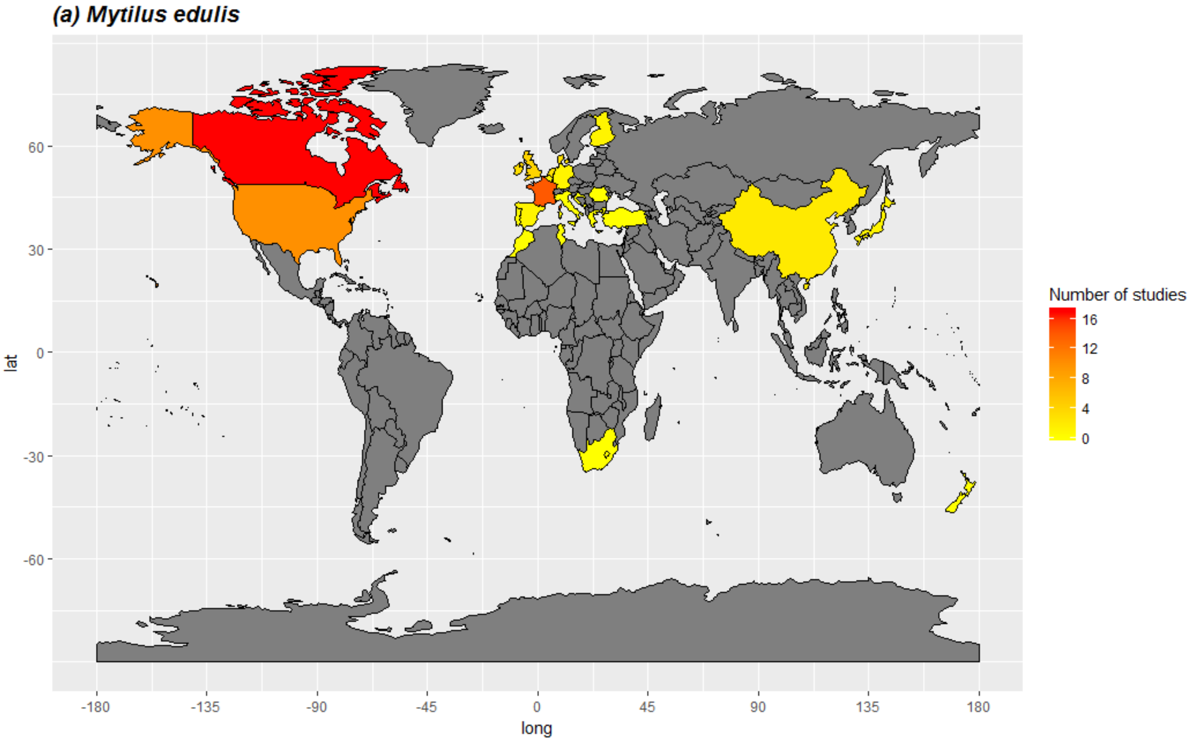


Figure 3. Geographical distribution of the included studies about (a) *Mytilus edulis* (N = 66), (b) *Mytilus galloprovincialis* (N = 48). Grey shading indicates countries without included research about mussel mortality risk factors. The other colours represent the number of studies for each country.



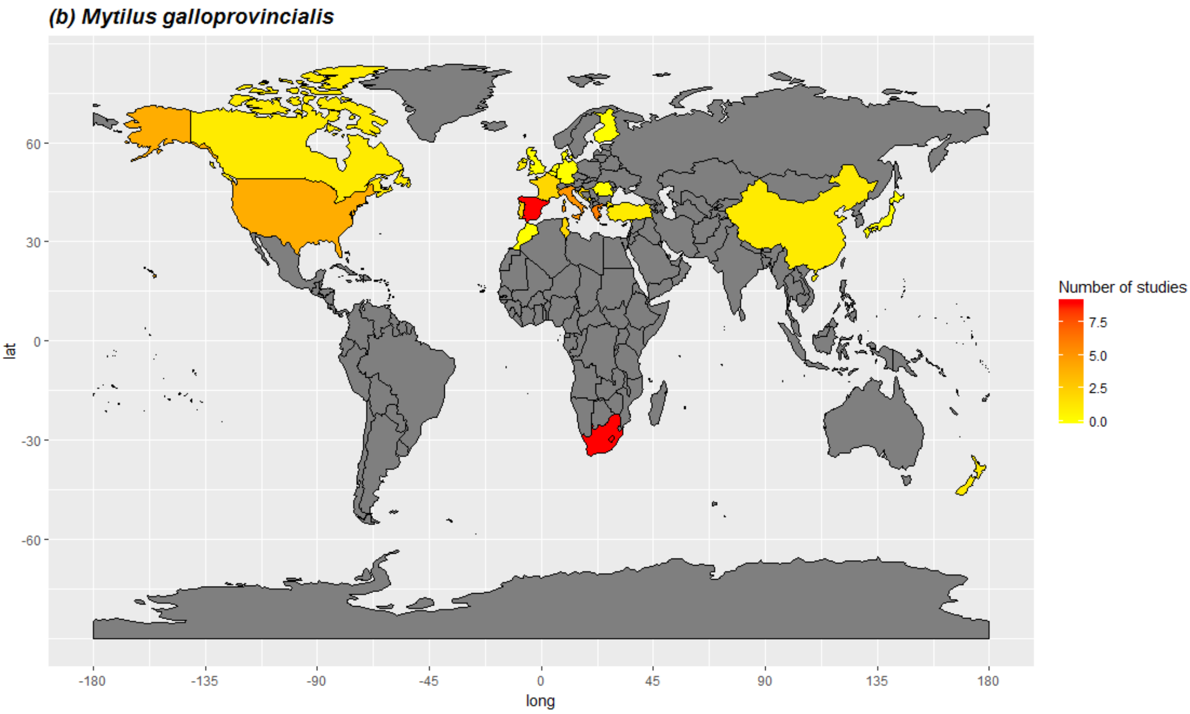


Figure 4. Graphical solution of the MCA on the first and second factorial axis, which explained respectively 15.5% and 12.5% of the total inertia of the 14 variables, for the 13 descriptive characteristics of N=114 studies related to risk factors of mussel mortality. Each variable is plotted on the graph according to the coordinates on factorial axis 1 (horizontal) and 2 (vertical).

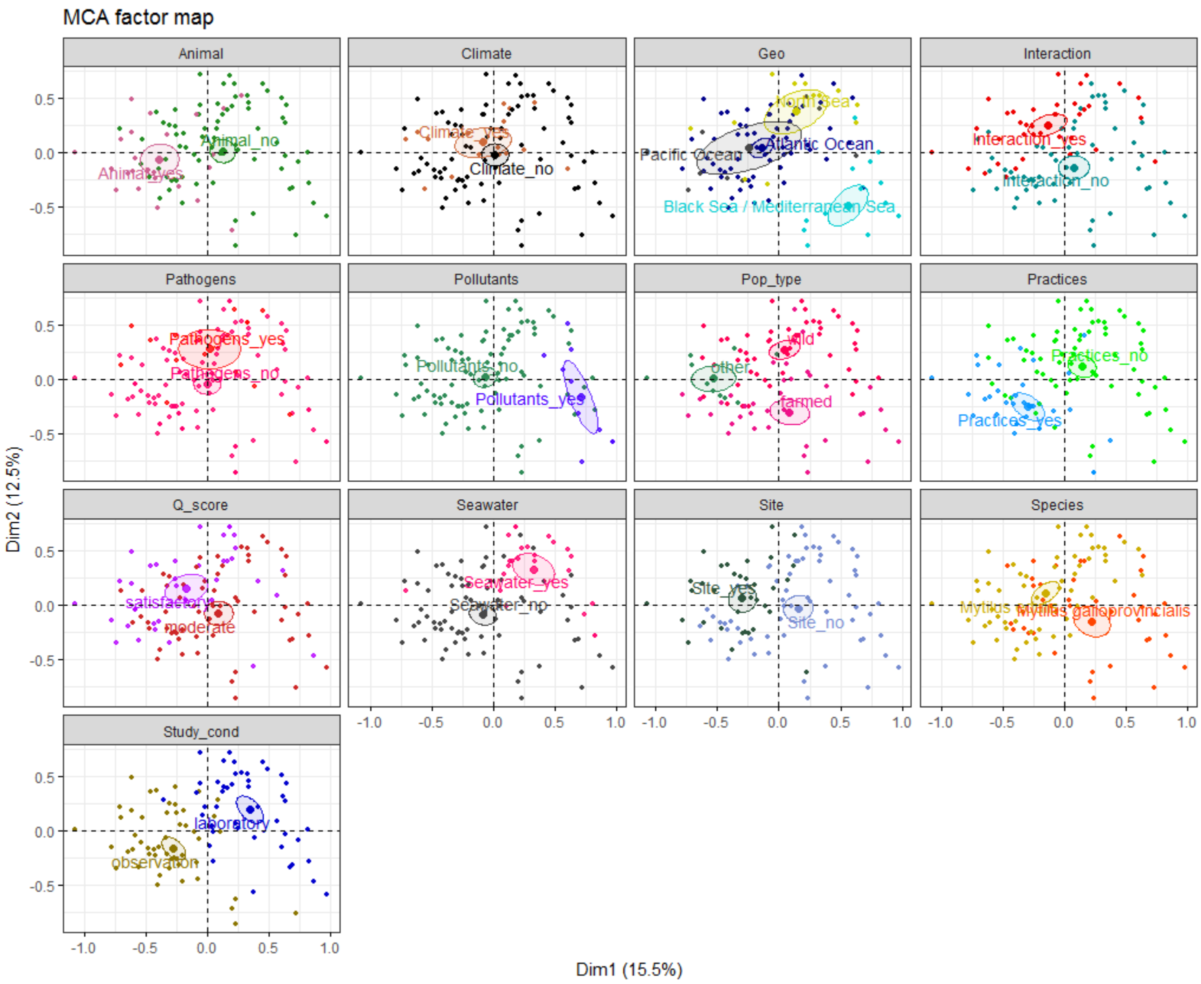


Figure 5. Number of studies investigating interactions between risk factor topics of mussel mortality by mussel species. The upper part of the matrix is for *M. edulis* and the lower part is for *M. galloprovincialis*, e.g. interactions between mussel and site characteristics were explored by 4 studies for *M. edulis* and 1 study for *M. galloprovincialis*.

M. edulis (columns); ***M. galloprovincialis*** (rows)

	Mussel	Site	Climate	Seawater	Pollutants	Pathogens	Practices
Mussel	0 / 2	4	0	0	0	1	3
Site	1	2 / 3	1	2	0	1	4
Climate	0	0	0 / 1	0	0	0	1
Seawater	0	0	0	1 / 3	1	0	0
Pollutants	0	0	0	0	0 / 0	0	0
Pathogens	1	1	0	1	0	0 / 0	0
Practices	0	1	0	1	0	1	0 / 1

Appendix I. Search equation used for searches in the Web of Science database.

Appendix II. Citations excluded at the full text examination step and reasons for their exclusion (N=117 citations).

Appendix III. Table synthetizing key results of the 114 studies included in the narrative synthesis.

Appendix IV. Graphical solution of the MCA on the first and second factorial axis, which explained respectively 15.5% and 12.5% of the total inertia of the 14 variables, for descriptive characteristics of 114 studies related to risk factors of mussel mortality. Each variable is plotted on the graph according to the coordinates on factorial axis 1 (horizontal) and 2 (vertical).

Appendix I. Search equation used for search in the Web of Science database

Request code	**Field**	**Request** (topic)
1.	Bivalves species	mussel* OR "Mytilus edulis" OR "M* edulis" OR "blue mussel*" OR "Mytilus galloprovincialis" OR "M* galloprovincialis "
2.	Mortality Disease Immunity	mortalit* OR "summer mortalit*" OR survival OR diseas* OR infection* OR illness OR epizoot* OR "health effect" OR immun* OR immunit* OR "immun* system*"
3.		1 AND 2
4.	Risk factor topics *Husbandry practices* *Animal* *Seawater characteristics* *Pollutants from terrestrial and marine environments* *Geographical characteristics* *Pathogens* *Larval recruitment*	"risk* factor*" OR stress OR factor* OR multifactor* OR husbandry OR management OR farming OR rearing OR "farm* practice*" OR "rear* practice*" OR aquaculture OR cultivation OR "shellfish* culture*" OR genetics* OR ploidy OR triploid* OR diploid* OR energetic OR physiol* OR age OR grow* OR weight OR length OR size OR environmental OR environment OR "environ* interact*" OR temperature OR salinity OR pH OR acidification OR pollut* OR *chemical* OR contaminant* OR "*water* qualit*" OR plan?ton OR sediment OR hydrodynamic* OR spatial OR temporal OR "marine current" OR "*water current" OR pathogen* OR virus OR parasite* OR bacteri* OR OsHV* OR "ostreid herpesvirus" OR herpes OR vibrio OR "v* aestuarianus" OR "v* splendidus" OR perkinsus OR Marteilia OR bonamia OR "v* tapetis" OR mi?rocytos OR recruitment OR settlement OR "larval abundance"
5.		3 AND 4
6.	Human foodborne pathogens	norovirus OR "vibrio parahaemolyticus" OR "vibrio vulnificus" OR "vibrio cholerae"
7.		5 NOT 6
8.	Time period	2006-2017
9.		7 AND 9

Appendix II. Citations excluded at the full text examination step and reasons for their exclusion (N=117 citations)

Citation	**Reason(s) for exclusion**
Arzul, I., Chollet, B., *et al.* (2017). Suspicion of infection with *Marteilia refringens* in mussels from Norway. *Institute of Marine Research, Po Box 1870, NORDES 517 Bergen, Norway,* Ref. Ifremer LGPMM/PAT/EURL/DS/BC/IA 17-032, 2 p.	Full text not available
Avelelas, F., R. Martins, *et al*. (2017). Efficacy and Ecotoxicity of Novel Anti-Fouling Nanomaterials in Target and Non-Target Marine Species. *Marine Biotechnology* **19**(2): 164-174.	Low field transposition score
Ayad, M. A., M. A. Fdil, *et al*. (2011). Effects of Cypermethrin (Pyrethroid Insecticide) on the Valve Activity Behavior, Byssal Thread Formation, and Survival in Air of the Marine Mussel *Mytilus galloprovincialis*. *Archives of Environmental Contamination and Toxicology* **60**(3): 462-470.	Low field transposition score
Babarro, J. M. F., Labarta, U., *et al.* (2007). Energy metabolism and performance of *Mytilus galloprovincialis* under anaerobiosis. *Journal of the Marine Biological Association of the United Kingdom* **87**(4): 941-946.	Exposure: risk factors for mortality not examined
Banni, M., Sforzini, S., *et al.* (2017). Assessing the impact of Benzo[a]pyrene on Marine Mussels: Application of a novel targeted low density microarray complementing classical biomarker responses. *Plos One* **12**(6).	Outcome : mortality risk is not the focus
Basti, L., Endo, M., *et al.* (2010). Histopathological effects of the toxic dinoflagellate *Heterocapsa circularisquama* on short-neck clam *Ruditapes philippinarum* and blue mussel *Mytilus galloprovincialis*. *Aquaculture*, San Diego, California, USA.	Exposure: risk factors for mortality not examined
Basti, L., Endo, M., *et al.* (2013). Sequencing of organ damage in the Mediterranean mussel *Mytilus galloprovincialis* following exposure to the harmful alga *Heterocapsa circularisquama*. *Aquaculture*, Nashville, Tennessee, USA.	Outcome : mortality risk is not the focus
Bat, L., F. Uestuen, *et al*. (2013). Effects of some heavy metals on the sizes of the mediterranean mussel *Mytilus galloprovincialis* Lamarck, 1819. *Fresenius Environmental Bulletin* **22**(7): 1933- 1938.	Low field transposition score (2 studies)
Benabdelmouna, A., Garcia, C., Ledu, C., Lamy, P., Maurouard, E., Degremont, L. (2018). Mortality investigation of *Mytilus edulis* and *Mytilus galloprovincialis* in France: An experimental survey under laboratory conditions. *Aquaculture* **495**, 831-841.	Low quality score to identify risk factors (1 study)
Benabdelmouna, A., Saunier, A., *et al.* (2018). Genomic abnormalities affecting mussels (*Mytilus edulis-galloprovincialis*) in France are related to ongoing neoplastic processes, evidenced by dual flow cytometry and cell monolayer analyses. *Journal of Invertebrate Pathology* **157**: 45-52.	Outcome : mortality risk is not the focus
Bernard, I. and Charles, M. (2017). Investigation on blue mussel high mortality in France: a phenomenon with high spatio-temporal variability but no conclusive cause. *2nd International Symposium on the Advances in Marine Mussel Research*, Sète, France.	Duplicate not detected at the title and abstract step
Bernard, I., Allain, G. (2016). Les mortalités de moules en 2014 et 2015 vues par les professionnels - Compte-rendu de la phase 1 : synthèse sur l'émergence, la propagation et l'installation des mortalités. Rapport technique CRC Bretagne Nord, 28 p.	Low quality score to identify risk factors
Bihari, N., Fafandel, M., Piskur, V. (2007). Polycyclic aromatic hydrocarbons and ecotoxicological characterization of seawater, sediment, and mussel *Mytilus galloprovincialis* from the Gulf of Rijeka, the Adriatic Sea, Croatia. *Archives of Environmental Contamination and Toxicology* **52**, 379-387.	- Low quality score to identify risk factors - Low field transposition score
Bodkin, J. L., Coletti, H. A., *et al.* (2018). Variation in abundance of Pacific Blue Mussel (*Mytilus trossulus*) in the Northern Gulf of Alaska, 2006-2015. *Deep-Sea Research Part II-Topical Studies in Oceanography* **147**: 87-97.	Outcome : mortality risk is not the focus
Bownes, S. J. and McQuaid, C. D. (2009). Mechanisms of habitat segregation between an invasive and an indigenous mussel: settlement, post-settlement mortality and recruitment. *Marine Biology* **156**(5): 991-1006.	Exposure: risk factors for mortality not examined
Brenner, M., K. Broeg, *et al*. (2012). Effect of air exposure on lysosomal tissues of *Mytilus edulis* L. from natural intertidal wild beds and submerged culture ropes. *Comparative Biochemistry and Physiology a-Molecular & Integrative Physiology* **161**(3): 327-336.	Low field transposition score

Bullard, S., Whithlatch, R., *et al.* (2006). Impacts of the colonial ascidian *didemnum* sp. on mussels, oysters and scallops. *98th Annual meeting of the National Shellfisheries Association*, Monterey, California USA.	Exposure: risk factors for mortality not examined
Bulleri, F., Airoldi, L., *et al.* (2006). Positive effects of the introduced green alga, *Codium fragile* ssp tomentosoides, on recruitment and survival of mussels. *Marine Biology* **148**(6): 1213-1220.	Outcome : mussel mortality is not the focus
Burgos-Aceves, M. A. and Faggio, C. (2017). An approach to the study of the immunity functions of bivalve haemocytes: Physiology and molecular aspects. *Fish & Shellfish Immunology* **67**: 513-517.	- Study type : review study - Outcome : mortality risk is not the focus
Burioli, E. A. V. (2017). First description of disseminated neoplasia in *Mytilus edulis* in Northern Brittany (France) and development of a rapid diagnostic tool. *2nd International Symposium on the Advances in Marine Mussel Research*, Sète, France.	Exposure: risk factors for mortality not examined
Calderwood, J., O'Connor, N. E., *et al.* (2014). Determining optimal duration of seed translocation periods for benthic mussel (*Mytilus edulis*) cultivation using physiological and behavioural measures of stress. *Aquaculture* **434**: 288-295.	Outcome : mortality risk is not the focus
Capelle, J. J., van Stralen, M. R., *et al.* (2017). Population dynamics of subtidal blue mussels *Mytilus edulis* and the impact of cultivation. *Aquaculture Environment Interactions* **9**: 155-168.	Outcome : mortality risk is not the focus
Capelle, J. J., Wijsman, J. W. M., *et al.* (2014). Spatial organisation and biomass development after relaying of mussel seed. *Journal of Sea Research* **85**: 395-403.	Outcome : mortality risk is not the focus
Capelle, J. J., Wijsman, J. W. M., *et al.* (2016). Effect of seeding density on biomass production in mussel bottom culture. *Journal of Sea Research* **110**: 8-15.	Outcome : mortality risk is not the focus
Capelle, J., Wisjman, J., *et al.* (2012). The effect of spatial heterogeneity in mussel density on the productivity of a commercial mussel bed. *104th Annual meeting of the National Shellfisheries Association*, Seattle, Whashington, USA.	Duplicate not detected at the title and abstract step
Charles, M. (en cours : 2016-2019). Surmortalités des moules (*Mytilus edulis* et *Mytilus galloprovincialis*). Etude des pathogènes et des composés chimiques qui peuvent influencer l'état physiologique des moules.	Full text not available: ongoing PhD
Christensen, H. T., Dolmer, P., *et al.* (2015). Aggregation and attachment responses of blue mussels, *Mytilus edulis*-impact of substrate composition, time scale and source of mussel seed. *Aquaculture* **435**: 245-251.	Outcome : mortality risk is not the focus
Coppola, F., A. Almeida, *et al*. (2017). Biochemical impacts of Hg in *Mytilus galloprovincialis* under present and predicted warming scenarios. *Science of the Total Environment* **601**: 1129-1138.	Low field transposition score
Coray, C. (2007). Assessing the health of Halifax Harbour's intertidal ecosystem: Impacts of marine pollution on community structure, reproductive health of key predator populations (*Nucella lapillus*), and immunomodulation in blue mussels (*Mytilus edulis* and *Mytilus trossulus*). *Masters Abstracts International*. **Vol. 45, no. 05:** 143.	Full text not available
CREOCEAN (2014). Etude sur l'origine des mortalités de moules sur le secteur d'élevage de Oye-Plage et Marck. Rapport technique CRC Normandie-Mer du Nord, 125 p.	Low quality score to identify risk factors
de los Rios, A., Perez, L., *et al.* (2016). Measuring biological responses at different levels of organisation to assess the effects of diffuse contamination derived from harbour and industrial activities in estuarine areas. *Marine Pollution Bulletin* **103**(1-2): 301-312.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Deruytter, D., Vandegehuchte, M. B., *et al.* (2017). Salinity, Dissolved Organic Carbon, and Interpopulation Variability Hardly Influence the Accumulation and Effect of Copper in *Mytilus edulis*. *Environmental Toxicology and Chemistry* **36**(8): 2074-2082.	Outcome : mortality risk is not the focus
Domeneghetti, S., Varotto, L., *et al.* (2014). Mortality occurrence and pathogen detection in *Crassostrea gigas* and *Mytilus galloprovincialis* close-growing in shallow waters (Goro lagoon, Italy). *Fish & Shellfish Immunology* **41**(1): 37-44.	- Exposure: risk factors for mortality not examined - Study type : descriptive study
Drapeau, A., Comeau, L. A., *et al.* (2007). The effect of sock spacing on the productivity of mussel on a longline system. *Canadian technical report of fisheries and aquatic sciences*. **2685:** 22.	Outcome : mortality risk is not the focus
Eggermont, M., Tamanji, A., *et al.* (2014). Isolation of blue mussel *Mytilus edulis* pathogenic Vibrios from wildcaught adults. *European Aquaculture Society conference*, Donostia-San Sebastian, Spain.	Duplicate not detected at the title and abstract step
Fafandel, M. and Bihari, N. (2007). PAH content and toxicity of sediment, seawater and mussel tissue in Gulf of Rijeka. *CIESM Congress Proceedings,*	Outcome : mortality risk is not the focus

Rapp. Comm. int. Mer Médit.	
Faria, M., Soares, A. M. V. M., *et al.* (2018). Effects of Camellia sinensis crude saponin on survival and biochemical markers of oxidative stress and multixenobiotic resistance of the Mediterranean mussel, *Mytilus galloprovincialis*. *Science of the Total Environment* **625**: 1467-1475.	Full text not available
Galinou-Mitsoudi, S., Savvidis, Y., *et al.* (2006). Interaction between mussel culture and hydrodynamics: a preliminary study in the gulfs of Thessaloniki and Thermaikos, Greece. *Journal of Biological Research-Thessaloniki* **6**: 139-145.	Exposure: risk factors for mortality not examined
Garcia, C., Osta Amigo, A., *et al.* (2016). Mortality of mussels in France. *Annual Meeting of the National Reference Laboratories for Mollusc Diseases*, Nantes, France.	Duplicate not detected at the title and abstract step
Garcia, C., Osta Amigo, A., *et al.* (2016). Mortality of mussels in France. *Annual Meeting of the National Reference Laboratories for Mollusc Diseases*, Nantes, France.	Exposure: risk factors for mortality not examined
Garcia, C., Ropert, M., *et al.* (2017). Atypical Marteilia refringens infection in mussels in Normandy, France. *Annual Meeting & Technical Workshop of NRLs for Mollusc diseases*, Oranmore, Ireland.	Exposure: risk factors for mortality not examined
Garner, Y. L. and Litvaitis, M. K. (2013). Effects of wave exposure, temperature and epibiont fouling on byssal thread production and growth in the blue mussel, *Mytilus edulis,* in the Gulf of Maine. *Journal of Experimental Marine Biology and Ecology* **446**: 52-56.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Glize, P., Tetard, X., *et al.* (2010). Elevage conchylicole au large en Baie de Bourgneuf : Approche zootechnique et cartographique. SMIDAP. 122 pp.	Outcome : mortality risk is not the focus
Goedknegt, M. A., Bedolfe, S., *et al.* (2018). Impact of the invasive parasitic copepod *Mytilicola orientalis* on native blue mussels *Mytilus edulis* in the western European Wadden Sea. *Marine Biology Research* **14**(5): 497-507.	Outcome : mortality risk is not the focus
Gombac, I., Fonda, I., *et al.* (2011). Prevalent diseases and pathogens of Slovene cultured mediterranean mussels (*Mytilus galloprovincialis*). *Slovenian Veterinary Research Volume* **48**(SUPPL.13): 98-100.	Document in Slovenian
Gombac, M. and Jencic, V. (2010). Protozoan infestation dynamics and occurrence of neoplasias in digestive gland of Mediterranean mussels (*Mytilus galloprovincialis*) in the Slovene sea in correlation with sea temperature, salinity and oxygenation. *Annual Meeting of the National Reference Laboratories for Mollusc Diseases*, Nantes, France.	Outcome : mortality risk is not the focus
Guesdon, S., Travers, M. A., *et al.* (2017). Microbial balance, and triggering of recent mussel mortality events in France: is there a link? *2nd International Symposium on the Advances in Marine Mussel Research*, Sète, France.	Duplicate not detected at the title and abstract step
Gulshad, M. (2003). Alagal bloom and mass mortality of fishes and mussels along Kozhikode coast. *Marine Fisheries Information Service, Technical and extension series*. Cochin, India, Central Marine Fisheries Research Institute, Indian Council of Agricultural Research. **175**.	Publication date <2006 (error in the database)
Hamer, B., Z. Jaksic, *et al*. (2008). Effect of hypoosmotic stress by low salinity acclimation of Mediterranean mussels *Mytilus galloprovincialis* on biological parameters used for pollution assessment. *Aquatic Toxicology* **89**(3): 137-151.	Low field transposition score (1 study)
Hanna, S. K., R. J. Miller, *et al*. (2013). Impact of Engineered Zinc Oxide Nanoparticles on the Individual Performance of *Mytilus galloprovincialis*. *Plos One* **8**(4).	Low field transposition score
Hernroth, B. E. and Baden, S. P. (2018). Alteration of host-pathogen interactions in the wake of climate change - Increasing risk for shellfish associated infections? *Environ Res* **161**: 425-438.	Study type : review study
Hopkins, G. A., M. Prince, *et al*. (2016). Desiccation as a mitigation tool to manage biofouling risks: trials on temperate taxa to elucidate factors influencing mortality rates. *Biofouling* **32**(1): 1-11.	Low field transposition score (1 study)
Ifremer-LERN (2017-2019). Programmation du Centre de Référence de l'Huître - Moules 2017.	Full text not available
Jones, S. J. and Wethey, D. S. (2010). Mussels, models, and mortality: exploring the respective roles of air and seawater temperatures in the southern range limit contraction of *Mytilus edulis*. *Integrative and Comparative Biology* **50**: E85-E85.	Duplicate not detected at the title and abstract step
Jones, S.J., Mieszkowska, N., Wethey, D.S. (2009). Linking Thermal Tolerances and Biogeography: *Mytilus edulis* (L.) at its Southern Limit on the East Coast of the United States. *Biological Bulletin* 217, 73-85.	Low quality score to identify risk factors (1 study)
Karagiannis, D., I. N. Vatsos, *et al*. (2011). Effects of atrazine on the viability and the formation of byssus of the mussel *Mytilus galloprovincialis*. *Aquaculture*	Low field transposition score (2 studies)

International **19**(1): 103-110.	
Karayucel, S., Celik, M. Y.*, et al.* (2015). Effects of stocking density on survival, growth and biochemical composition of cultured mussels *(Mytilus galloprovincialis*, Lamarck 1819) from an offshore submerged longline system. *Aquaculture Research* **46**(6): 1369-1383.	Outcome : mortality risk is not the focus
Khalaman, V. V. and Komendantov, A. Y. (2007). Mutual effects of several fouling organisms of the white sea (*Mytilus edulis, Styela rustica*, and *Hiatella arctica*) on their growth rate and survival. *Russian Journal of Marine Biology* **33**(3): 139-144.	Exposure: risk factors for mortality not examined
Kock, M., Farre, M.*, et al.* (2010). Integrated ecotoxicological and chemical approach for the assessment of pesticide pollution in the Ebro River delta (Spain). *Journal of Hydrology* **383**(1-2): 73-82.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Kristensen, P.S., Lassen, H. (1997). The production of relaid blue mussels (*Mytilus edulis* L.) in a Danish fjord. *Ices Journal of Marine Science* **54**, 854-865.	Low quality score to identify risk factors
LeBlanc, N. (2006). Mussel genetics in relation to selection methods for high quality seed and treatment for tunicates. *Dissertation Abstracts International* **68**: 169.	Full text not available
Leblanc, N., Davidson, J.*, et al.* (2006). The effects of anti-fouling treatments for *Styela clava* on long-line cultured *Mytilus edulis* in Prince Edwards Island, Canada. *98th Annual meeting of the National Shellfisheries Association*. Monterey, California, USA.	Duplicate not detected at the title and abstract step
LeBlanc, N., Davidson, J.*, et al.* (2006). The effects of anti-fouling treatments for *Styela clava* on long-line cultured *Mytilus edulis* in Prince Edward Island, Canada. *Journal of Shellfish Research* **25**(2): 748.	Outcome : mortality risk is not the focus
LeBlanc, N., Davidson, J.*, et al.* (2007). The effect of anti-fouling treatments for the clubbed tunicate on the blue mussel*, Mytilus edulis*. *Aquaculture* **264**(1-4): 205-213.	Outcome : mortality risk is not the focus
LeBlanc, N., Landry, T., Davidson, J., Tremblay, R., McNiven, M. (2010). The effect of elevated water temperature stress on the mussel *Mytilus edulis* (L.), survival and genetic characteristics*. Canadian Technical Report of Fisheries and Aquatic Sciences* 2900. 19 p.	Low quality score to identify risk factors (1 study)
Lupo, C. and Prou, J. (2016). Enhanced surveillance of mussel mortality to improve early detection and investigation of outbreaks of infectious diseases. *Annual Meeting of the National Reference Laboratories for Mollusc Diseases*, Nantes, France.	Duplicate not detected at the title and abstract step
Lupo, C. and Prou, J. (2016). Enhanced surveillance of shellfish mortality to improve early detection and investigation of outbreaks of exotic or emerging infectious diseases: An example of a mass mortality outbreak of mussels, France 2014. *Preventive Veterinary Medicine* **132**: 57-66.	Exposure: risk factors for mortality not examined
Maar, M., Timmermann, K.*, et al.* (2010). A model study of the regulation of blue mussels by nutrient loadings and water column stability in a shallow estuary, the Limfjorden. *Journal of Sea Research* **64**(3): 322-333.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Marcheselli, M., C. Rustichelli, *et al*. (2010). Novel Antifouling Agent Zinc Pyrithione: Determination, Acute Toxicity, and Bioaccumulation in Marine Mussels (*Mytilus Galloprovincialis*). *Environmental Toxicology and Chemistry* **29**(11): 2583-2592.	Low field transposition score (2 studies)
Marigomez, I., Mugica, M.*, et al.* (2017). Chronic environmental stress enhances tolerance to seasonal gradual warming in marine mussels. *Plos One* **12**(3).	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Marin, M. G., Boscolo, R.*, et al.* (2006). Field validation of autometallographical black silver deposit (BSD) extent in three bivalve species from the Lagoon of Venice, Italy (*Mytilus galloprovincialis, Tapes philippinarum, Scapharca inaequivalvis*) for metal bioavailability assessment. *Sci Total Environ* **371**(1-3): 156-167.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Matozzo, V., Ercolini, C.*, et al.* (2018). Assessing the health status of farmed mussels (*Mytilus galloprovincialis*) through histological, microbiological and biomarker analyses. *Journal of Invertebrate Pathology* **153**: 165-179.	Outcome : mortality risk is not the focus
Matozzo, V., Fabrello, J.*, et al.* (2018). Ecotoxicological risk assessment for the herbicide glyphosate to non-target aquatic species: A case study with the mussel *Mytilus galloprovincialis*. *Environmental Pollution* **233**: 623-632.	Outcome : mortality risk is not the focus
Meneghetti, F., Moschino, V.*, et al.* (2006). Interaction between mussels	Full text not available

(Mytilus galloprovincialis Lmk) and habitat in an experimental area of the North Adriatic Sea: evaluation of biological responses. *Biologia marina mediterranea*: 703-706.	
Mesas, A. and Tarifeno, E. (2015). Upper lethal temperatures for the mussel *Mytilus galloprovincialis* (Lamarck, 1819), in central coast of Chile. *Latin American Journal of Aquatic Research* **43**(3): 473-483.	Document in Spanish
Mezzelani, M., Gorbi, S.*, et al.* (2018). Long-term exposure of *Mytilus galloprovincialis* to diclofenac, Ibuprofen and Ketoprofen: Insights into bioavailability, biomarkers and transcriptomic changes. *Chemosphere* **198**: 238-248.	Outcome : mortality risk is not the focus
Michaelidis, B., Portner, H. O.*, et al.* (2014). Advances in predicting the impacts of global warming on the mussels *Mytilus galloprovincialis* in the mediterranean sea. *The Mediterranean Sea: Its history and present challenges*. S. Goffredo and Z. Dubinsky (eds.), Springer Science+Business Media Dordrecht**:** 319-339.	Study type : review study
Moreira, R., Balseiro, P.*, et al.* (2018). Bivalve transcriptomics reveal pathogen sequences and a powerful immune response of the Mediterranean mussel (*Mytilus galloprovincialis*). *Marine Biology* **165**(4).	Outcome : mortality risk is not the focus
Morello, S. L. and Etter, R. J. (2017). Estimating the impact of consumers in ecological communities: Manual removals identify the complex role of individual consumers in the Gulf of Maine. *Journal of Experimental Marine Biology and Ecology* **495**: 89-102.	Outcome : mortality risk is not the focus
Morello, S. L. and Etter, R. J. (2018). Transition probabilities help identify putative drivers of community change in complex systems. *Ecology* **99**(6): 1357-1369.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Mortensen, S. (2018). Marteilia case in Scandinavia. *Annual Meeting of the National Reference Laboratories for Mollusc Diseases*. La Rochelle, France.	Outcome : mortality risk is not the focus
Moschino, V., E. Delaney, *et al*. (2011). Biomonitoring approach with mussel *Mytilus galloprovincialis* (Lmk) and clam *Ruditapes philippinarum* (Adams and Reeve, 1850) in the Lagoon of Venice. *Environmental Monitoring and Assessment* **177**(1-4): 649-663.	Low field transposition score
Motta, C. M., Tizzano, M.*, et al.* (2018). Biocide triclosan impairs byssus formation in marine mussels *Mytilus galloprovincialis*. *Environmental Pollution* **241**: 388-396.	Outcome : mortality risk is not the focus
Muller, E. B., Hanna, S. K.*, et al.* (2014). Impact of engineered zinc oxide nanoparticles on the energy budgets of *Mytilus galloprovincialis*. *Journal of Sea Research* **94**: 29-36.	Outcome : mortality risk is not the focus
Nesto, N., Romano, S.*, et al.* (2007). Bioaccumulation and biomarker responses of trace metals and micro-organic pollutants in mussels and fish from the Lagoon of Venice, Italy. *Marine Pollution Bulletin* **55**(10-12): 469-484.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined *3*
Nikiforov, S. M. and Zvyagintsev, A. Y. (2008). Allozyme diversity among local populations of the pacific mussel *Mytilus trossulus* (Bivalvia : Mytilidae) from polluted areas of Peter the Great Bay (Sea of Japan). *Russian Journal of Marine Biology* **34**(1): 45-50.	Outcome : mortality risk is not the focus
Nikolova, G., Karamalakova, Y.*, et al.* (2018). Comparative analysis of real-time oxidative stress biomarkers measured in mussels (*Mytilus galloprovincialis*) and veined rapa whelks (*Rapana venosa*) in relation to two seasons - An electron paramagnetic resonance study. *Bulgarian Chemical Communications* **50**(Special Issue C): 58-63.	Outcome : mortality risk is not the focus
O'Connor, N. E., Crowe, T. P.*, et al.* (2006). Effects of epibiotic algae on the survival, biomass and recruitment of mussels, *Mytilus* L. (Bivalvia : Mollusca). *Journal of Experimental Marine Biology and Ecology* **328**(2): 265-276.	Outcome : mortality risk is not the focus
Oden, E., E. A. V. Burioli, *et al*. (2016). Multilocus sequence analysis of *Vibrio splendidus* related-strains isolated from blue mussel *Mytilus* sp during mortality events. *Aquaculture* **464**: 420-427.	Low field transposition score
Passarelli, M. C., I. Riba, *et al*. (2018). What is the best endpoint for assessing environmental risk associated with acidification caused by CO2 enrichment using mussels? *Marine Pollution Bulletin* **128**: 379-389.	Low field transposition score
Peperzak, L. and Poelman, M. (2008). Mass mussel mortality in The Netherlands after a bloom of *Phaeocystis globosa* (prymnesiophyceae). *Journal of Sea Research* **60**(3): 220-222.	Exposure: risk factors for mortality not examined
Pépin, J. F., A. Benabdelmouna, *et al*. (2018). Mortalités de moules bleues dans les secteurs mytilicoles : description et facteurs liés -MORBLEU-,	Low field transposition score (1 study)

R.INT.RBE/SG2M-LGPMM. .	
Pépin, J.F., Benabdelmouna, A., Bierne, N., Bouget, J.F., Chabirand, J.M., Costes, L., Dégremont, Garcia, C., Génauzeau, S., Geairon, P., Grizon, J., Guesdon, S., Lamy, J.-B., Ledu, C., Le Jolivet, A., Le Moine, O., Le Noc, S., Morga, B., Normand, J., Palvadeau, H., Polsenaere, P., Robert, S., Saunier, A., Schmitt, A., Seugnet, J.L., Tourbiez, D., Travers, M.A. (2017). Mortalités de moules bleues dans les secteurs mytilicoles charentais et vendéens : description et facteurs liés -MORBLEU-. R.INT.RBE/SG2M-LGPMM. https://archimer.ifremer.fr/doc/00391/50288/	Low quality score to identify risk factors (1 study)
Petes, L. E. (2007). Effects of environmental stress on intertidal mussel reproduction. *Dissertation Abstracts International* **68**(no. 06, suppl. B): 196.	Duplicate not detected at the title and abstract step
Petes, L. E., Menge, B. A., *et al.* (2007). Environmental stress decreases survival, growth, and reproduction in New Zealand mussels. *Journal of Experimental Marine Biology and Ecology* **351**(1-2): 83-91.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Polsenaere, P., Soletchnik, P., *et al.* (2017). Potential environmental drivers of a regional blue mussel mass mortality event (winter of 2014, Breton Sound, France). *Journal of Sea Research* **123**: 39-50.	Exposure: risk factors for mortality not examined
Quaglio, F., Quaglieri, E., *et al.* (2017). Histological and microbiological investigations in farmed mussels (*Mytilus galloprovincialis*) of La Spezia Gulf, Italy to evaluate health status. *18th International Conference on Diseases of Fish and Shellfish*, Belfast, United-Kingdom.	Outcome : mortality risk is not the focus
Renault, T. (2011). BIVALIFE, a FP7 project focusing on the management of infectious diseases affecting oysters and mussels. *Annual Meeting of the National Reference Laboratories for Mollusc Diseases*, La Rochelle, France.	Duplicate not detected at the title and abstract step
Renault, T. (2014). BIVALIFE - Controlling infectious diseases in oysters and mussels in Europe - Periodic Report. 266157_BIVALIFE_Periodic_Report-12_20140428_192012_CET.	Low quality score to identify risk factors (2 studies)
Rius, M. and McQuaid, C. D. (2006). Wave action and competitive interaction between the invasive mussel *Mytilus galloprovincialis* and the indigenous *Perna perna* in South Africa. *Marine Biology* **150**(1): 69-78.	Exposure: risk factors for mortality not examined
Romero, A., M. D. Costa, *et al.* (2014). Occurrence, seasonality and infectivity of Vibrio strains in natural populations of mussels *Mytilus galloprovincialis*. *Diseases of Aquatic Organisms* **108**(2): 149-163.	Low field transposition score (2 studies)
Rosioru, D. M. (2014). Ecological resilience of *Mytilus galloprovincialis* from the Romanian Black Sea coast at environmental variations. *Journal of Environmental Protection and Ecology* **15**(3): 924-932.	Low field transposition score (2 studies)
Rowley, A. F., Cross, M. E., *et al.* (2014). The potential impact of climate change on the infectious diseases of commercially important shellfish populations in the Irish Sea-a review. *Ices Journal of Marine Science* **71**(4): 741-759.	- Study type : review study - Outcome : mortality risk is not the focus
Ruellet, T., Meirland, A. (2010). Evaluation des pertes mytilicoles du secteur de Quend-Plage les Pins et de Saint-Quentin-en-Tourmont au cours du mois de mai 2010. Saint Valery sur Somme, GEMEL, 8 p.	Low quality score to identify risk factors
Sandee, S. D., Van Hamme, J. D., *et al.* (2016). Testing microbial pathogens as a cause of early juvenile mortality in wild populations of benthic invertebrates. *Marine Ecology Progress Series* **562**: 53-63.	Population : larvae stage studied
Schneider, K.R., Van Thiel, L.E., Helmuth, B. (2010). Interactive effects of food availability and aerial body temperature on the survival of two intertidal *Mytilus* species. *Journal of Thermal Biology* **35**, 161-166.	Low quality score to identify risk factors
Scro, A. K., Materna, C., *et al.* (2016). The occurrence and severity of disease in populations of blue mussels, *Mytilus edulis*, in Rhode Island coastal waters. *Aquaculture*, Las Vegas, Nevada, USA.	Absence of result in this conference proceedings
Serracca, L., Prearo, M., *et al.* (2014). Four-Year Surveillance of *Marteilia refringens* in Shellfish Farms in the Gulf of La Spezia (Liguria, Italy). *Turkish Journal of Fisheries and Aquatic Sciences* **14**(4): 893-896.	Outcome : mortality risk is not the focus
Sforzini, S., Oliveri, C., *et al.* (2018). Application of a new targeted low density microarray and conventional biomarkers to evaluate the health status of marine mussels: A field study in Sardinian coast, Italy. *Science of the Total Environment* **628-629**: 319-328.	Outcome : mortality risk is not the focus
SMEL-LABEO (2016). Programme CACHEMYRE. CRC Normandie-Mer du Nord.	Outcome : mortality risk is not the focus
SMIDAP (2017). Programme CAPEMOULES 2 Bis. SMIDAP & CRC Pays de la Loire.	Duplicate not detected at the title and abstract step

Soletchnik, P. and Robert, S. (2016). Eléments de connaissance sur la mortalité et la reproduction de la moule bleue (*Mytilus edulis*) sur la façade atlantique, RST/ ODE / LER / LERPC – juillet 2016. https://archimer.ifremer.fr/doc/00345/45634/	Exposure: risk factors for mortality not examined
Steeves, L. E., Filgueira, R. n.*, et al.* (2018). Past, Present, and Future: Performance of Two Bivalve Species Under Changing Environmental Conditions. *Frontiers in Marine Science* **5**(184).	Outcome : mortality risk is not the focus
Sundt, R. C., Pampanin, D. M.*, et al.* (2006). The BEEP Stavanger Workshop: Mesocosm exposures. *Aquatic Toxicology* **78**: S5-S12.	- Outcome : mortality risk is not the focus - Exposure: risk factors for mortality not examined
Theodorou, J. A., Tzovenis, I.*, et al.* (2015). Risk analysis of the Mediterranean mussel farming in Greece. *European Aquaculture Society Conference*, Rotterdam, The Netherlands.	Full text not available
Travers, M.-A., B. Morga, *et al*. (2015). Pathogens detected during mortality events of mussels in France in 2014. *Annual meeting of NRLs for Mollusc diseases and the technical workshop*, Saintes, France.	Low field transposition score
Travers, M.-A., Morga, B.*, et al.* (2015). Pathogens detected during mortality events of mussels in France in 2014. *Annual meeting of NRLs for Mollusc diseases and the technical workshop*, Saintes, France.	Duplicate not detected at the title and abstract step
Vlahogianni, T. H. and A. Valavanidis (2007). Heavy-metal effects on lipid peroxidation and antioxidant defence enzymes in mussels *Mytilus galloprovincialis*. *Chemistry and Ecology* **23**(5): 361-371.	Low field transposition score
Wepener, V., Bervoets, L.*, et al.* (2008). Metal exposure and biological responses in resident and transplanted blue mussels (*Mytilus edulis*) from the Scheldt estuary. *Marine Pollution Bulletin* **57**(6-12): 624-631.	Exposure: risk factors for mortality not examined
Wethey, D. S., Woodin, S. A.*, et al.* (2011). Response of intertidal populations to climate: Effects of extreme events versus long term change. *Journal of Experimental Marine Biology and Ecology* **400**(1-2): 132-144.	Outcome : mortality risk is not the focus
Wu, H. F., Ji, C. L.*, et al.* (2013). Proteomic and metabolomic responses in hepatopancreas of *Mytilus galloprovincialis* challenged by *Micrococcus luteus* and *Vibrio anguillarum*. *Journal of Proteomics* **94**: 54-67.	Outcome : mortality risk is not the focus
Yanick, J. F., J. W. Heath, *et al*. (2003). Survival and growth of local and transplanted blue mussels (*Mytilus trossulus*, Lamark). *Aquaculture Research* **34**(10): 869-875.	Low field transposition score
Zardi, G. I., K. R. Nicastro, *et al*. (2006). Sand stress as a non-determinant of habitat segregation of indigenous (*Perna perna*) and invasive (*Mytilus galloprovincialis*) mussels in South Africa. *Marine Biology* **148**(5): 1031-1038.	Low field transposition score (1 study)

Appendix III. Table synthetizing key results of the 114 studies included in the narrative synthesis

Study ID	Reference	Country	Mussel species	Study conditions	Methodological quality score	Risk factor topic(s)	Risk factor(s) studied	Interactions accounted	Key results
177	Dionne *et al.* (2006)	Canada	*Mytilus edulis*	Observation	High	-Animal characteristics, -Site characteristics, -Husbandry/fishery practices	-Mussel size -Predation by diving ducks -Protective socking material	Yes	mortality by predation decreases with the use of tighter mesh socks (against ducks), especially in large mussels
323	Penney *et al.* (2006)	Canada	*Mytilus edulis*	Observation	High	-Animal characteristics -Site characteristics -Husbandry/fishery practices	-Genotypes (*M. edulis, M. trossulus* and hybrids) -Farming site -Spat translocation	Yes	- initial genetic heterogeneity between the 2 sites - no effect of the proportion of different species on mortality - site effect on mortality of different genotypes - transplanted mussels: mortality *M. trossulus* > *M. edulis* or hybrids - conclusion: interaction of site and genotype effects on mortality - at one of the 2 sites: local spat mortality higher than transplanted spat mortality
1098	Lok *et al.* (2007)	Turkey	*Mytilus galloprovincialis*	Observation	Moderate	Animal characteristics	-Initial size of seed (7 classes)	No	-mortality <5% in each class -no effect of mussel size on low mortality levels
1118	Suni *et al.* (2007)	Finland	*Mytilus edulis*	Laboratory	Moderate	Pollutants	-Diesel oil	No	-exposure to diesel oil associated with 100% mortality - exposure to diesel oil + its removal by cotton fibres does not cause mortality but histological lesions (inflammation, degeneration, cell death)
1159	Ramon *et al.* (2007)	Spain	*Mytilus galloprovincialis*	Observation	Moderate	Husbandry/fishery practices	-Spat origin	No	effect of spat origin on mortality in August: local spat mortality < transplanted spat
1204	Anestis *et al.* (2007)	Greece	*Mytilus galloprovincialis*	Laboratory	Moderate	Seawater characteristics	-Seawater temperature	No	- mussel mortality observed if water temperature > 26°C - if seawater temperature > 26°C, mortality increases with increasing temperature
1717	Rosen & Lotufo (2007)	United States of America	*Mytilus galloprovincialis*	Laboratory	Moderate	Pollutants	Explosive compounds: -TNT: 2,4,6-trinitrotoluene -RDX: hexahydro-1,3,5, -triazine -HMX: octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine	No	- no lethal effect with RDX < 30 mg/L- - no lethal effect with HMX < 2 mg/L- -89% mortality if TNT = 30 mg/L
2303	Schields *et al.* (2008)	Canada	*Mytilus galloprovincialis*	Observation	High	-Animal characteristics -Husbandry/fishery practices	-Genotype of mussels (*M. galloprovincialis, M. edulis, M. trossulus*) -Site: native vs. transplanted (characterized by different seawater temperatures)	No	- site effect: mortality on transplanted site < mortality on native site - no difference in mortality between native (*M. trossulus*) / hybrids / introduced (*M. galloprovincialis*) genotypes - no difference in mortality between intrasite genotypes
2493	LeBlanc *et al.* (2008)	Canada	*Mytilus edulis*	Observation	High	Husbandry/fishery practices	-Exposure to high air temperature (27.2°C +/- 0.5 for 11 hours) before deployment in the field -Exposure to high water temperature (32.6°C for 6 hours) before deployment in the field	No	-treatment of mussels with high seawater temperature or high aerial temperature at the <10mm stage before field deployment reduces mortality - higher degree of heterozygosity in surviving mussels from mortality events

2684	Nicastro *et al.* (2008)	South Africa	*Mytilus galloprovincialis*	Observation	Moderate	-Site characteristics -Climate characteristics	-Position in the bed: centre vs. edge -Bay vs. open coast habitat -Season	No	-mortality on the open coast > mortality in the bay -difference not significant between mortality at the edge of beds or at the centre -% mussel movement correlated to % mortality of the previous month -seasonality of mortality : higher mortality at the end of summer Explanation of the authors: the observed mortality is due to hydrodynamic stress, which is higher on the coast than in the bay, and also higher at the edge of the bed than in the centre. After a mortality event, the mussels move to reorganize the bed into a safer arrangement.
2698	Zardi *et al.* (2008)	South Africa	*Mytilus galloprovincialis*	Observation	High	Site characteristics	-Wave height -Sediment amount	No	- mortality increases with wave height increasing -absence of effect of sediment amount on mortality
2800	Babarro & De Zwaan (2008)	The Netherlands	*Mytilus edulis*	Laboratory	Moderate	Pathogens	-Anaerobic bacteria	No	-3 anoxic conditions, obtained from 3 different methods: no difference in survival between anoxic/air and nitrogen EDM conditions -so not a real study of the effect of the risk factor 'anoxia' - effect of acclimatization with chloramphenicol: increased survival (X2) Explanation of the authors: importance of anaerobic bacteria as a risk factor of mortality?
3874	Anestis *et al.* (2010)	Greece	*Mytilus galloprovincialis*	Laboratory	Moderate	Climate characteristics	Range between air and seawater temperature	No	-exposure to air temperature > water temperature => mortality - mortality increases if the temperature range between water and air increases
3960	Ali & Taylor (2010)	United Kingdom	*Mytilus edulis*	Laboratory	Moderate	-Seawater characteristics -Pollutants	-Seawater temperature -Salinity -Zinc -Cadmium	Yes	- mortality with low salinity (20 psu) - low salinity: mortality Cd > mortality Zn - absence of effect of seawater temperature on mortality - significant interaction between low salinity & high seawater temperature
4172	Bownes & McQuaid (2010)	South Africa	*Mytilus galloprovincialis*	Observation	High	Site characteristics	- Site effect - Location effect on the site -Height on the shore	Yes	- mortality *M. galloprovincialis :* - site-dependent - no location effect - no effect of the height on the shore
4367	Nicastro *et al.* (2010)	South Africa	*Mytilus galloprovincialis*	Observation	Moderate	Site characteristics, Climate characteristics	- Bay vs. open coast habitat - Wave height - Sand depth - Season	No	- in general: coastal mortality > bay mortality except in June (winter) - mortality increases with increasing sand depth, notably in bays - wave height effect: no correlation between % coastal mortality and wave height; correlation between % mortality in bays in the previous month and wave height - coast : higher mortality in winter-spring (June-October) / bay : 2 mortality peaks in summer (February) and winter (June)
4409	Plass-Jonhson *et al.* (2010)	South Africa	*Mytilus galloprovincialis*	Observation	High	Site characteristics	-Benthic and pelagic predation	No	differences in survival between cage types, which protect against benthic and/or pelagic predation

4680	Jones *et al.* (2010)	United States of America	*Mytilus edulis*	Observation	Moderate	-Seawater characteristics -Climate characteristics	- Seawater temperature - Air temperature	No	-multiple exposure to air temperatures > 32°C appears to be followed by significant mortality -average air or water temperature are the best predictors of mortality (R^2=0.89 or 0.98 depending on the site)
5066	Paetzold & Davidson (2011)	Canada	*Mytilus edulis*	Laboratory	Moderate	Husbandry/fishery practices	A1ntifouling disinfectant (Virkon© containing potassium hydrogen sulphate, sodium dodecyl-benzenesulphonate, sulphamic acid and inorganic buffers)	No	- absence of effect of Virkon disinfectant at doses tested on mussel mortality
5373	Danellakis *et al.* (2011)	Greece	*Mytilus galloprovincialis*	Laboratory	High	Pollutants	Olive oil mill wastewater	No	olive oil press waste water => mortality at concentrations of 1 and 0.2% v/v
6141	Tsarpali & Dailianis (2012)	Greece	*Mytilus galloprovincialis*	Laboratory	Moderate	Pollutants	Leachate (= liquid effluent from waste by fermentation / rainwater)	No	mussel mortality increases from leachate concentrations > 0.5%
6756	Gardner (2013)	New Zealand	*Mytilus galloprovincialis*	Observation	Moderate	-Site characteristics -Husbandry/fishery practices	-Site (n=3) -Site: native vs. transplanted	No	-site-dependent mortality -mortality transplanted site > native site
7240	Dowd & Somero (2013)	United States of America	*Mytilus galloprovincialis*	Laboratory	High	-Animal characteristics -Seawater characteristics -Climate characteristics	-Mussel species (*M. galloprovinciallis* vs. *M. trossulus* vs. *M. californianus*) -Seawater temperature -Air vs. seawater thermal range -Number of repetitions of aerial thermal stress	No	-mortality species *M. trossulus* > *M. galloprovincialis* > *M. californianus* -effect on mortality of an increase in seawater temperature from 13 to 33°C -no effect of repeated (x3) aerial heat stress on mortality
7454	Marquet *et al.* (2013)	Portugal & South Africa	*Mytilus galloprovincialis*	Observation	High	-Pathogens -Site characteristics	-Endolithic infestation -Height on the shore	Yes	-absence of effect of shore height on endolith mortality -endolith mortality is higher in the invaded environment (South Africa) than in the native environment (Portugal)
7718	Hiebenthal *et al.* (2013)	Germany	*Mytilus edulis*	Laboratory	Moderate	-Animal characteristics -Seawater characteristics	-Growth -Condition index -Lipofuscin accumulation -Shell resistance -Seawater temperature	No	-mortality increases with temperature between 20 and 25°C -mortality increases with decrease in growth -mortality increases with decrease in condition index -no association with the force required to break the shell -mortality increases with increase in lipofuscin accumulation
7791	Gazeau *et al.* (2018)	Spain	*Mytilus galloprovincialis*	Laboratory	High	Seawater characteristics	-Seawater temperature -Seawater pH	Yes	-no effect of pH decrease -mortality increases if temperature > 25°C
9018	Tsarpali *et al.* (2015)	Greece	*Mytilus galloprovincialis*	Laboratory	Moderate	Pollutants	-imidazolium ionic liquids: .1-butyl-3-methylimidazolium tetrafluoroborate .1-methyl-3-octylimidazolium tetrafluoroborate	No	-imidazolium ionic liquids have toxic effects on mussels (mortality but not only) - 1-butyl-3-methylimidazolium tetrafluoroborate => mortality if concentration > 10 mg/L : LC50=128.3 mg/L (IC95%: 45.5-253.5) without acetone and LC50=73.6 mg/L (20-3263) with acetone - 1-methyl-3-octylimidazolium tetrafluoroborate => mortality if concentration > 0.5 mg/L : LC50=0.512 mg/L (0.33-0.63) without acetone and LC50=2.31 mg/L (0.67-7.05) with acetone
9560	Waser *et al.* (2015)	The Netherlands	*Mytilus edulis*	Laboratory	High	Site characteristics	-Predation by the crab *Carcinus maenas* -Presence of the oyster *Crassostrea gigas*	Yes	-presence of oysters reduces mussel mortality -greater effect if the crab is small -greater effect if the mussel is small

10039	Gestoso *et al.* (2016)	Spain	*Mytilus galloprovincialis*	Laboratory	High	-Seawater characteristics -Husbandry/fishery practices	-Seawater temperature -Seawater pH -Mixed mussel species	Yes	-pH effect: higher mortality if pH=7.65 -pH effect decreases if species mixture -no seawater temperature effect -type of assembly effect: more mortality if monospecific assembly
10084	Barrento & Powell (2016)	United Kingdom	*Mytilus edulis*	Observation	High	Husbandry/fishery practices	- 48H depuration or 48H emersion storage on ice before transport -temperature during transport: 0°C vs. 5°C -humidity during transport -re-soaking time: 24H vs. 1H -re-soaking temperature: 5 vs. 10°C	Yes	-2 to 7% mortality throughout the transport chain -not significant difference of mortality in the absence of depuration before transport vs. with depuration during 48H - mortality after transport: no effect of depuration (depuration or storage on ice) or transport (humidity or temperature) conditions -re-soaking: mortality of the condition without depuration and ambient temperature > mortality of the depuration and ice condition
10215	Olabarrial *et al.* (2016)	Spain	*Mytilus galloprovincialis*	Laboratory	High	-Husbandry/fishery practices -Climate characteristics	-Air temperature -Mixed mussel species	No	-higher mortality if air temperature is high -*M. galloprovincialis* mortality: monospecific aggregation > if mixed species
10226	Gammoudi *et al.* (2017)	Tunisia	*Mytilus galloprovincialis*	Observation	Moderate	Site characteristics	-Predation by plathelminth (flatworm) polyclade *Imogine mediterranea*	No	-median exposure time resulting in 50% mortality = 4.5 days (CI95% 2.7-8.9) (median of the 3 worm size classes) -mortality increases with increasing worm exposure time and increasing worm size
10565	Moschino *et al.* (2016)	Italy	*Mytilus galloprovincialis*	Observation	Moderate	Pollutants	-Metals: As, Cd, Cr, Cu, Hg, Ni, V, Pb, Zn, Al, Fe -PAHs -Phthalates -Alkylphenols -PCBs	No	-mortality at exposed site > mortality at control site -association of mortality and Aluminium, Iron, Lead, Total metals and total PAHs
10632	Zardi *et al.* (2016)	South Africa	*Mytilus galloprovincialis*	Observation	High	Pathogens	-External parasitism (endoliths)	No	-in periods of high heat (temperature not specified): mortality among non-infested mussels 49% higher than among infested mussels
10727	Cottrell *et al.* (2016)	Scotland	*Mytilus edulis*	Laboratory	High	-Seawater characteristics -Site characteristics	-Sediment size -Seawater temperature -Burial sediment duration -Suspended organic matter concentration	Yes	-mortality increases with fine sediment -mortality increases with suspended organic matter concentration increases -mortality increases with seawater temperature increase -mortality increases with burial duration increases -significant interaction between sediment size *suspended organic matter (any concentration)
10825	Sun *et al.* (2016)	China	*Mytilus edulis*	Laboratory	Moderate	Seawater characteristics	-Seawater pH	No	-mortality increases with decreasing pH: pH=8.1 ⇔ 0% mortality pH = 6.5 ⇔ 6.7% HCl mortality and 23.3% CO_2 mortality
bi24	Tremblay *et al.* (1998)	Canada	*Mytilus edulis*	Observation	Moderate	-Animal characteristics -Husbandry/fishery practices	-Mussel size (<30 mm vs. >30 mm) -Degree of multiple-locus heterozygosity -Energy requirements for metabolism maintenance -Suspended cages vs. suspended socks	No	-absence of mussel size effect -higher degree of heterozygosity in "resistant" stocks -higher energy maintenance needs in stocks with high mortality -absence of effect of suspended cages vs. suspended socks
10057_1	Hutchison *et al.* (2016)	United Kingdom	*Mytilus edulis*	Laboratory	Moderate	Site characteristics	-Burial depth -Burial duration -Sediment size	Yes	-mortality increases with increasing burial duration -mortality increases with fine sediment -no effect of burial depth -not significant interaction between burial duration

									* burial depth
10057_2	Hutchison *et al.* (2016)	United Kingdom	*Mytilus edulis*	Laboratory	Moderate	-Seawater characteristics -Site characteristics	-Burial depth -Burial duration -Seawater temperature	Yes	-mortality increases with increasing burial duration -mortality increases with seawater temperature increases -mortality increases with depth of burial increases -not significant interaction between burial duration*seawater temperature
10112_a	Benabdelmouna & Ledu (2016)	France	*Mytilus edulis*	Observation	Moderate	Animal characteristics	-Frequency of individuals having more than 10% of cytogenetic abnormalities in haemocytes in the mussel population	No	correlation with mortality=0,945
10112_b	Benabdelmouna & Ledu (2016)	France	*Mytilus galloprovincialis*	Observation	Moderate	Animal characteristics	-Frequency of individuals having more than 10% of cytogenetic abnormalities in haemocytes in the mussel population	No	correlation with mortality=0,945
10292_1	Travers *et al.* (2016)	France	*Mytilus edulis*	Observation	Moderate	-Seawater characteristics -Climate characteristics	-Air temperature -Pluviometry -Phytoplankton diversity (environmental DNA)	No	-absence of association between mortality and pluviometry -absence of association between mortality and air temperature -association between mortality and low phytoplankton diversity index -higher relative abundances of phylum communities Ciliophora, class Euglenoidea
10292_4	Pépin *et al.* (2017)	France	*Mytilus edulis*	Observation	Moderate	Animal characteristics	-Spawning period	No	- appearance of mortalities associated with an active gametogenesis phase (stages 3A and 3B) -cessation of mortalities in July and end of egg laying (stages 0 and 1 observed in September)
10292_5	Pépin *et al.* (2017)	France	*Mytilus edulis*	Observation	High	Animal characteristics	-Unselected vs. selected intraspecific genotype (progeny of mussels that survived a mortality episode)	No	-effect of the selected intraspecific genotype: 78% mortality in unselected genotype vs. 46% mortality in selected genotype
10292_7	Pépin *et al.* (2017)	France	*Mytilus edulis*	Laboratory	Moderate	-Pathogens -Animal characteristics	-Not identified infectious agent -Selected (i.e. which parents survived from a previous mortality event) vs. non-selected intraspecific genotype	No	-horizontal transmission of something leading to mortality: compatible with an infectious hypothesis -final cumulative mortality: 77% in non-selected mussels vs. 63% in selected mussels
10292_8	Pépin *et al.* (2017)	France	*Mytilus edulis*	Observation	High	Animal characteristics	-Selected (i.e. which parents survived from a previous mortality event) vs. non-selected intraspecific genotype -Frequency of individuals having more than 10% of cytogenetic abnormalities in haemocytes in the mussel population	No	-selected intraspecific genotype: survival gain of 47% on average vs. unselected genotype -no significant association between mortality and percentage of cytogenetic abnormalities in haemocytes
10292_10	Pépin *et al.* (2017)	France	*Mytilus edulis*	Observation	Moderate	Site characteristics	-Site effect	No	-variations in mortality rates between the sites monitored
10292_12	Pépin *et al.* (2018)	France	*Mytilus edulis*	Laboratory	Moderate	Animal characteristics	-Frequency of individuals having more than 10% of cytogenetic abnormalities in haemocytes in the mussel population -Neoplastic process in the haemocytes	No	-mussel batches with the highest percentage of cytogenetic abnormalities have the highest mortality levels -presence of neoplastic cells in the haemocytes of mussels with a high percentage of cytogenetic abnormalities
1228_1	Akaishi *et al.* (2007)	Canada	*Mytilus edulis*	Laboratory	High	Pollutants	-Untreated wastewater	No	mortality increases from untreated wastewater concentration >50%.

2012_1	Hamer *et al.* (2008)	Croatia	*Mytilus galloprovincialis*	Laboratory	Moderate	Seawater characteristics	-Seawater salinity -Seawater temperature	No	-at 13°C: no effect of salinity acclimatization -LT50 at 27°C: T0: 5.74, IC95% [5.45-6.02] 37 psu : 5.32, IC95% [5.01-5.62] 28 psu : 4.26, IC95% [too broad] 11 psu : 2.76, IC95% [2.42-3.08] => 27°C: mortality increases with acclimatization below 28 psu
2587_1	Lowen (2008)	Canada	*Mytilus edulis*	Observation	Moderate	Animal characteristics	-Mussel species: *M. edulis, M. trossulus* and hybrids	No	-No difference in mortality level between *M. edulis* and *M. trossulus* -Hybrid *edulis* (female *edulis*) mortality > mortality of *M. edulis* and *M. trossulus* -Hybrid *trossulus* (female *trossulus*) mortality not different from other genotypes
2587_2	Lowen (2008)	Canada	*Mytilus edulis*	Observation	Moderate	Husbandry/fishery practices	-Stocking density -Mixed mussel species	No	-no stocking density effect on mortality level, except mortality *M. edulis* < mortality *M. trossulus* if density= 30 mussels/cages with mixed species condition
2886_1	Schneider (2008)	United States of America	*Mytilus galloprovincialis*	Laboratory	Moderate	-Animal characteristics -Climate characteristics	-Mussel species -Air vs. seawater thermal range	No	-if seawater temperature = 18°C : mortality *M. galloprovincialis* > mortality *M. trossulus* -If seawater temperature = 18°C / air temperature increases from 20 to 30°C : absence of effect of aerial body temperature on mussel mortality, regardless of mussel species
2886_2	Schneider (2008)	United States of America	*Mytilus galloprovincialis*	Laboratory	Moderate	Climate characteristics	-Mussel species -Air vs. seawater thermal range	No	-if water temperature = 12°C : mortality *M. galloprovincialis* > mortality *M. trossulus* -if water temperature = 12°C / air temperature increases from 20 to 30°C : mortality *M. galloprovincialis* decreases at air temperature = 30°C
3024_1	Jones *et al.* (2009)	United States of America	*Mytilus edulis*	Laboratory	Moderate	-Seawater characteristics -Climate characteristics	-Seawater temperature -Number of exposures to elevated seawater temperature -Number of exposures to elevated air temperature	No	-mortality increases from 30°C (air or water) -mortality increases (up to 100%) with increasing number of exposures (air or seawater)= multiple exposure decreases thermal tolerance
3267_1	Vickerson (2009)	Canada	*Mytilus edulis*	Observation	Moderate	Husbandry/fishery practices	-Temperature during 24H transport (with / without ice) -Antifouling treatment (30 s) before or after transport (300 ppt brine / hydrated lime / vinegar) -Rinsing of the mussels after the antifouling treatment	No	Data for 24H transport (only available): -no difference in mortality between brine treatments -mortality between hydrated lime treatments without rinsing > mortality other hydrated lime treatments -mortality vinegar treatment without rinsing before transport and not stored in ice (35.4%) > mortality vinegar treatment without rinsing before transport and stored in ice during transport (33.7%) >> other vinegar treatment (<10%) -the 3 antifouling treatments : correlation between % mortality and biomass (r=0.377 / 0.377 / 0.804)
365_2	Altieri & Witman (2006)	United States of America	*Mytilus edulis*	Observation	Moderate	-Animal characteristics -Seawater characteristics	-Hypoxia -Mussel size -Mussel growth rate	Yes	under hypoxic conditions: -mortality increases with increasing mussel size -correlation between % mortality and growth rate: R^2=0.49

365_3	Altieri & Witman (2006)	United States of America	*Mytilus edulis*	Observation	High	-Site characteristics	-Starfish predation	No	under hypoxic conditions: no effect of cages (against predation) on mussel survival during hypoxia, i.e. predation does not play a particular role in hypoxia concurrences
3834_a	O'Connor (2010)	Ireland	*Mytilus edulis*	Observation	High	-Pathogens -Animal characteristics -Site characteristics	-Presence of perennial epibiont algae *Fucus serratus* (exposed sites) vs. mixture of *F. serratus* * *F. spiralus* * *Ascophyllum nodosum* (sheltered sites) -Initial mussel size -Exposed site vs. sheltered wave site	Yes	-mortality on sheltered sites < wave-exposed sites -wave sheltered site: mussels with epibionts have a 50% higher risk of dying compared to mussels without epibionts -no effect of initial mussel size on epibiont-related mortality
3834_b	O'Connor (2010)	Ireland	*Mytilus galloprovincialis*	Observation	High	-Pathogens -Animal characteristics -Site characteristics	-Presence of perennial epibiont algae *Fucus serratus* (exposed sites) vs. mixture of *F. serratus* * *F. spiralus* * *Ascophyllum nodosum* (sheltered sites) -Initial mussel size -Exposed site vs. sheltered wave site	Yes	-mortality on sheltered sites < wave-exposed sites -wave sheltered site: mussels with epibionts have a 50% higher risk of dying compared to mussels without epibionts -no effect of initial mussel size on epibiont-related mortality
6023_1	Christensen *et al.* (2012)	Denmark	*Mytilus edulis*	Laboratory	Moderate	-Site characteristics	-Predation by crab -Origin of mussels: bottom bed vs. farmed suspended	No	-association between mussel mortality and crab predation, whatever the origin of the mussel spat
6023_2	Christensen *et al.* (2012)	Denmark	*Mytilus edulis*	Observation	High	-Site characteristics -Husbandry/fishery practices	-Predation by crab -Origin of mussels: bottom bed vs. farmed suspended	No	-predation-related mortality in farmed suspended mussels < bottom bed mussels
7869_2	Romero *et al.* (2014)	Spain	*Mytilus galloprovincialis*	Laboratory	Moderate	-Pathogens -Seawater characteristics	-Bacteria *Vibrio aestuarianus* -Bacteria *Vibrio splendidus* clade -Emersion from water during 8h vs. permanent immersion to reproduce hypoxic stress	Yes	-15°C : mortality <5%, no effect of emersion -25°C: increased mortality if emersion and seawater contaminated with *Vibrio splendidus* clade or *Vibrio aestuarianus*
8146_1	Bressan *et al.*(2014)	Italy	*Mytilus galloprovincialis*	Laboratory	Moderate	Seawater characteristics	-pH of the seawater	No	-up to the 5th month: 5.6% mortality in controls and 5.5% mortality in the treated group (variable pH) -mortality in the treated group increases at the 6th month to 11%. => mortality increases if prolonged exposure (6 months) to a low and constant pH (7.4)
8146_2	Bressan *et al.*(2014)	Italy	*Mytilus galloprovincialis*	Laboratory	Moderate	Seawater characteristics	-pH of the seawater	No	-7.25% mortality in the control group and 7.00% mortality in the treated group => no effect of exposure to a low and constant pH (7.4) for 3 months on mortality
8841_1	Brousscau *et al.* (2014)	United States of America	*Mytilus edulis*	Observation	Moderate	Site characteristics	-Predation by the Japanese crab *Hemigrapsus sanguineus*	No	-presence of *Hemigrapsus sanguineus* crab is associated with an increase in mortality (predation) of about 25%.
8841_2	Brousscau *et al.* (2014)	United States of America	*Mytilus edulis*	Observation	Moderate	Site characteristics	-Predation by Japanese crab *Hemigrapsus sanguineus*	No	-presence of *Hemigrapsus sanguineus* crab is associated with an increase in mortality (predation)

9283_1	Carella *et al.* (2105)	Italy	*Mytilus galloprovincialis*	Laboratory	Moderate	Pathogens	-Toxic dinoflagellate algae *Ostreopsis* cf *ovata*	No	-concentration 300 cells/ml: 7% mortality (1 mold/15) after 24H and 10% after 48H -concentration 500 cells/ml: 15% mortality (2 mold/15) after 24H and 40% after 48H -concentration 1000 cells/ml: 93% mortality (14 mold/15) after 24H => mussel mortality is proportional to the concentration of toxic algae
996_1	Zardi *et al.* (2006)	South Africa	*Mytilus galloprovincialis*	Observation	Moderate	Site characteristics	-Sand burial	No	-mortality increases with duration of sand burial increases -after 6 days, 50% of the mussels are dead
996_2	Zardi *et al.* (2006)	South Africa	*Mytilus galloprovincialis*	Laboratory	High	Site characteristics	-Sand burial	No	-suspended sand: LT50 = 14 days -sand burial: LT50 = 6 days
bi2	Eggermont *et al.* (2014)	Belgium	*Mytilus edulis*	Laboratory	Moderate	Pathogens	-Opportunistic heterotrophic bacteria	No	-treated condition: 100% mortality in 6 days -control with antibiotic: 25% mortality -other controls: 0% mortality
bi5	Myrand & Gaudreault (1995)	Canada	*Mytilus edulis*	Observation	Moderate	-Animal characteristics -Site characteristics -Husbandry/fishery practices	-Selected (survivors from a previous mortality event) vs. non-selected intraspecific genotype -Site -Geographic origin of spat	Yes	-no effect of intraspecific genotype -no difference in mortality between sites -intrasite: effect of spat origin -intersite: same effect of spat origin -non significant interaction site*spat origin
bi6	Karayücel & Karayücel (2000)	Scotland	*Mytilus edulis*	Observation	Moderate	Husbandry/fishery practices	-Depth of the farming structures: 2 m vs. 6 m -Position inside the farming structure (inflow vs. outflow)	No	-no effect of the depth of the farming structure -no effect of the position inside the farming structure, related to marine currents
bi7	Tsuchiya (1983)	Japan	*Mytilus edulis*	Observation	High	-Animal characteristics -Site characteristics -Climate characteristics	-Mussel size -Height on the shore -Elevated air temperature (heat wave)	No	-no link between mussel size and mortality -higher mortality if high position on the shore -link between wave heat and mortality
bi8	Stirling & Okumus (1994)	Scotland	*Mytilus edulis*	Observation	Moderate	-Site characteristics -Husbandry/fishery practices	-Site -Geographic origin of spat: local vs. translocated	No	-no site effect -no effect of spat origin
bi10	Petraitis (1998)	United States of America	*Mytilus edulis*	Observation	Moderate	Site characteristics	-Position on the shore: high vs. low -Predation by the snail *Nucella lapillus*	No	- 64% of deaths due to predation by the snail -no association between predator abundance and mortality -higher mortality on the higher shore
bi11	Myrand *et al.* (2000)	Canada	*Mytilus edulis*	Observation	High	-Animal characteristics -Husbandry/fishery practices characteristics -Climate characteristics	-Physiological state of mussels: gametogenesis, energy reserves -Suspended cages at 16 m (open water) vs. 6 m depth (lagoon) -Season	No	-mortality in the lagoon (6 m depth) higher than mortality in the open sea (16 m depth) -foreshore: link between the beginning of mortality and the end of the second spawning + low energy reserves -mortality higher in summer (June-September)
bi12_1	Lauzon-Gay *et al.* (2005)	Canada	*Mytilus edulis*	Observation	High	-Animal characteristics -Site characteristics -Husbandry/fishery practices	-Seed size -Site -Initial density in socks	No	-no site effect -Month 10: mortality of small mussels higher than that of medium and large mussels -Month 18: mortality of high initial densities higher than that of low initial densities, regardless of size
bi12_2	Lauzon-Gay *et al.* (2005)	Canada	*Mytilus edulis*	Observation	High	-Animal characteristics -Husbandry/fishery practices	-Seed size -Initial density in socks	Yes	-no initial density effect -mortality of small mussels higher than mortality of medium and large mussels -mortality of high initial densities higher than that of low initial densities, regardless of size

bi15	Mallet *et al.* (1987)	Canada	*Mytilus edulis*	Observation	Moderate	-Site characteristics -Husbandry/fishery practices -Climate characteristics	-Site -Origin of spat: local vs. transplanted -Geographic origin of spat -Season	Yes	-no site effect -spat geographical origin effect -no native vs. transplanted origin effect -no single significant seasonal effect -origin*season significant interaction -origin*site significant interaction
bi16	Incze *et al.* (1980)	United States of America	*Mytilus edulis*	Observation	Moderate	Seawater characteristics	-Surface seawater temperature -Size, abundance and nature of particles in seawater: total chlorophyll, nanoplankton (<20 µm)	No	-increase in seawater temperature (20°C threshold) + sudden decrease in the quantity of particles before a mortality episode
bi18_a	Fuentes *et al.* (2002)	Spain	*Mytilus edulis*	Observation	High	Animal characteristics	-Interspecific genotype	No	-genotype effect: *M. edulis* hybrid mortality higher than *M. galloprovincialis* mortality
bi18_b	Fuentes *et al.* (2002)	Spain	*Mytilus galloprovincialis*	Observation	High	Animal characteristics	-Interspecific genotype	No	-genotype effect: *M. edulis* hybrid mortality higher than *M. galloprovincialis* mortality
bi19	Gardner & Thompson (2001)	Canada	*Mytilus edulis*	Laboratory	Moderate	Animal characteristics	-Species *M. edulis* vs. *M. trossulus*	No	-in coastal regime: low mortality, difference could not be tested (too small sample) -in estuarine regime: *M. trossulus* mortality higher than that of *M. edulis*
bi21	Mallet *et al.* (1990)	Canada	*Mytilus edulis*	Observation	Moderate	-Animal characteristics -Site characteristics -Husbandry/fishery practices	-Age: juveniles vs. adults -Site (not detailed) -Geographic origin of spat	Yes	-age effect: juvenile mortality higher than adult mortality -no site effect -spat origin effect
bi22	Fuentes *et al.* (1992)	Spain	*Mytilus galloprovincialis*	Observation	Moderate	-Site characteristics -Husbandry/fishery practices	-Site -Geographic origin of spat -Position inside the farming structure (fore vs. aft part of the raft)	Yes	-no site effect -effect of spat origin -no effect of position inside the farming structure
bi25	Fuentes *et al.* (1994)	Spain	*Mytilus galloprovincialis*	Observation	Moderate	-Site characteristics -Husbandry/fishery practices	-Site -Geographic origin of spat -Position inside the farming structure (fore vs. aft part of the raft)	No	-site effect -effect of the position inside the farming structure: mortality at the front of the structure lower than mortality at the back of the structure (relative to current) - effect of spat origin: mortality of sites in the north > mortality of sites in the south
LG57	Glize *et al.* (2017)	France	*Mytilus edulis*	Observation	Moderate	-Site characteristics -Husbandry/fishery practices	-Site -Geographic origin of spat -Geographic origin of spat: local vs. transplanted from an area not affected by mortality events	No	-mortality varied between sites -no difference in mortality levels between the 2 origins, on 7 of the 8 sites -on 1 site: 14.3% mortality for local origin vs. 0.8% origin "not affected by mortality"
LG59	SMIDAP (2016)	France	*Mytilus edulis*	Observation	Moderate	-Husbandry/fishery practices	-Geographic origin of spat: local vs. transplanted from an area not affected by mortality events	No	absence of association between spat origin and mortality
LG60	SMIDAP (2016-2017)	France	*Mytilus edulis*	Observation	Moderate	-Husbandry/fishery practices	-Geographic origin of spat -Geographic origin of spat: local vs. transplanted from an area not affected by mortality events	No	-absence of association between spat origin and mortality -mortality of the local mussels > mortality of the mussels transplanted from an area not affected by mortality events
LG82_a	Bernard *et al.* (2018a) Bernard *et al.* (2018b)	France	*Mytilus edulis*	Observation	Moderate	-Pathogens -Animal characteristics -Seawater characteristics -Site characteristics -Husbandry/fishery practices -Climate characteristics,	-Bacteria, *Marteilia refringens* -Mussel species, age, origin, transmissible neoplasia -Seawater temperature -Site -Geographic origin of spat -Season	No	-absence of association between *Marteilia refringens* and mortality -absence of association between bacteriological profile of mussels and mortality -association between haemocytic tissue infiltration and mortality -absence of association between haemocytic neoplasia and mortality -association between seawater temperature and

									mortality: thermal threshold between 19-20°C -site effect -effect of geographical origin of the animals -peak mortality in spring
LG82_b	Bernard *et al.* (2018a) Bernard *et al.* (2018b)	France	*Mytilus galloprovincialis*	Observation	Moderate	-Pathogens -Husbandry/fishery practices -Climate characteristics,	-Bacteria -Geographic origin of spat -Season	No	-absence of association between bacteriological profile of mussels and mortality -effect of geographical origin of the animals -peak mortality in spring
LG83	Glize & Gourmelen (2018)	France	*Mytilus edulis*	Observation	Moderate	-Site characteristics -Husbandry/fishery practices	-Site -Geographic origin of spat: local vs. transplanted from an area not affected by mortality events	No	-effect of the site on mortality : mortality of sites in the North higher than mortality of sites in the South -absence of association between spat origin and mortality
maj1003	Clements *et al.* (2018)	Canada	*Mytilus edulis*	Laboratory	High	-Seawater characteristics	-Acidification of seawater -Increase in seawater temperature	Yes	-no effect of CO2 concentration in seawater on mortality -effect of temperature increase on mortality, which increases with time increases -with high temperature: observed decrease in glycogen. The authors make a link (not demonstrated by this study) between glycogen reduction and increased mortality -no effect of the interaction of elevated seawater temperature*acidification
maj1351	Ajjabi *et al.* (2018)	Tunisia	*Mytilus galloprovincialis*	Laboratory	High	-Husbandry/fishery practices	-Polyculture with macroalgae culture *Gracilaria verrucosa*	No	-controls (monoculture): 16.25% mortality -polyculture (regardless of algae concentration): no mortality
maj1428	Gvozdenovic *et al.* (2017)	Montenegro	*Mytilus galloprovincialis*	Observation	Moderate	-Husbandry/fishery practices	-Polyculture with fish and flat oysters vs. mussel monoculture	No	-no difference in cumulative mortality between the 3 sites, nor kinetics (data not used in the article, Table 1) -no effect of mussel farming near fish farms on mussel mortality
maj1757	Oliveira *et al.* (2017)	Portugal	*Mytilus galloprovincialis*	Laboratory	High	-Pollutants	-Carbamazepine	No	-no mortality observed at 96H exposure -at 28 days of exposure: 6.0 microg/L : 12.5% mortality 9.0 microg/L : 6.3% mortality
maj1890	Eggermont *et al.* (2017)	Netherlands	*Mytilus edulis*	Laboratory	Moderate	-Pathogens	-Cultivable bacteria	No	-100% mortality in 1 week -control with rifampin: 25% mortality in 1 week -17 isolates during mortality: 8 belonging to the *Splendidus* clade of *Vibrios* and the others to the genus *Photobacterium*
maj2462	Kovacic *et al.* (2017)	Croatia	*Mytilus galloprovincialis*	Observation	Moderate	-Husbandry/fishery practices	-Geographic origin of spat: local vs. translocated	No	- varying mortality depending on the origin of the mussels (from 13.13% to 37.66%): lower mortality in translocated mussels
maj2616	Theodorou *et al.* (2017))	Greece	*Mytilus galloprovincialis*	Observation	Moderate	-Husbandry/fishery practices	-Stocking density during immersion before transport for sale (7.5 / 10 / 10 / 12.5 /15.5 kg per bag) -Re-immersion time (11 / 25 / 37 / 46 days)	No	-no difference in mortality between the different storage densities, at each time step (? Little consistent with Figure 1) -mortality < 10% up to 11 days of storage for densities <12.5 kg, with the exception of density 12.5kg: up to 25 days
maj2926	Moschino *et al.* (2017)	Italy	*Mytilus galloprovincialis*	Observation	Moderate	-Site characteristics	-Site (N=4)	No	Site effect
maj989	Li *et al.* (2018)	China	*Mytilus galloprovincialis*	Laboratory	Moderate	-Pollutants	-ZnO	No	-coarse suspension ZnO: LC50 = 2.62 mg Zn/L [1.00-4.00] -nanoparticles ZnO: LC50 = 0.78 mg Zn/L [0.64-1.00], 100% mortality at 14 days per 100 mg/L and 21 days per 10 mg/L

									-ZnSO4 : LC50 = 0.25 mg Zn/L[0.10-0.40] 100% mortality at 4 days per 10 mg/L and higher concentrations
maj2_129a	Lenz *et al.* (2018)	Finland, Germany, Portugal	*Mytilus galloprovincialis*	Laboratory	Moderate	-Seawater characteristics	-Number of thermal stresses	No	-no difference in mortality between group A exposed twice to stress and group B exposed only once to stress -no effect of a first exposure to an elevated temperature on the mortality level following a second exposure to the same stress
maj2_129b	Lenz *et al.* (2018)	Finland, Germany, Portugal	*Mytilus edulis*	Laboratory	Moderate	-Seawater characteristics	-Number of thermal stresses	No	mortality after a second exposure to an elevated temperature is lower than mortality after a first exposure to the same stress
maj2_147_1	Stevens & Gobler (2018)	United States of America	*Mytilus edulis*	Laboratory	High	-Seawater characteristics	-Decreased pH -Decrease in dissolved oxygen	Yes	-effect of pH decrease on mortality: mortality increases when pH decreases 0% mortality in the control group 2% mortality when pH decreased, statistically significant difference (P<0.05) -no effect of oxygen depletion -no effect of pH decrease* oxygen depletion
maj2_147_2	Stevens & Gobler (2018)	United States of America	*Mytilus edulis*	Laboratory	High	-Seawater characteristics	-Elevated seawater temperature -Decreased pH -Decrease in dissolved oxygen	Yes	-no pH decrease effect -no oxygen decrease effect -no elevated water temperature effect -non significant interaction pH decrease* oxygen decrease -non significant interaction pH decrease*elevated temperature -non significant interaction oxygen decrease * elevated temperature -non significant interaction pH decrease*oxygen decrease*elevated temperature
maj2_152_1	Bertolini *et al.* (2018)	Ireland	*Mytilus edulis*	Laboratory	Moderate	-Site characteristics	-Predation by the crab *Carcinus maenas* -Habitat complexity	Yes	-effect of habitat complexity on mortality in crab predation: mortality decreases with habitat complexity increases, regardless of mussel size -effect of predator size: total mussel mortality (small and large) increases with crab size increases
maj2_152_2_2	Bertolini *et al.* (2018)	Ireland	*Mytilus edulis*	Laboratory	Moderate	-Site characteristics	-Predation by the starfish *Asterias rubens* -Habitat complexity	Yes	-absence of effect of habitat complexity on total mussel mortality in case of starfish predation -effect of habitat complexity on small mussel mortality in case of starfish predation : mortality decreases with habitat complexity increases -effect of predator size : total mussel mortality (small and large) increases with starfish size increases
maj2_153	Peden *et al.* (2018)	France	*Mytilus edulis*	Laboratory	Moderate	-Climate characteristics	-Animals chronically exposed to pollution (from a polluted site) -Number of thermal stresses	Yes	-acclimatisation to elevated temperature reduces mortality associated with a heat wave: mortality in acclimatised group = 8.3% / in non-acclimatised group = 51.7%
maj2_155_1_1_a	Benabdelmouna *et al.* (2018)	France	*Mytilus edulis*	Laboratory	Moderate	-Pathogens	-Bacteria *Vibrio Splendidus* clade -Bacteria *Vibrio aestuarianus* -Virus OsHV-1 -*Marteilia refringens* and other notifiable pathogens	No	-in moribund mussels: no detection of notifiable parasites, OsHV-1, *Vibrio aestuarianus* but detection of *Vibrio Splendidus* clade, except in August -horizontal transmission of an infectious agent between adult mussels, resulting in mortality -absence of formal evidence of involvement of *Vibrio* bacteria of the genus *Splendidus*

maj2_155_1_b	Benabdelmouna *et al.* (2018)	France	*Mytilus galloprovincialis*	Laboratory	Moderate	-Pathogens	-Bacteria *Vibrio Splendidus* clade -Bacteria *Vibrio aestuarianus* -Virus OsHV-1 -*Marteilia refringens* and other notifiable pathogens	No	-in moribund mussels: no detection of notifiable parasites, OsHV-1, *Vibrio aestuarianus* but detection of *Vibrio Splendidus* clade, except in August -horizontal transmission of an infectious agent between adult mussels, resulting in mortality -absence of formal evidence of involvement of *Vibrio* bacteria of the genus *Splendidus*
maj2_235_1	Wang *et al.* (2018)	China	*Mytilus edulis*	Laboratory	High	-Seawater characteristics	-Decreased seawater temperature -Elevated seawater temperature	No	-high mortality at high (35°C) or cold (4°C) temperatures 4°C : 28% mortality / 9°C : 20% / 15°C : 4% / 25°C : 5% / 30°C : 7% / 35°C : 20% mortality
maj2_486	Nicastro *et al.* (2018)	South Africa	*Mytilus galloprovincialis*	Observation	High	-Pathogens -Husbandry/fishery practices	-Endolithic infestation -Intensity of trampling during bed harvesting	Yes	endolithic infestation of mussels increases the mortality by trampling (i.e. crushing)
maj2_624	Binzer *et al.* (2018)	Denmark	*Mytilus edulis*	Laboratory	High	-Pathogens	-Toxic algae *Karlodinium armiger*	No	-LC50 at 24H = 9.4*10^3 +/- 2.7*10^3 cells/mL -LC50 at 48H = 6.1*10^3 +/- 0.3*10^3 cells/mL -no mortality in controls -mussel mortality observation from 4*10^3 cells/mL (24H and 48H) - critical concentrations: 6.3*10^3 cells/mL at 24H and 3.5*10^3 cells/mL at 48H => the toxic algae *Karlodinium armiger* is associated with mussel mortality at concentrations greater than 4*10^3 cells/mL. The authors hypothesize that the direct contact of toxins with mussels is deleterious.

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Appendix IV. Graphical solution of the MCA on the first and second factorial axis, which explained respectively 15.5% and 12.5% of the total inertia of the 14 variables, for descriptive characteristics of 114 studies related to risk factors of mussel mortality. Each variable is plotted on the graph according to the coordinates on factorial axis 1 (horizontal) and 2 (vertical).